12-20-2017

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Abstract
Soybeans, foods derived from soybeans (e.g., tofu, soymilk, soy infant formula, tempeh) and food and dietary supplement ingredients derived from soybeans (e.g., soybean oil, soybean proteins, isoflavones) have been under intensive research for their health effects especially over the past 25 years. 2 This intensive research derives from the recognition of soybeans as having desirable nutritional properties, containing about twice the protein of other legumes/serving, with good protein quality, such that some soybean protein ingredients have protein digestibility corrected amino acid scores commensurate with proteins thought to be optimal to meet human protein needs (Messina 1999). Soybean oil is used as the nutritional standard fat source for the AIN-93G diet for growing rodents(Reeves 1997); its high content of polyunsaturated fats, including a high ratio of α-linolenic: linoleic acids (~ 1: 7.5)(Messina 1999) make it well-aligned to meet human as well as rodent requirements for n-3 and n-6 essential fatty acids.

Disciplines
Food Science | Human and Clinical Nutrition

Chapter 23. Nutritional, nutraceutical and functional properties of soybeans

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Introduction

Soybeans, foods derived from soybeans (e.g., tofu, soymilk, soy infant formula, tempeh) and food and dietary supplement ingredients derived from soybeans (e.g., soybean oil, soybean proteins, isoflavones) have been under intensive research for their health effects especially over the past 25 years.

This intensive research derives from the recognition of soybeans as having desirable nutritional properties, containing about twice the protein of other legumes/serving, with good protein quality, such that some soybean protein ingredients have protein digestibility corrected amino acid scores commensurate with proteins thought to be optimal to meet human protein needs (Messina 1999). Soybean oil is used as the nutritional standard fat source for the AIN-93G diet for growing rodents(Reeves 1997); its high content of polyunsaturated fats, including a high ratio of α-linolenic: linoleic acids (~ 1: 7.5)(Messina 1999) make it well-aligned to meet human as well as rodent requirements for n-3 and n-6 essential fatty acids.

Soybeans are also a nearly unique source of isoflavones in the human diet. These phytoestrogens associated with soybean proteins may mimic human estrogens in useful ways, such as in alleviating menopausal symptoms, and perhaps protecting from heart disease and some types of cancer(Messina 1999). In 1999, a US Food and Drug Administration health claim was approved stating that soybean foods and foods with ingredients that provide 25 g of soybean protein per day as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease(Stein 2000).

In South Korea, several soybean ingredients are endorsed by the government's functional food code, permitted to carry claims of health benefits at specified doses. Soy protein, soy isoflavones and soy fiber as well as lecithin are listed in South Korea's functional food code(Lupton and others 2014). This review will examine recent human clinical studies related to the efficacy and safety of soybean foods and food or dietary supplement ingredients including soybean oils, proteins, isoflavones and selected other compounds for which soybeans are a significant source.

Nutritional effects of soybean oils

A recent systematic literature review of 15 randomized controlled trials of nearly 60,000 participants linked decreased intake of saturated fats in favor of increased intake of polyunsaturated fats (PUFAs) with modest decrease of cardiovascular disease risk(Hooper and others 2015), supporting a positive role for soybean oil in human health. However, partial hydrogenation of soybean and other vegetable oils to yield cheap, functional food fats suitable for production of pastries and other baked goods was determined also to increase dietary content of trans-fatty acids.

A 35 day randomized cross-over study was performed with 30 mildly hypercholesterolemic postmenopausal women (LDL cholesterol ≥ 120 mg/dL) who consumed diets with 25% of energy from fat, 2/3 of which was from either partially hydrogenated soybean oil (PHSO) or corn oil. The corn oil diet lowered LDL cholesterol by 10% compared with the PHSO diet; trans-fatty acid content was 4.3% of energy in the PHSO diet vs. 0.3% in the corn oil diet; PUFA content of the corn oil diet was twice that of the PHSO diet(Vega-Lopez and others 2009).

