



# **MYTHS & FACTS**

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Soyfoods are common in Asian and many health-conscious Western diets, and thus it is pertinent to explore the safety of soy as documented in the body of accumulated research. Consumers can be encouraged to continue feeding their families soyfoods for generations to come.

## Introduction

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 and because of an increased interest in plant-based diets. Possible benefits include reduced risk of coronary heart disease,<sup>1.3</sup> osteoporosis<sup>4.6</sup> and some forms of cancer.<sup>7</sup> Many of the proposed benefits of soyfoods are attributed to their uniquely rich isoflavone content. However, isoflavones, which are diphenolic molecules with estrogen-like properties, are also the primary reason for concerns about the potential adverse effects of soyfoods.

In 1999, as part of the process for approving the coronary heart disease-health claim, the U.S. Food and Drug Administration (FDA) extensively reviewed the scientific literature and concluded that soyfoods are safe for all except those who are allergenic to soy protein.<sup>8</sup> Most of the concerns being raised today were considered by the FDA; although not unexpectedly, considerably more research has been published since their comprehensive

review. 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 specifically to address safety issues.<sup>9</sup> Nevertheless, a similar conclusion was reached through a meta-analysis conducted by Austrian researchers, which was undertaken specifically to address the safety of isoflavone supplements.<sup>10</sup> Still, discussions about the safety of soy continue to appear in the scientific literature and popular media.

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

# How Much Soy Protein do Asians and Americans Consume?

There is considerable confusion about the role soy plays in the diets of Asian populations and about how much soy protein and isoflavones 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 United States.

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 to 2 g per day, representing about 2% of total protein intake.<sup>11</sup> Since soy protein intake is low, isoflavone intake is also very low. This is the case not only due to the low soy protein intake but also because the protein used by the food industry is often quite low in

isoflavones. According to a recent analysis, which used the USDA isoflavone database and the National Health and Nutrition Examination Survey III 24-hour dietary recall data to estimate intake, Americans ingest only 2.35 mg isoflavones daily {Bai, 2014 #17061}. There are approximately 25 mg isoflavones in one cup of soymilk.



## Traditional Japanese diets include 10 g/day soy protein for 10% of total protein needs.

In Japan, the daily intake of soy protein by older individuals is approximately 8 to10 g, which represents slightly more than 10% of their total protein intake.<sup>12</sup> Chinese soy intake varies markedly among regions. Large studies from Shanghai, a high-soy-consuming area, indicate men consume anywhere from about 9 g to as much as 12 to 13 g of soy protein per day,<sup>13</sup> the latter figures represent about 15% of total protein intake.<sup>14</sup> Shanghainese women consume about 9 g per day.<sup>15</sup> Individuals in the upper one-quarter of intake consume about 15 to 20 g soy protein daily. Ten grams of soy protein translates to about 1.5 servings since one serving of a traditional soyfood provides about seven 7 g protein, although some soyfoods can provide considerably more than this amount.

Approximately half of the soy consumed in Japan comes from unfermented foods, with four foods – tofu, miso, natto and fried tofu – accounting for about 90% of all soy consumption.<sup>16,17</sup> In Shanghai, and throughout much of China, most of the soyfoods consumed are unfermented, and soymilk, tofu and processed soy products other than tofu account for about 80% of total soy consumption.<sup>1</sup>

In conclusion, U.S. intake data indicates that most Americans need to substantially increase their soy intake to match the levels common to the traditional cuisines of many Asian populations. Doing so is relatively easy with the wide variety of fermented and unfermented soyfoods readily available.

## 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, at least in some individuals and under certain circumstances. Indeed, some types of in vitro and animal studies have raised concern. The fact that some studies raise concern 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 scientific literature overall. Furthermore, they often don't assign proper weight to the type (in vitro, animal, human, clinical, epidemiologic, etc.) of study being highlighted.

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. 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 affected by the presence of others.<sup>18, 19</sup>

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.<sup>20-25</sup> 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 are naturally found in soybeans.

