

What Are The Advantages and Dangers of Soy Protein?

USANA uses soy as a major source of protein in its bars and drink mixes. A variety of factors have gone into this decision. The most important involve the fact that soy protein is nutritionally complete and high quality, and soy consumption has been linked with several long-term health benefits. In addition, soy protein is ecologically friendly. Its production has a much lower environmental impact than does the production of most animal protein foods.

This does not mean we don't appreciate the nutritional value of other proteins. Whey protein, for example, is also high quality from a nutritional perspective, and may have some advantages for those whose primary goal is to build muscle. It also has some advantages in taste and mouthfeel, although newer soy isolates are catching up in the sensory arena. We also recognize the value of rice, pea, and other protein concentrates, but note that few of these are as complete or balanced as soy and whey.

In general, though, our position is that a healthy diet includes protein from a wide variety of sources - including whole foods (legumes, whole grains, meat, dairy, and fish) as well as healthy processed foods. In this context, we believe that soy, whey, and other protein isolates and concentrates can play a role as components of healthy, well-balanced diets.

That said, we are also aware that the world of protein isolates and concentrates is filled with controversy. Much of what we see on the Internet and in certain popular magazines is strongly pro-whey and anti-soy, or strongly pro-soy or anti-whey, as if one or the other of these protein sources were "all good" or "all bad" for all people in all situations. In most instances, such stories are associated (either overtly or covertly) with food marketing campaigns. They are part of the "sticks and stones" that get thrown back and forth between the soy, whey, and meat factions who compete for your food dollars.

Is there any truth in what they are saying? Many times there is, but too often those truths are "half truths" or "facts spun out of context" with the intent of swaying purchasing behavior.

Is soy the preferred protein source for everyone? No. Clearly there are people who are sensitive or allergic to soy, and these individuals should avoid or limit their intakes of soy protein. Similarly, there are people who are allergic to dairy and who should avoid whey protein. People who are vegetarian or vegan may want to avoid whey protein because it is animal-based.

But to USANA scientists, these are not sufficient grounds for making the choice between whey and soy proteins an all-or-nothing, black-and-white proposition for the vast majority of people.

The industrial-grade bickering that has characterized much of the soy versus whey debate has left many consumers confused, concerned, and generally hungry for objective information on what they should eat. The purpose of this position paper is to summarize in an objective way our interpretation of what nutritional science has to say about several key issues that lie at the heart of arguments for and against soy protein.

1. The Nutritional Value of Soy Protein.

Several scales for assessing the nutritional value of protein have been developed over the years. These have been used to rate various proteins for their ability to support growth, supply important amino acids, and generally satisfy the human protein requirement. The first broadly accepted standard was the Protein Effectiveness Ratio (PER). Developed in 1919, this method focused on the growth-supporting characteristics of a given protein, and it used rats (rather than humans) as the test animal. Because of the metabolic differences between rodents and humans, this method has been largely discredited and is rarely used today.

A second method, the Biological Value (BV) scale, is based on the retention of protein nitrogen by the body. It is thought to be a good measure of protein utilization. The BV scale stretches from 0 to 100, with a score of 100 indicating that virtually 100% of a given protein's nitrogen is retained by the body. Some people - particularly in the sports world - use this method, but it is not widely accepted within the community of nutritional scientists.

Most nutritionists (and many in the sports sector) now consider the Protein Digestibility Corrected Amino Acid Score (PDCAAS) to be the international standard for assessing protein quality. This approach, developed by the Food and Agriculture Organization and endorsed by the U.S. Food and Drug Administration, considers the amino acid balance of a given protein as it compares with the amino acid needs of humans, with specific reference to 2-5 year old children. It also takes into account the digestibility of the protein, or how fully the protein is broken down and absorbed by the body. The PDCAAS scale stretches from 0.0 to 1.0, with a score of 1.0 indicating that the protein completely satisfies human needs from a quality perspective.

During the 1990's, whey protein became the protein of choice among bodybuilders, due in large part to an intense and successful marketing campaign sponsored by the dairy industry. That marketing promotion was based on the fact that some whey protein isolates have a rating of 100 on the BV scale. In comparison, egg-white protein (the traditional standard for bodybuilders) typically ranks in the 90's, while most fish, beef, and soy proteins rank in the 70's on the BV scale. (You will see a wide variety of BV scores for these foods because different people express the ratios in different ways, and the techniques for measuring BV are imprecise and not easily replicated from one experiment to another.)