Various strategies to substitute other fats and oils for trans-fatty acid sources reduced cardiovascular disease risk factors according to a meta-analysis of controlled human trials (Mozaffarian and Clarke 2009). Some recent research has developed ways to remove trans-fatty acids from PHSOs. An example is the hydrolysis of fatty acids from PHSO with a commercially available *Candida antarctica* lipase A favoring hydrolysis of trans- over cis-unsaturated fatty acids by ~4-fold. This processing was capable of removing ~3/4 of the trans-fatty acids from PHSO(Jala and others 2013). It seems feasible to improve PHSO products by removing their trans-fatty acids. But retaining functionality in terms of good eating quality of baked goods will also require attention.

A recent 4 week study of 34 participants who ate 20 g of either palm oil mayonnaise or soybean oil mayonnaise showed significantly lower total cholesterol (185 mg/dL vs 196 mg/dL) and LDL cholesterol (118 mg/dL vs. 125 mg/dL) after soybean oil intake compared with palm oil(Karupaiah and others 2016). This specifically demonstrated a modest benefit of soybean oil compared with another common food fat. Information on the connection between dietary fatty acid composition and heart disease continues to be refined. Soybean oil is among the healthier choices in dietary fats, but even with removal of trans fats from PHSO, the lesser PUFA content of PHSO compared with soybean oil warrants consumer advice to choose diets de-emphasizing PHSO–containing foods, as one among many strategies to diminish cardiovascular disease risk.

Nutritional and nutraceutical functions of soybean proteins and associated constituents on cardiovascular disease risk factors

Studies continue to emerge on the efficacy of soybean protein to benefit human health. This review will attempt to distinguish among human clinical studies that focused on providing soybean proteins per se vs. studies providing soybean proteins within foods from whole soybeans. In human clinical trials, few studies have distinguished effects of soybean proteins from the effects of the isoflavones or other constituents that are carried into the diet by soybean proteins.

A study of groups of 30-33 moderately hypercholesterolemic women showed that after 12 weeks of supplementing their diets with 42 g of protein from milk, soy with 80 mg isoflavones or soy with only trace amounts of isoflavones, LDL cholesterol was lowered to a greater extent by soy protein containing isoflavones than by soy protein without isoflavones. Neither treatment differed from milk protein in final LDL cholesterol(Gardner and others 2001).

An abstract from a trial published at the same time, of a study of groups of 16-18 moderately hypercholesterolemic women given 28 g supplemental protein for 4 weeks showed that soy beta-conglycinin with 60 mg isoflavones lowered LDL and total cholesterol at 4 weeks compared with baseline but beta-conglycinin without isoflavones did not. Women given a casein control treatment also showed lower LDL cholesterol after 4 weeks compared with baseline. The three treatments did not differ in effects on LDL cholesterol or total cholesterol after 4 weeks(Lee and others 2001).

A group of 90 postmenopausal, prehypertensive, moderately hypercholesterolemic women given 40 g whole soy flour containing 50 mg isoflavones showed lower LDL cholesterol and C-reactive protein after 6 months of treatment compared with groups of 90 women given 60 mg daidzein in milk powder or milk powder alone over that time period. All 270 women were shown to produce equol, a daidzein metabolite of interest to various health endpoints, so the ability to make equol did not efficacy of isoflavone-containing foods(Liu and others 2015b).

Groups of 80-82 hypercholesterolemic adults were given 25 g soy protein, 12.5 g soy protein + 12.5 g whey protein or 25 g whey protein; none of the three treatments lowered LDL cholesterol after 6 weeks of treatment(Padhi and others 2015).

A meta-analysis of 5 clinical trials of a total of 104 hypercholesterolemic participants given soy isoflavones (15 mg/d or more) in soy protein or as a supplement for 3-6 months compared with control participants given soy protein with < 5 mg isoflavones/d or a placebo supplement showed no benefit of isoflavones to lower LDL cholesterol(Qin and others 2013). A meta-analysis that included 35 randomized controlled trials of soy foods, soy ingredients and/or isoflavones examined effects on LDL-cholesterol in 2670 participants given these products for 1-12 months, with a mean soy protein intake of of 30 g (range of 14-50 g/d). This analysis showed mean benefit of soy products of a 5 mg/dL decrease in total and LDL-cholesterol. Isoflavones per se showed no benefit on serum lipids(Tokede and others 2015).

