Soy and Safety

2011 EDITION

One serving of a traditional soyfood, such as 1 cup of soymilk, provides about 25 mg of isoflavones.

Traditional soyfoods have played an important role in East Asian diets for centuries, and have been consumed by health-conscious individuals in Western countries for decades. More recently, soyfoods have become increasingly popular among mainstream consumers in the West, largely because of research suggesting they offer health benefits independent of the nutrients they provide. Possible health benefits include reducing risk of coronary heart disease,[1-3] osteoporosis[4-6] and some forms of cancer.[7] Many of the proposed benefits of soyfoods are attributed to their being essentially unique dietary sources of isoflavones, a group of diphenolic molecules with estrogen-like properties. However, it is precisely for this reason that questions about the potential adverse effects of soyfoods have been raised.

The FDA concluded that soyfoods are safe in its review when approving the health claim for soy protein and coronary heart disease.

In 1999, as part of the process for approving the health claim for soy protein and coronary heart disease, the U.S. Food and Drug Administration (FDA) reviewed the scientific literature and concluded that soyfoods were safe.[8] During the past decade, considerably more research has been conducted, although most of the concerns being raised today were previously considered by the FDA. In 2005, the Agency for Healthcare Research and Quality identified only minor problems associated with the intake of large amounts of soy, such as mild gastrointestinal disturbances, although most of the research they evaluated wasn't designed to specifically address safety issues.[9] However, a similar conclusion was reached by Austrian researchers in a recently published meta-analysis, which was undertaken to specifically address the safety of phytoestrogen supplements.[10] Nevertheless, discussions about the safety of soy continue to appear in the scientific literature and popular media.

How Much Soy Protein do Asians and Americans Consume?

There exists considerable confusion in some circles about the role soy plays in the diets of Asian populations and precisely how much soy Americans consume. Soy protein is widely used by the food industry and is found in small amounts in an extensive array of foods in the U.S. However, soy protein is added to foods primarily for its functional properties, i.e., to improve shelf stability and texture. Consequently, U.S. daily per capita soy protein intake is only 1-2 g/day. That represents about 2 percent of total protein intake.[11] Obviously, because soy protein intake is so low, U.S. isoflavone intake is also very low (<2 mg/day). Furthermore, although each gram of protein in minimally processed or traditional soyfoods is associated with about 3.5 mg isoflavones, the protein used by the food industry is often quite low in isoflavones.

In Japan, the daily intake of soy protein among those consuming a traditional diet is approximately 10 g, which represents more than 10 percent of their total protein intake.[12] Large studies from Shanghai, China, show men consume about 12-13 g of soy protein per day,[13] which represents about 15 percent of total protein intake,[14] and that women consume about 9 g/day.[15] Individuals in the upper one-quarter of intake consume about 15-20 g soy protein daily. Ten grams of soy protein translates to about 1.5 servings since 1 serving of a traditional soyfood provides about 7 g protein, although some soyfoods can provide considerably more than this.

In Japan, about half of soy intake comes via unfermented foods, and four foods – tofu, miso, natto and fried tofu – account for about 90 percent of all soy consumption.[16, 17] In Shanghai, most of the soy consumed is unfermented, and soymilk, tofu and processed soy products other than tofu account for about 80 percent of total soy consumption.[1]

In conclusion, these intake data indicate that most Americans need to substantially increase their soy intake to match the levels common to the traditional cuisines of many Asian populations. This can easily be done through a variety of fermented and unfermented soyfoods.

Considerations in Evaluating Soy Research

Most scientists can probably agree that there is a legitimate basis for discussion about potential adverse effects of soy consumption in some individuals under certain circumstances. Some types of in vitro and animal studies have raised concern but this is hardly surprising given the sheer volume of research conducted. Almost 2,000 soy-related scientific papers are published annually. Unfortunately, sensationalized media stories – and especially online articles lacking editorial oversight – often focus on a tiny minority of studies unrepresentative of the overall scientific literature.

The relevance of in vitro and animal studies to humans is always a matter of debate. Clearly, in vitro conditions cannot duplicate the complexity of living organisms, human or otherwise. Further, by necessity, these studies typically examine the effects of isolated compounds, which may be quite different from the effects seen when these compounds are examined in their natural milieu. The biological impact of one nutrient or non-nutrient in a food can be dependent upon the presence of others.[18, 19]

The vast majority of the data show that soyfoods and isoflavones are safe.

Studies in rats and mice, while certainly part of the scientific literature, often have limited value for predicting effects in humans because of the many physiological and anatomical differences between rodents and humans. In the case of soy, there is an additional caveat; most animals, including rodents and non-human primates, metabolize isoflavones very differently than humans.[20-24] Therefore, one may derive, at most, only very limited insight about the possible effects of soyfoods in humans based on the results from studies in which rodents are fed isoflavone-rich soy protein or mixed isoflavones as exist in soybeans.

It is also important to recognize that many highly investigated foods and food components have been linked with adverse effects in at least some studies and this includes foods that are recommended by most nutritionists for their roles as part of a healthy diet. For example, whole grains contain phytate (as do soyfoods), which can decrease mineral absorption.[25] Nevertheless, the nutrition community recommends the intake of whole grains because the overwhelming preponderance of evidence indicates that they are nutritionally beneficial.[26, 27] The point is that when evaluating any food – including soy – it is necessary to not only evaluate the totality of the evidence but to carefully consider the strengths and weaknesses of study designs.

Fast Facts about Isoflavones

- *Isoflavones are one of five chemical classes of anticarcinogens found in soy.*
- *Soyfoods are the only significant natural dietary source of isoflavones.*
- *Research shows isoflavones may prevent the onset of osteoporosis and may protect against various forms of cancer.*

Evaluating the Evidence:

Hormonal Balance

Isoflavones bind to and transactivate estrogen receptors and can potentially influence steroid hormone synthesis and metabolism via their effects on enzymes involved in a variety of metabolic pathways.[28, 29] Not surprisingly, there has been considerable investigation into the effects of isoflavone-rich soy products and isoflavone supplements on hormone levels in both men and women. Some of this research was aimed at determining whether decreases in testosterone and estrogen levels might account for the proposed role of soy in reducing risk of prostate and breast cancer, respectively.

