



To Soy or Not to Soy: Effects of Soybeans on Breast Cancer, Menopause and Heart Disease

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Originating in China, soybeans have been cultivated for more than 5,000 years. They were introduced to America in the 19th century, and since the 1940s, they have become one of the most important economic crops in this country. During the 2011-12 season, the U.S. was the largest soybean producer in the world with more than 35 percent of worldwide production (Taylor and Koo 2014). Various products are made from soybeans; a list of products can be found in Table 1 on page 2 (Berk 1992; Revival Products 2016).

The United Soybean Board monitors consumer attitudes toward soy. In 1998, 67 percent of consumers considered soy products to be healthy, and by 2011, this percentage had increased to 81 percent (USB 2012). With better understanding of soy's health benefits and increasing consumer acceptance, soy product use has reached a much wider market.

On Oct. 26, 1999, based on all the scientific evidence, the U.S. Food and Drug Administration issued a ruling on the health claims of soy protein. The ruling states that, "Diets low in saturated fat and cholesterol that include 25 g of soy protein a day may reduce the risk of heart disease." In the ruling, the FDA proposed that the soy food should contain 6.25 g of soy protein per serving in order to qualify for this health claim. This ruling is the most significant event for the soybean growing and processing industry in the past few decades.

It is known that eating soy-based foods lowers cholesterol (Qin et al. 2013; Messina, Messina, and Jenkins 2012), calms hot flashes, prevents breast cancer (Messina, Messina, and Jenkins; Takagi, Tago, and Kaga 2015) and prostate cancer (Castle and Thrasher 2002; Adjakly et al. 2013), aids weight loss (Ragle and Sawitzke 2012), and helps osteoporosis

(Hirota and Hirota 2015). Some of these benefits have been attributed to a unique characteristic of soybeans — a high concentration of isoflavones (a type of plant estrogen called "phytoestrogen"). However, some claims about soy consumption have been based on preliminary evidence and are not confirmed. This publication discusses the benefits and concerns regarding the consumption of soybean products and soy isoflavones related to breast cancer, menopause, and heart disease.

What Is in Soybeans?

According to the U.S. Department of Agriculture (2015) nutrient database, the largest commercial interests in soy are proteins and oils. Soybean compositions vary depending on variety, location, climate, and farming practices. Dry, mature, raw soybeans typically contain 40 percent protein, 20 percent lipids, and 10 percent dietary fiber. Soy protein contains all essential amino acids for human nutrition, and soybean oil contains a high level of unsaturated fatty acids (omega-6 and omega-3 fatty acids). Soybeans also contain many non-nutritional components such as isoflavones, which are considered to be healthy components. While isoflavones occur in many types of legumes, soybeans contain the highest concentration (1.5-1.8 mg of total isoflavones per gram of dry soybeans). In soybeans, three isoflavones are present as glycoside forms that contain sugar molecules (Imai 2015). Once ingested (or fermented), sugar molecules are detached and converted to bioactive aglycone (without sugar molecules) forms (genistein, daidzein, and glycitein) in the gut. Average isoflavone intake levels in Asian countries are higher than those in U.S. by four to 20 times (Chun, Chung, and Song 2009; Messina, Nagata, and Wu 2006).

Table 1. Descriptions of soybean products.

