**Soy**

**Overview**

This section contains the following key information:

* [Soy](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000407766&Filter=set:QC+GlossaryTermName+with+Concept+Set) foods (e.g., soy milk, miso, tofu, and soy flour) contain [phytochemicals](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044709&Filter=set:QC+GlossaryTermName+with+Concept+Set) that may have health benefits, including for cancer prevention, and, among these, soy [isoflavones](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046660&Filter=set:QC+GlossaryTermName+with+Concept+Set) have been the focus of most of the research.
* Soy isoflavones are [phytoestrogens](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000330175&Filter=set:QC+GlossaryTermName+with+Concept+Set). The major isoflavones in [soybeans](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000415913&Filter=set:QC+GlossaryTermName+with+Concept+Set) are [genistein](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046107&Filter=set:QC+GlossaryTermName+with+Concept+Set) (the most abundant), [daidzein](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000285740&Filter=set:QC+GlossaryTermName+with+Concept+Set), and glycitein.
* Genistein affects components of multiple growth and [proliferation](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044572&Filter=set:QC+GlossaryTermName+with+Concept+Set)-related pathways in [prostate cancer](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000445079&Filter=set:QC+GlossaryTermName+with+Concept+Set) [cells](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046476&Filter=set:QC+GlossaryTermName+with+Concept+Set), including the [COX-2](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000589403&Filter=set:QC+GlossaryTermName+with+Concept+Set)/[prostaglandin](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000559143&Filter=set:QC+GlossaryTermName+with+Concept+Set), [epidermal growth factor](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000653114&Filter=set:QC+GlossaryTermName+with+Concept+Set) (EGF), and [insulin-like growth factor](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000653119&Filter=set:QC+GlossaryTermName+with+Concept+Set) (IGF) pathways.
* Some [preclinical studies](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044517&Filter=set:QC+GlossaryTermName+with+Concept+Set) have indicated that the combined effect of multiple isoflavones may be greater than that of a single isoflavone.
* Some [animal studies](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000454774&Filter=set:QC+GlossaryTermName+with+Concept+Set) have demonstrated prostate cancer [prevention](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000439419&Filter=set:QC+GlossaryTermName+with+Concept+Set) effects with soy and genistein; however, other animal studies have yielded conflicting results regarding beneficial effects of genistein on prostate cancer [metastasis](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046710&Filter=set:QC+GlossaryTermName+with+Concept+Set).
* [Epidemiologic](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000257225&Filter=set:QC+GlossaryTermName+with+Concept+Set) studies have generally found high consumption of nonfermented soy foods to be associated with a decreased risk of prostate cancer.
* A few [clinical trials](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045961&Filter=set:QC+GlossaryTermName+with+Concept+Set) of soy [protein](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046092&Filter=set:QC+GlossaryTermName+with+Concept+Set) or whole soy products have provided preliminary evidence of the ability of soy and soy products to modulate intermediate endpoint biomarkers implicated in prostate carcinogenesis ( steroid hormones, PSA pro-inflammatory cytokines and chemokines, proliferative biomarkers) in men with localized prostate cancer.
* To date, these early phase clinical trials with isoflavones,soy and soy products for prevention and treatment of prostate cancer have been limited to relatively short durations of intervention, sample sizes with low statistical power, targeting heterogeneous prostate cancer patient populations (in high risk, early and later stage disease) as well as varying doses of isoflavones, soy and soy products and have not demonstrated evidence of reducing prostate cancer progression.
* Other trials evaluating the role of isoflavones, soy or soy products in reducing the **management of a**[ndrogen deprivation](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000559086&Filter=set:QC+GlossaryTermName+with+Concept+Set" \t "_blank)  **therapy side-effects have** found no improvement in side effects following isoflavone treatment, compared with placebo.
* Isoflavones, soy and soy products are generally well tolerated in patients with prostate cancer. In clinical trials, the most commonly reported [side effects](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046580&Filter=set:QC+GlossaryTermName+with+Concept+Set) were mild [gastrointestinal](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045692&Filter=set:QC+GlossaryTermName+with+Concept+Set) symptoms.