However, according to the conclusions of two recently published meta-analyses, the purported chemopreventive effects of soyfoods are unlikely to be related to their effects on blood hormone concentrations. The vast majority of studies have shown no effects on circulating reproductive hormone levels in men[30, 31] or women[32-34] in response to the intake of soy protein or isoflavones. One meta-analysis, which included 32 studies and 36 treatment groups, evaluated the effects of soy products on total and free testosterone in men.[35] The other, which included 47 studies, evaluated the effects of soy products on levels of estradiol and other reproductive hormones in pre- and postmenopausal women.[36]

Fertility

Given the large populations of Asian countries that traditionally consume soy, it is somewhat ironic and almost nonsensical that concerns that soy intake impairs fertility have been raised. On the other hand, in many respects the biological effects of isoflavones first came to the attention of the scientific community in the 1940s because of breeding problems experienced by female sheep in Western Australia grazing on a type of clover rich in isoflavones.[37-39] Furthermore, two decades ago it was established that isoflavone-rich soy, which was part of the standard diet of cheetahs in North American zoos, was a factor in the decline of fertility in these animals.[40] However, problems in the latter arose because felines are only poorly able to glucuronidate phenolic compounds, a major step in the bodily elimination of isoflavones – a good example of differences in isoflavone metabolism between animals and humans.[41-43] In the case of the sheep, serum levels of equol – a bacterially synthesized metabolite of the soybean isoflavone daidzein – far exceeded anything approaching human levels simply because daily isoflavone intake was estimated to be several grams[44] versus the 40 mg common to Asian populations.[12]

In women, soyfoods do appear to increase the length of the menstrual cycle. However, ovulation is not prevented, but is simply delayed by 1 day.[36] Interestingly, longer cycles are associated with a decreased breast cancer risk.[45] In men, a small pilot epidemiologic study found that soy consumption was associated with lower sperm concentration but there were many weaknesses to this study. In fact, much of the decreased sperm concentration occurred because there was an increase in ejaculate volume in men consuming higher amounts of soy.[46] Furthermore, in contrast to this one epidemiologic study, all three of the clinical studies conducted show that isoflavones have no effect on sperm concentration or quality.[46-48] Interestingly, a case report actually noted that isoflavones increased sperm count. Daily isoflavone supplementation for 6 months in the male partner of an infertile couple with initially low sperm count led to normalization of sperm quality and quantity and allowed the couple to conceive.[49]

Soy, Isoflavones and Thyroid Function

The first animal studies investigating the effects of soy intake on thyroid function were published 70 years ago.[50-52] Concerns about the anti-thyroid effects of soy are based primarily on in vitro research[53, 54] and studies in rodents administered isolated isoflavones.[55, 56] Although several cases of goiter were attributed to the use of soy infant formula, this problem was eliminated in the mid-1960s with the advent of iodine fortification of the formula.[50, 51, 57]

A comprehensive review published in 2006 that included 14 clinical trials concluded there was little evidence that soyfoods or isoflavones adversely affect thyroid function in healthy men or women.[58] Studies published since this review are supportive of the conclusion.[59-62] One of these is a 3-year study that included more than 200 postmenopausal women who were given isoflavone supplements at either 80 mg/day or 120 mg/day (personal communication, Lee Alekel, Iowa State University). Another noteworthy study, which also supports the safety of soy, was 3 years in duration and the intervention product was high-dose genistein (the isoflavone shown in vitro to inhibit the activity of thyroid peroxidase). In addition to measuring thyroid hormones (thyroid stimulating hormone, thyroxine and triiodothyronine) it also assessed very sensitive indicators of thyroid function, thyroid hormone receptor and retinoid receptor expression from peripheral blood monocytes.[63]

Isoflavone Content of Soyfoods

One serving of a traditional soyfood provides about 20 to 35 mg of isoflavones.

Soyfood	Serving size	Total (mg) isoflavone/ serving
Miso	1 Tbsp	7
Soybeans, Green, Cooked	1/2 cup	50
Soybeans, Black, Cooked	1/2 cup	40
Soybeans, Yellow, Cooked	1/2 cup	78
Soybeans, Roasted, Plain	1/4 cup	78
Soymilk, Plain, Unfortified	1 cup	10
Soymilk, Plain, Fortified	1 cup	43
Soy Flour, Defatted	1/4 cup	42
Soy Flour, Full-Fat	1/4 cup	33
Soy Flour, Low-Fat	1/4 cup	50
Soy Crumbles	1/2 cup	9
Soy Protein Isolate Powder, Plain	1/3 cup	53
Textured Soy Protein, Dry	1/4 cup	33
Tempeh	1/2 cup	53
Tofu	1/2 cup	25

Although soy has no effect on thyroid function in euthyroid individuals, soyfoods may increase the amount of thyroid medication needed by hypothyroid patients, not because of an effect on the thyroid but rather because soy protein may interfere to some extent with the absorption of the medication.[64-67] Soy is not alone in this regard as many herbs, drugs and fiber supplements have similar effects.[68-76] In any event, it is not necessary for thyroid patients (with the exception of infants with congenital hypothyroidism) to avoid soyfoods since thyroid medication is taken on an empty stomach and dosages can easily be adjusted to compensate for any effects of soy.

Finally, there are two clinical situations that warrant consideration in which the relationship between soy intake and thyroid function have not been explored. One involves individuals with subclinical hypothyroidism, which represents about 5 percent of the general adult population but a higher percentage among individuals over the age of 60 years.[77] This condition is defined as having normal levels of the two primary thyroid hormones, thyroxine and triiodothyronine, but elevated levels of thyroid stimulating hormones.[78] There is no evidence that soyfoods pose a problem for subclinical hypothyroid patients but research specifically addressing this issue has not been conducted. Therefore, individuals with subclinical hypothyroidism who begin to consume soy should be sure to monitor their thyroid function. The second situation involves individuals whose iodine intake is marginal or inadequate. In the United States, iodine intake is generally quite good, however subpopulations may not be getting sufficient amounts of this mineral.[79] In any event, with an individual whose iodine intake is suboptimal, the appropriate recommendation is to increase iodine intake, not to avoid soyfoods.

Soyfoods and Breast Cancer Risk

The estrogen-like effects of isoflavones form the theoretical basis for concern that soyfoods might be contraindicated for women at increased risk of breast cancer and for breast cancer patients with estrogen-sensitive tumors.[80-84] Isoflavones bind to estrogen receptors, stimulate the growth of human estrogen receptor positive (ER+) breast cancer cells in vitro and, in certain types of experimental rodent models, stimulate the growth of existing estrogen-responsive mammary tumors.[85, 86] However, not all rodent models show that soy stimulates the growth of existing mammary tumors[87, 88] and even in rodent models where stimulation occurs, minimally processed soyfoods do not have this effect.[89] More importantly, the human data suggest that isoflavones, regardless of the source, do not exert stimulatory effects on breast tissue.

In none of the five clinical trials – three involving postmenopausal, one premenopausal and one both pre- and postmenopausal women in which researchers took breast tissue biopsies before and after exposure to isoflavones – were effects on cell proliferation noted.[32, 90-93] Increased cell proliferation is generally regarded as a risk factor for cancer. Isoflavone exposure also has no effect on breast tissue density (increased density is a marker of cancer risk).[94-97] In contrast to the lack of effects of isoflavones, estrogen plus progestin hormone therapy, which increases breast cancer risk,[98] increases breast tissue density and breast cell proliferation.[99, 100]

The American Cancer Society states that breast cancer patients can safely consume up to 3 servings of traditional soyfoods daily.

