

SoyConnection

Health & Nutrition News About Soy

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**FACTS
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MYTHS**

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In This Issue

- Soy Myths and Misconceptions
- Polyunsaturated Fat Favorably Affects Glycemic Control
- Soy Turkey Chili and Layered Tofu Salad with Warm Soy Sauce Dressing Recipes



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SOLID RESEARCH COUNTERS COMMON MYTHS ABOUT SOY

Editor's Note: There continues to be confusion among consumers about the health attributes of soyfoods. To this point, a recent survey found that whereas the vast majority of health professionals view soyfoods very positively, little more than half of the public agrees. Four specific concerns about soyfood use are addressed below. They are misconceptions about male feminization, soy and breast cancer, thyroid function and fertility. First, the overall conclusion or take-away is presented on each topic, and then the evidence underlying the concern is discussed, followed by a summary of the evidence refuting the concern.

By Mark Messina, PhD

Background

The health effects of soyfood consumption have been rigorously investigated over the past 25 years. Much of this research is aimed at understanding the effects of soyfoods and soybean components, such as isoflavones, on chronic disease risk. Proposed benefits of soyfoods include protection against coronary heart disease (CHD),¹ breast² and prostate³ cancer, osteoporosis⁴ and alleviation of menopausal symptoms.⁵ However, soyfoods are not without controversy. There are concerns, based mostly on in vitro and animal studies, that soyfoods may exert untoward effects in some individuals; primarily because they contain isoflavones.

However, animal studies have limited value for predicting clinically-relevant effects because of the many physiological and anatomical differences between rodents and humans.⁶ In the case of soy, there is an additional caveat; most animals, including rodents and non-human primates, metabolize isoflavones very differently than humans.⁷⁻¹³ Furthermore, and more importantly, in contrast to animal data, the clinical and epidemiologic research overwhelmingly supports the safety and potential benefit of soyfood consumption.

Much of the interest in soyfoods is because they are uniquely-rich sources of isoflavones. Isoflavones are classified as phytoestrogens but they are also, and arguably more accurately classified as selective estrogen receptor modulators (SERMs).¹⁴ SERMs have estrogen agonistic effects in some tissues, estrogen antagonist effects in other tissues, and in some cases may not affect tissues responsive to the hormone estrogen. The ability of isoflavones to function as SERMs is almost certainly due in part to their preference for binding to and activating estrogen receptor (ER)-beta in comparison to ER-alpha.¹⁴ In contrast, estrogen binds to and activates these two receptors with equal affinity. When activated, ER-beta can have different and sometimes opposite physiological effects in comparison to the activation of ER-alpha and is generally viewed as possessing tumor-suppressing actions.¹⁵ Isoflavones may also exert effects independent of their interaction with estrogen receptors.¹⁶ Therefore, it is not appropriate to equate isoflavones with estrogen or soyfoods with isoflavones since the soybean, like all foods, is a collection of multiple biologically active molecules.¹⁷

Male feminization

Takeaway

Clinical studies show neither soyfoods nor isoflavones affect testosterone levels or sperm or semen parameters or otherwise exert feminizing effects. In addition, soy protein enhances lean tissue accretion and strength in response to resistance exercise.¹⁸⁻²⁰

Evidence underlying concern

Conceptually, concerns about feminization are based on the estrogen-like effects of isoflavones. Experimentally, some rodent work has shown that high-dose isoflavones, especially when exposure occurs very early in life, lower testosterone levels²¹⁻²⁴ and possibly adversely affect spermatogenesis.^{25,26} In addition, there are two case reports describing a single individual who experienced feminizing effects (e.g., gynecomastia, loss of libido, lower testosterone and raised estrogen levels) that allegedly occurred as a result of soyfood consumption.^{27,28} A small cross-sectional study found soy intake was inversely related to sperm concentration (but not total sperm count) in the male partners of subfertile couples attending a fertility clinic.²⁹

