Isoflavones, a subclass of flavonoids, are commonly referred to as phytoestrogens (plant estrogens) because they bind to estrogen receptors (ER) and exert estrogen-like effects under certain experimental conditions. Although they are found in an extensive array of plants such as garbanzo beans, alfalfa and red clover, soybeans and foods made from them are the only commonly consumed foods that provide nutritionally relevant amounts of isoflavones.\(^1\)

Soybeans contain three types of isoflavones—genistein, daidzein and glycitein, which account for approximately 50, 40 and 10%, respectively, of the total isoflavone content of soybeans. In whole soybeans and unfermented soyfoods such as tofu, isoflavones are found primarily as glycosides, with an attached sugar molecule. In fermented soyfoods such as miso and tempeh, more of the isoflavones are present in the aglycone form. This is an important consideration in measuring the isoflavone content of foods since the sugar molecule accounts for about 40% of the weight of the glycoside form. In this fact sheet, isoflavone amounts are expressed in aglycone equivalent weights, which is the most accurate representation.

As a general guide, traditional soyfoods contain about 3.5 mg of isoflavones per gram of protein.\(^1\) The isoflavone content of processed soyfoods such as meat analogs can be much lower due to processing losses. Isoflavone intake varies widely throughout Asia, but is around 30 to 50 mg per day in Japan and Shanghai, China, representing an intake of one to two servings of soyfoods per day.\(^2\) Older people consuming more traditional diets may have much higher intakes than younger people. In contrast, US daily isoflavone intake is less than 3 mg.\(^3\)

While epidemiological research has looked at the health effects of traditional soyfoods such as tofu, soymilk, and tempeh, clinical trials have used isolated soy protein or isoflavone supplements.

### Metabolism and Biological Properties of Isoflavones

Isoflavone metabolism differs greatly among individuals. In particular, about one-third of non-vegetarian Westerners host intestinal bacteria that metabolize daidzein into equol, a metabolite that may have important health benefits. In contrast, approximately 50 to 60% of Asians are equol producers. Equol production among vegetarians may be comparable to that of Asians although data are limited.\(^4\) Although isoflavones bind to estrogen receptors, they differ from estrogen at both the molecular and clinical levels. Isoflavones preferentially bind to and activate estrogen-receptor-β (ERβ) in comparison to estrogen-receptor-α (ERα), whereas estrogen binds to both with equal affinity. As a result, isoflavones appear to exert
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tissue-selective effects and hence are classified as SERMs (selective estrogen receptor modulators). In contrast to estrogen, which has estrogenic effects in all tissues that possess ERs, SERMs can have estrogen-like effects, anti-estrogen effects, or no effects in different parts of the body that are affected by estrogen. Consequently, the effects of isoflavones cannot be predicted based on the effects of estrogen.

Breast Cancer

Higher soy intake is associated with a reduced risk of breast cancer among Asian women. However, evidence suggests that soy confers protection only if consumed in childhood and/or adolescence while breast tissue is developing. One serving per day during this time may reduce lifetime risk by as much as 25 to 50 percent.

Although animal studies have raised concerns about the effects of isoflavones on breast tumors, extensive clinical data indicate that isoflavone exposure has no effect on markers of breast cancer risk including breast tissue density and breast cell proliferation. Furthermore, data from more than 11,000 women with breast cancer show that women who consume soyfoods after their diagnosis have a better prognosis, with reduced recurrence and improved survival. The American Cancer Society, the American Institute for Cancer Research and several medical and academic institutions have concluded that women with breast cancer can safely consume soyfoods.

Prostate Cancer

Among Asian men, higher soy intake is associated with a nearly 50% reduction in prostate cancer risk. In addition, several, but not all, intervention studies have found that isoflavone exposure slows the rise in prostate specific antigen levels in men with prostate cancer. Preliminary data suggest that isoflavones may also help to alleviate side effects in men undergoing radiation for the treatment of prostate cancer. While the data are encouraging, the relationship between prostate cancer and isoflavones has yet to be definitively determined.

Heart Disease

Adding isolated soy protein to diets can lower blood cholesterol by as much as 4% and there is some evidence that traditional soyfoods may have the same benefits. Further reductions occur when soyfoods replace foods that are high in saturated fat. Soy protein may also modestly lower blood pressure. There is also evidence that soyfoods exert coronary benefits beyond effects on blood cholesterol and blood pressure by enhancing endothelial function.

