# Soyfoods Safety Issues



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**TRADITIONAL SOYFOODS, SUCH AS TOFU AND MISO**, have played important roles in Southeast Asian diets for centuries and have been consumed by health-conscious individuals in Western countries for decades. They are excellent sources of high-quality protein and contain less saturated fat than many other commonly consumed protein sources. Recently, soyfoods have become increasingly popular in the West due in part to research indicating they may reduce the risk of certain chronic diseases including coronary heart disease,[1-3] osteoporosis,[4,5] and some forms of cancer.[6] Given these health and nutritional attributes, there would seem to be little reason for uncertainty about the value of adding soyfoods to the diet.

However, in recent years, concerns have been raised about the safety of soyfoods, primarily because they contain isoflavones. Isoflavone supplements have been implicated to a greater extent than soyfoods, but concerns are expressed about both. These concerns exist despite the U.S. Food and Drug Administration's conclusion that soyfoods are safe following their review of the literature included as part of the process for approving the health claim for soy protein and coronary heart disease in 1999.[7] Also, the Agency for Healthcare Research and Quality[8] identified only minor problems, such as mild gastrointestinal disturbance, associated with the intake of large amounts of soy in its review in 2005.

## Considerations in Evaluating Soy Research

Much of the discussion about the safety of soyfoods occurs on the Internet, often offering links to results of scientific studies. Given the volume of research that has been conducted on soy and isoflavones, it is not surprising that some studies show adverse effects. However, focusing on only these few studies gives a skewed perception of the safety of soyfoods. It is important to keep in mind that the preponderance of the data show soyfoods and isoflavones to be safe.

As in all research areas, there are findings that directly conflict with the majority of data. Most of the studies showing undesirable effects of soy are in vitro studies or have been conducted in animals so their relevance to humans should be considered with caution. In vitro conditions cannot duplicate the complexity of living organisms, human or otherwise. Further, the general approach in these studies is to examine the effects of isolated compounds which are often very different from the effects seen when these compounds are examined in their natural environment. This is because the biological impact of one nutrient or non-nutrient in a food can be dependent upon the presence of others.[9]

*The FDA evaluated the safety of soy when they approved the health claim stating, "25 grams of soy protein per day, as a part of diet low in saturated fat and cholesterol, may reduce the risk of heart disease."*

*One serving of a traditional soyfood, such as 3 to 4 ounces of tofu or 1 cup of soymilk, provides about 25 mg of isoflavones.*

Regarding animal studies, in addition to the many physiological and anatomical differences between rodents and humans, many animals, including rodents and non-human primates, metabolize isoflavones very differently than humans.[10-14] Therefore, one may derive only very limited insight about the possible effects of soyfoods on humans based on the results of studies in which rodents are fed isoflavone-rich soy protein or mixed isoflavones as exist in soybeans.

This is not to suggest that all in vitro and animal data should be ignored. Some types of studies, especially those related to safety assessments, can not ethically be conducted in humans. However, whenever possible, conclusions about health effects should be based on human data.

Finally, it should be noted that most highly investigated foods or food components have been linked with adverse effects in at least some studies. Studies have linked dairy milk consumption with colorectal[15] and prostate cancer,[16] and whole grains with a decrease in mineral absorption;[17] nevertheless, the nutrition community recommends these foods because the preponderance of evidence indicates that they are nutritionally beneficial.

*The preponderance of research data demonstrate neither soy isoflavones nor soyfoods affect hormone levels in men or women.*

## Fertility and Hormonal Imbalance

There has been considerable investigation into the effects of isoflavone-rich soy products and isoflavone supplements on hormone levels in both men and women. Much of the focus of this research was on determining whether decreases of testosterone and estrogen levels might indicate a possible role of soy in reducing prostate and breast cancer, respectively. However, the proposed chemopreventive effects of soyfoods appear to be due to some other mechanism since the vast majority of studies have shown no effects on hormone levels in response to the intake of soy protein or isoflavones in men[18, 19] or women.[20-22]

Nor is there any evidence that isoflavones contribute to infertility in humans, despite the effects seen in some animals when exposure to isoflavones is very high.[23-26] Although comparisons among different cultures should be made with caution, the large populations in Asian countries give support to the idea that soy does not cause infertility. The fertility problems seen in some animals are believed to be due to differences between the way in which isoflavones are metabolized in humans and non-humans.[27-29] Studies in humans show that soy does not prevent ovulation[30] in women or affect sperm quality in men.[31] Nevertheless, given the paucity of data, more fertility-related research is warranted.