Data refuting concern

Problems described in the two referenced case reports occurred because soy intake was excessive and in the context of unbalanced and nutrient-deficient diets.^{27,28} Both men consumed 360 mg isoflavones per day, which is approximately nine-fold greater³⁰ than the mean isoflavone intake among older Japanese men. One of the men consumed 12 cups of soymilk per day for as long as six months,²⁷ and the other perhaps as many as 20 servings of soyfoods daily for one year.²⁸

In contrast to the drop in testosterone levels reported in some rodent studies, a meta-analysis that included 15 placebo-controlled treatment groups with baseline and ending measures and an additional 32 reports involving 36 treatment groups found no effects of soy protein or isoflavone intake on testosterone, sex hormone binding globulin, free testosterone or the free androgen index.³¹ Studies published subsequent to this analysis are consistent with these findings^{32,33} including one study involving men with subclinical hypogonadism.³⁴ In addition, no effects on estrogen levels in men have been noted in numerous clinical studies ranging in duration from six weeks to six months, despite isoflavone exposure as high as 150 mg/day isoflavones.³⁵

In contrast to the aforementioned cross-sectional study which found an inverse association between soy intake and sperm concentration,²⁹ all three clinical studies found that isoflavones do not affect sperm or semen parameters.³⁶⁻³⁸ In addition, the research group responsible for the cross-sectional study subsequently found in another cross-sectional study involving 184 men from couples undergoing in vitro fertilization that the male partner's intake of soyfoods and soy isoflavones was unrelated to fertilization rates.³⁹

Finally, soy protein has been shown to increase strength and lean tissue in response to resistance exercise as well as beef¹⁹ and even whey protein in some studies¹⁸ and has recently been shown to be efficacious at stimulating muscle protein synthesis when part of a mix that included milk proteins.⁴⁰

Soy and breast cancer patients

Takeaway

Clinical studies investigating the effects on markers of breast cancer risk, and epidemiologic studies evaluating recurrence and mortality, show that soyfoods can be safely consumed by women with breast cancer. This conclusion is consistent with the positions of the American Cancer Society⁴¹ and the American Institute for Cancer Research.⁴² In addition, the European Food Safety Authority concluded that isoflavone supplements do not adversely affect the breast tissue of postmenopausal women.⁴³ The World Cancer Research Fund International concluded there is a possible link between soy intake and improved *survival* from breast cancer.⁴⁵

Evidence underlying concern

The estrogen-like effects of isoflavones provide a theoretical basis for concern that soyfoods may adversely affect the prognosis of breast cancer patients. Experimentally, in ovariectomized athymic mice implanted with MCF-7 cells, an estrogen-sensitive human breast cancer cell line, isoflavones stimulate the growth of existing mammary tumors^{46,47} and inhibit the efficacy of cancer drugs.^{48,49} Limited work has found that in early stage breast cancer patients short-term isoflavone exposure increased the expression of genes that promote cell proliferation.⁵⁰

Evidence refuting concern

Not only are isoflavones different from estrogen but the evidence that

estrogen therapy increases breast cancer risk is unimpressive. In fact, in the Women's Health Initiative trial, which involved over 10,000 women, estrogen therapy statistically significantly reduced risk of developing invasive breast cancer.⁵¹ It is the combination of estrogen plus progestin that appears to increase breast cancer risk (soy has no progestin activity), not estrogen therapy itself.⁵²

Although one particular rodent model does show isoflavones, and in particular genistein (the primary soybean isoflavone), stimulate the growth of existing mammary tumors,⁵³ just slightly tweaking this model in a more physiologic direction causes a complete loss of the tumor-stimulatory effect.⁵⁴ More importantly, clinical studies show that in adults, neither soy protein nor isoflavone supplements affect markers of breast cancer risk including mammographic density^{55,56} and breast cell proliferation.^{50,57-61} Furthermore, cell proliferation is not increased even when the expression of genes associated with proliferation is increased.^{50,57} It is notable that in contrast to the lack of effects of isoflavones, combined hormone therapy, which increases breast cancer risk, increases in vivo breast cell proliferation four- to ten-fold.⁶²⁻⁶⁴