These recent studies support a modest benefit of foods or ingredients providing soy protein and its associated isoflavones on serum lipids associated with cardiovascular disease risk. Extreme variability among participants in isoflavone bioavailability as observed, for example, by Liu et al.(Liu and others 2015b) may be interfering with an ability to discern an action of isoflavones. The importance of isoflavones bioavailability to lessening cholesterol was illustrated in a study of 38 Golden Syrian hamsters fed soy protein for 4 weeks. Compared with casein-fed controls, the soy protein-fed hamsters had significantly lower LDL-cholesterol. But **all** of the cholesterol-lowering effect of soy protein could be attributed to 9 of the 38 individuals who excreted about 4 times greater amounts of isoflavones than did the majority of the hamsters(Ye and others 2006). A similar proportion of women (~25%) fed soy foods in single meals showed more than 2-fold greater urinary excretion of isoflavones than did the majority of participants(Xu and others 1995). This phenomenon was apparently determined by the gut microbiome, as isoflavone-degrading microbial species have been putatively identified as common in the human gut in a study using genomic methods to identify human fecal bacterial species, associating bacterial species profiles with fecal isoflavones degradation in anaerobic incubations, and confirming the ability of particular bacterial species when added back to human feces to cause isoflavones disappearance from the fecal incubation mixtures(Renouf and Hendrich 2011). It remains to be determined if a subset of humans with a “high isoflavones excreting” phenotype may account for the observed modest benefits on serum lipids of ingestion of soy protein or soy foods. It seems that the combination of soy protein and isoflavones but not isoflavones per se are required for the cholesterol-lowering effects of soy protein.

Soybean proteins and associated constituents: effects on blood pressure, kidney and arterial function

Research has been done recently on other effects of soybean foods and ingredients on the cardiovascular system, beyond serum lipids. Sixty post-menopausal women replaced non-soy protein with 25 g of protein from soy nuts for 8 weeks. After 8 weeks on diets with and without the soy nuts, systolic blood pressure and C-reactive protein (CRP) were decreased significantly by ingesting soy in 49 women who did not have characteristics of metabolic syndrome.

In 11 women with metabolic syndrome, only those 4 of these 11 women who were equol producers showed decreased diastolic blood pressure, CRP, and serum triglycerides. 28 of 49 women without metabolic syndrome who were equol producers also showed significantly decreased diastolic blood pressure after eating soy nuts(Acharjee and others 2015). This suggests a novel strategy to benefit individuals with metabolic syndrome: introduction of equol-producing bacteria into their guts. This would require significant preliminary work to establish the safety and efficacy of such a manipulation of human gut microbes.

In groups of 90 prehypertensive, postmenopausal women, 40 g soy flour or 60 mg daidzein in milk powder both prevented decreased glomerular filtration rate that occurred in women given 40 g milk powder per day as a placebo after 6 months(Liu and others 2014). In this study, neither blood pressure nor brachial flow-mediated dilation, an indicator of arterial function, were different between treatment groups(Liu and others 2015b). Based on limited data, healthy postmenopausal women may particularly benefit from whole soy foods to help to maintain healthy blood pressure. More work on this potential benefit of soybean foods in both sexes and across the lifespan is indicated.

Soybean proteins and associated constituents: effects on blood glucose and diabetes

Effects of soy on blood glucose is another important public health interest, with burgeoning rates of type 2 diabetes across the globe. Three groups of ~50 women with fasting glucose status of 100-126 mg/dL, 2 h postprandial blood glucose of 140-200 mg/dL or newly diagnosed type 2 diabetes not requiring medication were given 10 g soy protein alone, soy protein with 50 mg daidzein or with 50 mg genistein for 6 months. Responses to oral glucose tolerance tests and fasting glucose and hemoglobin A1C did not differ between the treatments(Ye and others 2015).