Finally, four prospective epidemiologic studies provide important insight into the soy and breast cancer relationship. The findings from these studies are reassuring in regard to safety and even suggestive of benefit. In one, neither soy nor isoflavone intake was related to the disease-free survival of Chinese breast cancer patients over the 5.2 year follow-up period.[101] In this study, of the 1,001 patients for whom data on receptor status were available, approximately 63 percent were ER+. The limitation of this study is that soy intake was assessed prior to diagnosis.

In the second study, data from the Shanghai Breast Cancer Survival Study (SBCSS), a population-based cohort study of breast cancer survivors, were analyzed to investigate the effect of soy intake after diagnosis on breast cancer prognosis.[102] During the median follow-up period of approximately 3.9 years, the hazard ratio associated with the highest quartile of soy protein intake was 0.71 for total mortality and 0.68 for recurrence compared with the lowest quartile of intake. In fact, in this study, high soy intake was as protective as tamoxifen use. In an editorial accompanying the *Journal of the American Medical Association* article, researchers from the National Cancer Institute and Fred Hutchinson Research Center in Seattle remarked, "Patients with breast cancer can be assured that enjoying a soy latte or indulging in pad thai with tofu causes no harm and, when consumed in plentiful amounts, may reduce risk of disease recurrence."[103]

A third study, which was conducted in the United States, involved 1,954 breast cancer survivors who were followed for 6.3 years. During this time, there were 282 breast cancer recurrences. Suggestive trends for a reduced risk of cancer recurrence were observed with increasing quintiles of isoflavone intake compared to no intake among postmenopausal women and among tamoxifen users.[104]

Interestingly, the benefit of soyfood intake on survival was more pronounced among women with ER+ breast cancer. However, among patients who had not previously used tamoxifen, there was an increased risk associated with higher genistein intake but relatively few women fell into this category, raising the possibility that these findings may have occurred by chance.

Most recently, a study conducted in Harbin, China, found that among postmenopausal breast cancer patients with ER+ and progesterone receptor positive tumors, soy consumption was associated with an approximate 30 percent decrease in recurrence, although overall mortality was not affected.[105] Although there was no interaction between tamoxifen and soy intake, which is consistent with the results of the SBCSS, soy intake enhanced the efficacy of anostrozole, an aromatase inhibitor.

The clinical and epidemiologic findings described above are certainly consistent with the position of the American Cancer Society that breast cancer patients can safely consume up to 3 servings of traditional soyfoods daily.[106] A recent commentary concluded that, with the clinical studies showing isoflavones do not adversely affect breast tissue and recent epidemiologic studies showing soy consumption improves breast cancer prognosis, the current default position of oncologists advising their breast cancer patients to limit or avoid soy intake is no longer justified.[107] However, the commentary also noted that the data do not justify actively recommending soy specifically for the purpose of improving prognosis. Rather, a position in between these two extremes was deemed most defensible. That is, to agree to allow women consuming soy who develop breast cancer to continue doing so and to allow breast cancer patients who want to begin consuming soy, for whatever reason, to do so. Nevertheless, breast cancer patients should discuss any dietary changes with their primary healthcare provider.

Effects of Soy on Mineral Status

Soyfoods are frequently used in place of animal foods, many of which are good sources of iron, zinc and, in the case of dairy foods, calcium. Relatively little red meat is needed to meet daily iron and zinc requirements, so questions about the effects of soy on the status of these two minerals pertains mostly to those eating a predominately plant-based diet.[108]

As noted previously, soybeans, like other legumes and whole grains, are high in phytate,[109] which reduces the absorption of some minerals, including zinc and iron.[110] Zinc absorption from soyfoods is only modestly lower than that from other sources. However, because soybeans contain relatively little zinc, unfortified soyfoods are not particularly good sources of this mineral.[111-114] Zinc status is difficult

to assess[115, 116] so those consuming a plant-based diet are advised to identify good plant sources of zinc in their diet or to take a zinc supplement.[117-121]

In contrast to zinc, soyfoods are relatively high in iron.[122] Until recently, it was believed that the iron in essentially all plant foods, including soyfoods, was poorly absorbed. However, new research utilizing improved methodology indicates that iron absorption from soy may be much higher than previously thought because most of the iron in soy is in the form of ferritin. Although there is debate about the bioavailability of ferritin iron, two important clinical studies in which subjects were fed soyfoods or soybean ferritin show it to be highly bioavailable.[123, 124] In support of these observations are the results from a study designed specifically to examine the effect of soyfoods on mineral status. In this study, young premenopausal women consumed either 2-3 servings of soyfoods daily or non-soyfoods matched for type of food (i.e., soy burgers in place of hamburgers, soymilk in place of cow's milk). Results showed there were no statistically significant effects of soy on urinary and serum zinc, serum hemoglobin and iron, or transferrin saturation (see reference for a description of this study).[48]

In addition to phytate, soybeans are also high in oxalate – another compound that binds calcium and reduces its absorption.[125] Oxalate is one reason that spinach, despite being high in calcium, is not a good source of this mineral. However, despite the presence of both phytate and oxalate, calcium absorption from soybeans is surprisingly good.[126] This is also true for calcium-set tofu[127] and calcium-fortified soymilk.[128, 129] In fact, the absorption of calcium from these foods is comparable to the absorption of calcium from cow's milk. Bioavailability of calcium from calcium-fortified products, such as soymilk, depends to some extent on the type of supplemental calcium used.[127] When calcium carbonate is used as the fortificant in soymilk, absorption is similar to that seen with cow's milk.[128] In contrast, calcium absorption from soymilk fortified with tricalcium phosphate is about 25 percent lower than from cow's milk.[130] However, because of the high amounts of tricalcium phosphate added, the amount of calcium available to the body from both types of calcium-fortified soymilk is similar to that from cow's milk.[128]

Finally, questions have been raised about the solubility of calcium in soymilk. Some research indicates that, even with vigorous shaking, the calcium in soymilk comes out of the solution.[131] While some sedimentation occurs in certain soymilks, this sediment is re-suspended with mild shaking for the majority of soymilk purchased in the United States.

Allergies

Soy protein can cause allergic reactions in sensitive individuals, as is the case for essentially all food proteins. Soy protein is one of the eight foods responsible for approximately 90 percent of all food-induced allergic reactions in the United States.[132] But, these foods are not equally allergenic and allergy to soy protein is relatively rare.[133] A recent nationally representative telephone survey found that only approximately 1 out of 2,500 adults reported having a doctor-diagnosed allergy to soy protein.[134] The results of this survey indicate that cow's milk allergy (CMA) is about 40 times more common than soy allergy. The rate of soy allergy is undoubtedly higher in children than adults, as children are more likely to have food allergies in general. However, by age 10, an estimated 70 percent of children will outgrow their soy allergies.[135]

According to the American Academy of Pediatrics (AAP), extensively hydrolyzed protein formula should be considered as the first alternative for infants with documented CMA (especially for IgE-mediated reactions), because 10-14 percent of these infants will also have a soy protein allergy.[136] However, recently conducted UK research found that 60 percent of all infants with CMA were initially treated with soy and of those, only 9 percent of patients remained symptomatic.[137] In contrast, of the 18 percent of patients treated with extensively hydrolyzed formula, 29 percent remained symptomatic. The results from a small retrospective study from Portugal, which evaluated children with persistent CMA, also suggest soy formula may have advantages over hydrolyzed formulas.[138]

Recent research shows that only about 1 out of 2,500 American adults are allergic to soy protein.