However, when the PDCAAS approach is employed, soy protein isolates, whey protein isolates, and egg white protein all score a complete 1.00, meaning they all exhibit very high - and essentially equivalent - nutritional value in supporting human health.

The high PDCAAS score for soy protein isolates speaks to two important points. First, soy protein is well-digested and absorbed by humans. (This is the "D" of PDCAAS). Second, soy protein is complete. It contains all the essential amino acids in a proper balance for human growth, development, and health. (This is the "AA" of PDCAAS.)

Some authors have claimed that soy is lacking in the essential amino acid methionine, as if to imply that soy contains no methionine. This is incorrect. Soy may not be *rich* in methionine, but it contains enough to supply human needs under most circumstances. Furthermore, it is important to point out that human methionine requirements can be partially met by another sulfur-containing amino acid (cysteine). When cysteine + methionine content is considered, soy protein is nutritionally excellent.

2. Soy Allergies and Sensitivities.

Soy is on the Food and Agriculture Organization's list of the eight most prevalent food allergens. This list includes milk, eggs, fish, crustacea, wheat, peanuts, tree nuts, and soy. Together, these foods account for about 90% of food allergies.

That said, it is important to understand that these high-profile food allergies differ widely in their incidence, severity, and symptoms, and that soy protein - relative to milk and nut proteins, for example - is a relatively mild allergen. Consider the following:

- Milk and peanut allergies are each 5-6 times more prevalent than soy allergies. In fact, the true incidence of soy allergy - as confirmed by double blind, placebo-controlled food challenges - is quite low. Research indicates that allergic reactions to soy occur predominately in children less than four years of age, and most estimates agree that <1.0% of children (probably 0.2-0.4% of children) have true soy allergies. Moreover, 90% of children who have reactions to soy outgrow the allergy by age four. Given these statistics, it is safe to assume that <0.1% of adults (fewer than 1 in 1,000) are allergic to soy.
- Food allergen reaction thresholds, or the minimum oral dose of protein that elicits an allergic response, tend to be several orders of magnitude (more than 100-1000 times) higher for soy than for milk and peanut proteins. In other words, it takes 100-1000 times more soy protein than milk or peanut protein to initiate an allergic response in sensitive people.
- Soy allergies tend to produce mild symptoms relative to other food allergies. In a summary report of clinical food challenge studies, it was noted that in 80% of reported cases, symptoms of soy allergies were minimal to mild, with the remaining 20% being moderate. No severe allergic reactions to soy were reported. In comparison, milk and peanut allergies produced minimal-to-mild symptoms in 50-70% of cases, moderate symptoms in 20-30% of cases, and severe symptoms in 10-15% of cases.

In summary, soy proteins can produce allergic reactions in some people, but relative to milk, peanut, and the other high-profile food allergens, reactions to soy are less common, more difficult to trigger, and less severe.

Beyond true allergic reactions, some people may be sensitive to the "non-digestible" sugars and fiber in soy. These components can cause abdominal bloating and gas, just like the sugars and fibers in most beans and just like the lactose in milk. Such symptoms are generally reduced, if not eliminated, when people use highly refined soy protein isolates which are 90-92% soy protein and only 3-4% carbohydrate (fiber plus simple and complex sugars and starches).

3. Soy and Weight Loss

Some claim that soy-based meal-replacement formulas are ineffective for weight loss. However, the fact is that soy protein has been used effectively as a component of weight loss diets for more than 20 years. Animal studies have shown that soy protein and its associated bioactive isoflavones and peptides can have beneficial effects on glucose metabolism, fat metabolism, insulin sensitivity, metabolic rate, food intake and weight loss. Studies in humans have further shown that increased intakes of soy or animal protein can increase metabolic rate, decrease appetite, and increase satiety. Furthermore, randomized clinical trials and clinical weight loss studies have shown that diets based on soy protein are

every bit as effective - if not more effective - than diets based on dairy protein when it comes to helping people lose weight and abdominal fat.

The truth is that weight loss is much more a function of reducing caloric intake and increasing calories burned through exercise, as opposed to simply using soy or whey protein in the diet.

4. Soy and Thyroid Function.

Some claim that soy foods should be avoided because they contain compounds (isoflavones) that disrupt thyroid function. We view this as a "half truth" that has little relevance for healthy individuals who consume soy at moderate levels as part of a healthy, balanced diet.