Adding tofu (25 g protein) to a standard meal of 50 g glucose from rice significantly diminished glucose response over time compared with rice alone, whereas 25 g of protein from chicken, fish or egg white did not significantly decrease the blood glucose response to rice in 15 Chinese men in a randomized cross-over study(Quek and others 2016). This effect of tofu suggests a benefit for glycemic control in individuals with pre-diabetes or diabetes. The mechanism for this effect is not yet clear, but potentially suggests a role for isoflavones as the other proteins fed are not associated with these compounds.

In a group of 34 women with gestational diabetes, substituting soy protein for half of the animal protein in their diets for 6 weeks during gestation improved fasting plasma glucose, triglycerides and homeostatic model assessment of insulin resistance (HOMA-IR) status compared with a control group of 34 women, matched for week of gestation and BMI(Jamilian and Asemi 2015). Diets provided 0.8 g total protein/kg body weight. At birth, the women who had eaten soy protein had significantly fewer babies with hyperbilirubinemia or the need to be hospitalized. Additional studies are needed to confirm this finding that promises an important benefit for pregnant women and newborn infants. The inclusion of soy protein in human diets, rather than isoflavones per se, seems to confer benefits on blood glucose, but men have not been studied much. Because type 2 diabetes is strongly associated with obesity,

obesity prevention as well as approaches to preventing and mitigating diabetes might well include further study of soybean foods and soy protein.

Soybean proteins and associated constituents: effects on obesity

Type 2 diabetes risk is the disease most strongly associated with obesity(Eckel and others 2011). It follows that some nutrition research has been directed toward the effects of soybean foods and components on obesity. Over 16 weeks in a randomized design, groups of approximately 60 eighteen-year-old women consumed soy protein or casein beverages containing 20 g protein and 500 kcals (Berger and others 2014). Neither protein shake prevented slight weight gain (~ 1lb) in this population. A high protein soy snack delayed onset time of eating dinner and decreased appetite in 31 adolescents (age 17 years) compared with a high fat snack or no snack(Leidy and others 2015). In 21 adults fed lunch meals matched for macronutrient content either with beef or soy as the protein source (24 g of each), onset of eating dinner and overall appetite were similar for both treatments(Douglas and others 2015). These studies suggest that soy protein may not especially benefit satiety or prevent obesity. Soy protein snacks might be useful in controlling appetite, but probably not more so than other high protein foods of good amino acid quality.

Soybean proteins and associated constituents: effects on cancer risk

Human epidemiological studies have tended to support the association of decreased cancer risk with increased intake of soybean foods(Messina and others 1994). This association remains the subject of considerable research. Genistein has been investigated in animal models and a small number of clinical trials of prostate cancer patients(Perabo and others 2008). The animal models indicate a potential for genistein to prevent prostate cancer. The human trials have studied prostate cancer patients for varying lengths of time, but for not longer than 6 months, with no obvious benefits across a range of doses (60-600 mg genistein/day) and across a range of cancer stages(Perabo and others 2008).

A more recent meta-analysis of 2 prostate cancer prevention trials and 6 prostate cancer treatment trials indicated a significant reduction of prostate cancer risk, especially in men older than 65 years taking 60 mg isoflavones/day for 12 months or soy protein isolate containing isoflavones for 6 months compared with placebo treatments(van Die and others 2014). The prostate cancer treatment trials of soy/isoflavones showed no clear benefits of soy components on prostate-specific antigen (PSA) or sex hormones(van Die and others 2014).

In a review of breast cancer epidemiological studies of the relation between soy foods and/or isoflavone contents of the body, only one of the 6 large prospective cohort studies showed a positive association between miso soup and dietary isoflavone intake and decreased breast cancer risk (179 cases of breast cancer in 21,852 Japanese women)(Enderlin and others 2009). The other 5 such studies showed no association between dietary soy intake and breast cancer risk, in studies totaling more than 200,000 women in Great Britain, France, Japan and the US. It may be that the range of soy food intakes studied was too narrow to see a benefit of soy. Of 28 case control studies associating soy/isoflavone intake with breast cancer risk, more than half the studies showed decreased risk of breast cancer with increased soy/isoflavone intake, but 2 studies showed increased risk of breast cancer with increased isoflavone intake(Enderlin and others 2009). Groups of 70 women recently diagnosed with early stage breast cancer ate 26 g of soy protein or milk protein for 7-30 days before breast surgery. In a subset of women clustered as having especially high plasma genistein levels after treatment, their mammary tissue showed more than 2-fold greater expression of a set of genes (e.g., fibroblast growth factor receptor-2 (FGFR2)) related to stimulation of cell proliferation(Shike and others 2014).