Soybean product	Description
Whole soybean products	
Edamame	Edamame is lightly steamed young green soybeans.
Soybean sprouts	Soybean sprouts are the germinating seeds of soybeans under shade conditions. Compared to mature soybeans, soybean sprouts contain substantial amounts of good proteins and much higher amounts of various vitamins.
Soy nuts	Soy nuts are made from soaked soybeans that have been fried, baked, or roasted with various flavors applied. In recent years, soy nuts have become more popular as a snack in the western world.
Soybean flours	Soybean flours are made from roasted soybeans that have been ground into fine flour; they can be found as full-fat or defatted versions. They are widely used to increase the protein content of many food items, such as baked goods and pasta.
Soybean meals	Soy meals are ground soybeans after soybean oil is extracted. They contain greater than 40 percent protein by weight and are an important protein source for the feed industry.
Soybean oil	Soybean oil is one of the most important vegetable oils in the world. In 2012-13, soybean oil made up 27 percent of the world's vegetable oil production.
Tofu	Tofu is a curd made by coagulating soy protein using mineral salts or acid.
Fermented soy products	
Miso	Miso is a popular Japanese food made by fermenting rice and soybean with a mixture of molds, yeast, and bacteria. The traditional miso manufacturing process starts with fermenting cooked rice with spores, followed by a second fermentation of the fermented rice and cooked soybean mix by molds, yeasts, and bacteria, which yields a paste material.
Soy sauce	Similar to miso, traditional soy sauce is manufactured by fermenting a mix of wheat and soybean by various bacteria and yeasts, creating a very complex flavor and aroma through chemical and biochemical reactions during the fermentation.
Natto	Natto is a traditional Japanese soy food made by fermenting soybeans with bacteria. It has become much more popular in recent years among U.S. consumers due to its perceived health benefits.
Tempeh	Tempeh is a fermented soybean product that originated in Indonesia. It is made by fermenting dehulled and partially cooked soybeans with mold. The network formed by mold forms a block, making it like a fermented soybean loaf.
Processed soybean products	
Soy protein isolate	Soy protein isolate contains a very high level of protein (>90 percent), and it is nearly carbohydrate and fat-free. It is widely used in the food industry in protein drink dry mixes, infant formulas, soups, liquid nutritional meals, soymilk, frozen desserts, dressings, bakery items, breakfast cereals, pet foods, pastas, cheese alternatives, snack foods, and protein supplement products.
Texturized meat alternatives	As food processing technology advances, soy protein, either alone or in combination with other vegetable proteins, can be processed into various texturized meat substitute products. This type of product (dry, refrigerated, or frozen) has a texture and color typically similar to meat and can be used to make vegetarian hamburger patties, meatballs, or sausages.
Soy milk, cheese, and dairy alternatives	Soy milk is produced by grinding soybeans in water or by mixing soy proteins in liquid. Soymilk contains similar amounts of protein and fat as cow's milk, and it is free of lactose and cholesterol. Soy dairy alternatives are made from a combination of soymilk with tofu and soy protein isolates.
Soy-based nondairy desserts	Nondairy, soy-based desserts include ice cream, soy whipped cream topping, soy-containing frozen desserts, and bakery items.
Nutritional supplements	Various supplement products have been produced from soybean processing, and popular ones are vitamin E, lecithin, and isoflavones.

Soybeans and soybean products contain varying amounts of isoflavones (2-150 mg/serving; table 2; Higdon 2004; Bhagwat et al. 2008). The dietary isoflavone supplements contain a wider range of isoflavones in aglycones (0.01-400 mg/g; Nurmi et al. 2002; Collison 2008). The chemical structure of isoflavones is similar to the female hormone estrogen, and isoflavones can bind to estrogen receptors and act as an estrogen (Vitale et al. 2013). Due to this estrogen-like activity, effects of isoflavones on hormone-regulated health conditions have been studied extensively.

Health Effects of Soy Consumption

The explosion of research on soy and human health has produced a lot of information and gives a better understanding of soy's health benefits from the molecular level. Based on findings, soy products can play a positive role in improving health; however, some health claims are only partially supported and have been challenged by new evidence.

Soy Consumption and Breast Cancer

Breast cancer is the second leading cause of death in the U.S.; 1 in 8 women could be diagnosed during their lifetime (ACS 2016). More than 95 percent of breast cancer cases occur in women with no family history, and more than 60 percent of breast cancers are sensitive (responsive) to estrogen and progesterone hormones. These cancers are called estrogen-receptor-positive and progesterone-positive when diagnosed, which means estrogen- or progesterone-like compounds can stimulate tumor growth. Women who are 40 to 55 years old are at high risk; approximately 77 percent of breast cancer cases occur in postmenopausal women over 50.

Breast cancer rates in Europe and North America are four to six times higher than those in Asian countries (Mourouti and Panagiotakos 2013), and many lifestyle factors could contribute to this difference. Epidemiological studies have provided evidence that higher soy consumption could have protective effects against breast cancer in Asian countries (Boyapati et al. 2005; Wu et al. 2008). However, trials involving pure soy isoflavones have shown mixed results.

