

Position Paper on Soy

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EXECUTIVE SUMMARY

PUTTING THE SOY DEBATE IN PERSPECTIVE

Journalists and scientists have raised questions regarding the health benefits of soy and its components. Some select individuals and/or organizations even go as far as alluding to soy having a “dark side.”

As soy research experts will admit, it is difficult to reach a solid consensus on an area of research that continues to grow in sheer quantity. More difficult is the fact that studies are often conducted using a wide variety of soy products and varying protocols. As a result, much confusion is generated on the health effects of soy.

Many negative articles surrounding soy only focus on one particular study without conducting a balanced review of the extensive soy research. In contrast to these articles, a thorough evaluation of existing soy research will reveal many positive findings regarding the health benefits of soy. Some soy controversies have arisen from research protocols and approaches that are now viewed as outdated with results that are no longer relevant. Moreover, due to the lack of specificity in labeling terms such as “soy” or “soy protein,” it is often unclear what soy food or component is being examined in any particular study.

It is important to consider these points when reviewing any study on soy and health. Certainly, a preponderance of evidence supports the benefits of soy foods—particular soy protein and soy isoflavones—for the overall promotion of good health.

KEY POINTS

- √ Metagenics supports the inclusion of soy foods in the diet due to their reported safety and efficacy.
- √ It is well known that soy has a history of safe use, as demonstrated by its long history of consumption by Asian populations.
- √ Opinion leaders such as the U.S. Food and Drug Administration (FDA) support the inclusion of soy in the diet. After a yearlong scientific review, the FDA granted a health claim regarding soy protein and its potential to reduce the risk of heart disease.
- √ Substantial epidemiological and experimental data suggest that soy consumption may positively affect many aspects of health, including cardiovascular health, cancer risk reduction, menopausal symptom relief, and osteoporosis prevention.

THE BENEFITS OF SOY

IS SOY SAFE?

Historically, soy foods have been an integral part of the Asian diet. Therefore, Asian populations have consumed soy and its components in substantial quantities over long periods of time. Cumulative data gathered from epidemiological studies over the past several decades have not demonstrated that dietary soy consumption poses any substantial risk to human health overall. On the contrary, it has been shown that soy foods can provide protective effects against a number of chronic diseases.

ARE THERE CONFLICTING DATA ON SOY?

With the level of growth seen in the soy research field, it remains a challenge for scientists to come to a solid consensus on aspects of soy as they relate to human health. In addition, many different types of studies are performed using a variety of soy products. Conclusions from only one or a few studies on specific soy preparations cannot be simply generalized about the consumption of soy on the whole. As a result, much confusion is generated regarding the health effects of soy.

Much of the published soy research to date consists of epidemiological studies in which the relationship between soy intake and health outcomes in Asian populations is examined. These studies are based primarily on the intake of traditional soy foods derived from soybeans, such as tofu or soymilk or as soy protein added to foods. For the most part, the public health community and opinion leaders such as the U.S. Food and Drug Administration (FDA) and American Heart Association (AHA) agree that these soy foods are healthy additions to the diet.¹

Controversy around soy appears to relate primarily to the difference between observed health outcomes from these epidemiological studies on soy food intake and the data obtained using specific isolated and concentrated fractions of soy.² In contrast to epidemiological studies that look at soy food consumption, research data from animal or human intervention studies use fractions of soy (e.g., soy concentrates or isolates, isolated isoflavone mixtures, pure genistein). By not fully specifying what has been used in epidemiological studies, it is often difficult to understand what researchers mean when they use terms such as “soy” or “soy protein.”³ It is known that these different forms of soy products can produce varying results. Additionally, differences in soy components also arise from the variety of soybean used, specific processing techniques, and/or growing and storage conditions.³

HOW MUCH SOY ARE WE EATING?