## Soy, Isoflavones, and Thyroid Function

There is a long history of research into the effects of soy on thyroid function.[32-34] Concerns about anti-thyroid effects of soy are based primarily on in vitro[35, 36] and animal studies involving isoflavones.[37, 38] In addition, several early cases of goiter were attributed to the use of infant soy formula; however, this issue was resolved in the mid-1960s by fortifying soy formula with iodine.[32, 33, 39]

### Fast Facts about Isoflavones

- *Isoflavones are one of five chemical classes of anticarcinogens found in soy.*
- *Soyfoods are the only significant natural dietary source of isoflavones.*
- *Research shows isoflavones may prevent the onset of osteoporosis and may protect against various forms of cancer.*
- *One serving of a traditional soyfood provides about 20 to 35 mg of isoflavones.*

A recent review of 14 clinical trials concluded that there is little evidence that soyfoods or isoflavones adversely affect thyroid function in healthy men or women.[40] Studies published subsequent to the review also found no effect on thyroid function. Soyfoods may increase the amount of thyroid medication needed by patients with hypothyroidism,[41-44] but this is also true of many foods, herbs and drugs, including fiber supplements.[45-53] It is not necessary for thyroid patients (with the exception of infants with congenital hypothyroidism) to avoid soyfoods; medication dosages can easily be adjusted to compensate for any effects of soy.

Preliminary results from research currently underway indicate that soy also has no adverse effects on thyroid function in people who are marginally hypothyroid. This condition occurs in a fairly large number of Americans, especially older people, and is defined as having normal levels of thyroxine and triiodothyronine but elevated levels of thyroid stimulating hormone.[54]

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## Soyfoods and Breast Cancer Risk

The estrogen-like effects of isoflavones form the theoretical basis for concern that soyfoods might be contraindicated for women at increased risk of breast cancer or for those with estrogen-sensitive tumors.[55-59] Isoflavones bind to estrogen receptors, stimulate the growth of estrogen receptor positive breast cancer cells in vitro, and in certain types of experimental rodent models stimulate the growth of existing estrogen-responsive mammary tumors.[60, 61] However, even in the rodent models, unprocessed soyfoods do not cause tumor stimulation.[62] More importantly, human data suggest that isoflavones do not exert stimulatory effects on breast tissue.

In 4 clinical trials, 3 involving postmenopausal women and 1 involving premenopausal women, researchers took biopsies before and after exposure to isoflavones to test for increased breast cell proliferation (a marker of increased cancer risk). All 4 trials found no increase in breast cell proliferation and no effects on other measures of estrogenicity related to isoflavone exposure.[20, 63-65]

*The National Cancer Institute states that, for breast cancer survivors, "soyfoods, as a part of a healthy diet and in moderate amounts, are safe to consume."*

Similarly, 4 other studies found that isoflavone exposure does not increase breast tissue density.[66-69] In contrast, estrogen plus progestin therapy increases breast tissue density and breast cell proliferation,[70, 71] and increases breast cancer risk.[72]

Finally, the epidemiologic study most relevant to the soy-breast cancer controversy found that neither soy nor isoflavone intake was related to disease-free survival over the 5.2 year follow-up period.[73] In this study, of the 1,001 (total cohort included 1,459 subjects) Chinese breast cancer patients for whom data on receptor status was available, approximately 63 percent were estrogen receptor positive.

Despite the evidence showing no stimulatory effects of either soyfoods or isoflavones on human breast tissue, breast cancer patients should always discuss any dietary changes with their healthcare provider.

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## Isoflavone Content of Soyfoods

*One serving of a traditional soyfood provides about 20 to 35 mg of isoflavones.*

| Soyfood | Serving size | Total (mg) isoflavone/ serving |
|---|---|---|
| Miso | 1 Tbsp | 7 |
| Soybeans, Green, Cooked | 1/2 cup | 50 |
| Soybeans, Black, Cooked | 1/2 cup | 40 |
| Soybeans, Yellow, Cooked | 1/2 cup | 78 |
| Soybeans, Roasted, Plain | 1/4 cup | 78 |
| Soymilk, Plain, Unfortified | 1 cup | 10 |
| Soymilk, Plain, Fortified | 1 cup | 43 |
| Soy Flour, Defatted | 1/4 cup | 42 |
| Soy Flour, Full-Fat | 1/4 cup | 33 |
| Soy Flour, Low-Fat | 1/4 cup | 50 |
| Soy Crumbles, Meat Alternative | 1/2 cup | 9 |
| Soy Protein Isolate Powder, Plain | 1/3 cup | 53 |
| Textured Soy Protein, Dry | 1/4 cup | 33 |
| Tempeh | 1/2 cup | 53 |
| Tofu | 1/2 cup | 25 |