**General Information & History**

Although records of soy use in China date back to the 11th century BC, it was not until the 18th century that the plant reached Europe and the United States. The soybean is an incredibly versatile plant: it can be processed into a variety of products including soy milk, miso, tofu, soy flour, and soy oil.[[1](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_1)]

Soy foods contain a number of phytochemicals that may have health benefits but isoflavones have garnered the most attention. Among the isoflavones found in soybeans, genistein is the most abundant and may have the most [biological](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044510&Filter=set:QC+GlossaryTermName+with+Concept+Set) activity.[[2](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_2)] Other isoflavones found in soy include daidzein and glycitein.[[3](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_3)] Isoflavones are quickly taken up by the gut and can be detected in [plasma](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045839&Filter=set:QC+GlossaryTermName+with+Concept+Set) as soon as 30 minutes after the consumption of soy products. Studies suggest that maximum levels of isoflavone plasma [concentration](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000683342&Filter=set:QC+GlossaryTermName+with+Concept+Set) may be achieved by 6 hours after soy product consumption.[[5](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_5)] Isoflavones are phytoestrogens (they bind to [estrogen receptors](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046409&Filter=set:QC+GlossaryTermName+with+Concept+Set)) with a greater binding [affinity](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000655052&Filter=set:QC+GlossaryTermName+with+Concept+Set) for estrogen receptor beta than for estrogen receptor alpha.[[6](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_6)]

A link between isoflavones and prostate cancer was first observed in epidemiological studies which demonstrated a lower risk of prostate cancer in populations consuming considerable amounts of dietary sources of soy. (Messina 2004 and Messina 2006). Subsequent studies evaluating the role of soy in experimental models further showed anticancer properties of soy, specifically relevant to prostate carcinogenesis. These early studies have led to a few clinical trials in humans using soy food products or supplements targeting men with varying stages of prostate cancer. Although these studies showed modulation of intermediate endpoint or surrogate biomarkers of prostate cancer progression, the evidence relating soy or soy products have been mxed.

**Preclinical/Animal Studies**

***In vitro* studies**

A number of [laboratory studies](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044512&Filter=set:QC+GlossaryTermName+with+Concept+Set) have examined ways in which soy components affect prostate cancer cells. In one study, human prostate cancer cells and normal prostate [epithelial](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045682&Filter=set:QC+GlossaryTermName+with+Concept+Set) cells were treated with either an ethanol vehicle (carrier) or isoflavones. Treatment with genistein decreased COX-2 [mRNA](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000662001&Filter=set:QC+GlossaryTermName+with+Concept+Set) and [protein](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046092&Filter=set:QC+GlossaryTermName+with+Concept+Set) levels in cancer cells and normal epithelial cells more than did treatment with the vehicle. In addition, cells treated with genistein exhibited reduced [secretion](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000643082&Filter=set:QC+GlossaryTermName+with+Concept+Set) of prostaglandin E2 (PGE2) and reduced mRNA levels of the prostaglandin [receptors](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044958&Filter=set:QC+GlossaryTermName+with+Concept+Set) EP4 and FP, suggesting that genistein may exert [chemopreventive](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045487&Filter=set:QC+GlossaryTermName+with+Concept+Set) effects by inhibiting the synthesis of prostaglandins, which promote [inflammation](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044042&Filter=set:QC+GlossaryTermName+with+Concept+Set).[[10](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_10)] In another study, human prostate cancer cells were treated with genistein or daidzein. The isoflavones were shown to down regulate [growth factors](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045705&Filter=set:QC+GlossaryTermName+with+Concept+Set) involved in [angiogenesis](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046529&Filter=set:QC+GlossaryTermName+with+Concept+Set) (e.g., [EGF](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000653115&Filter=set:QC+GlossaryTermName+with+Concept+Set) and IGF-1) and the [interleukin](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046069&Filter=set:QC+GlossaryTermName+with+Concept+Set)-8 [gene](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045693&Filter=set:QC+GlossaryTermName+with+Concept+Set), which is associated with cancer [progression](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044078&Filter=set:QC+GlossaryTermName+with+Concept+Set). These findings suggest that genistein and daidzein may have chemopreventive properties.[[11](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_11)] Both genistein and daidzein have been shown to reduce the proliferation of LNCaP and PC-3 prostate cancer cells [*in vitro*](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045733&Filter=set:QC+GlossaryTermName+with+Concept+Set). However, during the 72 hours of [incubation](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045734&Filter=set:QC+GlossaryTermName+with+Concept+Set), only genistein provoked effects on the dynamic [phenotype](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000460203&Filter=set:QC+GlossaryTermName+with+Concept+Set) and decreased invasiveness in PC-3 cells. These results imply that invasive activity is at least partially dependent on [membrane](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046294&Filter=set:QC+GlossaryTermName+with+Concept+Set) fluidity and that genistein may exert its antimetastatic effects by changing the mechanical properties of prostate cancer cells. No such effects were observed for daidzein at the same dose.[[12](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_12)]