Various ranges of soy intake have been proposed. While Asian populations consume an average of 10 to 50 grams of soy per day, Americans generally consume only 1 to 3 grams daily.⁴ Although soy has been used extensively in Asian cultures for many centuries, soy foods continue to remain a niche market in the United States.¹ Despite the fact that soy product consumption has generally increased, a recent article from the

United Soybean Board confirmed that most Americans report no or only a modest intake of soy products. In fact, one-quarter of Americans reported consuming soy foods once a week or more, while 38% of respondents admitted to never consuming soy products.⁵

WHAT ARE THE DIFFERENT SOY-BASED PRODUCTS?

Soybeans can be processed to yield a number of soy foods, including:⁶

Fermented soy products (e.g., tempeh and soy sauce)	Produced by inoculating the soybeans with various species of bacteria, fungi, and/or molds
Soy milk	Made by soaking, grinding, and straining the soybeans
Tofu	Soy milk that is boiled to coagulate the proteins and then pressed to remove the water
Soy oil	The extracted oil of the soybean refined for human consumption
Soy lecithin	The phospholipid component of the crude oil removed during the degumming process
Soy meal	Obtained by grinding the cake or chips that remain after removing most of the oil from the soybeans
Soy flour	Prepared by removing the water-soluble, non-protein constituents of the defatted flakes or flours to a concentrate of 70% soy protein
Soy protein concentrates	Prepared by removing the water-soluble, non-protein constituents of the defatted flakes or flours to a concentrate of 70% soy protein
Soy protein isolates	The purest form of soy protein—prepared from defatted, dehulled soybean flakes to an isolate of 90 to 95% protein

WHAT IS THE NUTRITIONAL VALUE OF SOY?

MACRONUTRIENT COMPOSITION

The soybean seed is 13% to 25% oil, 30% to 50% protein, and 14% to 24% carbohydrate that includes 2% to 5% fiber. The ratio of polyunsaturated to saturated fatty acids (P:S ratio) is 82:18 in soy oil. Soy oil contains 55% linoleic acid (18:2n-6), 21% oleic acid (18:1n-9), 9% palmitic acid (16:0), 6% stearic acid (18:0), and 9% other fatty acids.

THE COMPLETENESS OF SOY PROTEIN

Soy is a nutritionally *complete* protein that has an unusually well-rounded amino acid profile for a plant protein. Soy contains adequate quantities of all essential amino acids necessary for the building and maintenance of human tissues.⁷

One historical controversy in the soy literature is related to this issue of complete protein. The old method of evaluating protein quality—known as the protein efficiency ratio (PER)—was based on the response of growing rats to a particular protein source. Due to the different protein needs for humans as compared to rats, early studies using the PER values suggested that soy was not a complete protein source. However, after an adequate study protocol to assess a human's response to a particular protein source was developed, these early findings have been shown to be inaccurate. In fact, according to the newer method for protein quality determination—known as the Protein Digestibility Corrected Amino Acid Score (PDCAAS), which has been adopted by both the FDA and World Health Organization (WHO)—soy has the same score as egg white and milk protein.⁸⁻¹⁰ In general, soy is considered to be equivalent to animal protein.

Soy protein isolates and concentrates are high quality complete proteins that are well tolerated in comparison to animal protein sources (e.g., casein). In fact, soy protein can serve as the sole source of protein intake for both adults and children.¹¹ While protein accounts for 20% to 30% of the weight for most legumes, it accounts for roughly 35% to 38% of the weight for soybeans.¹² The amount of protein varies among different soy products: soy flour is comprised of 50% protein, soy concentrate is comprised of 70% protein, and soy isolate is comprised of 90% protein.

