Soy

SCIENTIFIC NAME
Glycine max, synonyms Glycine soja, Dolichos soja, Glycine gracilis, Glycine hispida, Phaseolus max, Soja hispida, Soja max

FAMILY
Fabaceae/Leguminosae.

...read less

CAUTION: See other monograph for specific products made from soy, such as Alpha-GPC, Avocado Soy Unsaponifiables, Nattokinase, and Soybean Oil.

Other Common Names

Cosse de Soja, Cosse de Soya, Daidzein, Daidzéine, Edamame, Estrogène Végétal, Fermented Soy, Fève de Soja, Fève de Soya, Fibre de Soja, Fibre de Soya, Frijol de Soya, Genistein, Génistéine, Haba Soya, Haricot de Soja, Haricot de Soya, Hydrolyzed Soy Protein, Isoflavone, Isoflavone de Soja, Isoflavone de Soya, Isoflavones, Isolated Soy Protein, Isolated Soybean Protein, Lait de Soja, Lait de Soya, Legume, Miso, Natto, Phytoestrogen, Phyto-œstrogène, Plant Estrogen, Protéine de Haricot de Soja Isolée, Protéine de Haricot de Soya Isolée, Protéine de Soja, Protéine de Soya, Protéine de Soja Isolée, Protéine de Soya Isolée, Protéine de Soya Isolée, Shoyu, Soja, Sojabohne, Soy Bean, Soy Fiber, Soy Germ, Soy Isoflavone, Soy Isoflavones, Soy Milk, Soy Polysaccharide, Soy Protein, Soy Protein Isolate, Soya, Soya Bean, Soja Fermenté, Soya Fermenté, Soybean, Soybean Curd, Soybean Isoflavone, Soybean Isoflavones, Soymilk, Tempeh, Texturized Vegetable Protein, Tofu, Touchi.

Overview

Soybean is a legume that originated in China, but is now grown in other countries, including North and South America (90991,90992). Soybeans are processed into soy milk, soy fiber, or soy protein, which includes soy powder, soy protein concentrate, and isolated soy protein products (90993). Soy is a primary source of phytoestrogens called isoflavones, a class of compounds that are structurally similar to endogenous estrogen (90954).

WARNINGS

The Food Allergen Labeling and Consumer Protection Act (FALCPA) of 2004 recognizes soy as a major food allergen in the United States and requires that soy contents be labeled on packaged food and supplement products (105410).

Safety

LIKELY SAFE ...when soy protein is used orally and appropriately. Soy protein products in doses up to 60 grams, providing up to 185 mg isoflavones, daily have been safely used in studies lasting up to 16 weeks (842,2293,2294,2296,3025,3402,3977,4755,6412,8530)(10372,11805).

POSSIBLY SAFE ...when soy extracts are used orally and appropriately, short-term. Soy extracts containing concentrated isoflavones in doses of 35-120 mg daily have been used with apparent safety for up to 6 months (4751,6455,7802,12040,12048,13209,95994,95999).

CHILDREN: **LIKELY SAFE** ...when consumed in amounts commonly found in foods or as a component of infant formula (3400,4912,7331). Soy milk that's not designed for infants should not be used as a substitute for infant formula. Regular soy milk can lead to nutrient deficiencies (12045). Most evidence shows that exposure to soy formula or other soy products in infancy does not cause early onset of puberty or health or reproductive problems later in life (7331,11080,108245). However, some small cohort studies have suggested that higher soy intake during childhood may be associated with an increased risk of precocious puberty (108240) and may be weakly correlated with the development of breasts in children less than 2 years of age (75520). This is in contrast to an observational study in Chinese children ages 7-9 years which suggests that higher soy intake is associated with delayed puberty (108252). One small cohort study has also found that use of soy infant formula may be associated with an increased risk of endometriosis in adulthood, although endometriosis was also correlated with prematurity, which may have confounded the findings (101803). **POSSIBLY UNSAFE** ...when used orally as an alternative to cow's milk in children with severe milk allergy (75359). Although soy protein-based infant formulas are often promoted for children with milk allergy, children with a severe allergy to cow's milk are also frequently sensitive to soy protein (9883). There is insufficient reliable information available about the safety of soy products when used in amounts higher than typical food quantities for children.

PREGNANCY: **LIKELY SAFE** ...when used orally in amounts commonly found in foods (4912). **POSSIBLY UNSAFE** ...when used orally in medicinal amounts. Soy contains mildly estrogenic constituents (3373,3988,3989,3990,3994,6029,75303). Theoretically, therapeutic use of soy might adversely affect fetal development; avoid using.

LACTATION: **LIKELY SAFE** ...when used orally in amounts commonly found in foods (4912). A single 20-gram dose of roasted soybeans, containing 37 mg isoflavones, produces four to six times less isoflavones in breast milk than provided in a soy-based infant formula (2290). There is insufficient reliable information available about the safety of long-term use of therapeutic amounts of soy during lactation.

Adverse Effects

General: Orally, soy is well tolerated.

Most Common Adverse Effects:

Orally: Bloating, constipation, diarrhea, and nausea.

All ROAs: Allergic reactions.

Endocrine

In the 1950s and 1960s, cases of altered thyroid function, particularly goiter, were reported in children taking soy formula. However, adding iodine to soy formula or replacing soy flour in formula with soy protein isolate has nearly eliminated the risk of altered thyroid function in most infants (75353,75651).

In adults, there is some evidence that soy intake can alter thyroid function. Results from one clinical trial suggests that consuming soybeans 30 grams daily for as little as one month can increase thyroid-stimulating hormone (TSH) and decrease thyroxine, causing diffuse goiters, constipation, fatigue, and lethargy in some Japanese men. Recovery was achieved by discontinuing soybean intake (75206,75353). There is also some evidence that soy inhibits thyroid hormone synthesis resulting in increased secretion of TSH in some postmenopausal patients (7806). However, this seems to only occur in people with iodine deficiency (6466,75311). In postmenopausal patients with normal levels of iodine, taking a soy extract for 6 months does not seem to significantly affect thyroid hormone levels (13010).

Evidence from a single case-control study suggests that consumption of soy-based formulas may be associated with an observed three-fold increase in the risk of breast development in Puerto Rican children less than 2 years-old (75520). The correlation has been attributed to the estrogenic activity of soy. However, other risk factors, including a maternal history of ovarian cysts and consumption of meat products were also associated with the increased risk of breast development prior to 2 years of age. Also, the investigators noted that in over half of the cases, the child had not been exposed to soy or any of the other risk factors. Therefore, factors other than soy consumption may be more strongly associated with the increased risk of breast development prior to 2 years of age.

Gastrointestinal

Gastrointestinal upset, such as constipation, diarrhea, bloating, and nausea are the most common side effects of soy (2297,11033,11082,15851,75491,95999). Reports of "bad taste" and taste intolerance have also been documented in clinical research (15851,39007,75491). Firmer stools, diarrhea, colitis, and intestinal mucosal damage has been reported in infants fed soy protein formula (75161,75448,75516,75525).

Genitourinary

Orally, soy might increase discomfort during menstrual periods. Evidence from a small, retrospective cohort study has found that consuming soy formula as an infant may slightly increase the duration and discomfort of menstrual periods later in life. However, the investigators noted that these differences may not be clinically significant (7331).

Orally, frequent soy consumption might be a risk factor for uterine leiomyoma, an estrogen-dependent benign tumor located on the uterus. Observational research found that consumption of soy milk or soybean at least four times weekly is associated with a 7-fold increased odds of uterine leiomyoma (98869).

There is some concern that use of soy-based formulas in infants might result in long-term health complications. However, results from a retrospective cohort study has found that intake of soy-based formula as an infant does not affect height, weight, body mass index, pubertal maturation, menstrual history, or pregnancy history, nor does it increase the risk of reproductive organ disorders, hormonal disorders, libido dysfunction, or birth defects in the offspring of adults who received soy formula as infants (7331,11080). Additionally, research in adults shows that urinary phytoestrogens are not associated with endometriosis risk (101804). However, some population research has found that regular exposure to soy-based formulas during infancy is associated with an increased risk for endometriosis (101803).

Immunologic

Orally, soy can cause allergic reactions such as skin rash and itching in some people (6412). In an 11-year-old female, allergy to soy protein resulting in a delayed itching papular rash was thought to be responsible for the reaction to injected benzathine benzylpenicillin containing possible soy protein-contaminated soy lecithin (96422).

Topically, soy-based ingredients were responsible for the development of hand atopic dermatitis in a young female using cosmetic lotions in the workplace. Percutaneous sensitization resulted in the development of anaphylaxis to oral soy (96000).

Neurologic/CNS

Orally, one clinical study showed that insomnia was more common in postmenopausal adults taking soy isoflavone supplements when compared with those receiving placebo (9917). Some research suggests that dietary consumption of tofu during midlife might decrease cognitive function in later years. Evidence from one retrospective cohort study suggests that males who consume at least two servings of tofu weekly during midlife have increased risk of cognitive impairment in late life (19% vs. 4%) compared to those who consume tofu less frequently. Although the effect of tofu was considered to be marginal compared to other factors such as age, education, or history of stroke, results from the study suggest that the effect of significant midlife consumption of tofu is comparable to the effect of an age difference of 4 years or an education difference of 3 years. However, numerous other factors, such as lifestyle and health, could be involved (6415,6416). Therefore, these findings are too preliminary to be used as a basis for clinical recommendations.

Oncologic

There is controversy about the role of soy in breast cancer. Population studies suggest that soy is protective against breast cancer. Asian females who eat a traditional diet high in soy seem to have a lower risk of developing breast cancer (4590,5939,9674). Early exploratory studies have suggested that soy stimulates proliferation of normal human breast tissue

(3980,3981). However, taking a soy tablet containing 50 mg soy isoflavones daily for 12 months does not alter mammographic or breast MRI tissue density in adults at high risk of breast cancer, with non-endocrine treated breast cancer, or previously treated for breast cancer and without evidence of recurrence (95999).

There is some concern that soy supplements, but not soy foods, might increase the risk of endometrial hyperplasia due to its estrogenic effects. Population and clinical research suggests that soy foods do not have a proliferative effect on endometrial cells (7358,2429,7654,9676,9917), and increased dietary soy and phytoestrogens are associated with reduced endometrial cancer risk (7338,10372). However, the effects seem to be different with concentrated soy isoflavone extract. While taking products providing isoflavones 120 mg daily for 6 months does not increase endometrial thickening (13209), taking higher doses such as isoflavones 150 mg daily for 5 years might increase the risk of simple endometrial hyperplasia (12105). However, there is no evidence that soy isoflavones increase the risk of atypical hyperplasia which has a much higher risk of developing into endometrial cancer than simple endometrial hyperplasia (12105,90973).

There is also concern that increased soy intake increases the risk for other types of cancer. Some observational research has found that higher dietary intake of soy is associated with a higher risk for bladder cancer and pancreatic cancer (9677,105609).