Soy Infant Formula

Soy infant formula (SF) has been in use for more than 50 years. Currently, it accounts for about 13 percent of all dollars spent on infant formula in the United States. An estimated 20 million infants have used SF over the past 40 years. SF produces normal growth and development; nevertheless, SF use has become controversial because of its high isoflavone content. In 2009, the U.S. National Toxicology Program (NTP) concluded there was minimal concern about the safety of SF. However, in response to this conclusion, the AAP submitted a letter to the NTP, which is now part of the public record, stating that, in their view, there was negligible concern about the safety of SF. The five levels of concern are negligible, minimal, some, concern and serious concern. Over the next few years, considerable insight to the health effects of SF will be gained as a result of research underway at the Arkansas Children's Nutrition Center, University of Arkansas for Medical Sciences. At this center, the health status of infants fed breast milk, cow's milk formula and SF is being compared. Thus far, findings indicate that all health parameters assessed in infants fed SF are well within the normal range.[139, 140]

A Word about Soyfood Processing

Tofu and miso are the most commonly consumed soyfoods in Japan and China, whereas in the United States, many people choose more processed forms of soy such as meat analogs and energy bars.[141] Numerous human studies demonstrate that processed soy products provide the same high-quality protein as traditional soyfoods.[142]

Depending on processing methods, however, the isoflavone content of these foods can be markedly reduced.[143] The isoflavone content of a large number of soy-containing foods can be found in an online database created by Iowa State University and the United States Department of Agriculture at: http://www.nal.usda.gov/fnic/foodcomp/Data/isoflav/isoflav.html.

Many traditional soyfoods such as miso, tempeh and natto undergo fermentation. While mineral absorption may be very slightly improved with fermentation and may give rise to other possibly beneficial compounds, there is little evidence that these foods are superior to unfermented ones. In fact, several epidemiologic studies show protective effects of non-fermented but not fermented soyfoods.[144] Non-fermented soyfoods have been consumed in Japan[145] and China[146] for at least 500 years and 1,000 years, respectively. In Japan, where many fermented foods are quite popular, at least half of the total soy consumed comes from foods that are not fermented[16, 17] and in China most of the soy is consumed in nonfermented form.[1]

Summary and Conclusions

When evaluating the safety of soyfoods, it is imperative to consider the totality of the scientific research. This research indicates that soyfoods can be safely incorporated into the diets of essentially all healthy individuals with the exception of those allergic to soy protein. Nevertheless, because all foods have the potential to cause undesirable effects in some individuals, people with specific health concerns should consult their healthcare provider regarding unique nutritional needs.