ISOFLAVONES

Isoflavones are plant-derived substances that have a chemical structure similar to that of estrogen. Due to this unique structure, isoflavones have weak estrogen-like effects in various tissues, such as reproductive, cardiovascular, and skeletal tissues.^{13,14} There has been concern regarding the estrogenic effects of soy isoflavones; however, it has been estimated that isoflavones are 1/400th to 1/1000th the potency of synthetic estrogen.¹⁵

The primary isoflavones in soy, **genistein** and **daidzein**, are thought to be responsible for many of the protective effects of soy. A recent review of published literature reveals that a majority of the interest in soy is due to its isoflavone content. Isoflavones are either connected to a glucose molecule, and are known as glycone (genistin and daidzin), or have this sugar molecule removed, and are known as aglycone (genistein and daidzein). In a number of individuals, a large portion of genistein and daidzein is further metabolized to p-ethyl phenol, and equol or O-demethyl-angolensin (O-Dma), respectively. Emerging data suggests that intestinal microflora affects isoflavone absorption and metabolism.² This factor may contribute to the explanation of different isoflavone levels among individuals even when soy intake is apparently similar. Both the isoflavone precursors and metabolites have estrogenic activity and may act via genomic (which involves binding to the nuclear estrogen receptor) and nongenomic (e.g., antioxidant activity, altered protein activity) mechanisms.¹³

On average, a typical serving of a first generation soy food such as tofu or soymilk contains around 35 to 40 mg of isoflavones.

DOES SOY PREVENT MINERAL ABSORPTION?

Soy products provide a good balance of nutrients, including minerals. The bioavailability

of minerals such as zinc and iron from soy is influenced by the form of the soy product, and depends on whether fiber and/or phytic acid is present. Generally found in high-fiber foods, **phytic acid** (inositol hexaphosphate) can bind minerals in the gastrointestinal tract, thereby decreasing their absorption during digestion. The relatively high level of minerals in soy partially overcomes this effect. However, when soy products provide a significant amount of calories in the diet, removal of phytic acid to increase mineral bioavailability and/or supplementation with minerals can be employed to increase the nutritive value of soy products.

WHAT ARE PROTEASE INHIBITORS AND ARE THEY HARMFUL?

Raw soybeans contain a family of proteins called **protease inhibitors** that can bind to trypsin and other proteolytic digestive enzymes and inhibit their action. Similar to other proteins, protease inhibitors can be destroyed by heat treatment. Cooking soybeans or processing soy partially denatures the proteins, thereby decreasing their activity. The heat processing of soy protein also increases its digestibility.⁷ Protease inhibitors are ubiquitous in food. For example, raw potato contains twice the trypsin protease inhibitor activity of raw soy flour, and raw egg contains an amount comparable to soy.

Animal studies suggest that protease inhibitors may cause pancreatic cancer. However, there is no direct evidence that a low-level intake of the inhibitors associated with soy is harmful to humans.⁷ In contrast, several studies have suggested that certain soy protease inhibitors may in fact be anti-cancer agents.¹⁶

DOES SOY HAVE A NEGATIVE IMPACT ON THYROID FUNCTION?

There have long been questions about soy ingestion and its potential effects on thyroid function, due to the presence of compounds known as **goitrogens**. Some studies suggest that soy and soy isoflavones inhibit the production of thyroid hormones.¹⁷ Well-designed human clinical studies, however, have demonstrated that soy has a minimal effect on overall thyroid function in healthy individuals.^{18,19} These studies indicate that a majority of individuals will not experience long-term negative effects on thyroid function from consistent consumption of high levels of soy. Individuals who have a history of thyroiditis and/or consume a diet marginally deficient in iodine may be more susceptible to these effects.

WHAT ROLE DOES SOY PLAY IN CARDIOVASCULAR DISEASE?

In 1999, the FDA approved a health claim for soy protein and its effect on lowering cholesterol levels (“Diets low in saturated fat and cholesterol that include 25 grams of soy protein a day may reduce the risk of heart disease”).²⁰ It is important to note that health claims of this type are only allowed when significant scientific agreement has been reached. This particular health claim was approved after an extensive, yearlong review of studies supporting the cholesterol-lowering effects of soy protein.¹