Because isoflavones are estrogenic, and some mammary neoplasms proliferate in response to estrogen(Renoir and others 2013), it is reasonable to be cautious in recommending soy foods to prevent breast cancer as the research cited above supports the concept that some women with breast cancer might be harmed by soy foods or isoflavones supplements. A clinical trial of women at high risk for breast cancer or who had previously had breast cancer provided 50 mg isoflavones or a placebo to groups of 46 or 49 women, respectively, for 12 months. Mammogram density, an early indicator of breast cancer, did not differ between the two groups(Wu and others 2015). Thus recent work does not support soy or isoflavone interventions for women with breast cancer, breast cancer survivors or women at high risk for breast cancer. Soy or isoflavones may not be harmful to most of those women, but more progress in individualizing cancer prevention strategies is needed. Soy foods remain somewhat promising in their ability to **prevent** breast and prostate cancer, and identification of characteristics that can better guide decisions on cancer preventive strategies may be on the near horizon.

Soybean proteins and associated constituents: effects on menopause

Along with increased risk of chronic diseases such as cancer, aging involves menopause. Soy protein, presumably due to estrogenic effects of isoflavones seems to benefit symptoms of menopause and post-menopause. A randomized double-blind trial of groups of 20 post-menopausal women given soy powder with 90 mg isoflavones or low dose hormone therapy for 16 weeks showed reduced vaginal dryness with both of these treatments compared with placebo(Carmignani and others 2015). Only the hormone therapy improved vaginal maturation index.

In a group of 30 postmenopausal women in Iran given 33 g soy protein containing 54 mg isoflavones/day for 8 weeks, menopausal symptoms according to the Kupperman index abated significantly compared with a group of 31 placebo-treated women(Husain and others 2015). Post-menopausal women given isoflavone supplements ranging from 50-220 mg/d for 50 days in a randomized cross-over design (n = 14) showed improved bone calcium retention compared with baseline, but did not experience as much bone calcium retention as when given risedronate(Pawlowski and others 2015). The participants in this study experienced this benefit of isoflavones regardless of their ability to produce equol.

Recently, an analysis of numerous studies on isoflavones and vasomotor symptoms (hot flushes) during menopause resulted in a consensus that doses of isoflavones up to 150 mg/day may serve as a first choice option for relief of these symptoms that is both effective and safe(Schmidt and others 2016). Thus, with respect to several aspects of health during and after menopause, soy foods containing isoflavones and isoflavones as dietary supplements may be recommended.

Soybean proteins and associated components: effects on reproductive function

The estrogenicity of soybean foods, ingredients and supplements, while apparently beneficial during menopause has also put these dietary constituents under scrutiny for adverse effects on reproductive function(Maqbool and others 2016). Very high doses of phytoestrogenic isoflavones from subterranean clover in livestock forage caused infertility in cattle and sheep(Lindner 1976). Claims that the long history of use of soybean foods in human diets has not been associated with adverse reproductive effects have led to research.

A long term project on infant formula quality that examined nutritional effects of soy and cow's milk formulas presented the chance to examine health effects of early dietary exposure to soybean isoflavones. Adults ages 20-34 who had ingested soy (n = 248) or cow's milk formula (n = 563) as infants showed no differences in reproductive history or function except slightly more menstrual discomfort and slightly longer menstruation in women fed soy formula compared with those fed cow's milk formula as babies(Strom and others 2001).