It is also important to recognize that many highly investigated foods and food components have been linked with adverse effects in a small minority of studies including foods that are recommended by most nutritionists for their healthful properties. For example, whole grains contain phytate (as do soyfoods), which can decrease mineral absorption.<sup>26</sup> Nevertheless, the nutrition community recommends the intake of whole grains because the overwhelming preponderance of evidence indicates that they are nutritionally beneficial.<sup>27, 28</sup> Conclusions about the healthfulness of any food need to be based on the totality of the evidence with careful consideration given to the strengths and weaknesses of study designs.

## **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.<sup>29, 30</sup> Not surprisingly, there has been much investigation of 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 hormonally-influenced cancers.

The vast majority of studies show no effects on circulating reproductive hormone levels in men or women in response to the intake of soy protein or isoflavones.

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

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circulating reproductive hormone levels in men<sup>31, 32</sup> or women<sup>33, 35</sup> in response to intakes of soy protein and 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.<sup>36</sup> 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.<sup>37</sup> In addition, a comprehensive review of the clinical research, found no evidence that isoflavone exposure affects circulating estrogen levels in men.<sup>38</sup> Estrogen is typically thought of as a female hormone but men also synthesize estrogen; in fact, estrogen levels in older men are higher than in older women.<sup>39</sup>

## **Fertility**

Given the large populations of Asian countries that have historically consumed soy, it is somewhat ironic and almost nonsensical that concerns regarding soy intake and 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.<sup>40-42</sup> 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.<sup>43</sup>

However, problems in the latter are thought to have arisen 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.<sup>44,46</sup> 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,<sup>47</sup> which dwarfs the 40 mg typically consumed by older Japanese.<sup>12</sup>

#### 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.

In women, soyfoods appear to increase the length of the menstrual cycle. However, ovulation is not prevented, but is simply delayed by one day.<sup>37</sup> Interestingly, longer cycles are associated with a decreased breast cancer risk.<sup>48</sup> In men, a small pilot epidemiologic study found that very modest soy consumption was associated with lower sperm concentration (sperm count was not decreased) 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, a finding which seems biologically implausible.<sup>49</sup> 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.<sup>49-51</sup> Interestingly, a case report actually noted that isoflavones increased sperm count. Daily isoflavone supplementation for six months in the male partner of an infertile couple with initially low sperm count led to normalization of sperm quality and quantity and allowed the couple to conceive.<sup>52</sup>

## Soy, Isoflavones and Thyroid Function

The first animal studies investigating the effects of soy intake on thyroid function were published 80-years ago.<sup>53-55</sup> Concerns about the anti-thyroid effects of soy are based primarily on in vitro research<sup>56, 57</sup> and studies in rodents administered isolated isoflavones.<sup>58, 59</sup> 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.  $^{\rm 53,\,54,\,60}$ 

A comprehensive review published in 2006 that included 14 clinical trials found that the totality of the evidence showed that neither soyfoods nor isoflavones adversely affect thyroid function in healthy men or women.<sup>61</sup> Studies published since this review are supportive of the conclusion.<sup>62-66</sup> One of these is a 3-year study that included more than 200 postmenopausal women who were given isoflavone supplements at either 80 mg or 120 mg per day (personal communication, Lee Alekel, National Institutes of Health). Another noteworthy study, which supports the safety of soy, was also three years in duration. In this case, 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) investigators study assessed thyroid hormone receptor and retinoid receptor expression from peripheral blood monocytes, which are thought to be very sensitive indicators of thyroid function.<sup>67</sup>

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 because soy protein may interfere to some extent with the absorption of the medication.<sup>68-71</sup> Soy is not unique in this regard, however, as many herbs, drugs, fiber and calcium supplements have similar effects.<sup>72-80</sup> 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.