Some experiments have compared the effects of individual isoflavones with isoflavone combinations on prostate cancer cells. In one study, human prostate cancer cells were treated with a soy [extract](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000407760&Filter=set:QC+GlossaryTermName+with+Concept+Set) (containing genistin, daidzin, and glycitin), genistein, or daidzein. The soy extract induced [cell cycle](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000597111&Filter=set:QC+GlossaryTermName+with+Concept+Set) arrest and [apoptosis](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046524&Filter=set:QC+GlossaryTermName+with+Concept+Set) in prostate cancer cells to a greater degree than did treatment with the individual isoflavones. Genistein and daidzein activated apoptosis in noncancerous [benign prostatic hyperplasia](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046509&Filter=set:QC+GlossaryTermName+with+Concept+Set) (BPH) cells, but the soy extract had no effect on those cells. These findings suggested that products containing a combination of active [compounds](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000422394&Filter=set:QC+GlossaryTermName+with+Concept+Set) (e.g., *whole foods*) may be more effective in preventing cancer than individual compounds.[[13](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_13)] Similarly, in another study, prostate cancer cells were treated with genistein, [biochanin A](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044148&Filter=set:QC+GlossaryTermName+with+Concept+Set), quercetin, doublets of those compounds (e.g., genistein + quercetin), or with all three compounds. All of the treatments resulted in decreased cell proliferation, but the greatest reductions occurred using the combination of genistein, biochanin A, and quercetin. The triple combination treatment induced more apoptosis in prostate cancer cells than did individual or doublet compound treatments. These results indicate that combining phytoestrogens may increase the effectiveness of the individual compounds.[[14](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_14)]

At least one study has examined the combined effect of soy isoflavones and [curcumin](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046049&Filter=set:QC+GlossaryTermName+with+Concept+Set). Human prostate cancer cells were treated with isoflavones, curcumin, or a combination of the two. Curcumin and isoflavones in combination were more effective in lowering PSA levels and expression of the [androgen](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045592&Filter=set:QC+GlossaryTermName+with+Concept+Set) receptor than were curcumin or the isoflavones individually.[[15](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_15)]

**Animal studies**

[Animal models](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000043996&Filter=set:QC+GlossaryTermName+with+Concept+Set) of prostate cancer have been used in studies investigating the effects of soy and isoflavones on the disease. Wild-type and [transgenic](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000691466&Filter=set:QC+GlossaryTermName+with+Concept+Set) [adenocarcinoma](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046216&Filter=set:QC+GlossaryTermName+with+Concept+Set) of the mouse prostate (TRAMP) mice were fed control diets or diets containing genistein (250 mg genistein/kg chow). The TRAMP mice fed with genistein exhibited reduced cell proliferation in the prostate compared with TRAMP mice fed a control diet. The genistein-supplemented diet also reduced levels of ERK-1 and ERK-2 (proteins important in stimulating cell proliferation) as well as the growth factor receptors EGFR and IGF-1R in TRAMP mice, suggesting that down regulation of these proteins may be one mechanism by which genistein exerts chemopreventive effects.[[16](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_16)] In one study, following the appearance of spontaneous [prostatic intraepithelial neoplasia](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044345&Filter=set:QC+GlossaryTermName+with+Concept+Set) [lesions](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000046324&Filter=set:QC+GlossaryTermName+with+Concept+Set), TRAMP mice were fed control diets or diets supplemented with genistein (250 or 1,000 mg genistein/kg chow). Mice fed low-dose genistein exhibited more cancer cell metastasis and greater osteopontin expression than mice fed the control or the high-dose genistein diet. These results indicate that timing and dose of genistein treatment may affect prostate cancer outcomes and that genistein may exert biphasic control over prostate cancer.[[17](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_17)] In a study reported in 2008, athymic mice were implanted with human prostate cancer cells and fed a control or genistein-supplemented diet (100 or 250 mg genistein/kg chow). Mice that were fed genistein exhibited less cancer cell metastasis, but no change in primary tumor volume, than did mice fed a control diet. Furthermore, other data suggested that genistein inhibits metastasis by impairing cancer cell detachment.[[18](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_18)] In contrast, in a study reported in 2011, there were more metastases in secondary [organs](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000257523&Filter=set:QC+GlossaryTermName+with+Concept+Set) in genistein-treated mice than in vehicle-treated mice. In this latter study, mice were implanted with human prostate cancer [xenografts](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044095&Filter=set:QC+GlossaryTermName+with+Concept+Set) and treated daily with genistein dissolved in peanut oil (80 mg genistein/kg body weight/day or 400 mg genistein/kg body weight/d) or peanut oil vehicle by gavage. In addition, there was a reduction in tumor cell apoptosis in the genistein-treated mice compared with the vehicle-treated mice. These findings suggest that genistein may stimulate metastasis in an animal model of [advanced](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000478743&Filter=set:QC+GlossaryTermName+with+Concept+Set) prostate cancer.[[19](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_19)]