Research Findings on Soy Consumption and Breast Cancer

- Soybeans, tofu, and miso had protective effects: a 20 to 23 percent decrease in breast cancer risks in China and Japan (He and Chen 2013).
- Isoflavone intake from soy foods lowered the risk of breast cancer recurrence among postmenopausal women (Dong and Qin 2011).
- Daidzein is an isoflavone contained in soybeans. Higher daidzein intake from soy products lowered breast cancer recurrence by 60 percent compared to low daidzein intake by postmenopausal women treated with tamoxifen (Guha et al. 2009). Estrogen-receptor-positive breast cancer can be treated with anti-estrogen therapy in combination with surgery, chemotherapy, and radiation therapy. Tamoxifen is one of the anti-estrogen therapies.
- Soy isoflavones consumed at levels comparable to those in Asian populations lowered the risk of breast cancer recurrence in women treated with tamoxifen without drug interaction (Lash et al. 2008).
- If a woman consumes soybeans throughout her life, she is likely to have a protective effect against later onset of breast cancer. Lifetime consumption of soy can facilitate gut bacteria that can efficiently metabolize soy to bioactive isoflavones (Hilakivi-Clarke, Andrade, and Helferich 2010).
- Genistein is a major isoflavone contained in soybeans. Genistein, at doses relevant to human consumption of soy products and isoflavone supplements, acted like an estrogen and stimulated the growth of estrogen-receptor-positive breast tumors in mice (Ju et al. 2001).
- Genistein accelerated carcinogen-induced breast tumor formation in rats (Allred et al. 2004).
- Genistein interfered with the inhibitory effect of tamoxifen against estrogen-receptor-positive breast tumors in mice (Ju et al. 2002).
- In contrast to estrogen-receptor-positive breast cancers, estrogen-receptor-negative breast cancers were inhibited by genistein treatment in mice (Pan et al. 2012).

These research findings suggest the following:

- Whole soybean food products might have a protective effect against breast cancer incidence and breast cancer recurrence.
- Early-age soy consumption could be protective against later on-set breast cancer.
- Products and supplements containing genistein might not be safe for people with estrogen-receptor-positive breast cancer; and

In contrast to estrogen-receptor-positive breast cancer, women with estrogen-receptor-negative breast cancer might benefit from soy and soy isoflavone consumption.

Soy Consumption and Menopausal Symptoms

The ovaries maintain the health of the female reproductive system and produce two main hormones — estrogen and progesterone — that regulate menstruation and other bodily functions.

Menopause begins when the ovaries start making fewer reproductive hormones, usually when a woman is in her 40s. Starting from perimenopause (menopausal transition), reproductive hormone levels are irregular and gradually decrease. Estrogen levels decrease approximately tenfold after menopause, and these hormonal changes cause menopausal symptoms such as hot flashes, night sweats, anxiety, mood swings, sleep disorders, vaginal atrophy (thinning, drying, and inflammation of the vaginal walls), irregular bleeding, joint pain, osteoporosis, memory loss, increased abdominal fat, and thinning hair. In addition to the natural decline of reproductive hormones, removal of the ovaries (oophorectomy) can cause a surgically induced menopause, and anti-estrogen therapy (as described above) can cause a chemically induced temporary menopause (National Institute on Aging 2015; Mayo Clinic 2015).

Menopausal symptoms are not life-threatening conditions; however, they can affect quality of life, and many women seek symptom relief through various treatments. Hormone replacement therapy provides estrogen and/or progesterone (ACS 2015) and various combinations of other reproductive HRT are available.

In the early 2000s, many studies reported negative effects of HRT, including a higher risk for breast cancer and ovarian cancer and other hormone-regulated conditions. Specifically, those who use an estrogen-progesterone combination HRT have a higher risk for developing breast cancer than those who use either estrogen HRT or no HRT. Due to the negative impacts of HRT, some physicians avoid prescribing them, which leads some women to look for other alternatives to relieve postmenopausal symptoms. Soybean products or soy isoflavone products became popular as an alternative HRT due to their estrogenic activity.