The relationship between soy consumption and thyroid function has been studied for more than 70 years. Interest in the topic grew during the 1950's and 1960's when several cases of goiter were identified in infants who consumed soy formulas. Subsequently, using *in vitro* and animal research, scientists found that at high concentrations the soy isoflavones genistein and daidzein can inhibit the activity of thyroid peroxidase and 5'-deiodinase, key enzymes involved in thyroid hormone biosynthesis.

Since that time, 14 human clinical trials have evaluated the effects of soy foods and soy isoflavones on thyroid function. All involved presumably healthy subjects, and with few exceptions the soy product used was isolated soy protein.

With only one exception, all of the studies showed either no effects or minor and clinically irrelevant effects of soy on thyroid function. The one trial that noted marked anti-thyroid effects (and the one often cited in anti-soy literature) involved Japanese adults who were fed roasted soybeans that had been pickled and stored in rice vinegar. The soy protein and isoflavone content of this food was not characterized, and the study involved no control group. As such, its relevance must be questioned.

One large study evaluated the specific effects of soy isoflavone supplements on thyroid function. Postmenopausal women between the ages of 64 and 83 were given daily doses of 90 mg of soy isoflavones or a placebo. Thyroid hormone levels were tested at baseline and again at 90 and 180 days. After six months, any differences in thyroid hormones between the groups were statistically indistinguishable.

Today, most experts agree that soy foods and isolated soy protein have little if any effect on thyroid function in normal, healthy adults. That said, the potential for soy isoflavones to disrupt thyroid function should not be ignored by people who have compromised thyroid function and/or people with suboptimal iodine status. But these groups aside, we contend that soy is a good source of protein when consumed in moderate amounts as part of a healthy, balanced diet.

In support of this position, note that Asian populations have a long history of consuming soy products without significant occurrence of goiter. This also holds true for vegetarians who consume not only higher levels of soy, but high levels of fruits and vegetables that contain other flavonoids known to inhibit thyroid enzyme activity. These flavonoids include kaempferol (found in apples, onions, green tea), naringenin (found in citrus fruits), and quercetin (found in fruits and berries). Such compounds are widely distributed in plant-derived foods and are consumed at relatively high levels (up to 1 gram or more per day) by

vegetarians and vegans. Despite this, vegetarian diets have not been linked with decreased thyroid function.

5. Soy Phytates.

Plants store phosphorus, an essential nutrient for plants and animals, in their seeds to support the growth of young seedlings. This phosphorus is stored in the form of phytate (inositol hexametaphosphate). Plant phytates are considered by some to be “anti-nutrients” because phytates consumed in the human diet can complex with essential minerals like iron and zinc and inhibit absorption in the gut. Others, however, consider phytates to be important food constituents that act not only as natural food-preserving antioxidants, but also help reduce risk of heart disease and cancer in those who consume whole grains, beans, seeds and nuts.

Soybeans contain significant amounts of phytate (1.3-1.4%), and some point to this as a reason to avoid soy foods. However, it is important to note that most whole grains, beans, seeds, and nuts are also rich in phytates (Table 1), and there is a wealth of science to support the fact that these foods are important constituents of a healthy, well-balanced diet that supports longevity and reduced disease risk. As such, it is difficult to argue that soy should be avoided based on its phytate content when so many healthy foods contain comparable levels of phytates.

It is also important to note that on a percent basis, isolated soy protein contains far less phytate than do whole soybeans.

Table 1. Phytate contents of some common grains, beans, and nuts. Values from NR Reddy and SK Sathe (eds). Food Phytates. CRC Press, 2001.

Food	Phytate Content (%)
Whole Wheat	0.7-1.1
Wheat Flour	0.3-1.4
Wheat Bran	2.0-5.3
Corn	0.8-1.0
Oats	1.0
Barley	1.0
Brown Rice	0.9
Soybeans	1.3-1.4
Soy Protein Isolates	0.7-0.9
Kidney Beans	2.6-2.9
Lentils	0.4-0.5
Chick Peas	0.6
Small White Beans	1.2
Great Northern Beans	2.6-2.9
Peas	0.8-1.2
Hazel Nuts	1.9
Walnuts	0.6-2.4
Almonds	1.3-3.2
Cashews	0.6-2.0

6. Soy and Chronic Disease Risk with an Emphasis on Breast Cancer

The association between soy consumption and chronic disease risk is controversial. Epidemiological research suggests that soy consumption is associated with reduced risk of heart disease, osteoporosis, and some cancers, but the mechanisms underlying these relationships are unclear. Is soy itself beneficial, or do these protective associations exist because those who eat higher amounts of soy also eat lower amounts of animal protein and fat? Both factors are likely involved, but enough research exists to indicate that soy protein and soy isoflavones likely provide some direct benefits.