As supported by numerous controlled, human clinical trials, researchers agree that soy foods are beneficial for overall heart health. In the often-quoted meta-analysis of 38 controlled clinical trials, Anderson, et al. concluded that the consumption of soy protein rather than animal protein significantly decreased serum concentrations of total

cholesterol, low-density-lipoprotein (LDL) cholesterol, and triglycerides in hypercholesterolemic individuals.²¹ The changes in serum cholesterol and LDL cholesterol concentrations were directly related to initial serum cholesterol concentrations. In other words, soy protein consumption did not affect serum cholesterol concentrations in normolipidemic individuals but led to a decrease in total and LDL cholesterol levels in individuals with already elevated serum lipids. Although the exact mechanism of soy's cholesterol-lowering abilities is unknown, research suggests that the amino acid composition of the soy protein and the isoflavones are both important.^{22,23}

IS SOY ANTI- OR PRO-CANCER?

Soy contains various anti-cancer agents, including isoflavones, protease inhibitors, phytate, phytosterols, and saponins. Isoflavones may exert their anti-cancer activity in a number of ways. Some of the hypothesized mechanisms include the ability of isoflavones to weakly bind to estrogen receptors, which help block the harmful effects of estrogen, or inhibit certain enzymes that promote cancer cell growth.²⁴ As previously mentioned, studies have shown that certain protease inhibitors in soy prevent carcinogenesis in cell and animal models.¹⁶ Phytate is capable of binding minerals such as iron—a mineral with the potential to catalyze free radical production—and this may be one mechanism by which phytate can prevent cancer. Phytosterols, such as beta-sitosterol, have been shown to play a role in decreasing colon and prostate cancers. Lastly, studies have shown that saponins are anticarcinogenic, possibly due to their antioxidant activity and/or ability to regulate cellular proliferation.¹⁶

Epidemiological data demonstrate that the typical Asian diet is associated with a lower risk of colon and specific hormone-related (e.g., ovarian, prostate) cancers. An intake of soy foods early in life is hypothesized to be important for these protective effects.^{24,25} In recent years, soy has also become increasingly popular for its role in breast health. Overall, the research data on soy and breast cancer risk has been controversial.²⁶ The discrepancy in research as it pertains to breast cancer risk reduction is proposed by some researchers to be due to the lack of well-designed, long-term dietary intervention trials.⁴

From a mechanistic aspect, soy intake and, in particular isoflavones, may play an important role in breast health. It is well documented that a low lifetime exposure to estrogen is associated with a reduced risk of breast cancer. Soy isoflavones may shift estrogen metabolism towards the production of more beneficial metabolites, thereby aiding in breast cancer risk reduction. Two human clinical studies involving both pre- and post-menopausal women found that increased soy isoflavone consumption decreased urinary excretion of the genotoxic 16 α -OH and 4-OH estrogen metabolites and significantly increased the 2-OH:16 α -OH ratio.^{27,28}

Much of the controversy surrounding isoflavones and breast health comes from the in vitro studies with isoflavones. Isoflavones are considered to be phytoestrogens due to their estrogen-like effects, as demonstrated under specific in vitro experimental conditions. However, the biological effects of isoflavones have been shown to differ markedly from estrogen. One difference is the ability of isoflavones to preferentially bind one of the two estrogen receptors, similar to selective estrogen receptor modifiers

(SERMs), whereas estrogen binds robustly to both receptors. More research is needed to establish which tissues respond to isoflavones through these differential estrogen-receptor effects, as well as the indirect effects of isoflavones on various tissues.²

While there has been much discussion on whether women with estrogen receptor-positive tumors should avoid isolated soy components, the answer to that question has not been confirmed by research. Data are far from conclusive on this issue, and as a result, researchers are urging caution for women with active estrogen-dependent cancer. A distinction should be made between the clear benefit of soy protein for cardiovascular health and the inconclusive role of isoflavones for breast cancer risk reduction. Perhaps the comment by Daniel Sheehan, Ph.D., director of the Estrogen Knowledge Base Program at the FDA's National Center for Toxicological Research, along with his colleague, Daniel Doerge, Ph.D., stated it best: "While isoflavones may have beneficial effects at some ages or circumstances, this cannot be assumed to be true at all ages. Isoflavones are like other estrogens in that they are two-edged swords, conferring both benefits and risks."¹

DOES SOY HAVE A NEGATIVE EFFECT ON HORMONE LEVELS?