Finally, a meta-analysis of five prospective studies, two from the United States^{65,66} and three from China,⁶⁷⁻⁶⁹ involving over 11,000 women with breast cancer, found that post-diagnosis soy intake is associated with statistically significant reductions in breast cancer recurrence (hazard ratio, 0.85; 95% confidence interval: 0.77, 0.93) and mortality (hazard ratio, 0.79; 95% confidence interval: 0.72, 0.87).⁷⁰ Importantly, soy consumption was similarly beneficial in Asian and non-Asian women.⁷¹ Furthermore, in contrast to the results in ovariectomized athymic mice showing genistein negates the inhibitory effect of tamoxifen^{48,72} and an aromatase inhibitor⁴⁹ on mammary tumor growth, the prospective epidemiologic data suggest that soyfood intake may actually enhance the efficacy of these treatments.^{68,71}

Thyroid function

Takeaway

Clinical studies show neither soyfoods nor isoflavone supplements adversely affect thyroid function in healthy individuals with a normal functioning thyroid even when exposure occurs over several years and greatly exceeds typical Japanese intake. After a multi-year evalu-

Continued on pg. 4

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ation the European Food Safety Authority concluded that isoflavones do not adversely affect thyroid function in postmenopausal women.⁴³ Also, soyfoods are not contraindicated for hypothyroid patients.

Evidence underlying concern

Concerns about the anti-thyroid effects of soy are based primarily on in vitro research (genistein inhibits the activity of thyroid peroxidase, an enzyme involved in thyroid hormone synthesis)^{73,74} and studies in rodents administered isolated isoflavones.^{75,76} In addition, in the 1960s, several cases of goiter were identified in infants fed soy infant formula.^{77,78} Also, a few studies have found thyroid stimulating hormone levels were increased in response to soy, or isoflavone, exposure^{34,79} and one study reported that isoflavones exacerbated thyroid function in subclinical hypothyroid patients.⁸⁰ Finally, soy protein is thought to reduce the absorption of thyroid medication such as levothyroxine.⁸¹⁻⁸⁴

Evidence refuting concern

The totality of the evidence indicates that in generally healthy people with normal functioning thyroids, neither soy nor isoflavones adversely affect thyroid function.⁸⁵ No effect has been observed even in studies as long as three years in duration as well as when isoflavone intake exceeds typical Japanese intake two to three fold.^{86,87} Although in rodents, which as a species are especially sensitive to thyroid insults,⁸⁸ thyroid peroxidase activity is inhibited by isoflavones, thyroid function remains normal.⁷⁵

No cases of goiter specifically attributed to soy infant formula use have been reported in the literature since the late 1960s when the formula first began to be fortified with iodine and the source of protein was switched from soy protein isolate to soy protein concentrate. Concerns that isoflavones may impair thyroid function in those individuals whose iodine intake is marginal are not supported by the human data.⁸⁹

Although in a few studies thyroid stimulating hormone levels were elevated in response to soy/isoflavone exposure, in all cases levels remained well within the normal range.^{34,79} In one small study isoflavone exposure increased the likelihood of progressing from subclinical to overt hypothyroidism; however, in all patients enrolled there were robust decreases in blood pressure, insulin resistance and inflammation.⁸⁰ No conclusions about the possible harm or benefit of isoflavones in subclinical hypothyroid patients can be made at this time given the limited data.

Finally, soy protein is not unique in reducing the absorption of levothyroxine.⁸¹⁻⁸⁴ Food in general has this effect, as do fiber and calcium supplements, as well as many herbs and drugs.⁹⁰⁻⁹⁸ Soy protein is not contraindicated for hypothyroid patients as the consumption of soyfoods simply needs to be temporally separated from the ingestion of the medication (directions call for the medication to be taken on an empty stomach) or alternatively, the dose can be adjusted if necessary.⁹⁹

Fertility

Takeaway

Clinical studies show soy does not prevent ovulation or appreciably affect reproductive hormones in premenopausal women. Epidemiologic data suggest soy intake may negate the harmful effects of BPA on live birth rates in women undergoing assisted reproductive technology. In men, clinical studies show neither soy nor isoflavones affect sperm or semen parameters and epidemiologic data show male soy intake doesn't affect in vitro fertilization rates in their partners.