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

According to a recent position paper from the Pharmacy and Therapeutics Committee of the Lawson Wilkins Pediatric Endocrine Society, it is not necessary to avoid any particular food, or even to take thyroid hormone during the fasting state, but rather, it is important to maintain consistency in medication administration and dietary habits. As long as the medication is taken in a consistent manner and the amount of soyfoods consumed is relatively constant, soyfoods are not problematic.<sup>81</sup>

Questions remain about the effects of soy in individuals whose thyroid function may be compromised, such as subclinical hypothyroid patients and those whose iodine intake is marginal. Individuals consuming soy should be sure their iodine intake is adequate since there is a theoretical basis for postulating that soy could exacerbate thyroid function when iodine intake is inadequate.<sup>82</sup> In the United States, iodine intake is generally quite good, however subpopulations may not be getting sufficient amounts of this mineral.<sup>83</sup> In any event, when an individual whose iodine intake is suboptimal, the appropriate recommendation is to increase iodine intake, not to avoid soyfoods. Furthermore, clinical research published in 2012 strongly suggests even those whose iodine intake is inadequate are unlikely to be adversely affected by soy consumption {Sosvorva, 2012 #16614}.

Only recently has information on the effects of soy intake on thyroid function in subclinical hypothyroid patients become available. Estimates vary, but approximately 5% of the general adult population, and a higher percentage among individuals over the age of 60, have subclinical hypothyroidism.<sup>84</sup> With time, a certain percentage ( $\sim 2-6\%$ /year) of these patients, who have normal triiodothyronine and thyroxine levels but elevated levels of thyroid stimulating hormone, will spontaneously progress to overt hypothyroidism.<sup>85</sup> Only one study, a crossover study in which 60 middle-aged, overweight British patients (52 females) consumed in random order for eight weeks, 30 g isolated soy protein (ISP) containing 2 or 16 mg isoflavones separated by an eight week washout, evaluated the effects of soy on subclinical hypothyroid patients {Sathyapalan, 2011 #14675}. During the entire 6-month study period, 6 (10%) of the participants consuming the higher-isoflavone-ISP progressed to overt hypothyroidism whereas none did in the low isoflavone group. As a result, it was estimated that exposure to 16 mg per day isoflavones increased the likelihood of converting to overt hypothyroidism approximately 3.6-fold.

These results are unexpected given the relatively small isoflavone intake of the study participants and because the progression of subclinical to overt hypothyroidism among Japanese patients is not elevated;<sup>86</sup> nor does Japan have higher rates of hypothyroidism.<sup>87</sup> Nevertheless, the results of the British study can't be dismissed. It is important to note, however, that in the study participants overall (including those who became hypothyroid), there were dramatic reductions in systolic and diastolic blood pressure, insulin resistance and inflammation (as assessed by C-reactive protein). Therefore, in theory, isoflavones markedly reduced risk of cardiovascular disease and diabetes in people with subclinical hypothyroid function. Additional research is required before firm conclusions about the effects of soyfoods on thyroid function in these patients can be made.



#### **Isoflavone Content of Soyfoods**

Soyfood	Serving size	Total (Mg) Isoflavone/ serving
Miso	1 Tbsp	7
Soybeans, Green, Cooked	1⁄2 cup	50
Soybeans, Black, Cooked	½ cup	40
Soybeans, Yellow, Cooked	½ 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 сир	53
Textured Soy Protein, Dry	1⁄4 cup	33
Tempeh	1⁄2 cup	53
Tofu	1⁄2 cup	25

### **Soyfoods and Breast Cancer Risk**

The estrogen-like effects of isoflavones form the theoretical basis for concern that soyfoods are contraindicated for women who are at increased risk of breast cancer and women with estrogen-sensitive breast cancer.<sup>88-92</sup> Isoflavones bind to estrogen receptors, stimulate the growth of human estrogen receptor positive breast cancer cells in vitro and, in certain types of experimental rodent models, stimulate the growth of existing estrogen-responsive mammary tumors.<sup>93, 94</sup> However, not all rodent models show that soy or isoflavones stimulate the growth of existing mammary tumors<sup>95-97</sup> and even in rodent models that do, minimally processed soyfoods do not have this effect.<sup>98</sup> More importantly, the human data indicate that isoflavones, regardless of the source, do not exert harmful effects on breast tissue.