Cardiovascular Disease: With respect to heart disease, soy protein consumption has been linked to modest (3-5%) decreases in serum LDL cholesterol. Soy isoflavones may play some role in maintaining vascular function and preventing arterial stiffness, but the clinical significance of these benefits has not been defined.

Osteoporosis: Bone fracture rates are generally lower among Asian populations that regularly consume soy foods than among Western populations that seldom consume soy foods. Moreover, there is some clinical evidence that soy protein and soy isoflavone-rich diets have bone-sparing effects. The evidence is mixed, however, leading some experts to conclude that while soy foods and isoflavones should not be used as sole approaches to reducing osteoporosis risk, postmenopausal women who are concerned with bone health should be encouraged to incorporate soy foods into their diets.

Cancer / Breast Cancer: Epidemiological research has associated soy consumption with decreased risk of prostate, breast, and colon cancers. Soy products contain five known classes of anti-cancer agents including isoflavones (phytoestrogens), protease inhibitors, phytate, phytosterols, saponins, as well as other potential anticarcinogens such as phenolic acids, lecithin, and omega-3 fatty acids.

Isoflavones are currently the most intensively researched soy phytochemical with respect to breast cancer, although there is a growing body of literature supporting protease inhibitors as anticarcinogens. In addition, certain protease inhibitors - such as the Bowman-Birk inhibitor (BBI) found in soy - have been shown to prevent and suppress carcinogenesis in animal models without toxicity. A concentrated form of BBI (referred to as BBIC) has been granted Investigational New Drug Status for use in human cancer prevention trials.

The two primary isoflavones in soy are genistein and daidzein, and both are thought to be protective against cancer. Each of these compounds act as antioxidants that help to neutralize free radicals within the body. Additionally, these isoflavones are similar in structure to estrogen and are able to bind with estrogen receptors in a variety of tissues (particularly the estrogen receptor- β). That said, genistein and daidzein exhibit only weak estrogenic activity, perhaps only 1/400 to 1/1,000 the level of estradiol. Their activity is also far weaker than most other phytoestrogens, xenoestrogens, and estrogen antagonists (such as β -sitosterol, bisphenol A, octophenol, and tamoxifen). Since high levels of estrogen have been linked to breast cancer and other hormone-related cancers, isoflavones may be protective by binding estrogen receptors and blocking the harmful effects of the more potent form(s) of estrogen, thus functioning as overall antiestrogens.

Soy isoflavones have been shown to be protective against mammary cancer in rat models and in human mammary cancer cell lines grown in cell culture. However, no clinical trials have been published documenting soy's ability to reduce breast cancer in women at high risk.

Moderate, long-term consumption of soy foods containing isoflavones may contribute to the relatively low incidence of breast cancer in Asian countries. The incidence of breast cancer in Japan and China is one-fifth that of Western women. The average intake of soy protein in Southeast Asia ranges from 10-50g per day in contrast to 1-3g per day consumed by Americans. Asian women consume 20-80 mg of isoflavones daily; women in the U.S. have an average intake of less than 5 mg per day.

Several epidemiological studies have specifically examined the association between soy consumption and the incidence of breast cancer. Many - but not all - have shown that soy intake can be protective. In a study involving 200 Singapore Chinese women with breast cancer and 420 matched controls, a decreased risk of breast cancer was associated with high intakes of soy products in premenopausal women. A more recent case-control study done at the University of Southern California, Los Angeles, interviewed 597 Asian-American women with previous incidence of breast cancer and 966 controls. Risk of breast cancer decreased with increasing frequency of tofu consumption in both pre- and postmenopausal women. A recent and large study of 21,852 Japanese women aged 40-59 found that women with the highest intake of soy isoflavones reduced their risk of breast cancer by up to 54% compared to women with the lowest intake of soy isoflavones.

Dietary soy isoflavones have been shown to inhibit breast cancer in some animal models, but in other animal research they have been shown to stimulate breast cancer development when delivered at very high doses (equivalent to a human dose of 150 mg per day). Further laboratory research has shown that soy isoflavones can inhibit human breast cancer cell proliferation *in vitro*. Unfortunately, there are currently no long-term human clinical trials to help sort this issue out.