## Effects of Soy on Mineral Status

Soyfoods are frequently used in place of animal proteins, many of which are good sources of iron and zinc, and of dairy foods, which provide calcium. Consequently, there is a need to understand the impact of soy on mineral status. The consumption of relatively little red meat meets daily iron and zinc requirements, so questions about the effects of soy on the status of these two minerals pertains mostly to those eating a predominately plant-based diet.[74]

Soybeans, like other legumes and whole grains, are high in phytate,[75] which reduces the absorption of some minerals, especially divalent cations.[76] Zinc absorption from soyfoods is only modestly lower than that from other sources. But because soybeans are not naturally rich sources of this mineral, unfortified soyfoods are not particularly good sources of zinc.[77-80] Since zinc status is difficult to assess,[81, 82] vegetarians are advised to identify good plant sources of zinc in their diet or take a zinc supplement.[83-86]

In contrast to zinc, soyfoods are relatively high in iron.[87] Until recently, prevailing thought was that the iron in soyfoods and essentially all plant foods was poorly absorbed. However, new research using improved methodology indicates that iron absorption from soy may be higher than previously thought because most of the iron in soy is in the form of ferritin. Although there is some debate about the bioavailability of ferritin, some research shows it to be highly available.[88, 89] Also, clinical studies show that incorporating soy into the diet does not negatively impact iron status.

Finally, in addition to phytate, soybeans are high in oxalate, another inhibitor of calcium absorption. However, calcium absorption from soy is good despite the presence of oxalate and phytate.[90] The more relevant issue concerns the bioavailablity of calcium from calcium-fortified products, such as tofu and soymilk.

The issue of calcium absorption from soymilk is somewhat complex. First, absorption depends to some extent on the type of supplemental calcium used.[91] Absorption from soyfoods fortified with calcium carbonate is similar to the absorption of calcium from cow's milk.[92] In contrast, calcium absorption from soymilk fortified with tricalcium phosphate is about 25 percent lower than from dairy milk.[93] However, because of the high amounts of calcium added, the amount of calcium available to the body from both types of calcium-fortified soymilk is similar to that from cow's milk.[92]

Questions have also been raised about the solubility of calcium in soymilk. According to Heaney and Rafferty, even with vigorous shaking, the calcium in soymilk comes out of the solution.[94] However, while some sedimentation occurs in certain soymilks, with mild shaking, this sediment is re-suspended for the majority of soymilk purchased in the United States.

## Allergies

As with essentially all food proteins, soy protein can cause allergic reactions in sensitive individuals. Soy protein is classified as one of the eight foods responsible for approximately 90 percent of all food-induced allergic reactions in the United States, but allergy to soy protein is actually relatively rare.[95] A recently conducted nationally representative telephone survey found that only approximately 1 out of 2,500 adults reported having doctor-diagnosed allergies to soy protein.[96] The rate is undoubtedly higher in children, as children are more likely to have food allergies. However, most children outgrow their soy allergies early in life.

The FDA notes in the 2004 Food Allergen Labeling and Consumer Protection Act that highly refined oils, such as soybean oil, are non-allergenic because the protein that causes food allergy has been removed during processing.

*Recent research shows that only about 1 out of 2,500 American adults are allergic to soy protein.*

## A Word about Processing

Tofu and miso are the most commonly consumed soyfoods in Japan and China, while in the United States, many people choose more processed forms of soy such as meat alternatives and energy bars.[97] Numerous human studies demonstrate that processed soy products provide the same high-quality protein as traditional soyfoods.[98] In some cases, however, the isoflavone content is markedly reduced.[99] A database of the isoflavone content of foods by the USDA can be accessed at http://www.nal.usda.gov/fnic/foodcomp/Data/isoflav/isoflav.html .

Many traditional soyfoods such as miso, tempeh and natto undergo fermentation. While mineral absorption may be slightly improved with fermentation and this process also gives rise to other potentially beneficial compounds, there is little evidence that these foods are significantly superior to unfermented ones. Non-fermented soyfoods have been consumed in Japan[100] and China[101] for at least 500 and 1,000 years, respectively. In both countries today, at least half of the total soy consumed comes from non-fermented foods.[1, 102, 103]

## Summary and Conclusions

When evaluating the safety of soyfoods, it is important to look at the totality of the scientific research which indicates soyfoods can safely be incorporated into the diets of all healthy individuals with the exception of those allergic to soy protein.

It is also important to keep in mind that all foods have the potential to cause undesirable effects in some individuals. People with specific health concerns should consult their healthcare provider regarding their unique nutritional needs.

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