A meta-analysis of results from cohort and case-control studies evaluating the risk of stomach cancer related to consumption of fermented soy products is unclear and inconclusive. The highest quality data from cohort studies suggests that these products have no significant effect on stomach cancer (7340,7341). More research is required to determine if soy products have any correlation with stomach cancer.

Pulmonary/Respiratory

Inhaled soy dust and soy hull aeroallergen can trigger symptoms of asthma and allergic rhinitis (5084,5085,5086).

Effectiveness

POSSIBLY EFFECTIVE

Breast cancer. High dietary intake of soy might be beneficial for the prevention of breast cancer and breast cancer recurrence in some patients. However, soy supplements do not seem to be beneficial.

Details: For prevention, most population research has found that higher dietary intake of soy is associated with up to a 26% reduced odds of developing breast cancer when compared with a lower intake (7335,7336,11038,11807,75377,75587,90955,108251). One meta-analysis of population research found that patients who consumed more than 15 mg soy isoflavones daily made up about 25% of all cases of breast cancer, compared with 75% of cases in the group of patients consuming less than 15 mg daily (108251). The effects appear to vary depending on the ethnicity of the patient. Population research has consistently found that a high-soy diet in Asian and Asian-American females is associated with a significantly reduced risk of breast cancer (7335,7336,11038,11807,75377,75587,90955). However, the amount of soy consumed in a Western diet, even among those who consume the highest amounts of soy, was not found to have a preventative effect (11391,17109,90955,90967). The reason for the disparate findings are unknown but may be related to genetic differences or differences in quantification of soy intake (7663,94153). Also, the prophylactic benefit seems to apply regardless of whether high amounts of soy are consumed during adolescence or later in life (7335,7336,9674).

Limited population research has also found that consuming a diet high in soy is associated with up to a 25% reduced risk of breast cancer recurrence; however, it is unclear whether there is an association with reduced mortality in breast cancer patients (90956,90969,94154). The effect appears to be greater for certain subgroups of breast cancer patients. Increased dietary soy intake is associated with a 28% to 36% risk reduction in patients with estrogen receptor (ER)-negative tumors, a 30% risk reduction in patients with ER-positive/progesterone receptor (PR)-positive tumors, and a 25% to 36% risk reduction in postmenopausal patients (90956).

Some small clinical studies have also evaluated the use of soy isoflavone extract . One small clinical study in patients with breast cancer shows that taking a soy isoflavone extract 200 mg daily for 2 weeks prior to surgery does not seem to affect cancer cell growth when compared with a historical control (11042). Another small clinical study in patients at high risk for breast cancer or with a history of breast cancer shows that taking a soy tablet containing 50 mg soy isoflavones (Novasoy, Archer Daniels Midland Co.) daily for 12 months does not alter mammographic or breast tissue density when compared with placebo (95999).

Chronic kidney disease (CKD). Oral soy protein seems to improve some measures of disease severity in patients with CKD.

Details: Clinical research shows that consuming soy protein seems to reduce proteinuria in people with kidney disease (2286,2287,2288,75249,75634). Also, a meta-analysis of clinical research in patients with CKD who are not on dialysis shows that soy protein intake reduces serum levels of creatinine by 0.07 mg/dL, phosphorus by 2.5 mg/dL, and triglyceride by 18 mg/dL when compared with placebo or control (90989).

Diabetes. Diets high in soy seem to reduce the risk of type 2 diabetes. Also, oral soy protein, but not soy isoflavones, seems to modestly improve glycemic indices. It is unclear if soy is beneficial for lowering blood lipid levels or reducing cardiovascular (CVD) mortality risk in adults with type 2 diabetes.

Details: A meta-analysis of observational studies has found that higher dietary intake of tofu, soy protein, or soy isoflavones is associated with an 8% to 16% lower risk of developing diabetes when compared with a lower dietary intake (105608). In menopausal patients without diabetes, a meta-analysis of clinical research shows that intake of soy isoflavones 40-161 mg daily seems to improve glycemic indices when compared with control (96423).

Some research shows that soy can modestly improve glycemic indices in patients with diabetes. A meta-analysis of small low-quality clinical studies in patients with diabetes or metabolic syndrome shows that taking various formulations of soy protein modestly reduces fasting plasma glucose and insulin levels, as well as insulin resistance, when compared with control (96001). An older meta-analysis assessing both healthy patients and patients with diabetes shows that a whole soy diet reduces fasting blood glucose by about 4 mg/dL when compared with control (75493). Small clinical studies also suggest that an extract of the fermented soybean product, Touchi, acts as an alpha-glucosidase inhibitor. It seems to modestly lower blood glucose, glycated hemoglobin (HbA1c), and triglycerides in patients with type 2 diabetes (11762,75205). However, some conflicting evidence exists. A meta-analysis of small, low-quality clinical studies in patients with type 2 diabetes shows that taking soy isoflavones does not improve glycemic indices when compared with control (105610). Also, another meta-analysis of clinical research in patients with

type 2 diabetes shows that taking soy protein and/or soy isoflavones for 6-12 weeks does not improve glycemic indices when compared with either soy protein without isoflavones, other protein, or placebo (105610). Reasons for these conflicting results are unclear but may relate to differences in baseline blood glucose levels, the formulation of soy, or the duration of treatment.

Some research shows that soy may modestly improve the lipid profile in patients with diabetes. A meta-analysis of clinical research in patients with diabetes shows that taking soy protein and/or soy isoflavones for 6-12 weeks modestly reduces levels of total and low-density lipoprotein (LDL) cholesterol, but not high-density lipoprotein (HDL) cholesterol or triglycerides, when compared with control (105610).

Consuming soy foods might reduce the risk of mortality related to CVD in patients with diabetes. Population research suggests that consuming soy foods at least four days each week is associated with a 23% reduced risk of CVD mortality when compared with never consuming soy foods. Consuming soy foods less than four times weekly is not associated with CVD mortality risk (108242).

Soy is also of interest in the prevention or treatment of gestational diabetes. Population research has found that consumption of less than 40 grams of soy daily in the second trimester is associated with a 2.1-fold increased risk of gestational diabetes when compared with daily soy intake of 40 grams or more (108241). Also, a small clinical trial in patients with gestational diabetes shows that consuming a diet containing about 0.3 grams/kg soy protein for 6 weeks, beginning at 24-28 weeks' gestation, reduces blood glucose levels, insulin resistance, and triglyceride levels when compared with consuming a non-soy control diet (95993).

Diarrhea. Oral soy fiber seems to reduce acute diarrhea in infants, although it may not be beneficial in adults.
^ Details: Giving soy fiber-supplemented formula orally, either alone or in combination with oral rehydration solution, seems to reduce the duration of acute diarrhea in infants when compared with cow's milk formula or oral rehydration solution alone (2291,2292,75474,75517,75523,75531,75572). However, in some studies, a reduction in the duration of acute diarrhea was not observed when compared with cow's milk formula (75522,75542).

In adult patients receiving nutrition via intubation, preliminary clinical research suggests that treatment with soy-polysaccharide fiber does not improve the incidence of diarrhea when compared to control (75508).

Galactosemia. Oral soy protein can be used in infant formula to prevent symptoms of galactosemia.
^ Details: Soy does not contain the sugar galactose. Some research suggests that giving oral isolated soy protein-based formula in place of milk-based formula to infants seems to be helpful for preventing symptoms of galactosemia (3400).

Hyperlipidemia. Oral soy protein seems to modestly reduce lipid levels. However, purified soy isoflavone may not have the same benefit.
^ Details: Consuming soy protein orally, in place of other dietary protein, seems to modestly reduce total cholesterol and low-density lipoprotein (LDL) cholesterol by about 3% to 4% when compared with control (842,2293,2294,2296,2585,3402,4755,6412,7346,7803)(8530,10459,42059,75356,105598,105604). Additionally, some research shows that soy protein might be more effective in patients with more severe hyperlipidemia (75497). The FDA has approved labeling for specific soy products that states that they may be used for cholesterol reduction in combination with a diet low in saturated fat and cholesterol. To be eligible for this labeling, soy products must provide at least 6.25 grams of soy protein per serving, which is 25% of the effective daily intake (3977).

However, not all evidence is positive. Some studies have shown no benefit of soy protein or isoflavones on LDL cholesterol levels when compared to control (8521,9679,12034,17105,53771,75236)(75242,75274,75276). Furthermore, although a few clinical trials have shown significant decreases in triglycerides following supplementation with soy or soy protein isolate (75258,75365), most studies suggest that soy protein does not decrease triglycerides when compared to control (2293,6412,8530,12034,17105). The effect of soy protein on high-density lipoprotein (HDL) cholesterol is inconsistent. Most studies suggest that it does not increase HDL levels (2293,6412,8530,12034,75286)(75524), although some analyses of clinical research suggest that soy might increase HDL cholesterol levels by up to 4% when compared to control (75480,75497).

Doses of soy protein have ranged from 25-135 grams daily, providing 40-318 mg daily of isoflavones; however, higher doses do not seem to be more effective (17106,105598). Some evidence suggests that soy protein providing more isoflavones, or supplemented with isoflavones, might be more effective (3402,6413,10459), but this has not been consistently found in studies (3402). Most studies evaluating soy protein products containing little to no isoflavones suggest that these products are not effective (3402,7346,9679); however, purified soy isoflavone supplements alone do not seem to decrease LDL cholesterol (851,4738,7345,8502,10459,14066). In addition to soy protein, limited evidence suggests that soy fiber alone might reduce total cholesterol, LDL cholesterol, and triglyceride levels when compared with placebo (75686,75689). There is also some evidence that ultra-high temperature (UHT) treatment of soy milk destroys any cholesterol-lowering activity (17106).

Hypertension. Oral soy seems to modestly reduce blood pressure in some patients.
^ Details: A meta-analysis of the available clinical research shows that consuming soy products modestly lowers systolic and diastolic blood pressure by an average of 1.6 mmHg and 1.2 mmHg, respectively, when compared with control (105605). This analysis is limited by high risk of bias and the lack of a dose-response relationship. An older meta-analysis, as well as individual clinical studies, in patients with prehypertension or mild hypertension show that consuming soy protein 18-40 grams, providing 118-143 mg of isoflavones, daily or black soy peptide 4.5 grams daily for 8 weeks reduces systolic blood pressure by about 4-8 mmHg and diastolic blood pressure by about 3-5 mmHg when compared with control (1313990962,90965). In normotensive patients, soy protein does not seem to reduce systolic or diastolic blood pressure (90965).

Lactose intolerance. Oral soy protein can be used in infant formula to prevent symptoms of lactose intolerance.
^ Details: Providing isolated soy protein-based formula orally to infants is an acceptable alternative to milk-based formulas, especially for infants with symptoms of lactose intolerance (3400).