References

1. Zhang X, Shu XO, Gao YT, Yang G, Li Q, Li H, Jin F, Zheng W. Soy food consumption is associated with lower risk of coronary heart disease in Chinese women. J. Nutr. 2003, 133, 2874-8.
2. Kokubo Y, Iso H, Ishihara J, Okada K, Inoue M, Tsugane S. Association of dietary intake of soy, beans, and isoflavones with risk of cerebral and myocardial infarctions in Japanese populations: the Japan Public Health Center-based (JPHC) study cohort I. Circulation. 2007, 116, 2553-62.
3. Messina M, Lane B. Soy protein, soybean isoflavones, and coronary heart disease risk: Where do we stand? Future Lipidology. 2007, 2, 55-74.
4. Ma DF, Qin LQ, Wang PY, Katoh R. Soy isoflavone intake inhibits bone resorption and stimulates bone formation in menopausal women: meta-analysis of randomized controlled trials. Eur J Clin Nutr. 2007.
5. Marini H, Minutoli L, Polito F, Bitto A, Altavilla D, Atteritano M, Gaudio A, Mazzaferro S, Frisina A, et al. Effects of the phytoestrogen genistein on bone metabolism in osteopenic postmenopausal women: a randomized trial. Ann. Intern. Med. 2007, 146, 839-47.
6. Koh WP, Wu AH, Wang R, Ang LW, Heng D, Yuan JM, Yu MC. Gender-specific associations between soy and risk of hip fracture in the Singapore Chinese Health Study. Am. J. Epidemiol. 2009, 170, 901-9.
7. Shu XO, Jin F, Dai Q, Wen W, Potter JD, Kushi LH, Ruan Z, Gao YT, Zheng W. Soyfood intake during adolescence and subsequent risk of breast cancer among Chinese women. Cancer Epidemiol. Biomarkers Prev. 2001, 10, 483-8.
8. Food Labeling: Health Claims; Soy Protein and Coronary Heart Disease. Federal Register: (Volume 64, Number 206)], 1999:57699-57733.
9. Balk E, Chung M, Chew P, Ip S, Raman G, Kuplenick B, Tatsioni A, Sun Y, Wolk B, et al. Effects of soy on health outcomes. Evidence report/technology assessment No. 126 (prepared by Tufts-New England Medical Center Evidence-based Practice Center under Contract No. 290-02-0022.) AHRQ Publication No. 05-E024-2. Rockville, MD Agency for Healthcare Research and Quality, July 2005.
10. Tempfer CB, Froese G, Heinze G, Bentz EK, Hefler LA, Huber JC. Side effects of phytoestrogens: a meta-analysis of randomized trials. Am. J. Med. 2009, 122, 939-46 e9.
11. Smit E, Nieto FJ, Crespo CJ, Mitchell P. Estimates of animal and plant protein intake in US adults: results from the Third National Health and Nutrition Examination Survey, 1988-1991. J. Am. Diet. Assoc. 1999, 99, 813-20.
12. Messina M, Nagata C, Wu AH. Estimated Asian adult soy protein and isoflavone intakes. Nutr. Cancer. 2006, 55, 1-12.
13. Lee SA, Wen W, Xiang YB, Barnes S, Liu D, Cai Q, Zheng W, Shu XO. Assessment of Dietary Isoflavone Intake among Middle-Aged Chinese Men. J. Nutr. 2007, 137, 1011-1016.
14. Villegas R, Yang G, Liu D, Xiang YB, Cai H, Zheng W, Shu XO. Validity and reproducibility of the food-frequency questionnaire used in the Shanghai men's health study. Br. J. Nutr. 2007, 97, 993-1000.
15. Yang G, Shu XO, Jin F, Zhang X, Li HL, Li Q, Gao YT, Zheng W. Longitudinal study of soy food intake and blood pressure among middle-aged and elderly Chinese women. Am. J. Clin. Nutr. 2005, 81, 1012-7.
16. Wakai K, Egami I, Kato K, Kawamura T, Tamakoshi A, Lin Y, Nakayama T, Wada M, Ohno Y. Dietary intake and sources of isoflavones among Japanese. Nutr. Cancer. 1999, 33, 139-45.
17. Somekawa Y, Chiguchi M, Ishibashi T, Aso T. Soy intake related to menopausal symptoms, serum lipids, and bone mineral density in postmenopausal Japanese women. Obstet. Gynecol. 2001, 97, 109-115.
18. Rozen P, Lubin F, Papo N, Knaani J, Farbstein H, Farbstein M, Zajicek G. Calcium supplements interact significantly with long-term diet while suppressing rectal epithelial proliferation of adenoma patients. Cancer. 2001, 91, 833-40.
19. Bolca S, Wyns C, Possemiers S, Depypere H, De Keukeleire D, Bracke M, Verstraete W, Heyerick A. Cosupplementation of Isoflavones, Prenylflavonoids, and Lignans Alters Human Exposure to Phytoestrogen-Derived 17{beta}-Estradiol Equivalents. J. Nutr. 2009.
20. Wisniewski AB, Klein SL, Lakshmanan Y, Gearhart JP. Exposure to genistein during gestation and lactation demasculinizes the reproductive system in rats. J. Urol. 2003, 169, 1582-6.
21. Fielden MR, Samy SM, Chou KC, Zacharewski TR. Effect of human dietary exposure levels of genistein during gestation and lactation on long-term reproductive development and sperm quality in mice. Food Chem. Toxicol. 2003, 41, 447-54.
22. Ojeda SR, Andrews WW, Advis JP, White SS. Recent advances in the endocrinology of puberty. Endocr. Rev. 1980, 1, 228-57.
23. Robinson JD, Judd HL, Young PE, Jones OW, Yen SS. Amniotic fluid androgens and estrogens in midgestation. J. Clin. Endocrinol. Metab. 1977, 45, 755-61.
24. Gu L, House SE, Prior RL, Fang N, Ronis MJ, Clarkson TB, Wilson ME, Badger TM. Metabolic Phenotype of Isoflavones Differ among Female Rats, Pigs, Monkeys, and Women. J. Nutr. 2006, 136, 1215-21.
25. Larsson M, Rossander-Hulthen L, Sandstrom B, Sandberg AS. Improved zinc and iron absorption from breakfast meals containing malted oats with reduced phytate content. Br. J. Nutr. 1996, 76, 677-88.
26. Harris KA, Kris-Etherton PM. Effects of whole grains on coronary heart disease risk. Curr Atheroscler Rep. 2010, 12, 368-76.
27. Slavin J. Whole grains and human health. Nutr Res Rev. 2004, 17, 99-110.
28. Rice S, Mason HD, Whitehead SA. Phytoestrogens and their low dose combinations inhibit mRNA expression and activity of aromatase in human granulosa-luteal cells. J. Steroid Biochem. Mol. Biol. 2006, 101, 216-25.
29. Lacey M, Bohday J, Fonseka SM, Ullah AI, Whitehead SA. Dose-response effects of phytoestrogens on the activity and expression of 3beta-hydroxysteroid dehydrogenase and aromatase in human granulosa-luteal cells. J. Steroid Biochem. Mol. Biol. 2005, 96, 279-86.
30. Dillingham BL, McVeigh BL, Lampe JW, Duncan AM. Soy protein isolates of varying isoflavone content exert minor effects on serum reproductive hormones in healthy young men. J. Nutr. 2005, 135, 584-91.
31. Hamilton-Reeves JM, Rebello SA, Thomas W, Slaton JW, Kurzer MS. Isoflavone-Rich Soy Protein Isolate Suppresses Androgen Receptor Expression without Altering Estrogen Receptor-{beta} Expression or Serum Hormonal Profiles in Men at High Risk of Prostate Cancer. J. Nutr. 2007, 137, 1769-1775.
32. Cheng G, Wilczek B, Warner M, Gustafsson JA, Landgren BM. Isoflavone treatment for acute menopausal symptoms. Menopause. 2007, 14, 468-73.
33. Brown BD, Thomas W, Hutchins A, Martini MC, Slavin JL. Types of dietary fat and soy minimally affect hormones and biomarkers associated with breast cancer risk in premenopausal women. Nutr. Cancer. 2002, 43, 22-30.
34. Duncan AM, Underhill KE, Xu X, Lavalleur J, Phipps WR, Kurzer MS. Modest hormonal effects of soy isoflavones in postmenopausal women. J. Clin. Endocrinol. Metab. 1999, 84, 3479-84.
35. Hamilton-Reeves JM, Vazquez G, Duval SJ, Phipps WR, Kurzer MS, Messina MJ. Clinical studies show no effects of soy protein or isoflavones on reproductive hormones in men: results of a meta-analysis. Fertil. Steril. 2009.
36. Hooper L, Ryder JJ, Kurzer MS, Lampe JW, Messina MJ, Phipps WR, Cassidy A. Effects of soy protein and isoflavones on circulating hormone concentrations in pre- and post-menopausal women: a systematic review and meta-analysis. Hum. Reprod. Update. 2009, 15, 423-40.
37. Bennetts HW, Underwood EJ, Shier FL. A specific breeding problem of sheep on subterranean clover pastures in Western Australia. Aust J Agric Res. 1946, 22, 131-138.
38. Bradbury RB, White DR. Estrogen and related substances in plants. In: Harris RS, Marrian GF, Thimann KV, eds. Vitam. Horm. New York: Academic Press, 1954:207-230.
39. Lundh TJ-O, Petterson HL, Martinsson KA. Comparative levels of free and conjugated plant estrogens in blood plasma of sheep and cattle fed estrogenic silage. J. Agric. Food Chem. 1990, 38, 1530-1534.
40. Setchell KD, Gosselin SJ, Welsh MB, Johnston JO, Balistreri WF, Kramer LW, Dresser BL, Tarr MJ. Dietary estrogens--a probable cause of infertility and liver disease in captive cheetahs. Gastroenterology. 1987, 93, 225-33.
41. Setchell KD, Brown NM, Lydeking-Olsen E. The clinical importance of the metabolite equol-a clue to the effectiveness of soy and its isoflavones. J. Nutr. 2002, 132, 3577-84.
42. Rowland I, Faughnan M, Hoey L, Wahala K, Williamson G, Cassidy A. Bioavailability of phyto-oestrogens. Br. J. Nutr. 2003, 89 Suppl 1, S45-58.
43. Rowland IR, Wiseman H, Sanders TA, Adlercreutz H, Bowey EA. Interindividual variation in metabolism of soy isoflavones and lignans: influence of habitual diet on equol production by the gut microflora. Nutr. Cancer. 2000, 36, 27-32.
44. Urpi-Sarda M, Morand C, Besson C, Kraft G, Viala D, Scalbert A, Besle JM, Manach C. Tissue distribution of isoflavones in ewes after consumption of red clover silage. Arch. Biochem. Biophys. 2008, 476, 205-10.
45. Kurzer MS. Hormonal effects of soy in premenopausal women and men. J. Nutr. 2002, 132, 570S-3S.
46. Mitchell JH, Cawood E, Kinniburgh D, Provan A, Collins AR, Irvine DS. Effect of a phytoestrogen food supplement on reproductive health in normal males. Clin Sci (Lond). 2001, 100, 613-8.
47. Beaton LK, McVeigh BL, Dillingham BL, Lampe JW, Duncan AM. Soy protein isolates of varying isoflavone content do not adversely affect semen quality in healthy young men. Fertil. Steril. 2009.