As previously mentioned, soy isoflavones have been shown to lead to the production of beneficial estrogen metabolites in women.^{27,28} Additionally, a review of several studies demonstrated that soy consumption (32 to 200 mg of isoflavones per day) has been implicated in trends toward increased menstrual cycle length and decreased blood levels of estradiol, progesterone, and sex hormone-binding globulin.¹⁹ Although isoflavones have weakly estrogenic effects, it appears that the major biological influence is on endogenous estrogen metabolism and their ability to act as SERMs.

In men, there has been concern as to whether soy consumption might lead to infertility by decreasing testosterone levels and semen quality. Kurzer reviewed four published clinical trials investigating the effects of soy isoflavone consumption in men and reported that "...there are no adverse effects of soy isoflavone consumption on sperm quality, although there may be small effects of soy consumption on sex hormone-binding globulin and steroid hormones."¹⁹ It is also worthwhile to note that based on a variety of studies, it has been suggested that soy consumption may reduce prostate cancer risk without any significant adverse effects.²⁹⁻³⁵ Further studies to evaluate the effects of soy consumption on hormone metabolism by the prostate are needed for a better understanding of this effect of soy.

WILL SOY HELP REDUCE MENOPAUSAL HOT FLASHES?

Due to the Women's Health Initiative study on the risks of hormone replacement therapy (HRT/ERT), there has been heightened interest in the use of natural supplements as an alternative therapy for menopausal symptoms.³⁶ In both placebo-controlled and randomized diet comparison trials involving perimenopausal women, consumption of soy protein containing isoflavones appeared to decrease the intensity of hot flashes and improve the perceived severity of vasomotor symptoms.³⁷ There appears to be a strong placebo effect, and data from various studies demonstrates up to a 30% reduction of vasomotor symptoms in placebo groups. However, additional reductions of 10% to 20%

over the calculated placebo effect were found in intervention studies using soy foods, soy protein isolates, and soy extracts.³⁷⁻⁴¹ The majority of studies using 40 to 80 mg of isoflavones per day have shown beneficial effects on vasomotor symptoms and relief of hot flashes following soy consumption.⁴²⁻⁴⁴

CAN SOY BUILD STRONG BONES?

Although the research in this area is still in its infancy, soy isoflavones have been found to have a positive effect on bone health. This is most likely due to the estrogen-like actions of isoflavones.⁴⁵ While the exact mechanism is unknown, the specific estrogen receptor implicated in bone health is the same as that to which the isoflavones preferentially bind. Therefore, it is proposed that isoflavones can act directly on bone cells and promote bone conservation. Furthermore, several studies suggest that isoflavones stimulate osteoblastic bone formation and inhibit osteoclastic bone breakdown.⁴⁶

Specifically, animal studies have shown that dietary isoflavones positively affect bone mineral density and bone turnover.⁴⁵⁻⁴⁷ Moreover, human clinical trials suggest that soy isoflavones lead to short-term, decreased lumbar spine bone loss in peri- and post-menopausal women.⁴⁷ Long-term studies (approximately 2 to 3 years) are needed to establish whether these effects are sustained.

IS SOY ALLERGY COMMON?

Soy is considered a frequent human food allergen, and is included on the list of food proteins that account for approximately 90% of all food allergies.⁴⁸ Based on a review of human clinical and animal model data, however, Cordle stated that soy proteins tend to be less reactive than many other food proteins. In fact, soy has been used as an alternative for infants with allergies to cow's milk with relative success.⁴⁸ A meta-analysis of 17 studies of allergy patterns of high-risk infants revealed soy allergy occurring in 3% to 4% of subjects versus 25% for cow's milk.⁴⁹ Unless highly sensitive or allergic to soy protein, most individuals can safely incorporate moderate amounts of soy into their diet.

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