As such, controversy remains as to whether women with a family history of breast cancer - or women who have been diagnosed with estrogen dependent tumors - should avoid consuming soy products. Based on our research, we encourage at-risk and concerned women to discuss this matter with their doctors and oncologists.

To summarize, as we have reviewed the scientific literature and discussed this topic with experts, we have come to the following conclusions.

- Soy foods containing isoflavones appear to have protective effects against breast cancer, particularly when consumed lifelong (*e.g.* when consumed as part of a healthy, balanced diet beginning in childhood).
- Healthy dietary intakes of soy isoflavones, as reflected in Asian diets, appear to be in the range of 20-80 mg per day.
- High rates of soy isoflavone intake (≥ 150 mg per day) through consumption of isoflavone-fortified foods and supplements should be avoided, particularly by menopausal and post-menopausal women who are at risk for estrogen dependent breast cancer and who have not regularly eaten soy foods in their pasts.

Finally, it is important to maintain a sense of perspective. The relationships between diet and chronic disease risk are complex, and we may never have a complete set of answers to our questions concerning soy and long-term health. That said, we feel that the weight of the scientific evidence clearly indicates that soy foods, whether whole or prepared from soy protein isolates, can be safely consumed in moderation by the vast majority of healthy people as part of a healthy, well-balanced diet. Soy offers a balanced and nutritious source of protein that can be used to offset intakes of animal-based proteins. It also supplies a number of phytochemicals linked to long-term health. Soy also contains phytochemicals that

can interfere with certain physiological processes (phytates and enzyme inhibitors), but this is neither unique nor cause for alarm. Most whole plant-based foods contain similar compounds. And, if nutritional science has taught us anything it is that a diet rich in whole, plant-based foods is generally protective against chronic disease and generally health promoting.

7. Fermented Versus Non-Fermented Soy Foods

There are two principal categories of traditional soy foods: non-fermented and fermented. The main non-fermented foods include soymilk, tofu (bean curd), soybeans, and soynuts. These foods are consumed mainly for nourishment. The main fermented soyfoods include soy paste (*miso* in Japan) and fermented soybeans (*natto* in Japan). Fermented soy pastes are generally used as condiments in cooking, whereas fermented soybeans are also consumed as part of a meal.

There is not currently scientific agreement as to which type of soy is superior. The following are points to consider:

- Fermenting soy foods increases isoflavone bioavailability. However, it also decreases the actual isoflavone content of the food. Typical intakes of non-fermented soy foods are higher than fermented soy products and would contribute a much larger percentage of dietary isoflavones.
- Fermented soy may be easier for some people to digest, although digestion of non-fermented products is not a common problem and can generally be resolved.
- Fermented products have lower phytate levels. Again, this is not a major issue since mineral levels of people eating a typical mixed diet are not significantly affected by the phytic acid content in non-fermented soy. Additionally, phytic acid intake has been linked to a reduced risk of certain cancers.
- Fermented soy products can be quite high in sodium. A review of soy intake and stomach cancer indicated that risk increased with intake of fermented soyfoods (mainly miso), but decreased with intake of non-fermented soyfoods (mainly tofu). The increased cancer risk may be related to high sodium intake in those eating fermented products. Sodium intake is a well-known risk factor for stomach cancer.
- Statements that non-fermented soy is inferior to fermented soy are misleading. In a review of 26 animal studies of experimental carcinogenesis in which diets containing soy or soybean isoflavones were used, 17 (65%) reported protective effects. No studies reported that soy intake increased tumor development. The epidemiological data are also inconsistent, although consumption of non-fermented soy products (such as soymilk and tofu) tended to be either protective or not associated with cancer risk; however, no consistent pattern was evident with the fermented soy products (such as miso). Protective effects were observed for both hormone- and non-hormone-related cancers.

The established benefits of soy relating to heart disease, osteoporosis, cancers, and other chronic diseases are based on total intakes of soy foods, soy protein, or soy isoflavones. The published scientific literature has generally made no distinction in benefit between fermented and non-fermented soy foods. If anything, the majority of published soy research has involved non-fermented soy foods or products.

Again, USANA's position is that optimal nutrition starts with a healthy, well-balanced diet that includes a wide variety of plant-based foods. In this light, perhaps the best way to take

advantage of the health benefits of soy is to eat moderate amounts from a variety of both fermented and non-fermented sources.