48. Messina M, Watanabe S, Setchell KD. Report on the 8th International Symposium on the Role of Soy in Health Promotion and Chronic Disease Prevention and Treatment. J. Nutr. 2009, 139, 796S-802S.

49. Casini ML, Gerli S, Unfer V. An infertile couple suffering from oligospermia by partial sperm maturation arrest: can phytoestrogens play a therapeutic role? A case report study. Gynecol. Endocrinol. 2006, 22, 399-401.

50. Van Wyk JJ, Arnold MB, Wynn J, Pepper F. The effects of a soybean product on thyroid function in humans. Pediatrics. 1959, 24, 752-760.

51. Shepard TH, Gordon EP, Kirschvink JF, McLean CM. Soybean goiter. New Engl J Med. 1960, 262, 1099-1103.

52. Hydovitz JD. Occurrence of goiter in an infant on a soy diet. New England J Medicine. 1960, 262, 351-353.

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

54. Divi RL, Chang HC, Doerge DR. Anti-thyroid isoflavones from soybean: isolation, characterization, and mechanisms of action. Biochem. Pharmacol. 1997, 54, 1087-96.

55. Chang HC, Doerge DR. Dietary genistein inactivates rat thyroid peroxidase in vivo without an apparent hypothyroid effect. Toxicol. Appl. Pharmacol. 2000, 168, 244-52.

56. Chang HC, Churchwell MI, Delclos KB, Newbold RR, Doerge DR. Mass spectrometric determination of Genistein tissue distribution in diet-exposed Sprague-Dawley rats. J. Nutr. 2000, 130, 1963-70.

57. Pinchera A, MacGillivray H, Crawford JD, Freeman AG. Thyroid refractiveness in an athyreotic cretin fed soybean formula. N. Engl. J. Med. 1965, 273, 83-87.

58. 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. Thyroid. 2006, 16, 249-58.

59. Ryan-Borchers T, Boon C, Park JS, McGuire M, Fournier L, Beerman K. Effects of dietary and supplemental forms of isoflavones on thyroid function in healthy postmenopausal women. Topics Clinical Nutr. 2008, 23, 13-22.

60. Romualdi D, Costantini B, Campagna G, Lanzone A, Guido M. Is there a role for soy isoflavones in the therapeutic approach to polycystic ovary syndrome? Results from a pilot study. Fertil. Steril. 2008, 90, 1826-33.

61. Nahas EA, Nahas-Neto J, Orsatti FL, Carvalho EP, Oliveira ML, Dias R. Efficacy and safety of a soy isoflavone extract in postmenopausal women: a randomized, double-blind, and placebo-controlled study. Maturitas. 2007, 58, 249-58.

62. Khaodhiar L, Ricciotti HA, Li L, Pan W, Schickel M, Zhou J, Blackburn GL. Daidzein-rich isoflavone aglycones are potentially effective in reducing hot flashes in menopausal women. Menopause. 2008, 15, 125-32.

63. Bitto A, Polito F, Atteritano M, Altavilla D, Mazzaferro S, Marini H, Adamo EB, D'Anna R, Granese R, et al. Genistein aglycone does not affect thyroid function: results from a three-year, randomized, double-blind, placebo-controlled trial. J. Clin. Endocrinol. Metab. 2010, 95, 3067-72.

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

65. Fitzpatrick M. Soy formulas and the effects of isoflavones on the thyroid. N. Z. Med. J. 2000, 113, 24-6.

66. Bell DS, Ovalle F. Use of soy protein supplement and resultant need for increased dose of levothyroxine. Endocr Pract. 2001, 7, 193-4.

67. Conrad SC, Chiu H, Silverman BL. Soy formula complicates management of congenital hypothyroidism. Arch. Dis. Child. 2004, 89, 37-40.

68. Liel Y, Harman-Boehm I, Shany S. Evidence for a clinically important adverse effect of fiber-enriched diet on the bioavailability of levothyroxine in adult hypothyroid patients. J. Clin. Endocrinol. Metab. 1996, 81, 857-9.

69. Chiu AC, Sherman SI. Effects of pharmacological fiber supplements on levothyroxine absorption. Thyroid. 1998, 8, 667-71.

70. Shakir KM, Chute JP, Aprill BS, Lazarus AA. Ferrous sulfate-induced increase in requirement for thyroxine in a patient with primary hypothyroidism. South. Med. J. 1997, 90, 637-9.

71. Liel Y, Sperber AD, Shany S. Nonspecific intestinal adsorption of levothyroxine by aluminum hydroxide. Am. J. Med. 1994, 97, 363-5.

72. Sperber AD, Liel Y. Evidence for interference with the intestinal absorption of levothyroxine sodium by aluminum hydroxide. Arch. Intern. Med. 1992, 152, 183-4.

73. Sherman SI, Tielens ET, Ladenson PW. Sucralfate causes malabsorption of L-thyroxine. Am. J. Med. 1994, 96, 531-5.

74. Siraj ES, Gupta MK, Reddy SS. Raloxifene causing malabsorption of levothyroxine. Arch. Intern. Med. 2003, 163, 1367-70.

75. Rosenberg R. Malabsorption of thyroid hormone with cholestyramine administration. Conn. Med. 1994, 58, 109.

76. Harmon SM, Seifert CF. Levothyroxine-cholestyramine interaction reemphasized. Ann. Intern. Med. 1991, 115, 658-9.

77. Villar HC, Saconato H, Valente O, Atallah AN. Thyroid hormone replacement for subclinical hypothyroidism. Cochrane Database Syst Rev. 2007, CD003419.

78. Aoki Y, Belin RM, Clickner R, Jeffries R, Phillips L, Mahaffey KR. Serum TSH and total T4 in the United States population and their association with participant characteristics: National Health and Nutrition Examination Survey (NHANES 1999-2002). Thyroid. 2007, 17, 1211-23.

79. Caldwell KL, Miller GA, Wang RY, Jain RB, Jones RL. Iodine status of the U.S. population, National Health and Nutrition Examination Survey 2003-2004. Thyroid. 2008, 18, 1207-14.

80. Bouker KB, Hilakivi-Clarke L. Genistein: Does it Prevent or Promote Breast Cancer? Environ. Health Perspect. 2000, 108, 701-708.

81. Messina MJ, Loprinzi CL. Soy for breast cancer survivors: a critical review of the literature. J. Nutr. 2001, 131, 3095S-108S.

82. Affenito SG, Kerstetter J. Position of the American Dietetic Association and Dietitians of Canada: women's health and nutrition. J. Am. Diet. Assoc. 1999, 99, 738-51.