Menopausal symptoms. Oral soy seems to reduce hot flashes in patients with menopausal symptoms.
^ Details: Consuming soy protein 15-60 grams, providing 34-100 mg of isoflavones, daily seems to modestly decrease the frequency and severity of hot flashes in some menopausal adults. Improvement seems to be greater in those with a higher frequency of hot flashes at baseline (2296,2297,3978,3986,3987,7653,9917,11805,15220,17110,75478)(75486,75649,92661,95997). Taking concentrated soy isoflavone extracts, providing 35-200 mg of isoflavones, daily seems to have similar effects (4751,6455,7802,9916,10460,11805,11993,11994,13209,15220)(15850,75478,90950,90979,92661). Higher doses of 100-200 mg of isoflavones daily and higher frequency of dosing intervals seem to have greater benefit (90950). Furthermore, the amount of the

specific isoflavone genistein contained in a soy product may influence outcomes. According to one analysis, studies using products that provide at least 15 mg of genistein daily consistently show positive outcomes. Studies using products containing a lower concentration of genistein have produced inconsistent findings (15133). Not all research has found that soy extracts reduce hot flashes (7801,11806,14062,15038,15851,16762); some experts speculate that this is due to a high placebo response (9916).

Some clinical research has compared soy isoflavone extracts to conventional estrogen replacement. In one study, a concentrated soy isoflavone extract of genistein 54 mg daily reduced hot flashes by 22% to 29%, compared to 54% in those taking 17beta-estradiol as 1 mg daily plus norethisterone acetate 0.5 mg daily (11994). Additional preliminary research suggests that taking a soy isoflavone extract providing 60 mg isoflavones twice daily is comparable in efficacy to conjugated estrogens 0.625 daily for reducing menopausal symptoms. Conjugated estrogens seem to work more quickly; it seems to take up to 2 months to achieve the full effect of soy isoflavones (13209). One clinical trial compared soy isoflavones 10-40 mg daily to S-equol, a soy isoflavone metabolite. Soy isoflavones were less effective for reducing hot flash frequency when compared with S-equol (90960). This has led to some speculation that the effectiveness of soy in relieving hot flashes is influenced by a patient's ability to convert daidzen, a soy isoflavone, to S-equol (90950). It is theorized that patients who are S-equol producers are more likely to achieve symptom relief from soy. However, observational and clinical research does not support this theory (90990,94162).

Soy has also been evaluated for the management of other symptoms of menopause. Some clinical research in menopausal patients with depression suggests that taking soy 100 mg, providing 50 mg of soy isoflavones, in combination with sertraline 50 mg daily for three months improves depression severity when compared with sertraline or soy alone (90958). An analysis of two small clinical trials shows that supplemental soy providing 50-118 mg of isoflavones can reduce vaginal dryness scores by 0.26 when compared with control (92661). Also, an open-label study suggests that drinking a specific beverage (ViveSoy) containing soy protein 15 grams and soy isoflavones 50 mg orally daily for 12 weeks reduces overall urogenital symptoms when compared with a control group (95997). However, one small clinical study in perimenopausal patients shows that a soy-rich diet does not relieve urogenital symptoms, including vaginal dryness, itching, and urinary incontinence, when compared with a soy-free diet (75285).

Metabolic syndrome. Oral soy protein seems to improve glycemic control and other markers of metabolic syndrome.
^ Details: A meta-analysis of clinical research in patients with diabetes or metabolic syndrome shows that following a diet high in soy protein can decrease fasting plasma glucose and insulin levels, as well as insulin resistance, when compared with a control diet. Furthermore, dietary intake of soy protein modestly decreases diastolic blood pressure and low-density lipoprotein (LDL) cholesterol by a small amount in this population, although there is no effect on systolic blood pressure, high-density lipoprotein (HDL) cholesterol, or triglycerides (96001). Other clinical research shows that consuming a soy nut diet or a soy protein diet reduces fasting plasma glucose and LDL cholesterol levels when compared to baseline in postmenopausal adults with metabolic syndrome; however, the soy nut diet seems to more beneficial than either the soy protein diet or a Dietary Approaches to Stop Hypertension (DASH) diet (75378).

Muscle strength. Oral soy protein seems to increase muscle strength.
^ Details: Overall, soy protein combined with resistance training seems to increase muscle strength when compared with placebo (16748,75246,96942,98871). A meta-analysis of three clinical studies shows that consuming soy protein in addition to resistance training improves strength and lean body mass in untrained athletes (98871). Other clinical research shows that soy also improves muscle strength in trained athletes and postmenopausal adults (75246,96942). One study in Olympic endurance athletes shows that consuming isolated soy protein (Supro) 1.5 grams/kg daily for 8 weeks increases body mass and strength indices and reduces fatigue when compared with no protein supplementation (75246). Clinical research in postmenopausal adults undergoing resistance training 3 days weekly shows that taking soy protein 25 grams daily in skim milk for 16 weeks increases the maximum amount of weight lifted in one repetition by over 80% for both bench press and knee extension when compared to a maltodextrin placebo (96942).

Soy protein has also been compared with other protein supplements. A meta-analysis of preliminary clinical studies and other clinical research show that soy protein seems to work as well as whey, beef, and dairy (casein and whey) protein for improving muscle strength (75404,85941,98871,105591). However, the validity of these findings is limited by the small size and high heterogeneity of the studies.

Osteoporosis. Oral soy isoflavones seem to improve bone density and reduce the risk of osteoporosis in post-menopausal adults.
^ Details: Most clinical research suggests that soy protein or soy extract containing 75-90 mg of isoflavones can increase bone mineral density (BMD), or slow BMD loss, and improve biochemical markers of bone turnover in peri- and postmenopausal adults when compared with control (842,4951,6449,9775,11082,90972,90980). Lower doses of isoflavones do not seem to be as beneficial. However, some observational research in postmenopausal Japanese adults and Chinese females aged 30-40 years has found that consuming about 50 mg dietary soy isoflavones daily is associated with a higher BMD when compared with lower soy isoflavone intake (7342,11081). An observational study in postmenopausal Asian patients has found that consuming higher dietary soy protein is associated with a lower risk of developing fractures when compared with lower amounts (13181).

However, not all research has been positive. Some conflicting evidence suggests that soy protein does not improve BMD in some postmenopausal adults. The discrepancy in findings may be due to differences in soy formulations, concomitant treatments, or variable patient populations (4952,12034,14064,90978). For example, most evidence shows that soy does not affect BMD in premenopausal patients or bone turnover in adolescents (7660,8532,9684,11086).

It is theorized that only people who can convert daidzein, a soy isoflavone, to S-equol might obtain benefits from soy (4952). However, clinical research suggests that there is no difference in bone calcium retention between equol producers and nonproducers (95995).

POSSIBLY INEFFECTIVE

Benign prostatic hyperplasia (BPH). Oral soy does not seem to reduce BPH symptoms.
^ Details: Clinical research in patients with BPH shows that taking soy isoflavones 40 mg (Soylife 40, Acatris) daily for 12 months does not improve peak urine flow rate, residual urine volume, symptoms of BPH, or general quality of life when compared with placebo (90983).

Breast cancer-related hot flashes. Oral soy does not seem to reduce the risk for breast cancer-related hot flashes.
^ Details: Clinical research shows that consuming a soy beverage providing soy isoflavones 90 mg daily or taking a soy extract providing soy isoflavones 50 mg three times daily does not reduce hot flashes in breast cancer survivors (3991,7658,8499).

Observational research in breast cancer survivors has also found no association between hot flash incidence and soy isoflavone consumption (105602).

Colorectal cancer. Oral soy does not seem to reduce the risk for colorectal cancer.
Details: Some observational research from China and Japan has found that intake of soy protein or soy isoflavone is not associated with the risk of developing colorectal cancer (105601). Furthermore, some clinical research shows that soy protein powder 58 grams containing isoflavones 83 mg, taken daily for 12 months, does not reduce the proliferation of colorectal epithelial cells in patients with adenomatous polyps when compared to control (75282).

Exercise-induced muscle soreness. Oral soy does not seem to reduce muscle soreness after exercise.
Details: Some clinical research shows that taking soy isoflavone extract 120 mg orally for 30 days prior to exercise doesn't ameliorate muscle soreness caused by exercise when compared with placebo (8524).

INSUFFICIENT RELIABLE EVIDENCE to RATE
Alzheimer disease. It is unclear if oral soy improves cognition in patients with Alzheimer disease.
Details: Preliminary clinical research in patients with Alzheimer disease shows that taking soy isoflavones (Novasoy, Archer Daniels Midland Co.) 100 mg daily for 6 months does not improve cognition when compared with placebo (96424).

Androgen deprivation therapy (ADT)-associated hot flashes. One small clinical study in patients with prostate cancer receiving ADT shows that taking soy protein powder 20 grams, providing 160 mg of isoflavones, alone or along with venlafaxine 75 mg, once daily for 12 weeks does not improve the severity of hot flash symptoms when compared with milk protein, with or without venlafaxine (90981).

Asthma. It is unclear if oral soy reduces asthma symptoms.
Details: One population study has found that people with asthma who consume soy foods providing more than 250 mcg of genistein for every 1000 kcal consumed (e.g., 500 mcg/day for 2000 kcal diet) daily have increased lung function, as measured by FEV1 scores, when compared to those who consume less (11084). However, clinical research in adult and pediatric patients with poorly controlled asthma shows that taking soy isoflavones 50 mg twice daily for 24 weeks does not improve FEV1 scores, reduce the number of asthma episodes, or improve asthma symptoms when compared with placebo (90977).

Cardiovascular disease (CVD). It is unclear if soy consumption reduces the risk for CVD or CVD-related mortality. More research is needed to determine whether certain populations may benefit from increased soy intake.
Details: Due to mixed findings, it is unclear if consuming soy is associated with a reduced risk of CVD events. One population study has found that consuming at least 60 grams of soy daily over a 12-month period is associated with a 14% reduced risk of having a CVD event over the next 5 years, as well as a reduced risk of stroke, when compared with consuming less than 15 grams daily (108253). A study in Japan has found that consuming soy five or more times per week over a 10-year period is associated with fewer adverse cardiovascular outcomes in only a certain subset of patients when compared with consuming soy twice a week or less. Postmenopausal adults with the highest consumption had a 36% lower risk of stroke, a 45% lower risk of myocardial infarction, and a 65% lower risk of CVD mortality. However, risk was not significantly reduced in males or premenopausal adults (17108). In contrast, a study in Korea has found that consuming a median of 16.5 servings of soy per week is associated with a 64% reduced risk of CVD incidence in premenopausal, but not postmenopausal, adults when compared with a median of 4.7 servings per week. A subgroup analysis has found that the highest intake of tofu, but not soybeans, fermented soy paste, or soy milk, is associated with a reduced incidence of CVD (108243). Additionally, higher dietary intake of soy does not seem to be associated with a reduced risk of cardiovascular events in Western females (13040). The amount of phytoestrogens typically consumed in Western diets is significantly lower than the amount typically consumed in Asian diets. The form of soy food and isoflavone content might play a role in these discrepancies.