A recent analysis of reproductive organ development in children showed that groups of ~30 infants fed breast milk or formulas based on soy milk or cow's milk for the first year of life did not differ at 5 years of age in reproductive organ size (breast bud, ovaries, uteri, testes) assessed by sonogram(Andres and others 2015). The intent is for follow up of these children into adolescence, which will be important. Although the research is yet limited it supports a long history of use of soy infant formula without apparent longterm adverse reproductive effects.

In groups of ~70 healthy postmenopausal women given 80 or 120 mg isoflavones/day or placebo for 36 mos, endometrial thickness declined across this time period but did not differ among treatments. Circulating hormone levels (estradiol, estrone sulfate and thyroxine) and adverse events did not differ between treatments(Alekel and others 2015), supporting long term safety of isoflavone supplements after menopause. To date, soybean isoflavones either in soy infant formula or as dietary supplements, showed no ill effects on human reproductive system development or function.

Soybean proteins and other soybean associated components: effects on cognition

Because intake of isoflavones or soybean foods has been much studied at least in older women, effects of soy/isoflavones on cognition, which tends to decline with aging, have also been studied. A meta-analysis of 10 randomized placebo-controlled trials of soy isoflavones with a total of more than 1000 postmenopausal participants showed that mean summary cognitive function and visual memory test scores were significantly improved in women taking isoflavone supplements for 6 weeks-30 months(Cheng and others 2015). Six of the 10 trials included showed such a benefit of isoflavones; none of the included trials showed a detriment of isoflavones to cognitive function.

In 300 women given 25 g milk protein powder placebo or 25 g soy protein with 90 mg isoflavones for a mean of 2.7 years, composite global cognition score was not significantly associated with change in urinary isoflavones excretion over the trial period. General intelligence score was slightly but significantly inversely associated with urinary isoflavone excretion(St John and others 2014). This needs further investigation. In groups of 65 individuals with Alzheimer's disease, 100 mg isoflavones/day for 6 months showed no benefit versus a placebo across several cognitive and mood tests(Gleason and others 2015).

These results together support more study, especially of the ability of isoflavone supplements to prevent cognitive decline before the onset of overt cognitive disease. Soy lecithin may be of benefit as well. A 3 month trial of 300 mg phosphatidyl serine and 240 mg phosphatidic acid/day (PS + PA, derived from soy lecithin) in 31 healthy elders (60-80 years old) showed improved memory and less seasonal depression compared with 25 participants on a placebo(More and others 2014). A 2 month study of these same treatments in individuals with Alzheimer's disease showed maintenance of daily functioning and stabilization of mood in 53 participants on PS + PA, whereas daily functioning and positive mood declined in 39 participants given a placebo(More and others 2014). These trials indicate that research on soy foods and their components needs to continue in this field, and not just focused on isoflavones.

Other health or adverse effects of soybean foods and ingredients

Soybean-based infant formulas have a long history of use as an alternative to cow's milk formulas when breast feeding is not feasible. The addition of fructooligosaccharides (FOS) has been explored as a prebiotic strategy to increase infant gut contents of probiotic (beneficial) bacteria, mainly of the genera *Bifidobacteria* and *Lactobacilli*, which may protect from infectious illnesses. But cow's milk formulas containing FOS caused softer, watery stools, raising concerns about FOS as a formula additive. A recent clinical trial provided groups of ~50 newborn full term infants with soy formula or one of 2 soy formulas + FOS (2.5 g/L) for the first month of life(Lasekan and others 2015). No differences were found in stool consistency, body weight gain, formula intake, vomiting or hydration status (urine specific gravity) between the 3 treatment groups. This suggests that FOS supplementation of soy formula is feasible, and might provide a useful alternative to cow's milk formulas containing FOS.