[Radiation therapy](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044971&Filter=set:QC+GlossaryTermName+with+Concept+Set) is commonly used in prostate cancer, but, despite this treatment, disease [recurrence](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045861&Filter=set:QC+GlossaryTermName+with+Concept+Set) is common. Therefore, combining radiation with additional therapies may provide longer-lasting results. In one study, human prostate cancer cells were treated with soy isoflavones and/or radiation. Cells that were treated with both isoflavones and radiation exhibited greater decreases in cell survival and greater expression of proapoptotic [molecules](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045065&Filter=set:QC+GlossaryTermName+with+Concept+Set) than cells treated with isoflavones or radiation only. Nude mice were implanted with prostate cancer cells and treated by gavage with genistein (21.5 mg/kg body weight/d), mixed isoflavones (50 mg/kg body weight/d; contained 43% genistein, 21% daidzein, and 2% glycitein) and/or radiation. Mixed isoflavones were more effective than genistein in inhibiting prostate tumor growth, and combining isoflavones with radiation resulted in the largest inhibition of tumor growth. In addition, mice given soy isoflavones in combination with radiation did not exhibit [lymph node](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045762&Filter=set:QC+GlossaryTermName+with+Concept+Set) metastasis, which was seen previously in other experiments combining genistein with radiation. These preclinical findings suggest that mixed isoflavones may increase the efficacy of radiation therapy for prostate cancer.[[20](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_20)]

* **Human Studies**Human studies evaluating isoflavones and soy for prevention and treatment of prostate cancer have included epidemiological studies and early phase trials. Several Phase I-II randomized clinical studies have been conducted examining the impact of isoflavones as well as soy product use to examine the bioavailability, safety as well as effectiveness on prostate cancer prevention or treatment. To date, these studies have included a wide range of subject populations including high risk men, prostate cancer patient populations (localized and later stage disease), varying doses of isoflavones, soy and soy products, limited to relatively short durations of observation/intervention and sample sizes with low statistical power. .

**Epidemiologic studies**

In 2018, a [meta-analysis](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000691484&Filter=set:QC+GlossaryTermName+with+Concept+Set) of studies that investigated soy food consumption and risk of prostate cancer was reported. The results of this meta-analysis suggested that total soy foods, intake of isoflavones (genistein, diadzein) as well as high consumption of nonfermented soy foods (e.g., tofu and soybean milk) was significantly associated to decrease in the risk of prostate cancer. Fermented soy food intake, total isoflavone intake and circulating isoflavones were ot associated with a reduced risk of prostate cancer. [21](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_21), 22,23,44 ] However, these data from population studies must be interpreted with caution as the studies relied on self reported data obtained using varying forms of dietary data collection instruments with recall bias in addition to varying forms of individual or multiple isoflavones, soy supplements and soy foods. Additioanlly,these studies failed to account for other confounding genetic or behavioral variables that may affect the risk of prostate cancer.