#### Human data indicates that isoflavones, regardless of the source, do not exert harmful effects on breast tissue.

In none of the five clinical trials in which researchers took breast tissue biopsies before and after exposure to isoflavones — three involving postmenopausal, one premenopausal, and one with both pre- and postmenopausal women — were statistically significant effects on cell proliferation noted.<sup>33, 99-102</sup> 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).<sup>103-106</sup> For a comprehensive review of this data, see reference {Messina, 2013 #16493} {Fritz, 2013 #17036}. In contrast to the lack of effects of isoflavones, estrogen plus progestin hormone therapy, which increases breast cancer risk,<sup>107</sup> increases breast tissue density and breast cell proliferation.<sup>108, 109</sup>

The American Cancer Society concluded that soyfoods can be consumed by breast cancer patients.



Even more impressive than the lack of effect of soy noted in the clinical studies are the results of prospective epidemiologic studies, which show that post-diagnosis soy intake improves the prognosis of breast cancer patients. In 2012, Nechuta et al. {Nechuta, 2012 #15652} published a pooled analysis of three studies, two from the United States and one from China, which involved 9,514 patients and included a 7.4-year follow up period. Results showed that higher soy intake was associated with reduced mortality and tumor recurrence:

- 13% reduction in all-cause mortality
- 17% reduction in breast cancer-specific mortality
- 25% reduction in tumor recurrence (statistically significant)

Of the patients in this study, approximately half were from China and half from the United States and there were approximately equal numbers of pre-and postmenopausal women. Sub-analysis of the results failed to find statistically significant differences of soy intake according to whether women were pre-or postmenopausal, estrogen receptor negative or positive, or users or non-users of tamoxifen.

More recently, Chi et al. {Chi, 2013 #16490} conducted a meta-analysis of prospective studies, which included the three studies in the pooled analysis by Nechuta et al. {Nechuta, 2012 #15652} and two small Chinese studies, for a total of 11,206 breast cancer patients. They found post-diagnosis soy intake was associated with statistically significant 15 and 21% reductions in mortality and recurrence, respectively. One of the studies in this meta-analysis also found that soy intake enhanced the efficacy of anastrozole, an aromatase inhibitor. As a result of their findings, Chi et al. {Chi, 2013 #16490} recommended that breast cancer patients consume soyfoods. Both the American Cancer Society {Rock, 2012 #15829} and the American Institute for Cancer Research have concluded that soyfoods can be safely consumed by breast cancer patients.

### **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.<sup>110</sup>

New research indicates that iron absorption from soy may be much higher than previously thought because the majority of iron in soy is in the form of ferritin, which recent research has shown is highly bioavailable.

As noted previously, soybeans, like other legumes and whole grains, are high in phytate, <sup>111</sup> which reduces the absorption of some minerals, including zinc and iron.<sup>112</sup> 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.<sup>113-116</sup> Zinc status is difficult to assess<sup>117, 118</sup> and those consuming a plant-based diet are advised to identify good plant sources of zinc in their diet or to take a zinc supplement.<sup>119-123</sup>

In contrast to zinc, soyfoods are relatively high in iron.<sup>124</sup> 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 either soyfoods or soybean ferritin show it to be highly bioavailable.<sup>125, 126</sup>

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 — such as hamburgers in place of soy burgers or cow's milk in place of soymilk. Results showed there were no statistically significant effects of soy on urinary and serum zinc, serum hemoglobin and iron, or transferrin saturation {Zhou, 2011 #14712}.

While mineral absorption may be very slightly improved with fermentation and may give rise to other potentially beneficial compounds, there is little evidence that these foods are superior to unfermented ones.