Any association between consumption of soy-containing foods and CVD mortality is also unclear. A meta-analysis of observational studies conducted in China or Japan has found that the highest intake of soy-containing foods is not associated with a lower risk of CVD-related mortality when compared with the lowest intake (96941). A population study in patients with or without a prior history of CVD has also found that soy-containing food consumption is not associated with a lower risk of CVD-related mortality when compared with the lowest intake (108244). However, some research has found a positive effect of soy consumption on CVD mortality risk. A subgroup analysis of a meta-analysis has found that the highest intake of fermented soy products is associated with a 16% reduced risk of CVD mortality; higher intake of non-fermented soy is not associated with CVD mortality (96941). Population research in patients without a prior history of CVD has found that soy-containing food consumption is associated with a lower risk of myocardial infarction-related mortality when compared with the lowest intake (108244). Also, one population study in adults with type 2 diabetes has found that consuming soy-containing foods at least four days each week is associated with a 23% reduced risk of CVD mortality when compared with never consuming soy foods. Consuming soy foods less than four times weekly is not associated with CVD-related mortality (108242).

Cervical cancer. It is unclear if oral soy reduces the risk for cervical cancer.
Details: Population research has found that the highest dietary intake of soy over approximately 17 years is associated with a 57% decreased risk of cervical cancer when compared to the lowest intake of soy in females who also drank green tea. However, neither soy intake nor green tea intake alone was associated with a decreased risk of cervical cancer. Additionally, other population research has not confirmed an association between soy intake and cervical cancer (101800).

Child growth. It is unclear if oral soy protein enhances child growth.
Details: Preliminary clinical research in Colombian children 2-7 years of age shows that consuming a soy protein supplement dissolved in fruit juice on 6 days of every week for 1 year does not improve body mass index, body composition, weight, or height when compared with consuming fruit juice and whole milk. A sub-analysis shows that children consuming the soy protein supplement had an increase in weight-for-age when compared with the control group, indicating that the supplement may be beneficial for ensuring adequate weight and nutritional status during prepubertal growth (100320). However, the children in this study had normal or below average weight-for-age at baseline, limiting the applicability of these findings to other patient populations.

Cognitive function. It is unclear if oral soy improves cognitive function; research is conflicting.
Details: Some research shows that college students who increase consumption of soy foods providing isoflavones 100 mg daily have improved short- and long-term memory (9671). Postmenopausal patients aged 50-65 years who take a soy extract supplement providing isoflavones 60 mg daily also seem to have some improvement in some measures of cognitive function (12048). There is also evidence in postmenopausal patients aged 55-75 years that taking a soy extract supplement providing isoflavones 110 mg daily might improve verbal memory scores (12040). However, another study in this population shows that consuming 25.6 grams daily of soy protein providing 99 mg of isoflavones does not improve cognitive function (12034). Similarly,

population research in females aged 42-52 years has found that increasing dietary intake of the isoflavones genistein and daidzein is not associated with improved measures of cognitive function (15042). These differing findings might be explained by variations in study design and soy formulations.

Cognitive impairment. Oral soy has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: Preliminary clinical research in adults 55 years of age and older with mild cognitive impairment shows that taking a specific combination product (DW2009) containing fermented soybean powder and Lactobacillus plantarum daily for 12 weeks modestly improves composite cognitive function when compared with placebo (100319). It is not clear if this effect is due to soy, lactobacillus, or the combination.

Colic. It is unclear if oral soy is beneficial in infants with colic.
^ Details: Preliminary clinical research shows that consuming soy-based formula might reduce the duration of colic symptoms in infants with cows' milk intolerance (75509,75543). However, other clinical research shows that consuming soy-based formula does not improve crying in infants with colic when compared with dicyclomine hydrochloride 3 mg/kg daily (75573). Also, a meta-analysis of only high quality clinical research shows that soy milk formula does not improve the persistence of colic or the duration of crying in infants with colic when compared with control (75611).

Crohn disease. It is unclear if oral soy improves symptoms of Crohn disease.
^ Details: A small observational study in patients with inactive Crohn disease has found that taking oral soy-derived protein in combination with enteral treatment for 4 weeks is associated with increased bowel movements, improved symptoms such as fatigue and mental strain, and increased body weight when compared with standard enteral treatment alone (75175).

Diabetic nephropathy. It is unclear if oral soy improves kidney function in patients with diabetic nephropathy.
^ Details: A meta-analysis of small clinical trials in patients with diabetic nephropathy shows that consuming soy products, such as soy protein and soy milk, modestly reduces proteinuria and blood urea nitrogen (BUN), as well as levels of total and low-density lipoprotein (LDL) cholesterol, triglycerides, and fasting blood glucose, when compared with animal protein or cow's milk. However, there was no effect on any measures of kidney function (108247). Some individual small clinical trials show that replacing dietary animal protein with soy protein reduces urinary albumin excretion in patients with diabetic nephropathy (7348,12555,12556). However, one small clinical study shows that consuming soy milk 240 mL daily for 4 weeks does not affect urinary creatinine, blood urea nitrogen, proteinuria, or glomerular filtration rate in patients with diabetic nephropathy (90966).

Dyspepsia. Oral soy protein has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: A small clinical study in adults with mild or moderate dyspepsia shows that consuming 1 gram of toasted soy flour fermented with Lactobacillus delbrueckii up to three times daily for 3 weeks does not improve heartburn severity or frequency when compared with placebo (105599).

Endometrial cancer. It is unclear if oral soy protein reduces the risk for endometrial cancer.
^ Details: Most epidemiological research has found that increased soy intake is associated with a lower risk of endometrial cancer. Endometrial cancer incidence is lower in Japan, China, and other Asian countries where the typical diet is low in calories and high in soy, whole grain foods, vegetables, and fruits (7338,11036,90954). Also, a large meta-analysis of population research has found that the highest total and fermented soy intake is associated with a 17% to 19% reduced risk of developing endometrial cancer when compared to the lowest intakes in postmenopausal adults (96002). However, one clinical study shows that taking soy protein 25 grams daily providing 91 mg of aglycon equivalents of isoflavones and glycosides for three years does not reduce the risk of endometrial hyperplasia or cancer when compared with placebo in postmenopausal adults. However, this study may not have been adequately powered to detect small differences in the low rates of endometrial hyperplasia (90971).

Fibromyalgia. It is unclear if oral soy reduces fibromyalgia symptoms.
^ Details: Clinical research shows that consuming a shake containing soy protein 20 grams and soy isoflavone 160 mg once daily for 6 weeks does not improve physical functioning or symptoms of depression in patients with fibromyalgia when compared with placebo (75451).

Gastric cancer. It is unclear if oral soy reduces the risk for gastric cancer.
^ Details: Meta-analyses of population research have found that the highest intake of soy-containing foods and nonfermented soy products is associated with a 21% to 37% decreased risk of gastric cancer when compared with the lowest intake (95998,108246). Intake of at least 100 grams daily of nonfermented soy foods was found to be the most protective (95998). However, a high intake of fermented soy products is associated with an increased risk of gastric cancer, and intake of 1-5 cups daily of the fermented soy product miso soup is associated with an increased risk of gastric cancer in males (95998,108246).

Hepatitis C. It is unclear if oral soy is beneficial for hepatitis C.
^ Details: Preliminary clinical research in patients with hepatitis C shows that taking soy protein 32 grams daily for 12 weeks reduces the number of cases of steatosis by 47% and reduces alanine aminotransferase (ALT) levels by 13% when compared to baseline. However, it is no different than taking casein protein (90970).

Irritable bowel syndrome (IBS). A small study suggests that oral soy isoflavones might reduce IBS symptoms.
^ Details: A small clinical study in females with IBS shows that taking soy isoflavones 40 mg daily for 6 weeks improves symptoms of IBS, such as abdominal distention and abdominal pain severity and duration, by approximately 27% when compared with placebo. Quality of life is also improved. Some symptoms are also improved when soy isoflavones are taken in combination with vitamin D; however, the combination of soy isoflavones and vitamin D does not seem to improve symptoms better than soy isoflavones alone (96425).

Lung cancer. It is unclear if dietary soy reduces the risk for lung cancer.
^ Details: A meta-analysis of epidemiological research has found that although increased soy intake is not associated with a reduced risk of lung cancer overall, it is associated with a slightly reduced risk in nonsmoking adults (90985).

Mastalgia. It is unclear if oral soy is beneficial for mastalgia.
^ Details: A small clinical study suggests that soy milk providing 34 grams soy protein daily might reduce cyclical breast pain when compared with no intervention (2428).

Migraine headache. Oral soy has only been evaluated in combination with other ingredients; its effect when used alone is unclear.
^ Details: Clinical research shows that taking a combination of soy isoflavones 60 mg, dong quai 100 mg, and black cohosh 50 mg daily for 24 weeks reduces the frequency of menstrual-associated migraine attacks when compared with placebo (35797). It

is not clear if this effect is due to soy, the other ingredients, or the combination.

Neonatal jaundice. It is unclear if oral soy reduces the risk of neonatal jaundice.
^ Details: Clinical research shows that patients with gestational diabetes who consume a diet containing soy protein along with other plant and animal proteins for 6 weeks beginning at 24-28 weeks' gestation have a 73% reduced risk for newborn hyperbilirubinemia when compared with those consuming a control diet containing only non-soy plant and animal proteins (95993).

Nonalcoholic fatty liver disease (NAFLD). It is unclear if oral soy is beneficial for the treatment or prevention of NAFLD.
^ Details: Observational research in a Chinese population has found that increased frequency of dietary soy consumption is associated with a lower incidence of NAFLD when compared with lower consumption (105612). A meta-analysis of three small clinical trials in patients living in Iran with NAFLD shows that consuming soy milk, soy foods, or a genistein supplement for 8 weeks might reduce some liver transaminase levels when compared with control (105611). Another meta-analysis of small clinical trials in patients with NAFLD shows that consuming soy milk, soy foods, or a genistein supplement for 8 or 24 weeks modestly improves insulin resistance but does not improve body mass index, cholesterol levels, or liver transaminase levels (108239). These analyses are limited by their generally small population size and the heterogeneity of interventions.

Obesity. It is unclear if consuming oral soy protein as part of a calorie-restricted diet improves weight loss; research is conflicting.
^ Details: Some clinical research shows that consuming soy protein in conjunction with calorie restriction for 2-6 months helps reduce weight in those who are obese and overweight when compared with calorie restriction alone (11085,75397). Other clinical research shows that consuming soy protein for 16 weeks improves weight loss in overweight females when compared with consuming protein from meat (75620). Also, consuming black soy peptide 4.5 grams daily for 12 weeks reduces body weight and body fat mass more than placebo in overweight and obese adults (90961). In addition, some clinical evidence shows that eating biscuits supplemented with soy fiber 100 grams daily for 12 weeks reduces body weight, body mass index (BMI), and low-density lipoprotein (LDL) cholesterol when compared to control in overweight and obese patients (90960).