**Prevention studies:**

**Very few randomized, placebo controlled trials have been completed to evaluate the effect of isoflavones or soy in preventing prostate cancer progression. (Table\_\_). The studies targeted men with negative prostate biopsies with elevated serum PSA (2.5-10 mcg/ml at baseline). The duration of intervention was between 6 months[15] to 1 year[26-27], with varying formulations of isoflavones derived from soy [15,26] and red clover[27]. Although 2 of the 3 trials demonstrated a significant eduction in serum PSA, they failed to demonstrate any reduction in PCa progression [15,27]. In a single trial that showed no significant changes in serum PSA with intervention with isoflavones, demonstrated a reduction in prostate cancer progression at 1 year in a subgroup of men >65 years of age. Other than mild to moderate adverse events, no treatment-related toxicities were observed in all 3 trials.**

**Table \_\_: Randomized, placebo-controlled trials of isoflavones or soy in men with negative prostate biopsy and elevated serum PSA:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Soy/Isoflavone dose/day** | **Duration of Intervention** | **Target population (n)** | **Biomarkers of PCa risk assessed** | **Outcomes: Treatment-related change in PCa risk or Intermediate endpoint biomarkers of PCa Risk** |
| Soy isoflavones (40 mg; comprising 66% daidzein, 24% glycitin, and 10% genistin) and curcumin (100 mg) vs. placebo /day[15] | 6 months | Men with -ve Prostate biopsy and elevated PSA max 10mcg/ml (n=85) | Serum PSA | Decrease in Serum PSA (P<0.05) |
| 60 mgs isoflavone extract from red clover/day.[27] | 12 months | Men with -ve Prostate biopsy and elevated PSA max 10mcg/ml(n=20) | Serum PSA ,Prostate volume ,Steroid hormones, Liver function, Prostate symptom score, Sexual function, toxicities | Decrease in Serum PSA (P<0.05) |
| 60 mgs isoflavones/day [26] | 12 months | Men with -ve Prostate biopsy and elevated PSA max 10mcg/ml(n=158) | Serum PSA, PCa incidence,Toxicity, age-related reduction in PCa progression, equol vs.non-equol producers | Decrease in PCa incidence in men >65 years with isoflavones (P<0.05) |

**Treatment of prostate cancer**

**Isoflavones:**

**Clinical trials of isoflavones as well as soy supplements and soy products (Tables shown below) evaluated to treat localized prostate cancer prior to radical prostatectectomy have utilized a “window of opportunity” trial designs (from biopsy to prostatectomy), have primarily focused on evaluating serum and tissue biomarkers implicated in prostate carcinogenesis, bioavailability in plasma and prostate tissue as well as toxicity at various doses. Although these trials inform design of well-powered clinical trials in the future, they provide no meaningful data to inform clinical practice.**

**Table \_\_: Randomized, placebo-controlled trials of isoflavones in men with localized prostate cancer prior to prostatectomy:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Isoflavone dose/day** | **Duration of Intervention** | **Target population (n)** | **Toxicities**  **Biomarkers of PCa progression assessed** | **Outcomes: Treatment-related change in PCa progression or Intermediate endpoint biomarkers implicated in prostate carcinogenesis** |
| 30 mg genistein daily [32] | 3-6weeks | Localized PCa prior to prostatectomy. (n=54) | Serum PSA, Tumor tissue PSA, Total cholesterol, plasma genistein, thyroid ,sex hormones and toxicities. | Decrease in Serum PSA (P<0.05), Total cholesterol (P<0.01), Increase in plasma genistein (P<0.001)  Adverse events were few and mild. |
| Soy isoflavone capsules (total isoflavones, 80 mg/d /day.[33] | 6 weeks | Localized PCa prior to prostatectomy (n=86) | Serum PSA , serum-free and total testosterone, total cholesterol, 12 genes involved in cell cycle control, 9 genes involved in apoptosis. | 12 genes involved in cell cycle control and the 9 genes involved in apoptosis were down regulated in the tumor tissues of the isoflavone-treated men. |
| Isoflavones tablets (60 mg/d) [34,35] | 4-12 weeks | Localized PCa prior to prostatectomy (n=60) | Plasma isoflavones Serum-free testosterone, estradiol,SHBG and estrone, Correlation between plasma concentrations of isoflavones with changes in serum PSA with treatment , compared with the placebo arm. | Increase in plasma isoflavones (*P* <0.001) in the isoflavone-treated group vs.placebo.  Greater concentrations of plasma isoflavones daidzein (*P* = 0.02) and genistein (*P* =0 .01 were inversely correlated with changes in serum PSA. |
| Isoflavones capsules- 40, 60, or 80 mg of isoflavones or control arm [34,36] | 27-33 days | Localized PCa prior to prostatectomy (n=45) | Plasma isoflavones Serum-free testosterone, estradiol,SHBG and estrone, Tumor proliferation (Ki-67) | Increased plasma isoflavones at all doses, Increased serum total estradiol in the 40 mg (P=0.02) isoflavone-treated arm vs,placebo. Increased serum-free testosterone in the 60 mg isoflavone-treated arm (P=0.003). |
| Cholecalciferol (Vitamin D3)+200,000 IU+ genistein (G2535)600 mgs/day or placebo agents[45] | 21-28 days | Localized PCa prior to prostatectomy (n=15) | Serum and prostate tissue Vitamin D and Genistein,AR expression, TUNEL  Toxicities | Increased AR expression (p<0.05)  Increased TUNEL staining (P=0.1 in prostate tissue treated with Vitamin D+ genistein vs. placebo. |