83. American College of Obstetricians and Gynecologists. Use of botanicals for management of menopausal symptoms. ACOG Practice Bulletin. 2001, 28, 1-11.

84. American Cancer Society Workshop on Nutrition and Physical Activity for Cancer Survivors. Nutrition during and after cancer treatment: a guide for informed choices by cancer survivors. CA. Cancer J. Clin. 2001, 51, 153-187.

85. Ju YH, Allred CD, Allred KF, Karko KL, Doerge DR, Helferich WG. Physiological Concentrations of Dietary Genistein Dose-Dependently Stimulate 99.Sandstrom B, Kivisto B, Cederblad A. Absorption of zinc from soy protein meals in humans. J Nutr. 1987 Feb;117:321-7. Growth of Estrogen-Dependent Human Breast Cancer (MCF-7) Tumors Implanted in Athymic Nude Mice. J. Nutr. 2001, 131, 2957-2962.

86. Allred CD, Ju YH, Allred KF, Chang J, Helferich WG. Dietary genistin stimulates growth of estrogen-dependent breast cancer tumors similar to that observed with genistein. Carcinogenesis. 2001, 22, 1667-73.

87. Kang X, Jin S, Zhang Q. Antitumor and antiangiogenic activity of soy phytoestrogen on 7,12-dimethylbenz[alpha]anthracene-induced mammary tumors following ovariectomy in Sprague-Dawley rats. J Food Sci. 2009, 74, H237-42.

88. Mishra R, Bhadauria S, Murthy PK, Murthy PS. Glycine soya diet synergistically enhances the suppressive effect of tamoxifen and inhibits tamoxifen-promoted hepatocarcinogenesis in 7,12-dimethylbenz[alpha]anthracene-induced rat mammary tumor model. Food Chem. Toxicol. 2010.

89. Allred CD, Allred KF, Ju YH, Goeppinger TS, Doerge DR, Helferich WG. Soy processing influences growth of estrogen-dependent breast cancer tumors. Carcinogenesis. 2004, 25, 1649-57.

90. Sartippour MR, Rao JY, Apple S, Wu D, Henning S, Wang H, Elashoff R, Rubio R, Heber D, et al. A pilot clinical study of short-term isoflavone supplements in breast cancer patients. Nutr. Cancer. 2004, 49, 59-65.

91. Palomares MR, Hopper L, Goldstein L, Lehman CD, Storer BE, Gralow JR. Effect of soy isoflavones on breast proliferation in postmenopausal breast cancer survivors. Breast Cancer Res Treatment. 2004, 88 (Suppl 1), 4002.

92. Hargreaves DF, Potten CS, Harding C, Shaw LE, Morton MS, Roberts SA, Howell A, Bundred NJ. Two-week dietary soy supplementation has an estrogenic effect on normal premenopausal breast. J. Clin. Endocrinol. Metab. 1999, 84, 4017-24.

93. Khan SA, Michel N, Bryk M, Chatterton RT, Ivancic D, Zalles C, Hansen N, Bethke K, Jovanovic B, et al. A phase IIb trial of soy isoflavone supplementation to decrease breast cell proliferation in high risk women. San Antonio Breast Cancer Symposium (Abstract 1049). 2009.

94. Maskarinec G, Williams AE, Carlin L. Mammographic densities in a one-year isoflavone intervention. Eur. J. Cancer Prev. 2003, 12, 165-9.

95. Maskarinec G, Franke AA, Williams AE, Hebshi S, Oshiro C, Murphy S, Stanczyk FZ. Effects of a 2-year randomized soy intervention on sex hormone levels in premenopausal women. Cancer Epidemiol. Biomarkers Prev. 2004, 13, 1736-44.

96. Atkinson C, Warren RM, Sala E, Dowsett M, Dunning AM, Healey CS, Runswick S, Day NE, Bingham SA. Red-clover-derived isoflavones and mammographic breast density: a double-blind, randomized, placebo-controlled trial. Breast Cancer Res. 2004, 6, R170-9.

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

98. Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA. 2002, 288, 321-33.

99. Boyd NF, Lockwood GA, Martin LJ, Byng JW, Yaffe MJ, Tritchler DL. Mammographic density as a marker of susceptibility to breast cancer: a hypothesis. IARC Sci. Publ. 2001, 154, 163-9.

100. Boyd NF, Martin LJ, Li Q, Sun L, Chiarelli AM, Hislop G, Yaffe MJ, Minkin S. Mammographic density as a surrogate marker for the effects of hormone therapy on risk of breast cancer. Cancer Epidemiol. Biomarkers Prev. 2006, 15, 961-6.

101. Boyapati SM, Shu XO, Ruan ZX, Dai Q, Cai Q, Gao YT, Zheng W. Soyfood intake and breast cancer survival: a followup of the Shanghai Breast Cancer Study. Breast Cancer Res. Treat. 2005, 92, 11-7.

102. Shu XO, Zheng Y, Cai H, Gu K, Chen Z, Zheng W, Lu W. Soy food intake and breast cancer survival. JAMA. 2009, 302, 2437-43.

103. Ballard-Barbash R, Neuhouser ML. Challenges in design and interpretation of observational research on health behaviors and cancer survival. JAMA. 2009, 302, 2483-4.

104. Guha N, Kwan ML, Quesenberry CP, Jr., Weltzien EK, Castillo AL, Caan BJ. Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors: the Life After Cancer Epidemiology study. Breast Cancer Res. Treat. 2009.

105. Kang X, Zhang Q, Wang S, Huang X, Jin S. Effect of soy isoflavones on breast cancer recurrence and death for patients receiving adjuvant endocrine therapy. CMAJ. 2010.

106. Doyle C, Kushi LH, Byers T, Courneya KS, Demark-Wahnefried W, Grant B, McTiernan A, Rock CL, Thompson C, et al. Nutrition and physical activity during and after cancer treatment: an american cancer society guide for informed choices. CA. Cancer J. Clin. 2006, 56, 323-53.

107. Messina M, Abrams DI, Hardy M. Can clinicians now assure their breast cancer patients that soyfoods are safe? Womens Health (Lond Engl). 2010, 6, 335-8.

108. Johnson JM, Walker PM. Zinc and iron utilization in young women consuming a beef-based diet. J. Am. Diet. Assoc. 1992, 92, 1474-8.

109. Thompson DB, Erdman JWJ. Phytic acid determination in soybeans. J Food Sci. 1982, 47, 513-517.

110. Urbano G, Lopez-Jurado M, Aranda P, Vidal-Valverde C, Tenorio E, Porres J. The role of phytic acid in legumes: antinutrient or beneficial function? J. Physiol. Biochem. 2000, 56, 283-94.

111. Sandstrom B, Cederblad A. Zinc absorption from composite meals. II. Influence of the main protein source. Am. J. Clin. Nutr. 1980, 33, 1778-83.