However, contradictory evidence exists. Some clinical research shows that following a calorie-restricted diet and consuming soy-based meal replacements 3-5 times daily for 12-16 weeks, or eating soy protein-rich foods in place of animal protein for 2-12 weeks, does not improve weight loss in overweight or obese individuals when compared to a calorie-restricted diet alone (75277,75372,75376,90968). Also, in overweight and obese females following a free-choice diet, soy protein 56 grams daily for 23 weeks does not appear to improve weight loss when compared to eating an isoenergetic amount of carbohydrates (86077). Finally, a subgroup analysis of six preliminary clinical trials shows that soy products do not improve weight loss in postmenopausal adults (98870). The reason for these disparate findings is unclear but may be due to differences in the soy products used or differences in patient population. For example, a meta-analysis of clinical research shows that phytoestrogen consumption reduces weight in healthy postmenopausal adults but not in those with comorbid conditions (98870). However, the clinical validity of this analysis is limited because it did not evaluate the effect of soy-only phytoestrogens.

Soy protein has also been compared with whey protein. One small clinical study in overweight and obese adults shows that patients taking soy protein isolate 52 grams for 23 weeks had similar overall weight and fat loss as those taking whey protein concentrate 52 grams daily (86077). In contrast, another small clinical study in overweight males shows that taking soy isolate 60 grams before lunch daily for 12 weeks is less effective for weight loss when compared with taking whey protein concentrate 65 grams (91801).

Osteoarthritis. It is unclear if oral soy protein reduces osteoarthritis pain.
^ Details: Preliminary clinical research shows that taking soy protein 40 grams daily for three months improves range of motion, pain, and quality of life in osteoarthritis patients, particularly males, when compared to baseline. However, these beneficial effects seem to also be observed following supplementation with milk-based protein, indicating that the benefits may have resulted from a placebo effect (75266).

Overall mortality. It is unclear if dietary soy reduces overall mortality; the available research is conflicting.
^ Details: A meta-analysis of observational studies has found that the highest intake of soy products is not associated with a lower risk of overall mortality, mortality from cardiovascular disease, or mortality from cancer when compared with the lowest intake (96941). However, a more recent population study has found that consuming at least 60 grams of soy daily over a 12-month period is associated with a 17% reduced risk of overall mortality over the next 5 years when compared with consuming less than 15 grams daily (108253). Also, an observational study in Japanese patients followed over 14.8 years has found that although overall soy intake is not associated with any benefit, increased intake of fermented soy products, such as natto and miso, was found to be associated with a slightly reduced risk of mortality (105600).

Polycystic ovary syndrome (PCOS). It is unclear if oral soy reduces PCOS symptoms.
^ Details: Clinical research shows that taking soy isoflavones 50 mg daily for 12 weeks improves insulin levels and insulin resistance by a small amount when compared with placebo in patients with PCOS. Furthermore, taking soy isoflavones improves the free androgen index by approximately 25% and triglyceride levels by 14% when compared to baseline. However, taking soy isoflavones does not improve low- or high-density lipoprotein (LDL or HDL) cholesterol levels or markers of inflammation (95994).

Postmenopausal conditions. It is unclear if oral soy is beneficial for postmenopausal conditions.
^ Details: A meta-analysis of generally small clinical trials in postmenopausal adults shows that taking soy protein with isoflavones or soy isoflavones, usually for 3-24 months, has modest beneficial effects on total cholesterol, and possibly high-density lipoprotein (HDL) cholesterol, when compared with milk protein, soy protein without isoflavones, or placebo. However, there was no effect on low-density lipoprotein (LDL) cholesterol or triglyceride levels. Subgroup analyses show that reductions in LDL cholesterol levels occur when soy is used for less than 6 months, in individuals older than 55 years, and when the soy protein contains isoflavones (108249).

Preterm labor. It is unclear if oral soy reduces the risk for preterm labor.
^ Details: Clinical research in patients with gestational diabetes shows that consuming a diet containing soy protein along with other plant and animal proteins for 6 weeks, beginning at 24-28 weeks' gestation, does not reduce the likelihood for caesarean section, preterm delivery, or maternal hospitalization when compared with a control diet containing only non-soy plant and animal proteins (95993).

Premenstrual syndrome (PMS). It is unclear if oral soy reduces PMS symptoms.
^ Details: Preliminary clinical research in patients with PMS shows that taking isolated soy protein containing soy isoflavones 68 mg daily for two menstrual cycles reduces cramps and swelling when compared with placebo (75279).

Prostate cancer. It is unclear if oral soy is beneficial for the treatment or prevention of prostate cancer; research is conflicting.
^ Details: Observational and clinical research has evaluated the effects of soy intake on prostate cancer risk. Observational research has found that consuming an Asian diet, which contains 10 times more soy than the average American diet, is associated with a lower risk of prostate cancer; however, it is unclear whether it is the soy content of the diet or if genetic differences or environmental factors such as fat ingestion are responsible for this correlation (2298,12884,12886,12887). A meta-analysis of observational trials from North America, Europe, and Asia has found that highest intake of total soy foods, unfermented soy foods, or soy isoflavones is associated with a reduced risk of prostate cancer when compared with the lowest intakes. However, higher intake of fermented soy foods is not associated with a reduced risk (96939). Furthermore, some observational research in Japanese males has found a weak association between increased prostate cancer mortality and a higher dietary intake of soy isoflavones when compared with a lower intake (105607). Research evaluating the use of soy supplements is also conflicting. One clinical study shows that taking soy protein 40 grams daily for 6 months reduces the development of prostate cancer six-fold in those at risk of prostate cancer when compared with milk protein (75432). However, another clinical study in healthy adults aged 50-80 years shows that taking soy protein, providing 83 mg isoflavones, daily for a year does not affect PSA levels when compared with a soy protein drink without isoflavones (12888).

Soy products have also been evaluated in patients with prostate cancer. One clinical study shows that consuming a specific bread containing 50 grams of soy, providing 117 mg isoflavones, reduces PSA levels after about 3 weeks of treatment when compared with control (13140). Other preliminary clinical research in patients with rising PSA levels following prior therapy for prostate cancer shows that consuming 8 ounces of soy milk, standardized to contain 47 mg isoflavones, three times daily for 12 months slows the increase in PSA levels from 56% to 20% when compared with baseline (75435). However, one clinical study shows that taking soy protein 40 grams daily for 6 months does not reduce prostate size or improve PSA levels in those diagnosed with prostate cancer when compared with milk protein (75432). Also, in those with early stage prostate cancer, consuming a soy beverage daily providing genistein 60 mg does not seem to affect risk factors for progression of prostate cancer, including testosterone, estradiol, PSA, and sex hormone binding globulin (SHBG) levels (11033). Furthermore, consuming soy protein isolate 20 grams standardized to contain approximately 70 mg isoflavones daily for two years does not prevent prostate cancer recurrence following radical prostatectomy when compared with placebo (90953). Reasons for the discrepancies are not entirely clear, but may include the relatively short trial durations (up to 12 months) and heterogeneity of soy preparations and dosing regimens.

Rheumatoid arthritis (RA). It is unclear if oral soy reduces RA symptoms.
^ Details: Preliminary clinical research in patients with RA shows that consuming a liquid diet containing hydrolyzed soy protein (Top Up) daily for 4 weeks does not improve pain intensity, morning stiffness, or joint swelling and tenderness when compared to consuming a normal daily diet (75619).

Sarcopenia. It is unclear if oral soy reduces age-related muscle loss; evidence is conflicting.
^ Details: Some clinical research in postmenopausal adults shows that consuming soy protein containing isoflavones 99 mg daily for 12 months does not improve hand grip strength or physical performance when compared with a milk protein placebo (75283). However, another small clinical study in older adults with low muscle mass living in China shows that taking soy, or a whey-soy blended protein, 16 grams daily for 6 months, slightly attenuates muscle loss when compared with no intervention (105603).

Stroke. It is unclear if oral soy improves outcomes and overall function in people who have had a stroke.
^ Details: One small clinical study shows that older adults with a history of stroke who consumed soy milk 500 mL daily while participating in a rehabilitation program had greater improvements in hand grip strength, 8-feet walking speed, walking performance, and 6-minute walk test after 8 weeks when compared with placebo. However, consuming soy milk did not lead to greater improvements in lean mass or overall short physical performance battery (SPPB) scores when compared with placebo (100321).

Thyroid cancer. It is unclear if dietary soy reduces the risk for thyroid cancer.
^ Details: Epidemiological research has found that high dietary intake of soy is associated with a reduced risk of thyroid cancer when compared with lower intake (7662,12041).

Vaginal atrophy. It is unclear if topical soy improves vaginal atrophy.
^ Details: A small clinical study in postmenopausal adults with vaginal atrophy shows that applying one gram of soy extract 4% vaginal gel daily for 12 weeks reduces vaginal dryness and pain during sexual intercourse and improves vaginal endometrial thickness when compared with placebo (90964).

Wrinkled skin. Small studies suggest that oral and topical soy might reduce wrinkles.
^ Details: A small clinical study in middle-aged females shows that consuming soy isoflavone 40 mg daily for 12 weeks improves skin elasticity and the appearance of fine wrinkles when compared with placebo (75388). Another small clinical study in females with photodamaged skin shows that applying a soy moisturizer containing soybean trypsin inhibitor and Bowman-Birk protease inhibitor (Aveeno Positively Radiant Daily Moisturizer, Johnson & Johnson CCI) twice daily for 12 weeks improves skin pigmentation, fine lines, texture, tone, and appearance when compared with a placebo moisturizer (75410).

More evidence is needed to rate soy for these uses.

Dosing & Administration

- **Adult**

  Oral:

  Soy foods are available in many forms such as tofu, miso, and soy milk. Soy protein is most commonly used in daily doses of up to 40 grams for up to 6 months. Daily doses as high as 60 grams have been used for up to 4 months. Soy isoflavones up to 120 mg daily have been used for up to 6 months. See Effectiveness section for condition-specific information.

  Soy products may be standardized to specific soy isoflavones such as daidzein and genistein (96425),

  Topical:

Soy has been used in various topical formulations including as a gel and a moisturizer. See Effectiveness section for condition-specific information.

- **Children**

  Oral:

  Research is limited; typical dosing is unavailable.

- **Standardization & Formulation**

  Soy foods contain variable amounts of isoflavones. The typical amount of soy isoflavones per gram of soy product is as follows: soy flour, 2.6 mg; fermented soybeans, 1.3 mg; boiled soybeans, 0.6 mg; soy milk, 0.4 mg; soybean curd, 0.5 mg; fried soybean curd, 0.7 mg; soybean paste; 0.4 mg, and soy sauce, 0.016 mg (7342).