**Soy protein or whole soy products:**

**Table \_\_: Randomized, placebo-controlled trials of soy and soy products in men with localized prostate cancer prior to prostatectomy:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Soy or soy products (dose/day)** | **Duration of Intervention** | **Target population (n)** | **Toxicities**  **Biomarkers of PCa progression assessed** | **Outcomes: Treatment-related change in PCa progression or Intermediate endpoint biomarkers implicated in prostate carcinogenesis** |
| Soy supplement with 60 mg isoflavone vs. placebo supplement [37] | 12 weeks | Localized PCa prior to prostatectomy. (n=60) | Serum PSA, steroid hormone (Free testosterone, estrone, estradiol, SHBG) and toxicities. | No significant findings  Adverse events included GI side effects. |
| Soy supplements (three 27.2 mg tablets/d; each tablet contained 10.6 mg genistein, 13.3 mg daidzein, and 3.2 mg glycitein) or a placebo [38] | 2 weeks before surgery | Localized PCa prior to prostatectomy (n=19) | Serum and prostate tissue concenteration of isoflavones | Higher isoflavone concentration (x6) in tissue than in serum following treatment with the soy supplements. |
| Soy (high phytoestrogen), soy and linseed (high phytoestrogen), or wheat (low phytoestrogen) [39] | 8 weeks- 12 weeks(?) | Localized PCa prior to prostatectomy (n=29) | Total and freePSA, testosterone, sex hormone-binding globulin, free androgen index, and dihydrotestosterone | Reduction in total PSA (P = 0.02) ;Percentage of change in free/total PSA ratio (P = 0.01); Percentage of change in free androgen index (P = 0.04) |
| Soy isoflavone supplement (providing isoflavones, 81.6 mg/d) or placebo [10] | 2 weeks before surgery (Pilot) | PCa prior to prostatectomy (n=25)  Gleason 6-9) | COX-2 mRNA levels , p21 mRNA levels in prostatectomy | Decrease in COX-2 mRNA levels (P < .01) Increases in p21 mRNA levels (P < .01) in prostatectomy specimens obtained from the soy-supplemented group compared to placebo group. |

**Isoflavones and soy products in biochemical recurrence post treatment for Prostate cancer:**

Other studies have examined the role of isoflavones and soy products in prostate cancer patients with biochemical recurrence post treatment for prostate cancer. However, as shown in the table below, these early phase studies have not demonstrated any significant changes in serum PSA or PSA doubling time [28,29,31,46,47] with one study suggesting modulation of systemic soluble and cellular biomarkers consistent with limiting inflammation and suppression od MDSCs [47].