In addition to phytate, soybeans are also high in oxalate, another compound that binds calcium and reduces its absorption.<sup>127</sup> Oxalate is one reason that spinach, despite being high in calcium, is not a good source of this mineral. Despite the presence of both phytate and oxalate, calcium absorption from soybeans is surprisingly good.<sup>128</sup> This is also true for calcium-set tofu<sup>129</sup> and calcium-fortified soymilk.<sup>130, 131</sup> 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.<sup>129</sup> When calcium carbonate is used as the fortificant in soymilk, absorption is similar to that seen with cow's milk.<sup>130</sup> In contrast, calcium absorption from soymilk fortified with tricalcium phosphate is about 25% lower than from cow's milk.<sup>132</sup> 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.<sup>130</sup>

There have been questions about the solubility of calcium in soymilk. Some research indicates that, even with vigorous shaking, the calcium in soymilk comes out of the solution.<sup>133</sup> While some sedimentation may occur 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% of all food-induced allergic reactions in the United States.<sup>134</sup> However, these foods are not equally allergenic and allergy to soy protein is relatively rare.<sup>135</sup> A recent nationally representative telephone survey found that an estimated 1 in 2,500 adults reported having a doctor-diagnosed allergy to soy protein.<sup>136</sup> The results of this survey indicate that cow's milk allergy (CMA) is about 40 times more common than soy allergy. The prevalence of soy allergy is higher in children than adults, as children are more likely to have food allergies.<sup>137</sup> Consequently, it is estimated that by that age, only approximately 1 out of 1,000 children are allergic to soy.

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

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 to 14% of these infants will also have a soy protein allergy.<sup>138</sup> However, recently conducted British research found that of the 60% of all infants with CMA were initially treated with soy, only 9% of patients remained symptomatic.<sup>139</sup> In contrast, of the 18% of patients treated with extensively hydrolyzed formula, 29% remained symptomatic. The results from a small retrospective study from Portugal, which evaluated children with persistent CMA, also suggest that soy formula may have advantages over hydrolyzed formulas.<sup>140</sup>

Finally, in 2013, the first systematic review and meta-analysis of studies evaluating the prevalence of IgE-mediated soy allergies in infants and children was published {Katz, 2014 #16956}. The analysis, which included 40 studies, found that the prevalence of soy allergies ranged from 0 to 0.5% for the general population, 0.4 to 3.1% for the referred population (those referred to an allergy clinic for evaluation of food-related problems or other allergy issues), and 0 to 12.9% for allergic (atopic) children. The authors concluded concern about soy allergy is no reason to postpone the use of soy infant formula in IgE-mediated cow's milk allergy infants.

## **Soy Infant Formula**

Soy infant formula (SF) has been in use for more than 50-years. Currently, it accounts for about 13% of all dollars spent on infant formula in the United States. An estimated 20 million infants have used SF over the past 40-years. Soy formula 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 {McCarver, 2011 #15016}. 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.<sup>141-144</sup> Nevertheless, continued research in this area is warranted.

## **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.<sup>145</sup> Numerous human studies demonstrate that processed soy products provide very high-quality protein.<sup>146, 147</sup>

Depending on processing methods, the isoflavone content of these foods can be markedly reduced.<sup>148</sup> 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.ars.usda.gov/services/docs.htm?docid=6382

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 potentially 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.<sup>149, 150</sup> Non-fermented soyfoods have been consumed in Japan<sup>151</sup> and China<sup>152</sup> for at least 500-years and 1,000-years, respectively. In Japan, where many fermented foods are popular, at least half of the total soy consumed comes from foods that are not fermented<sup>16, 17</sup> and in China, most of the soy is consumed in non-fermented form.<sup>1</sup>

## **Summary and Conclusions**

When evaluating the safety of soyfoods, it is imperative to consider the totality of the scientific research and to place weight on studies according to their experimental design. The research overall 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.

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The 70 farmer-directors of USB oversee the investments of the soy checkoff to maximize profit opportunities for all U.S. soybean farmers. These volunteers invest and leverage checkoff funds to increase the value of U.S. soy meal and oil, to ensure U.S. soybean farmers and their customers have the freedom and infrastructure to operate, and to meet the needs of U.S. soy's customers. As stipulated in the federal Soybean Promotion, Research and Consumer Information Act, the USDA Agricultural Marketing Service has oversight responsibilities for USB and the soy checkoff. For more information, please visit SoyConnection.com.