  One study investigating the amount of isoflavones in soy products found that only 1 of 15 products contained isoflavones in the amount labeled by the manufacturer, with most products containing a lower amount (90974). Another study found that less than 25% of commercially available products contain within 90% of labeled soy isoflavone content. Higher prices did not correlate with higher quality products (11088).

  Touchi is a traditional Chinese soy product that is prepared by steaming then fermenting soybeans with koji (75205).

  Clinical trials have used sources of soy isoflavones. Mixed isoflavones have contained 50% daidzein, 42.5% genistein, and 7.5% glycetin (96425); 75% genistein, 20% daidzein, and 5% glycitein (95994); or 46% daidzein, 42% genistein, and 2% glycitein (Novasoy, Archer Daniels Midland Co.) (96424).

Interactions with Drugs

ANTIBIOTIC DRUGS

Interaction Rating = **Minor** Be watchful with this combination.
Severity = Mild • Occurrence = Possible • Level of Evidence = **D**

Theoretically, antibiotics may decrease the activity of soy isoflavones.

Details

Intestinal bacteria are responsible in part for converting soy isoflavones into their active forms. Antibiotics may decrease the amount of intestinal bacteria and decrease its ability to convert isoflavones (7657).

ANTIDIABETES DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **A**

Soy can lower blood glucose and have additive effects with antidiabetes drugs.

Details

Clinical research shows that whole soy diets and soy-based meals reduce fasting glucose levels in diabetic and non-diabetic individuals (75268,75296,75378,75493,96001). Also, individuals following a soy-based meal replacement plan seem to require lower doses of sulfonylureas and metformin to manage blood glucose levels when compared with individuals following a diet plan recommended by the American Diabetes Association (75268).

ANTIHYPERTENSIVE DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **A**

Theoretically soy protein may have additive effects with antihypertensive drugs and increase the risk of hypotension.

Details

Although some contradictory research exists (14254), most clinical evidence suggests that consuming soy protein modestly reduces systolic and diastolic blood pressure in individuals with prehypertension or hypertension (13139,75482).

CAFFEINE

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**

Theoretically, soy might reduce the clearance of caffeine.

Details

Soy contains genistein. Taking genistein 1 gram daily for 14 days seems to inhibit caffeine clearance and metabolism in healthy females (23582). This effect has been attributed to inhibition of the cytochrome P450 1A2 (CYP1A2) enzyme, which is involved in caffeine metabolism. It is unclear if this effect occurs with the lower amounts of genistein found in soy.

CYTOCHROME P450 2C9 (CYP2C9) SUBSTRATES

Interaction Rating = **Minor** Be watchful with this combination.
Severity = Moderate • Occurrence = Unlikely • Level of Evidence = **D**

Soy might modestly induce CYP2C9 enzymes. However, this effect does not seem to be clinically significant.

Details

In vitro research suggests that an unhydrolyzed soy extract might induce CYP2C9. However, the significance of this interaction is likely minimal. In healthy females taking a specific extract of soy (Genistein Soy Complex, Source Naturals), blood levels of losartan, a CYP2C9 substrate, were not significantly affected (16825).

DIURETIC DRUGS

Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**

Theoretically, soy might have additive effects when used with diuretic drugs.

Details

Animal research suggests that genistein, a soy isoflavone, increases diuresis within 6 hours of subcutaneous administration in rats. The effects seem to be similar to those of furosemide (75604). This effect has not been reported in humans.

ESTROGENS
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **D**
Theoretically, soy might competitively inhibit the effects of estrogen replacement therapy.
Details
Soy contains phytoestrogens and has been shown to have estrogenic activity in some patients (3860). Although this has not been demonstrated in humans, theoretically, concomitant use of soy with estrogen replacement therapy might reduce the effects of the estrogen replacement therapy.

LEVOTHYROXINE (Synthroid, others)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **B**
Soy products might reduce the absorption of levothyroxine in some patients.
Details
Preliminary clinical research and a case report suggest that soy-based formulas inhibit the absorption of levothyroxine in infants with congenital hypothyroidism (20636,20637,75548,90959). A levothyroxine dosage increase may be needed for infants with congenital hypothyroidism while using soy-based formulas, and the dose may need to be reduced when soy-based formulas are no longer administered. However, in postmenopausal adults, clinical research shows that taking a single dose of soy extract containing isoflavones 60 mg along with levothyroxine does not affect the oral bioavailability of levothyroxine (95996).

MONOAMINE OXIDASE INHIBITORS (MAOIs)
Interaction Rating = **Major** Do not take this combination.
Severity = High • Occurrence = Likely • Level of Evidence = **C**
Taking soy products containing high amounts of tyramine along with MAOIs can increase the risk of hypertensive crisis.
Details
Fermented soy products such as tofu and soy sauce contain tyramine, a naturally occurring chemical that affects blood pressure regulation. The metabolism of tyramine is decreased by MAOIs. Consuming more than 6 mg of tyramine while taking an MAOI can increase the risk of hypertensive crisis (15649). The amount of tyramine in fermented soy products is usually less than 0.6 mg per serving; however, there can be significant variation depending on the specific product used, storage conditions, and length of storage. Storing one brand of tofu for a week can increase tyramine content from 0.23 mg to 4.8 mg per serving (15649,15701,15702). Advise patients taking MAOIs to avoid fermented soy products that contain high amounts of tyramine.

PROGESTERONE
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = Moderate • Occurrence = Possible • Level of Evidence = **A**
Theoretically, combining soy isoflavones with transdermal progesterone may worsen bone density.
Details
Clinical research suggests that significant bone loss may occur in females with osteoporosis who receive a combination of transdermal progesterone with soy milk containing isoflavones when compared with placebo, soy milk alone, or progesterone alone (69859).

TAMOXIFEN (Nolvadex)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Possible • Level of Evidence = **B**
Theoretically, estrogenic soy isoflavones might alter the effects of tamoxifen.
Details
Laboratory research suggests that genistein and daidzen, isoflavones from soy, can antagonize the antitumor effects of tamoxifen under some circumstances (7072,14362,8966); however, soy isoflavones might have different effects when used at different doses. A relatively low in vitro concentration of soy isoflavones such as 1 microM/L seems to interfere with tamoxifen, whereas high in vitro concentrations such as those >10 microM/L might actually enhance tamoxifen effects. People on a high-soy diet have soy isoflavones levels ranging from 0.1-6 microM/L. Until more is known, advise patients taking tamoxifen to avoid therapeutic use of soy products.

WARFARIN (Coumadin)
Interaction Rating = **Moderate** Be cautious with this combination.
Severity = High • Occurrence = Possible • Level of Evidence = **D**
Theoretically, soy might interfere with the effects of warfarin.
Details
Soy milk has been reported to decrease the international normalized ratio (INR) in a patient taking warfarin. The mechanism of this interaction is not known (9672). However, animal and in vitro research suggests that soy may also inhibit platelet aggregation (3992). Dosing adjustments for warfarin may be necessary.

Interactions with Supplements

CAFFEINE-CONTAINING HERBS AND SUPPLEMENTS: Theoretically, soy might reduce the clearance of caffeine.
Details
Soy contains genistein. Taking genistein 1 gram daily for 14 days seems to inhibit caffeine clearance and metabolism in healthy females (23582). This effect has been attributed to inhibition of the cytochrome P450 1A2 (CYP1A2) enzyme, which is involved in caffeine metabolism. It is unclear if this effect occurs with the lower amounts of genistein found in soy. See caffeine-containing ingredients **here**.

GREEN TEA: Theoretically, soy protein may reduce the benefits of green tea when consumed concomitantly.
Details
Clinical evidence in healthy females shows that consuming a drink containing green tea extract in combination with soy protein reduces the bioavailability of total catechins, epigallocatechin gallate, and epicatechin gallate from green tea. Advise patients to separate dosing of green tea and soy protein products by at least three hours (90957).

HERBS AND SUPPLEMENTS WITH HYPOGLYCEMIC POTENTIAL: Soy might have hypoglycemic effects.

Details
Clinical research suggests that whole soy diets and soy-based meals reduce fasting glucose levels in diabetic and non-diabetic patients, including those taking antidiabetes medications (75268,75296,75378,75493,96001). Soy products might have additive effects and side effects when used with other supplements that decrease blood glucose levels. See other products with hypoglycemic potential here.

HERBS AND SUPPLEMENTS WITH HYPOTENSIVE EFFECTS: Theoretically, soy may reduce blood pressure.
Details
Some clinical evidence suggests that consuming soy protein modestly reduces systolic and diastolic blood pressure in individuals with prehypertension or hypertension (13139,90965). Although some contradictory evidence exists (14254), theoretically, soy protein may have additive effects when used with other herbs and supplements with hypotensive effects.

IRON: Soy might alter the absorption of iron.
Details
Clinical research suggests that taking soy sauce (Shoyu) polysaccharides 600 mg daily for 4 weeks increases iron levels in healthy females when compared with placebo (75362). Other clinical research suggests that various fermented soy products and dephytinized soy formula increase iron bioavailability in adults and infants when compared to control (20639,75564). However, some conflicting evidence suggests that soy protein isolate reduces the absorption of non-heme iron from foods (5053). These differing effects are likely due to the presence of phytic acid. This constituent inhibits iron absorption, but its concentration is reduced after fermentation.

MANGANESE: Soy might reduce manganese absorption from food.
Details
Clinical evidence suggests that soy formula reduces the bioavailability of manganese when compared with human milk or cow's milk. This effect has been attributed to the ability of phytic acid, a constituent of some soy products, to chelate elements such as manganese and reduce their absorption (61534).

ZINC: Soy might reduce zinc absorption from food.
Details
Clinical evidence suggests that administering soy-based formula to infants for 4 months reduces plasma zinc levels when compared with breastfeeding (20641). This effect has been attributed to the ability of phytic acid, a constituent of some soy products, to chelate elements such as zinc and reduce their absorption.

Interactions with Conditions

BREAST CANCER

The effects of soy in patients with breast cancer are unclear. Soy isoflavones have weak estrogenic effects, which has led to concerns about the use of soy in patients with breast cancer. There is evidence that soy might increase breast cell proliferation in healthy females (3980,3981). However, in a 2-week study of soy isoflavones 200 mg/day in patients with breast cancer, soy isoflavones did not seem to stimulate breast cancer cell growth (11042). Also, taking a soy tablet containing 50 mg soy isoflavones daily for 12 months did not alter mammographic or breast MRI tissue density in females at high risk of breast cancer, with non-endocrine treated breast cancer, or previously treated for breast cancer and without evidence of recurrence (95999).

CROSS-ALLERGENICITY

Soy might cause allergic reactions in individuals sensitive to the Fabaceae family. Members of this family include peanuts and soybeans (4079,4080).