**Table \_\_:Clinical trials of soy and soy products in men with biochemical recurrence post treatment for prostate cancer:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Isoflavones/ Soy or soy products (dose/day)** | **Duration of Intervention** | **Target population (n)** | **Toxicities**  **Biomarkers of PCa progression assessed** | **Outcomes: Treatment-related change in PCa progression or intermediate endpoint biomarkers implicated in prostate carcinogenesis** |
| Soy beverage daily (providing approximately 65-90 mg isoflavones)[28] (Non-radomized) | 6 months | Rising PSA s/p radiation for PCa dx (n=34) | PSA, PSA doubling time and toxicities. | No statistically significant findings  Adverse events included minor GI side effects. |
| Soy milk three times a day (isoflavones, 141 mg/d) (open-label study) [29] | 12 months | Rising PSA s/p treatment for PCa (n=20) | Serum PSA | No statistically significant findings |
| Supplement containing 450 mg genistein, 300 mg daidzein, and other isoflavones/day vs. placebo followed by open label [31] | 6 months iintervention followed by 6 months open label. | Active surveillance (n=59) | PSA, serum isoflavones | Significant increased in serum genistein and daidzein.  No other significant findings. |
| Beverage Powder containing soy protein isolate(20 grams protein) or Calcium Caseinate [46] | 2 years | Biochemical recurrence s/p radical prostatectomy (n=177) | PSA | No significant findings. |
| 2 slices Soy bread containing 34 mgs isoflavones/slice or 68 mgs/day) or soybreast containing almond powder.[47] | 56 days | Biochemical recurrence s/p radical prostatectomy (n=32) | Cytokines, chemokines | Reduced TH1 (P = 0.028) and myeloid-derived suppressor cell (MDSC)-associated cytokines (P = 0.035). Increased CD56(+) natural killer (NK) cells (P = 0.038). Decreased percentage of cells with a T regulatory cell phenotype (CD4(+)CD25(+)FoxP3(+)) (P = 0.0136). Decreased monocytic (CD33(+)HLADR(neg)CD14(+)) MDSC (P = 0.0056). |

**Management of** [Androgen deprivation](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000559086&Filter=set:QC+GlossaryTermName+with+Concept+Set" \t "_blank)  **therapy side-effects**

[Androgen deprivation](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000559086&Filter=set:QC+GlossaryTermName+with+Concept+Set) therapy is commonly used for [locally advanced](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045955&Filter=set:QC+GlossaryTermName+with+Concept+Set) and metastatic prostate cancer. However, this treatment is associated with a number of adverse side effects including sexual dysfunction, decreased [quality of life](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000045417&Filter=set:QC+GlossaryTermName+with+Concept+Set), and changes in [cognition](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000476290&Filter=set:QC+GlossaryTermName+with+Concept+Set). Two studies have examined men undergoing androgen deprivation therapy who were randomly assigned to receive a placebo or an isoflavone supplement (soy protein powder mixed with beverages; isoflavones, 160 mg/d) for 12 weeks. Neither study found an improvement in side effects following isoflavone treatment, compared with placebo.[[41](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_41), [42](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_42)]

In a study of men undergoing androgen deprivation therapy, participants were randomly assigned to receive high-dose isoflavone supplements (providing total isoflavones, 160 mg/d and containing 64 mg genistein, 63 mg daidzein, and 34 mg glycitein) or a placebo for 12 weeks. The results showed no difference between the two groups in PSA levels or in levels of [metabolic](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044056&Filter=set:QC+GlossaryTermName+with+Concept+Set) and [inflammatory](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000373080&Filter=set:QC+GlossaryTermName+with+Concept+Set) parameters (e.g., [glucose](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044033&Filter=set:QC+GlossaryTermName+with+Concept+Set), [interleukin-6](https://cdr.cancer.gov/cgi-bin/cdr/Filter.py?DocId=CDR0000044045&Filter=set:QC+GlossaryTermName+with+Concept+Set)).[[43](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_43)]

**Adverse Effects**

Overall, isoflavones,soy and soy products were well tolerated in clinical trials of high risk and prostate cancer patients.[[24](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_24), [27](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_27), [29](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_29), [31](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_31), [38](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_38), [41](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_41)] The most commonly reported side effects were gastrointestinal symptoms.[[28](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_28), [30](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_30), [31](https://cdr.cancer.gov/cgi-bin/cdr/QCforWord.py?DocId=CDR0000719335&DocType=Summary:bu&DocVersion=None&parmstring=yes&parmid=121443#CL_163_31)]

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