8. Environmental Considerations

Some people object to soy because it has become a leading example of industrial food production around the world. The U.S. alone produces some 70-80 million acres of soybeans each year. This production embraces principles of the "Green Revolution", namely monoculture, extensive use of chemical fertilizers, pesticides, herbicides, and genetically modified hybrids, high inputs of fossil fuels, poor land use practices leading to erosion, enormous government subsidies, and more. In short, soybeans are not being cultivated in a sustainable way, and this imposes an enormous burden on our environment.

Unfortunately, most of our basic foods stuffs (corn, wheat, rice, beef, chicken, milk, fish) are being produced and harvested in largely unsustainable ways. The problem lies with our "broken" approach to agriculture and food production in general. It is not an inherent feature of soy.

In fact, soy carries a number of advantages that greatly reduce its environmental impact as a source of protein. These advantages, in turn, mean that soy, when consumed as part of a balanced diet, can help to reduce the collective environmental impact of human diets. Such advantages include the following.

- Soybean plants fix nitrogen from the atmosphere and require little (if any) nitrogen fertilizer. In addition, by alternating soybeans with corn and other crops on a given piece of land, soy production can reduce the amounts of nitrogen fertilizer needed by those alternating crops.
- Soy offers a primary plant-based source of protein that is complete, balanced, and as nutritionally rich as most animal proteins - and it does this at a fraction of the environmental cost. Consider that a very high percentage of the corn and soybeans produced in the U.S. each year are fed to cattle, pigs, and chickens, and that the conversion of these grains into meat is inefficient. In fact, it requires 20 pounds of corn and soybeans to produce a single pound of beef. In comparison, it requires 4.5 pounds to produce a pound of chicken meat and 7.3 pounds to produce a pound of pork.

All in all, given the above factors, soy protein on a pound-for-pound basis carries an environmental cost that is only 10-20% that of a comparable pound of animal or dairy protein. Clearly, including soy as a significant source of our dietary protein helps us to eat lower on the food chain and reduce our dietary environmental impact.

Summary

In conclusion, USANA believes that soy is a healthy source of protein for the vast majority of people. Clearly there are people who are allergic and/or sensitive to soy, and those people need to limit their soy intakes or avoid soy all together. But the scientific research we have seen indicates that this group is relatively small.

That said, each of us is the best judge of what foods we should be eating. If you experience side effects from eating soy foods (even if you don't have a diagnosed soy allergy), it makes full sense for you to minimize or eliminate sources of soy intake.

We encourage everyone to become an active “student” of nutrition - to seek out objective information from a variety of sources concerning the foods they eat. We encourage everyone to question information that doesn't make common sense or that sounds too good or too scary to be true.

As always, the most solid, common sense advice we can provide concerning your protein sources is: a healthy diet is one that includes protein from a wide variety of sources, including whole foods (legumes, whole grains, meat, dairy, and fish) and healthy processed foods. In this context, we believe that soy, whey, and other protein isolates and concentrates can all play a role as components of healthy, balanced diets.

References and Suggested Reading

Bruce B, Messina M, Spiller GA. Isoflavone supplements do not affect thyroid function in iodine-replete postmenopausal women. 2003. *J Med Food* 6:309-16.

Cordle CT. Soy protein allergy: incidence and relative severity. 2004. *J Nutr* 134:1213S-9S.

Cotterchio M, Boucer BA, Manno M, Gallinger S, Okey A, Harper P. Dietary phytoestrogens intake is associated with reduced colorectal cancer risk. 2006. *J Nutr* 136:3046-53.

De Kleijn MF, van der Schouw YT, Wilson PW, Adlercreutz H, Mazur W, Frobbee DE, Jacques PF. Intake of dietary phytoestrogens is low in postmenopausal women in the United States: the Framingham study (1-4). 2001. *J Nutr* 131:1826-1832.

Divi RL, Doerge DR. Inhibition of thyroid peroxidase by dietary flavonoids. 1996. *Chem Res Toxicol* 9:16-23.

Doerge DR, Sheehan DM. Goitrogenic and estrogenic activity of soy isoflavones. 2002. *Environ Health Perspect* 110 Suppl 3:349-53.

Duffy C, Perez K, Partridge A. Implications of phytoestrogen intake for breast cancer. 2007. *CA Cancer J Clin* 57:260-77.