Research Findings on Soy Consumption and Menopausal Symptoms

- Soybean and soy isoflavone supplements have been investigated as a treatment to relieve hot flashes and other menopausal symptoms. Some studies found that soybeans and isoflavones reduced the frequency and severity of hot flashes (Bolanos-Diaz et al. 2011; Taku et al. 2012). Another study showed that soy isoflavones do not have enough estrogenic activity to have an impact on hot flashes and other menopausal symptoms (Fournier et al. 2007).
- A few studies have investigated the possibility of soy on age-related loss of memory or decline in thinking skills. One study showed a beneficial effect (Kritz-Silverstein et al. 2003) and others showed no effect (Kreijkamp-Kaspers et al. 2004; Fournier et al. 2007; Basaria et al. 2009). Some studies found that too much soybean consumption could lead to memory problems. Among older women of Japanese ancestry living in Hawaii, those who relied on the traditional soy-based diet were more likely to have cognitive problems than those who switched to a more western diet (White et al. 2000). This finding was confirmed by other long-term studies (Guo et al. 2000). A six-month study showed that soy isoflavone supplementation has a favorable effect on cognitive function, particularly verbal memory, in postmenopausal women (Kritz-Silverstein et al. 2003). Another study observed no effect on cognitive function from isoflavones (Krebs et al. 2004).
- Studies that evaluated bone loss (resorption) and/or formation found no consistent effect of soy

consumption on bone mineral density or bone formation. Some studies reported a slight reduction in bone loss among soybean users (Ricci et al. 2010; Taku, Melby, et al. 2010). Isoflavone mixtures are not effective in decreasing bone loss in both perimenopausal and postmenopausal Western women (Kreijkamp-Kaspers et al. (2004).

- Soy isoflavone supplementation did not improve overall quality of life in healthy Chinese postmenopausal women (Ho et al. 2007).

Based on these findings, the effects of soybean or soy isoflavone on menopausal symptoms are inconsistent across studies. Most of the human trials lasted only three to four months, thus long-term benefits need to be investigated. Considering the conflicting results, the efficacy of soy foods in improving menopausal symptoms remains unclear and more studies are needed.

Soy Consumption and Heart Disease

Heart disease is a broad term used to describe a range of diseases that affect the heart, including coronary artery disease, arrhythmias (irregular heartbeat), heart infections, heart defects, etc. Cardiovascular disease generally refers to conditions that involve narrowed or blocked arteries that can lead to a heart attack, angina (chest pain), or stroke. Cardiovascular disease is the leading cause of morbidity and mortality in the U.S. and is responsible for 1 in 4 deaths. Approximately 1 in 3, or 85.6 million Americans are living with some form of cardiovascular disease or the aftereffects of stroke.

Conditions and Symptoms

Arrhythmia - Normal heartbeats that pump blood rely on regular electrical impulses. Irregular electrical impulses (arrhythmias) can restrict or even stop the heart's ability to pump blood.

Atherosclerosis - The blood vessels become thick and stiff due to the buildup of plaque (fats, cholesterol, and other substances) in and on the artery walls, which can restrict blood flow.

Cardiomyopathy - A disease that causes changes in the heart muscle that reduce the heart's ability to pump blood and usually leads to chronic heart failure.

Coronary artery disease - Plaque narrows or partially obstructs coronary arteries and can result in reduced blood flow. This reduced flow can cause chest pain (angina), a warning sign of potential heart problems such as a heart attack.

Heart attack - Blockage of the blood flow to the heart by a buildup of plaques in the arteries.

Stroke - Blood supply to part of the brain is blocked or severely reduced, depriving brain tissue of oxygen and nutrients. This can be from clots that block the arteries or from bleeding due to ruptured blood vessels (AHA 2015).

Treatments

Treatment methods include lowering blood pressure by dilating arteries, lowering cholesterol by interfering with cholesterol synthesis, reducing water buildup and swelling, or preventing blood clots from forming in the coronary arteries through blood thinning medications (reduces the tendency for blood cells to stick together).