Beneficial interactions between foods or food ingredients and specific nutrients is an interesting and unstudied area. A recent example involving soybean saponins perhaps suggests that this topic deserves further attention. ZIP4 proteins in the small intestine are essential for zinc uptake. Enhancing ZIP4 expression and/or function enhances zinc absorption. Poor zinc status is a significant problem in low income world regions and in elders. Soybean extracts were tested for effects on ZIP4 in cell models simulating the human small intestine, including Caco-2 cells. Soyasaponin-rich soy extract and soyasaponin Bb, a major saponin glucoside in soybeans, in similar concentrations in purified form as present in the soy extract, significantly increased ZIP4 expression by blocking ZIP4 degradation in AsPC1 cells (human pancreatic tumor cells that express ZIP4 similarly to the human intestine)(Ayako and others 2015). Soyasaponins are not appreciably absorbed by humans, as shown in a small short term feeding trial of 8 women given a soyasaponin extract that showed the absence of saponins or their deglucosylated metabolites in urine(Hu and others 2004). It is feasible that the effect of soyasaponin Bb on ZIP4 derives from cell surface interactions between the saponin and ZIP4 protein domains. Effects of soybean foods or soyasaponin Bb on zinc status will need to be confirmed in vivo; such research is warranted based on the prospect of a novel benefit of soybean foods.

Soy protein might adversely influence heme iron uptake in comparison with pea or lentil proteins, according to a study of 15 women given single doses of each protein with heme iron. Soy protein permitted 10-20 % less heme iron absorption than did the other legume proteins(Weinborn and others 2015). The implications of this finding for iron uptake from intact foods remains to be seen, and would seem to be of practical significance only in extreme dietary circumstances such as someone ingesting very limited protein sources for fairly long periods of time that still included a source of heme iron (meat or seafood). Important interactions between soybean foods and nutrient uptake seemingly would have been discovered by now, given how commonly soybeans are included in human diets, at least in some major world regions. These studies on iron(Weinborn and others 2015) and zinc(Ayako and others 2015) suggest some need for such investigation.

Another interaction between soybean food intake and a nutritionally important endogenous substance, uric acid was studied in 450 postmenopausal women with prehypertension or prediabetes in China(Liu and others 2015a); data from 2 trials were combined in which soy protein or soy flour, or an analogous amount of isoflavone supplement was provided and compared with milk powder for 6 months. Isoflavones or milk powder treatment groups showed 10% decrease in serum uric acid from baseline, and soybean protein/flour caused less decrease in uric acid (5% decrease). Participants were asked to limit their intake of soy foods to 2 servings per week during the trial which might have caused the decrease in uric acid from baseline. It might be worth determining mechanisms for decreased uric acid by isoflavones or milk powder and what constituents in soy foods might interfere with that seeming effect of isoflavones.

A recent systematic review of botanical dietary supplements including soybean isoflavone supplements. 95 scientific papers reporting adverse effects of soybean supplements most prominently noted in 30 of the papers(Di Lorenzo and others 2015) the well-known allergenicity of soybean proteins which are among the eight major food allergens(Sathe and others 2016). The ingestion of a brand of soy milk containing seaweed disrupted thyroid function in 8 patients, but this seemed very likely to be due to an exceptionally high level of iodine from the seaweed in this soy milk (~25 mg/L)(Crawford and others 2010), and not due to the soy milk. Causal links between ingestion of soybean isoflavones and reproductive organ functional changes reported as adverse effects in this systematic review remain to be established. In summary, recent studies indicate no reason to worry about potential harm from intake of soy infant formulas. The human food supply contains an increasingly complex array of ingredients and mixtures, including dietary supplements. "Buyer beware" remains worthy advice in the use of food and supplements not bearing scientifically validated health claims. Food producers should also be vigilant to assure that potentially harmful amounts of constituents, which may even be essential nutrients (e.g. iodine), are avoided.

Summary and conclusions

Soybean foods, soy proteins and/or isoflavones, which are uniquely associated with soy protein, may benefit human health by lessening some cardiovascular disease risk factors, diminishing cancer risk and cognitive decline with aging. Isoflavones have been recently recommended by gynecological researchers as a first line of remedy for menopausal vasomotor symptoms. Considerable inter-individual variability in uptake of isoflavones due to their apparent degradation by gut microbes remains an impediment to ascertaining the health efficacy of these soybean constituents; more attention to this aspect of these compounds is consistent with advances in individualizing chronic disease prevention approaches. Human diets may benefit from increased inclusion of soybean foods.

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