Fournier DB, Erdman JW Jr, Gordon GB. Soy, its components, and cancer prevention: a review of the in vitro, animal, and human data. 1998. *Cancer Epidemiol Biomarkers Prev* 11:1055-65.

Gutendorf B, Westendorf J. Comparison of an array of in vitro assays for the assessment of the estrogenic potential of natural and synthetic estrogens, phytoestrogens and xenoestrogens. 2001. *Toxicology* 166:79-89.

Hydovitz JD. Occurrence of goiter in an infant on a soy diet. 1960. *N Engl J Med* 262:351-3.

Lee HP, Gourley L, Duffy SW, Esteve J, Lee J, Day NE. Dietary effects on breast-cancer risk in Singapore. 1991. *Lancet* 337:1197-200.

Liu Z, Li W, Sun J, Liu C, Zenhjg Q, Huang J, Yu B, Huo J. Intake of soy foods and soy isoflavones by rural adult women in China. 2004. *Asia Pac J Clin Nutr* 13:204-9.

McMichael-Phillips DF, Harding C, Morton M, Roberts SA, Howell A, Potten CS, Bundred NJ. Effects of soy-protein supplementation on epithelial proliferation in the histologically normal human breast. 1998. *Am J Clin Nutr* 68(Suppl):1431S-5S.

Messina M, Ho S, Alekel DL. Skeletal benefits of soy isoflavones: a review of the clinical trial and epidemiologic data. 2004. *Curr Opin Clin Nutr Metab Care* 7:649-58.

Messina M, McCaskill-Stevens W, Lampe JW. Addressing the soy and breast cancer relationship: review, commentary, and workshop proceedings. 2006. *J Natl Cancer Inst* 98:1275-84.

Messina M, Nagata C, Wu AH. Estimated Asian adult soy protein and isoflavone intakes. 2006. *Nutr Cancer* 55:1-12.

Messina M, Redmond G. Effects of soy protein and soybean isoflavones on thyroid function in healthy adults and hypothyroid patients: a review of the relevant literature. 2006. *Huroid* 16:249-58.

Munro IC, Harwood M, Hlywka JJ, Stephen AM, Doull J, Flamm WG, Adlercreutz H. Soy isoflavones: a safety review. 2003. *Nutrition Rev* 61:1-33.

Reddy NR, Sathe SK (eds). *Food Phytates*. 2001. CRC Press, Boca Raton.

Roberts P. *The End of Food*. 2008. Houghton Mifflin Co, New York.

Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris-Etherton P, Winston M. Soy protein, isoflavones, and cardiovascular health. 2006. *Circulation*, 113:1034-44.

Trock BJ, Hilakivi-Clarke L, Clarke R. Meta-analysis of soy intake and breast cancer risk. 2006. *J Natl Cancer Inst* 98:459-71.

Tuka K, Umegaki K, Sato Y, Endoh K, Watanabe S. Soy isoflavones lower serum total and LDL cholesterol in humans: a meta-analysis of 11 randomized controlled trials. 2007. *Am J Clin Nutr* 85:1148-56.

Wu AH, Ziegler RG, Horn-Ross PL, Nomura AM, West DW, Kolonel LN, Rosenthal JF, Hoover RN, Pike MC. Tofu and risk of breast cancer in Asian-Americans. 1996. *Cancer Epidemiol Biomarkers Prev* 11:901-6.

Yamamoto S, Sobue T, Kobayashi M, Sasaki S, Tsugane S. Soy, isoflavones, and breast cancer risk in Japan. 2003. *J Natl Cancer Inst* 95:906-13.

Yan L, Spitznagel E. A meta-analysis of soyfoods and risk of breast cancer in women. 2004. *Int J Cancer Prevention* 1:281-93.

Young VR, Pellett PL. Plant proteins in relation to human protein and amino acid nutrition. 1994. *Am J Clin Nutr* 59(suppl):1203S –12S.

Zhang Y, Song TT, Cunnick JE, Murphy PA, Hendrich S. Daidzein and genistein glucuronides in vitro are weakly estrogenic and activate human natural killer cells at nutritionally relevant concentrations. 1999. *J Nutr* 129:399-405.

Zuidmeer L, Goldhahn K, Rona RJ, Gisiason D, Madsen C, Summers C, Sodergren E, Dahlstrom J, Lindner T, Sigurdardottir ST, McBride D, Keil T. The prevalence of plant food allergies: a systematic review. 2008. *J Allergy Clin Immunol* 121:1210-8.