Evidence underlying concern

In the 1940s, breeding problems in Australian sheep grazing on a type of red clover high in isoflavones were reported and in the 1980s similar problems were noted in the captive cheetah fed a soy-containing diet.¹⁰⁰⁻¹⁰³ In male and female rodents, a few studies have found reproductive abilities are compromised by isoflavone exposure.¹⁰⁴⁻¹⁰⁶ In women, soyfoods appear to increase the length of the menstrual cycle¹⁰⁷ and in a small cross-sectional study soy intake was associated with a decrease in sperm concentration.²⁹

Evidence refuting concern

Reproductive problems noted in the sheep and captive cheetah were shown to result from excessive intake in the case of the sheep¹⁰⁸ and in the cheetah because of their limited ability to conjugate phenolic compounds such as isoflavones.¹⁰⁹⁻¹¹² In women, although soyfoods do appear to increase the length of the menstrual cycle by approximately one day, which may actually decrease breast cancer risk,¹¹³ ovulation is not prevented, but simply delayed.¹⁰⁷ Also, in premenopausal women, a meta-analysis of the clinical data found that neither soy nor isoflavone consumption affected estradiol, estrone or sex hormone binding globulin concentrations. In addition, the modest reductions (~20%) in the levels of follicle stimulating hormone and luteinizing hormone were not statistically significant when only studies at low risk of bias were considered.¹⁰⁷

In contrast to the concerns expressed, there are data suggesting soy may actually aid fertility. For example, a prospective study found that among 315 women who collectively underwent 520 assisted reproductive technology cycles soy isoflavone intake was positively related to live birth rates.¹¹⁴ Similarly, among women undergoing in vitro fertilization, soy consumption appeared to negate the adverse reproductive effects of the endocrine disruptor BPA.¹¹⁵

In men, although a small pilot cross-sectional study found that very modest soy consumption was associated with lower sperm concentration (sperm count was not decreased) there were many weaknesses to this study.²⁹ In fact, much of the decreased sperm concentration occurred because there was an increase in ejaculate volume in men consuming higher amounts of soy, a finding which seems biologically implausible. Furthermore, the research group responsible for this work subsequently found in a cross-sectional study involving 184 men from couples undergoing in vitro fertilization that male partner's intake of soyfoods and soy isoflavones was unrelated to fertilization rates.³⁹

Finally, and most importantly, all three of the clinical studies conducted show that isoflavones have no effect on sperm concentration or quality.³⁶⁻³⁸ In fact, a case report indicated that daily isoflavone supplementation for six months in the male partner of an infertile couple with initially low sperm count led to normalization of sperm quality and quantity.¹¹⁶

Overall conclusion

Health concerns about the consumption of soyfoods are based almost exclusively on in vitro and animal studies. In contrast, the overwhelming amount of evidence from clinical and epidemiologic studies refutes these concerns and directly supports the safety and potential benefits of soy consumption. The human data show that with few exceptions, such as those who are allergic to soy protein, soyfoods can make an important contribution to an overall healthful diet. 🍲

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Continued on pg. 6

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POLYUNSATURATED FAT FAVORABLY AFFECTS GLYCEMIC CONTROL

The health impacts of dietary fat and carbohydrate are hotly debated topics. Although health authorities are continuing to recommend that saturated fat (SFA) intake be reduced from current levels there has been recent controversy about the relationship between SFA and coronary heart disease (CHD) risk.

This controversy exists in part because it is now recognized that the macronutrient that replaces saturated fat greatly influences CHD risk. For example, when polyunsaturated fat (PUFA) replaced SFA, an analysis of over 130,000 men and women who were followed for as long as 32 years found that CHD risk was reduced by 25%. However, when refined carbohydrate and sugars replaced saturated fat, risk was not reduced.¹ Unfortunately, in their attempt to decrease SFA intake, many Americans increased their intake of refined carbohydrate.