In addition, a three-year intervention found that in young postmenopausal women, isoflavone-rich soy protein markedly inhibited the progression of subclinical atherosclerosis as assessed by changes in carotid intima media thickness. Prospective epidemiologic studies from Japan and Shanghai indicate that soy intake was associated with as much as a 50 to 75% reduction in the risk of stroke and fatal and non-fatal coronary heart disease among postmenopausal women. In contrast to the results in women, prospective studies in men have not reported protective effects against cardiovascular disease.

Bone Health

In epidemiologic studies among women in Asia soy intake is associated with substantially lower rates of fracture. However, findings from several large clinical trials providing between 80 and 300 mg of isoflavones daily to postmenopausal women found no improvement in bone mineral density. It is possible that lifelong soy intake is protective, but isoflavones show no protection when taken in adulthood only. Alternatively, it may be that components in soyfoods other than isoflavones account for the observed protection against fracture, although there are no suggestions as to what these components may be. At this time, the evidence that isoflavones promote bone health is unimpressive.
Menopausal Symptoms

Since 1995 when the first trial was published, more than 50 clinical trials have evaluated the impact of isoflavone-containing products on the alleviation of hot flashes. Results of a recently published meta-analysis found isoflavone supplements were efficacious at reducing both the number and severity of hot flashes. Sub-analysis of the data indicated that supplements providing ≥18.8 mg genistein (the median for all studies) reduced hot flash frequency by almost 27% whereas in trials providing less than this amount, frequency was reduced by only about 12.5%. The level of relief provided by isoflavones is consistent with the degree of benefit deemed satisfactory by women seeking non-hormonal treatments for hot flashes.

Safety of Isoflavones

Concerns about potential harmful effects of isoflavones are based primarily on in vitro or animal data. In contrast, almost without exception, human studies support the safety of both isoflavone supplements and isoflavone-rich soyfoods for adults. Clinical studies show little to no effects on circulating reproductive hormones in men or women. Also, the clinical evidence indicates that isoflavones do not affect sperm or semen. Exposure to high amounts of isoflavones does not affect thyroid function in people with normal thyroid function, although it is possible that isoflavones affect thyroid function in individuals with subclinical hypothyroidism. Finally, there have been conflicting results from both clinical and epidemiologic studies about the effects of isoflavones on cognitive function. A recent comprehensive review concluded that there was insufficient evidence to reach conclusions about the relationships between isoflavones and cognitive function.

Optimal Isoflavone Intake

Mean isoflavone intake among older Japanese adults ranges from about 30 to 50 mg/day. However, in many epidemiologic studies, lower disease rates were associated with isoflavone intakes that were considerably higher than these amounts. Western clinical studies have generally used between 50 and 100 mg/day of isoflavones; the lower end of this range appears to be sufficient for the alleviation of hot flashes and the higher end for the improvement in arterial health. Since one serving of a traditional soyfood provides about 25 mg of isoflavones, a reasonable soyfood intake recommendation is two to three servings per day.

<table>
<thead>
<tr>
<th>Isoflavone Content of Selected Foods</th>
<th>Total Isoflavone Content (mg)</th>
<th>Total Isoflavone Content (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food</td>
<td></td>
<td>Food</td>
</tr>
<tr>
<td>Soybeans, mature, ½ cup, cooked</td>
<td>47</td>
<td>Miso, 2 tablespoons</td>
</tr>
<tr>
<td>Tofu, firm, ½ cup</td>
<td>38.8*</td>
<td>Soy imitation chicken, 3 ounces</td>
</tr>
<tr>
<td>Soy flour, full-fat, ¼ cup</td>
<td>37.3</td>
<td>Soy hotdog, 2 ounces</td>
</tr>
<tr>
<td>Tempeh, ½ cup</td>
<td>36</td>
<td>Soy cheese, 1 ounce</td>
</tr>
<tr>
<td>Tofu, silken, ½ cup</td>
<td>31.2*</td>
<td>Soy infant formula, 4 ounces</td>
</tr>
<tr>
<td>Tofu, regular, ½ cup</td>
<td>29.7*</td>
<td>Soy veggie burger, 3 ounces</td>
</tr>
<tr>
<td>Edamame (green soybeans), ½ cup, cooked</td>
<td>28</td>
<td>Kidney beans, ½ cup, cooked</td>
</tr>
<tr>
<td>Soy flour, defatted, ¼ cup</td>
<td>27.5</td>
<td>Peanuts, 1 ounce</td>
</tr>
<tr>
<td>Soy protein isolate, 1 ounce</td>
<td>27.3</td>
<td>Pinto beans, ½ cup, cooked</td>
</tr>
<tr>
<td>Soymilk, 8 ounces</td>
<td>23*</td>
<td>Flaxseed, 1 tablespoon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Soy oil, 1 tablespoon</td>
</tr>
</tbody>
</table>
References