Research Findings on Soy Consumption and Heart Disease

In the past few decades, there have been numerous studies on the effects of soy consumption on heart disease. Epidemiological studies have found a lower incidence of cardiovascular disease in Asia than western countries; a lower incidence of cardiovascular disease is associated with higher soybean consumption. These studies often measured total cholesterol, low-density lipoprotein cholesterol (bad cholesterol), high-density lipoprotein cholesterol (good cholesterol), triglycerides, blood pressure, etc.

- Review papers concluded that consumption of soy protein rather than animal protein significantly decreased total cholesterol, LDL cholesterol, and triglycerides in blood (Stradling et al. 2013).
- Some studies showed the direct link between isoflavones in soy proteins and the lowering of total and LDL cholesterol (Anderson and Bush 2011). However, another study showed no effect of isoflavones on cholesterol levels (Basaria et al. 2009). No association between dose of isoflavones and cholesterol was found (Qin et al. 2013).

- Soy isoflavones had a blood-pressure-lowering effect in people with high blood pressure, but not in people with normal blood pressure (Liu et al. 2012).
- Soy isoflavone extracts decreased systolic blood pressure but not diastolic blood pressure in adults, and a dose-response relation was not observed (Taku, Lin, et al. 2010). When the heart beats, it contracts and pushes blood through the arteries to the rest of the body. This force creates pressure on the arteries, called systolic blood pressure. The diastolic blood pressure is the pressure in the arteries when the heart rests between beats.

Since the FDA’s 1999 ruling on health claims from soy consumption, many studies have further demonstrated the link between soy product consumption and reduced risk of CVD, including heart attack, stroke, and other forms of CVD. Eating soy and soy protein might help lower total cholesterol, LDL-c, triglycerides, and blood pressure. For all outcomes, there is no conclusive evidence of a dose-response effect for either soy protein or isoflavone. Benefits of soybeans or isoflavones against heart diseases observed by various animal and cell culture studies were not reproduced by human studies.

In 2006, the American Heart Association Science Advisory panel found that isolated soy protein with isoflavones has minimal effect in lowering LDL cholesterol (Sacks et al. 2006). Some studies reviewed in the nutrition committee of the AHA showed that eating 50 g of soy a day (equivalent of 1-1.5 pounds of tofu or 5-18 cups of soy milk) lowers LDL by only about 3 percent (Krauss et al. 2000). Although the finding does not agree with other studies, the AHA panel still recommends that soy products should be beneficial to cardiovascular and overall health because of their high content of polyunsaturated fats, fiber, vitamins and minerals, and low saturated fat content.

Summary

Effects of soybean or soy isoflavones on breast cancer, menopausal symptoms, and heart disease were discussed in this article.

- Soy on breast cancer: Whole soy product consumption throughout the lifetime can be good. However, isoflavones isolated from soybeans might not be good for estrogen-receptor-positive breast cancer.

- Soy on menopause: Soy or soy isoflavones could be good for delaying the process of osteoporosis by reducing hot flashes. However, memory and cognitive function were not affected by soy or soy isoflavone intake.
- Soy on heart disease: In general, soy and soy isoflavone intake is associated with a reduced risk of CVD because they can improve blood lipid profiles and reduce blood pressure.

Although there have been numerous studies to determine the effective and safe dosages of soybean products, mixed results have been reported. Human studies have used 20 to 50 g of soy protein per day (equivalent to two to 10 servings of soybeans and soybean products; table 2), or 40 to 150 mg of isoflavones per day (equivalent to one to five servings of soybean products or supplements). Much of the controversy surrounding soy focuses on isoflavones, particularly genistein. Therefore, it is recommended to consume whole soy products instead of products containing isolated protein or isoflavones.

Table 2. Content of protein and isoflavones in selected soybean products.

Food	Serving	Protein (grams)	Isoflavones (milligrams)
Edamame	2/3 cup	6-9	62
Green soybean	2/3 cup	7-9	65-154
Miso	1/2 cup	15	41-59
Meat alternatives	1 burger patty	3-10	3-15
	1 hot dog		
	3 sausage links		
Soy cheese	1 ounce	5	2-18
Soy milk	1 cup	3-10	3-30
Soy nuts	1 ounce	12	37
Tempeh	3 ounces	5-6	37-60
Tofu	3 ounces	6-13	20

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