HYPOTHYROIDISM

Theoretically, soy might worsen hypothyroidism in patients with low iodine levels. There is some evidence that soy might inhibit thyroid hormone synthesis and increase thyroid stimulating hormone (TSH) in infants with congenital hypothyroidism or in postmenopausal adults (7806,20637). There are also cases of hypothyroidism and goiter in infants fed soy formula (6466). However, this seems to occur primarily in people with low iodine levels (6466). In postmenopausal adults with normal levels of iodine, taking a soy extract for 6 months does not seem to significantly affect thyroid hormone levels (13010,90973).

KIDNEY FAILURE

Theoretically, patients with kidney failure could be more sensitive to the phytoestrogens in soy. In patients with kidney failure, phytoestrogens in soy may reach higher plasma concentrations, increasing the risk for toxicity (8522).

KIDNEY STONES (Nephrolithiasis)

There is some concern that soy products might increase the risk of kidney stones due to high oxalate content. Soy products can contain from 0.02-42 mg oxalate/gram or approximately 2-640 mg/serving of soy, depending on the soy food type (7073,11079). Highly processed soy foods such as soy milk, soy protein, and soy sauce generally contain lower amounts of oxalates. Soy foods with less processing like soy flour, textured vegetable protein, and tempeh contain higher amounts of oxalates.

MILK ALLERGY

Children who are severely allergic to cow's milk are frequently sensitive to soy as well (9883); use with caution.

URINARY BLADDER CANCER

Soy products might increase the risk for urinary bladder cancer. Soy foods should be avoided in patients who are at risk for, or have a history of, bladder cancer (9677).

Interactions with Lab Tests

None known.

Overdose

There is insufficient reliable information available about the presentation or treatment of overdose with soy.

Commercial Products Containing: Soy

View All

View Health Canada Licensed Products

View Certified Products

USP Verified Products

NSF Contents Certified Products

NSF Certified for Sport Products

Pharmacokinetics

Absorption: In the gastrointestinal tract, the soy isoflavones genistein and daidzein are hydrolyzed by beta-glucosidases in the jejunum, releasing the isoflavone aglycone forms of genistein and daidzein (3982,5937,9346). Genistein and daidzein are absorbed from the human gut, although about 85% of soy isoflavones are degraded in the intestines following ingestion (75574,75585). Daidzein is further metabolized by gut flora in some people to the estrogenic compound, equol, which is also absorbed (12049). The absorption of isoflavones from food may be saturable, suggesting improved effect if ingested throughout the day, but there is considerable variation in absorption from person to person (3380,3982,7344). In general, healthy intestinal flora appears to be important for proper absorption of soy (75549). Also, there is some variation in how isoflavones are absorbed from different soy products. Soy germ products result in higher plasma levels of daidzein and lower levels of genistein. Soy protein products result in higher levels of genistein. Soy foods such as tofu produce less dramatic rises of daidzein and genistein. Genistein from soy food sources appears to be more bioavailable than daidzein (7330). Isoflavone bioavailability is similar for most soy foods (4750). However, fermented soy contains a more easily absorbed form of isoflavones than those found in nonfermented products (75606).

Distribution: Genistein and daidzein are widely distributed in the body and undergo enterohepatic recycling (7330,75585). Peak concentrations appear at 4-8 hours after dietary intake, and excretion is within 24 hours (3982). They are found both free in serum and bound to plasma proteins. Both genistein and daidzein are conjugated to sulfate and glucuronide compounds. In plasma, 48% of genistein and 33% of daidzein are present as a glucuronide and 8% of genistein and 26% of daidzein are present as a sulfate (9673).

Metabolism: Isoflavonoid glycosides from soy are converted to hormone-like compounds by intestinal bacteria (75558). The elimination half-life of free genistein and free daidzein are 3.2 and 4.2 hours, respectively. The elimination half-life of total genistein and total daidzein are 9.2 and 8.2 hours, respectively (7661). The half-lives of genistein glucuronide and daidzein glucuronide are 3.2 and 8.4 hours, respectively. The half-lives of genistein sulfate and daidzein sulfate are 3.1 and 5.7 hours, respectively (9673).

Elimination: Soy isoflavones, including equol, O-desmethylangolensin, daidzein, and genistein, are primarily excreted in the urine (75314,75546). Only 1% to 2% of ingested isoflavones undergo fecal excretion (75574). Approximately 10% of consumed daidzein is excreted in the urine as its equol conjugate (75678). However, many patients are unable to biotransform daidzein to equol, so higher levels of daidzein and genistein may be seen in the urine (75629).

Mechanism of Action

General: The applicable part of soy is the bean. Soybeans are legumes that contain up to 50% protein; 24% carbohydrates; and 25% oil including stearic, linoleic, and palmitic acids. The active constituents of soybeans are the phytoestrogens, known as isoflavones and lignans (3387,3978,4753,6029,11041), and phytosterols such as beta-sitosterol, campesterol, and stigmasterol (8528). Lignans are commonly found in grains but are also found in legumes such as soy. Soy lignans include syringaresinol, secoisolariciresinol, pinoresinol, and others (11041). Soy protein also contains phospholipids including phosphatidylcholine and phosphatidylinositol, and various saponins (11040).

Soybeans are also rich in calcium, iron, potassium, amino acids, vitamins, and fiber. Soy protein contains all of the essential amino acids in sufficient quantities to support human life (2426). Non-fortified soy beverages such as soy milk contain only about 10 mg of calcium per serving (6414). Most soy milk products are fortified with calcium carbonate, which has an equivalent bioavailability to the calcium from cow's milk (11078). Tricalcium phosphate-fortified soy milk can contain from 80-500 mg of calcium per serving, but has a poor calcium bioavailability compared to cow's milk (6414,11078). Fermented soy foods, such as soy sauce, miso, tempeh, and natto, may have higher amounts of calcium and vitamin K2 (7342).

Fermented soy products such as tofu and soy sauce contain tyramine. The amount of tyramine in these products is usually relatively small, often less than 0.6 mg per serving; however, there can be significant variation depending on the specific product, storage conditions, and length of storage. For example, storing one brand of tofu for a week can increase tyramine content from 0.23 mg to 4.8 mg per serving (15649,15701,15702).

Soybeans and soy foods are the most significant dietary source of isoflavones (3387,3978,4753,6029). They contain the isoflavone glucosides genistein and daidzein in their inactive conjugated forms. In the gastrointestinal tract, genistein and daidzein are hydrolyzed by beta-glucosidases in the jejunum, releasing the isoflavone aglycone forms of genistein and daidzein (3982,5937,9346). Daidzein is further metabolized by gut flora to the estrogenic compound, equol. The extent of conversion of daidzein to equol varies among people due to differences in gut flora. Theoretically, people who do not convert significant amounts of daidzein to equol ("non-equol producers") might not experience the same pharmacological effects as people who do convert significant amounts ("equol producers"). However the ability to produce equol does not always determine the clinical benefits of soy (12049,95995). About 50% of the population does not produce equol (4952). To overcome this, some people are trying probiotics to attempt to increase isoflavone levels. But using probiotics in combination with soy supplements does not seem to increase plasma phytoestrogen levels or increase the conversion of isoflavones to equol (11037). The amount of isoflavones varies among the forms of soy. Soy milk and soy powder have a lower concentration of isoflavones than other soy products (7655). Soy protein usually contains 1-3 mg of isoflavones per gram of protein (7333).

Soy isoflavones are heterocyclic phenols with structural similarity to estradiol and selective estrogen-receptor modulators (SERMs). Soy isoflavones bind to both the alpha- and beta-estrogen receptors. But they have a higher affinity for the beta-estrogen receptor (3983,3992,6029,7344,7657).

The beta-estrogen receptor predominates in the heart, vasculature, bone, and bladder; and may account for some of soy's beneficial effects. Actions at the cellular level depend on the target tissue, receptor status of the tissue, and the level of endogenous estrogen (7344).

Antiasthma effects: Some evidence suggests that dietary soy is associated with reduced asthma severity. Preliminary evidence suggests that genistein, a soy isoflavone, decreases eosinophil leukotriene C(4) synthesis by 33% in asthma patients (75413). Leukotriene C(4) plays a role in bronchoconstriction.

Anticancer effects: In cancer, soy is thought to be beneficial due to preliminary evidence that suggests soy isoflavones have antioxidant, antiproliferative, and antiangiogenic activity (2296,3983). Soy also contains other anticarcinogenic compounds such as saponins, phytates, protease inhibitors, and phytosterols (9346).

There is a lot of controversy about soy's potential role in breast cancer. Some researchers think that soy is protective against breast cancer. Asian females who eat a traditional diet high in soy seem to have a lower risk of developing of breast cancer (4590,5939). This benefit persists even when Asian females immigrate to the western cultures where soy is less likely to be a regular component of the diet (9674). This suggests that exposure to soy early in life (i.e., before menopause), provides the most benefit against breast cancer. It is theorized that isoflavones found in soy enhance early cellular differentiation and maturation of mammary glands. More mature mammary glands seem to be less susceptible to carcinogens (4590). Animal models show that soy protein can prevent chemically induced breast cancer (3976). There is also some evidence that genistein can suppress breast cancer cell growth by arresting the cell cycle and stimulating apoptosis (3378,11035,75617). Additional research suggests that soy isoflavones might inhibit angiogenesis (11035). Other research suggests that genistein influences enzymes involved in signal transduction that regulate cell growth and replication (7337,75201). Genistein seems to exert multiple antiproliferative effects on both estrogen receptor positive (ER+) as well as estrogen receptor negative (ER-) human breast cancer cells (9346,10461). The ability of genistein to inhibit the growth of precancerous dysplastic cells in breast tissue might contribute to the prevention of breast cancer (8965). Also, genistein appears to decrease levels of 17beta-estradiol, an ovarian steroid involved in transformation and tumorigenesis in human breast epithelial cells (75581).

There is also some evidence that soy isoflavones can prolong the menstrual cycle and suppress midcycle surges of luteinizing hormone (LH) and follicle stimulating hormone (FSH), which may also decrease the risk of breast cancer (9346,11035). Other research suggests that soy isoflavones do not significantly increase plasma levels of estradiol, follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, testosterone, or dehydroepiandrosterone sulfate (DHEAS) in premenopausal and postmenopausal individuals (11086,11087,12571).

Some research suggests that soy consumption alters the ratios of various estrogen metabolites in the urine, reducing excretion of potentially carcinogenic estrogen metabolites. This suggests that soy might cause a shift in estrogen metabolism to produce more benign metabolites (2430). However, some researchers suggest that due to the estrogenic effects of soy, it might actually increase the risk of breast cancer (6030). There is also preliminary in vitro data suggesting that soy can stimulate proliferation of normal human breast tissue (3980,3981). However, taking a soy tablet containing 50 mg soy isoflavones daily for 12 months does not alter mammographic or breast MRI tissue density in females at high risk of breast cancer, with non-endocrine treated breast cancer, or previously treated for breast cancer and without evidence of recurrence (95999). Higher serum estradiol levels are associated with increased risk of breast cancer. There is evidence that drinking soy milk daily can reduce serum 17-beta-estradiol and progesterone levels in premenopausal patients. However, other research shows only a very modest effect of a high soy isoflavone diet on plasma hormones (2429,7654,9676).