The coronary benefit of PUFA replacing SFA in the diet is largely attributed to the reduction in LDL-cholesterol that results. However, new research suggests that the benefit of PUFA is not limited to this one metric as a recently published meta-analysis found pronounced benefits of PUFA on glycemic control.²

The analysis in question involved 102 controlled trials, including 239 diet arms and 4,220 adults. Using multiple-treatment meta-regression, Imamura et al.² estimated the dose-response effects of isocaloric replacements between SFA, monounsaturated fat (MUFA), PUFA and carbohydrate, adjusted for protein, trans fat, and dietary fiber.

The key findings from this analysis are highlighted below:

- Replacing 5% energy from carbohydrate with SFA had no significant effect on fasting blood glucose, but lowered fasting insulin.
- Replacing carbohydrate with MUFA lowered glycosylated hemoglobin and insulin resistance.
- Replacing carbohydrate with PUFA significantly lowered glycosylated hemoglobin and fasting insulin.
- Replacing SFA with PUFA significantly lowered glucose, glycosylated hemoglobin, C-peptide and insulin resistance.
- PUFA significantly improved insulin secretion capacity whether replacing carbohydrate, SFA or MUFA.

Not surprisingly, given the above findings, Imamura et al.² concluded that their meta-analysis “provides evidence that dietary macronutrients have diverse effects on glucose-insulin homeostasis. In comparison to carbohydrate, SFA, or MUFA, most consistent favorable effects were seen with PUFA, which was linked to improved glycaemia, insulin resistance, and insulin secretion capacity.” 🍌

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SOY TURKEY CHILI

Makes 24 servings

Ingredients

- 3 cups boiling water
- 2 cups texturized soy protein (TSP)
- 2 pounds ground turkey breast
- 3 cups onions, chopped
- 3 cups green peppers, chopped
- 1 tablespoon garlic, minced
- 1 tablespoon soybean oil (vegetable oil)
- 10 ounces canned diced tomatoes, including liquid
- 1½ quart canned tomato sauce
- 4 ounces canned green chilies, diced (½ cup)
- ⅓ cup chili powder or to taste
- 2 teaspoons salt
- 1 tablespoon jalapeno peppers, minced
- 3 quarts water



Instructions

1. In a large bowl, pour boiling water over soy protein.
2. In a 14-quart pot, sauté turkey, onions, peppers and garlic in oil over medium high heat until turkey is no longer pink.
3. Add rehydrated soy protein and remaining ingredients. Bring to a boil; reduce heat and simmer uncovered for 45 minutes.
4. Serve with assorted condiments such as shredded low fat cheddar cheese, yogurt, sour cream or minced onion.

Nutrition Per Serving: 97 calories, 16.0 gm protein, 7.5 gm carbohydrates, 1.3 mg fat, 27 mg cholesterol, 144 gm sodium, 3.1 gm dietary fiber

LAYERED TOFU SALAD WITH WARM SOY SAUCE DRESSING

Makes 12 servings

Salad

- 2 large heads iceberg lettuce, shredded
- 3 medium red onions, thinly sliced
- 3 quarts bean sprouts
- 9 medium tomatoes, cut into ½ inch cubes
- 3 pounds Silken tofu, cut into ½ inch cubes
- 1½ pound canned red salmon or light tuna
- 3 cups watercress (3 ounces), cut into 1-inch pieces (optional)



Dressing

- ¾ teaspoons bottled hot pepper sauce
- 1 cup soy sauce
- 1½ cup soybean oil (vegetable oil)
- 1½ cup green onions, minced
- 9 cloves garlic, mashed
- 1½ teaspoon sugar

Instructions

1. **For buffets**, layer salad ingredients in order of listing in a large shallow bowl or serving platter. Just before serving, heat ingredients for Warm Soy Sauce Dressing. Toss salad and serve.
2. **For a sit-down meal**, toss salad and serve about 2 cups per serving. Garnish with choice of cherry tomatoes, sliced red onions, sweet red or yellow peppers, sugar pea pods or sliced cucumbers.

Nutrition Per Serving (about 2 cups): 395.2 calories, 29.2 gm protein, 26.6 gm carbohydrates, 21.1 gm fat, 24.9 mg cholesterol, 1.0 gm saturated fat, 1787 mg sodium, 6.2 gm dietary fiber.



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