112. Sandstrom B, Kivisto B, Cederblad A. Absorption of zinc from soy protein meals in humans. J. Nutr. 1987, 117, 321-7.

113. Davidsson L, Almgren A, Sandstrom B, Juillerat M, Hurrell RF. Zinc absorption in adult humans: the effect of protein sources added to liquid test meals. Br. J. Nutr. 1996, 75, 607-13.

114. Lonnerdal B, Cederblad A, Davidsson L, Sandstrom B. The effect of individual components of soy formula and cows' milk formula on zinc bioavailability. Am. J. Clin. Nutr. 1984, 40, 1064-70.

115. de Portela ML, Weisstaub AR. Basal urinary zinc/creatinine ratio as an indicator of dietary zinc intake in healthy adult women. J. Am. Coll. Nutr. 2000, 19, 413-7.

116. Hunt JR. Moving toward a plant-based diet: are iron and zinc at risk? Nutr. Rev. 2002, 60, 127-34.

117. Messina V, Melina V, Mangels AR. A new food guide for North American vegetarians. Can J Diet Pract Res. 2003, 64, 82-6.

118. Messina V, Melina V, Mangels AR. A new food guide for North American vegetarians. J Am Diet Assoc. 2003, 103, 771-5.

119. Mangels AR, Messina V. Considerations in planning vegan diets: infants. J. Am. Diet. Assoc. 2001, 101, 670-7.

120. Messina V, Mangels AR. Considerations in planning vegan diets: children. J. Am. Diet. Assoc. 2001, 101, 661-9.

121. Messina VK, Burke KI. Position of the American Dietetic Association: vegetarian diets. J Am Diet Assoc. 1997, 97, 1317-21.

122. Karr-Lilienthal LK, Grieshop CM, Merchen NR, Mahan DC, Fahey GC, Jr. Chemical composition and protein quality comparisons of soybeans and soybean meals from five leading soybean-producing countries. J. Agric. Food Chem. 2004, 52, 6193-9.

123. Murray-Kolb LE, Welch R, Theil EC, Beard JL. Women with low iron stores absorb iron from soybeans. Am. J. Clin. Nutr. 2003, 77, 180-4.

124. Lonnerdal B, Bryant A, Liu X, Theil EC. Iron absorption from soybean ferritin in nonanemic women. Am. J. Clin. Nutr. 2006, 83, 103-7.

125. Sandberg AS. Bioavailability of minerals in legumes. Br. J. Nutr. 2002, 88 Suppl 3, S281-5.

126. Heaney RP, Weaver CM, Fitzsimmons ML. Soybean phytate content: effect on calcium absorption. Am. J. Clin. Nutr. 1991, 53, 745-7.

127. Weaver CM, Heaney RP, Connor L, Martin BR, Smith DL, Nielsen E. Bioavailability of calcium from tofu vs. milk in premenopausal women. J Food Sci. 2002, 68, 3144-3147.

128. Zhao Y, Martin BR, Weaver CM. Calcium bioavailability of calcium carbonate fortified soymilk is equivalent to cow's milk in young women. J. Nutr. 2005, 135, 2379-82.

129. Tang AL, Walker KZ, Wilcox G, Strauss BJ, Ashton JF, Stojanovska L. Calcium absorption in Australian osteopenic post-menopausal women: an acute comparative study of fortified soymilk to cows' milk. Asia Pac J Clin Nutr. 2010, 19, 243-9.

130. Heaney RP, Dowell MS, Rafferty K, Bierman J. Bioavailability of the calcium in fortified soy imitation milk, with some observations on method. Am. J. Clin. Nutr. 2000, 71, 1166-9.

131. Heaney RP, Rafferty K. The settling problem in calcium-fortified soybean drinks. J. Am. Diet. Assoc. 2006, 106, 1753; author reply 1755.

132. Food and Drug Administration (FDA). Food Allergen Labeling and Consumer Protection (FALCP) Act of 2004 hwcfgaap. http:// www.cfsan.fda.gov/~acrobat/alrgact.pdf.

133. Food and Drug Administration (FDA). Food Allergen Labeling and Consumer Protection (FALCP) Act of 2004. http://www.cfsan.fda.gov/~acrobat/alrgact.pdf,. 2004.

134. Vierk KA, Koehler KM, Fein SB, Street DA. Prevalence of self-reported food allergy in American adults and use of food labels. J. Allergy Clin. Immunol. 2007, 119, 1504-10.

135. Savage JH, Kaeding AJ, Matsui EC, Wood RA. The natural history of soy allergy. J. Allergy Clin. Immunol. 2010, 125, 683-686.

136. Bhatia J, Greer F. Use of soy protein-based formulas in infant feeding. Pediatrics. 2008, 121, 1062-8.

137. Sladkevicius E, Nagy E, Lack G, Guest JF. Resource implications and budget impact of managing cow milk allergy in the UK. J Med Econ. 2010, 13, 119-28.

138. Dias A, Santos A, Pinheiro JA. Persistence of cow's milk allergy beyond two years of age. Allergol. Immunopathol. (Madr). 2010, 38, 8-12.

139. Gilchrist JM, Moore MB, Andres A, Estroff JA, Badger TM. Ultrasonographic Patterns of Reproductive Organs in Infants Fed Soy Formula: Comparisons to Infants Fed Breast Milk and Milk Formula. J. Pediatr. 2009.

140. Li J, Dykman RA, Jing H, Gilchrist JM, Badger TM, Pivik RT. Cortical responses to speech sounds in 3- and 6-month-old infants fed breast milk, milk formula, or soy formula. Dev Neuropsychol. 2010, 35, 762-84.

141. Messina M, Nagata C, Wu AH. Estimated Asian adult soy protein and isoflavone intakes. Nutr Cancer. 2006, 55.

142. Rand WM, Pellett PL, Young VR. Meta-analysis of nitrogen balance studies for estimating protein requirements in healthy adults. Am. J. Clin. Nutr. 2003, 77, 109-27.

143. Murphy PA, Song T, Buseman G, Barua K, Beecher GR, Trainer D, Holden J. Isoflavones in retail and institutional soy foods. J. Agric. Food Chem. 1999, 47, 2697-704.

144. Kim J, Kang M, Lee JS, Inoue M, Sasazuki S, Tsugane S. Fermented and non-fermented soy food consumption and gastric cancer in Japanese and Korean populations: A meta-analysis of observational studies. Cancer Sci. 2010.

145. Shurtleff W. Database search of tofu and Japan before 1900. LaFayette: The Soyfoods Center, 2003.

146. Shurtleff W. Database search of tofu and China before 1900. Lafayette: The Soyfoods Center, 2003.

The United Soybean Board (USB) is a farmer-led organization comprised of 69 farmer-directors. Working with independent academic researchers affiliated with the National Institutes of Health (NIH) and academic institutions, USB has invested millions of dollars into health and nutrition research related to soy. Soybean farmers take pride in producing one of the healthiest food crops in the world. To access healthy soy recipes and more nutrition information, please visit SoyConnection.com.

0322-012011-1475