"Unopposed estrogen" from the estrogenic activity of soy and its effects on the uterus has been a concern. There doesn't seem to be any significant effects on vaginal cytology or endometrial biopsy in premenstrual or postmenopausal adults (2429,7654,9676,9917). Dietary phytoestrogens are associated with a reduced risk of endometrial cancer. In addition to their effect on estrogen, isoflavones and other phytoestrogenic substances in soy might inhibit aromatase, which converts androstenedione to estrone, and may in turn increase endometrial cancer risk (7338,10372). Also, some in vitro evidence shows that genistein can induce apoptosis in human uterine adenocarcinoma cell lines at the G2/M phase (75661).

Laboratory research suggests that genistein decreases the growth of both benign prostatic hyperplasia (BPH) and prostate cancer tissue (11238). Other preliminary research suggests that genistein might change androgen receptor expression and transcriptional activity of androgen-sensitive prostate cancer cells (12885,75221,75399). In addition, genistein appears to reduce the secretion of prostaglandin E2 from prostate cells. Prostaglandin E2 is known to stimulate the growth of prostate cancer (75455). Genistein also appears to induce apoptosis of human prostate adenocarcinoma cells (75660).

Antidiabetic effects: For diabetes, soy protein might reduce glucose levels due to its fiber content. There is also evidence that soy might improve glycemic control by inhibiting tyrosine kinase activity, improving insulin receptor affinity, improving glucose transport and increasing tissue sensitivity to insulin (8513). Touchi, a traditional Chinese food used as a seasoning agent, is prepared by steaming and then fermenting soybeans with the fungus Aspergillus. Touchi extract might be beneficial for diabetes patients because it seems to inhibit intestinal alpha-glucosidase and lower postprandial glucose levels in a dose-dependent manner. It may also lower triglyceride levels (11762).

Bone effects: For preventing postmenopausal osteoporosis, soy is thought to work due to its weak estrogenic effects on bone (5598,6029). Like estrogen, soy seems to have the most effect on the bone mineral density of the lumbar spine (7660). Soy seems to increase serum levels of osteocalcin, a marker of bone formation, in postmenopausal adults (7659). The soy isoflavone genistein appears to directly inhibit osteoclast activity (9346). High intake of soy also seems to lower parathyroid hormone levels, which might lower bone turnover (7660). In vitro tests suggest that genistein may promote the proliferation of osteoblasts by inhibiting oxidative damage (9682). Although some research suggests that soy protein and isoflavones do not seem to influence calcium absorption in postmenopausal adults, the evidence is mixed with respect to calcium retention (7343,11083,95995).

Cardiovascular effects: Soy has several pharmacological effects that might be beneficial for preventing cardiovascular disease (6029). It may lower homocysteine levels by unknown mechanisms, possibly related to the folic acid found in soy protein. Soy may also inhibit platelet aggregation (3992,8530,9776,75288,75295,75357). Soy might increase bile acid excretion, up-regulate low-density lipoprotein (LDL) receptors, inhibit endogenous cholesterol synthesis (2426,2594,6029,6030,7344,17106,75295,75667). Phytosterols in soy also contribute to the lowering of LDL cholesterol by competitively inhibiting cholesterol absorption in the small bowel (2594,8528).

Some preliminary evidence suggests that soy might prevent progression of coronary artery atherosclerosis (7333). The isoflavones found in soy, particularly genistein, inhibit oxidation of LDL particles, a process thought to play a role in early atherosclerosis (2586,6029,7347,9560,9561). The isoflavones seem to inhibit LDL oxidation by acting as free radical scavengers and by inhibiting cyclooxygenase (COX) (9683). In addition to preventing LDL oxidation, genistein also seems to protect vascular cells from oxidized LDL (8527). Some evidence suggests that genistein may prevent vascular remodeling, which is an important component of atherosclerotic plaque formation (8503). Genistein might produce these effects by inhibiting tyrosine kinase activity, and reducing the production of proteolytic enzymes and the migration of endothelial cells (9346). Genistein also appears to lower levels of vascular cell adhesion molecule-1, a protein that plays a role in the development of atherosclerosis (75440). Soy also seems to improve arterial compliance in perimenopausal females (851).

Unlike oral estrogen, phytoestrogens don't seem to elevate C-reactive protein (CRP) levels (9919), furthermore, some clinical research suggests that soy supplements might slightly lower CRP levels (105597,108250). However, lipoprotein (a), which has been identified as an independent risk factor for coronary heart disease, does not seem to be affected by soy in postmenopausal adults. In males, most research suggests that soy doesn't negatively affect lipoprotein (a) (7347,8530,8963,8964). The effect of soy on endothelial function, an early marker of vascular disease, is variable. In middle-aged males, soy might improve endothelial function. However, soy does not seem to affect endothelial function in postmenopausal adults and might worsen endothelial function in older males (8963,8964,14820,105596).

Soy seems to lower blood pressure, in particular the diastolic pressure (9346). Some clinical evidence shows that soybean powder can reduce diastolic blood pressure by increasing levels of adiponectin and nitric oxide (90975). Adiponectin stimulates the production of nitric oxide, which is involved in regulating blood pressure (90976).

Coagulant effects: Due to the estrogenic effects of soy isoflavones, there is some concern that soy might have pro-coagulant effects and potentially increase the risk for blood clots, similar to estrogen. But clinical evidence suggests that soy isoflavones have no significant effect on markers of coagulation, such as factor VII, or fibrinolysis (13168).

Dental effects: Preliminary clinical evidence shows that soy-based formula reduces plaque pH compared with other formulas (75582). By reducing plaque pH, soy formula may increase the development of tooth decay in infants.

Diuretic effects: In vitro evidence suggests that the soy isoflavone genistein can inhibit Na-K-Cl cotransporters similarly to the loop diuretic furosemide (75604).

Drug metabolizing effects: There is some evidence that isoflavones can inhibit oxidative and conjugative metabolism of drugs (4736). Isoflavones might also affect drug absorption and biliary excretion by interacting with drug transporters such as P-glycoprotein and the canalicular multispecific organic anion transporter (4736). Given the wide range of drugs and metabolites whose pharmacokinetics depends on these mechanisms, drug interactions with isoflavones might be more common than literature reports suggest.

Gastrointestinal effects: Reduction in duration of diarrhea in children fed soy formula may result from enhancement of sodium and water absorption by digested soy glucose and amino acids in the gut (75474).

Hormonal effects: Soy phytoestrogens might act as SERMs (3387,3990). In premenopausal adults with normal endogenous estrogen levels, soy phytoestrogens may have an anti-estrogen effect since soy isoflavones might displace endogenous estrogen from receptors. Consuming soy protein might also lower circulating levels of estradiol in premenopausal adults over the entire menstrual cycle (7663,7805,75226). In postmenopausal adults with low endogenous estrogens, soy phytoestrogens have a weak estrogenic effect (3373,3988,3989,3990,3994,6029,8529). Estrogenic effects of soy have also been attributed to benefit menopausal symptoms such as hot flashes. Genistein seems to relieve hot flashes in some females (11994). However, some research suggests that the incidence of hot flashes does not seem to correlate with serum levels of the phytoestrogens genistein, daidzein, and equol. Other components of soy, in addition to phytoestrogens, may be responsible for reduction in hot flashes (4752). The soy isoflavones, genistein and daidzein, seem to be responsible for the effects on thyroid hormones. These isoflavones seem to block production of thyroid hormone by interfering with thyroid peroxidase catalyzed iodination of thyroglobulin. This can result in increased thyroid stimulating hormone (TSH) and goiter. However, these clinical results appear most likely to occur in people with low iodine levels (6466). The effect on thyroid function is not likely to be clinically significant in patients with adequate dietary iodine intake (7806).

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to block production of thyroid hormone by interfering with thyroid peroxidase catalyzed iodination of thyroglobulin. This can result in increased thyroid stimulating hormone (TSH) and goiter. However, these clinical results appear most likely to occur in people with low iodine levels (6466). The effect on thyroid function is not likely to be clinically significant in patients with adequate dietary iodine intake (7806).

Neurological effects: Soy isoflavones have potential benefits on cognitive function. Preliminary evidence suggests that the effects of soy isoflavones seem to be equivalent to those of 17 beta-estradiol in up-regulating choline acetyl transferase and nerve growth factor. These chemical factors are thought to be essential for learning and memory. Soy also might decrease the phosphorylation of the brain protein tau. Phosphorylation of this protein is associated with the development of Alzheimer disease (9346).

Prostate effects: In prostate diseases, soy phytoestrogens are thought to be potentially beneficial due to estrogenic mechanisms as well as inhibition of 5-alpha-reductase and 17-beta-hydroxysteroid dehydrogenase (3984,3985). A diet high in soy foods seems to reduce serum estradiol levels and testosterone levels, but not PSA levels in healthy volunteers (7339,9683,9777,11039). However, in patients with prostate cancer consuming a soy beverage does not seem to decrease PSA or testosterone (11033).

Laboratory research suggests that genistein decreases the growth of both benign prostatic hyperplasia (BPH) and prostate cancer tissue (11238). Other preliminary research suggests that genistein might change androgen receptor expression and transcriptional activity of androgen-sensitive prostate cancer cells (12885).

Protection against heavy metal toxicity: Tofu, a soybean product, seems to inhibit the absorption of lead and prevent its build up in the body, possibly because of its phytic acid and calcium content (7656).

Weight loss effects: Postmenopausal adults with high dietary intake of the soy isoflavone genistein seem to have a lower body mass index, waist circumference, and fasting insulin levels than those with lower intake (7804). However, soy supplementation does not significantly increase concentrations of leptin, a protein associated with appetite and weight loss, in postmenopausal adults. In fact, some evidence suggests that soy supplementation can reduce leptin levels in patients who are obese or overweight (75428). But some evidence suggests that consumption of soy isoflavones as part of cereal bars increases levels of peptide YY, a satiety hormone (75340). In healthy female freshmen college students, consuming meal replacement shakes containing soy protein 20 grams and soy isoflavones 161 grams daily for 16 weeks did not prevent weight gain when compared with consuming casein-based meal replacements (90952).

Classifications

5-Alpha Reductase Inhibitors, Diuretics, Genistein-Containing Natural Ingredients, Ergogenic Aids

References

See Monograph References

Monographs are reviewed on a regular schedule. See our Editorial Principles and Process for details. The literature evaluated in this monograph is current through 4/12/2024. This monograph was last modified on 8/11/2022. If you have comments or suggestions, please tell the editors.