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Review Article

Soybean Nutrition

Sean O'Keefe[1], Laurie Bianchi[2] and Jyotsna Sharman[2]*

[1]Department of Food Science and Technology, Virginia Polytechnic Institute and State University, USA
[2]Department of Nutrition and Dietetics, Radford University, USA

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***Corresponding author**

Jyotsna Sharman, Department of Nutrition and Dietetics, Radford University, USA, Email: Jsharman2@radford.edu

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Abstract

This review is intended to provide information on recent research on the nutritional composition of the soybean, how soy can be used in the vegetarian and vegan diet, its use in diet therapy for some diseases, and how isoflavones in the soybean are related to health outcomes. Much research has been focused on the nutritional composition of soybeans in the past 30 years; in particular breeding and genetic engineering have the potential to alter soybeans. The protein, oil, and bioactive components of soy have been closely scrutinized; recent advances and challenges are outlined. The use of soy products has increased dramatically in the U.S. due to recognized correlations with positive health outcomes in those populations who consume much soy food products. Therefore, soy consumption has also been well studied for meeting nutritional needs of vegetarians and vegans, and those with health issues such as chronic kidney disease, cardiovascular disease, diabetes, and cancer. Finally, bioactive components of soybean, including isoflavones, have emerging promise, but there are conflicting results regarding correlations and effects on health outcomes, including reducing menopausal symptoms, reducing risk of bone disease and some cancers. The purpose of this review is to provide information regarding recent advances in the composition of the soybean, its use in health and disease.

History of the Soybean

The soybean plant, Glycine soja (wild) Glycine max (cultivated), has a long history of cultivation with an estimated beginning in China around 1700-1100 years C.E [1-3]. Soy was introduced to other regions beyond China such as Indonesia, the Philippines, and Japan during the first century C.E. As Europeans traveled to China and Japan, they were introduced to food products made from soybean such as miso and soy sauce, but did not make the connection between these products and the soybean. It was not until later in the 1700's that the soybean was introduced to Europe. The soybean plant was first brought to the U.S. in 1765 by Samuel Bowen [1]. It did not reach immediate success as a cultivated crop in the U.S. Hymowitz [1] provides an excellent summary of soy's rocky road to a widely cultivated crop. Initially, it had early appeal in the late 1800's/early 1900's in the U.S. as a high protein livestock feed. Since, the soybean has become one of the largest crops in the world with global production estimated at 293.97 MMT for 2014/15 [4]. Soy foods retail sales in the U.S. alone is estimated at $4.5 billion in 2013 [5]. The soybean is now one of the most highly genetically modified plants; in fact genome sequencing for this plant was accomplished before that of corn and cotton [6]. There is an abundance of research on the soybean and how soy affects human and animal nutrition.

Research in alterations of nutrient composition of the soybean

Protein

The soybean is a valuable legume because it does provide all of the essential amino acids for humans; however it is relatively low in the sulfur containing amino acids, cysteine and methionine. It is one of the few legumes that can be consumed as a complete protein. The soybean is comprised of approximately 37-42% protein [7-12]. The two main proteins of soybean are 11S glycinin, and 7S β-conglycinin, both globular in structure. Glycinins composed of acid/base polypeptide units and contains a higher percentage of sulfur-containing amino acids [8,13]. For this reason, a higher ratio of glycinin to β-conglycinin improves the protein quality of soy. β-conglycinins, a glycoprotein that has 3 homologous subunits, α, α', and β. Medic [12] and Wang [14] provide in depth reviews of the structure of these proteins. Nitrogen and sulfur fertilization can affect accumulation of one or the other of these proteins [15,16].

Soy protein is also responsible for initiating an allergenic response in susceptible individuals. Indeed, soy is one of the 8 foods responsible for causing the majority of food allergies. Both glycinin and β-conglycinin are believed to be responsible as allergens [17,18]. There are also other proteins, such as the protease inhibitors and whey fractions, within the soybean that cause allergenic responses [14], and there is the potential to breed and genetically modify the soybean to decrease allergenicity of soybean for human consumption [18].

Other proteins within the soybean are anti nutritional factors. Lectins are hemagglutinins; when consumed raw, lectins often cause alterations in small bowel histology and affect growth of animal

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[19-22]. Protease inhibitors comprise 6% of the total protein in the bean [9]. Protease inhibitors are responsible for reduction in protein hydrolysis in small bowel digestion. The two that are common to soybean include Bowman-Birk and Kunitz [14,16,23-25]. Although protease inhibitors are a relatively small percentage of the protein [25], consumed raw and in large amounts, they can impair protein digestion, and thus growth and affect pancreas physiology [26]. Heat inactivates these protease inhibitors [26,27] and lectin [28]. Since soy is usually heated for human consumption, they may not pose a problem to humans; however they can be a problem for livestock animals if they consume raw soy in their feed.

Because soybeans provide a relevant source of protein for livestock as well as humans, research has been focused on increasing the yield and quality of protein in the soybean, although not always successfully. It has been shown that protein content can be increased to as much as 50% of dry weight of the bean, however problems with yield of overall crop and decreased oil composition challenge this advancement [7,8,12,29]. It has been shown that increased nitrogen application to the bean has an inverse relationship with cysteine concentration of the bean, which is an undesirable consequence as a lower cysteine concentration further lowers biological value of soy [16,30]. Breeding for high amounts of a cysteine rich protein from Asian soybean with North American lines did not increase sulfur containing amino acids as cysteine appeared to be drawn from other cysteine rich proteins [31]. Alternatively, cysteine levels can be increased, but may result in increased production of protease inhibitors in the bean [32]; breeding for increased methionine has been shown to increase the amount of allergenic 2S albumin proteins also [33]. Medic [12] also provides a review of how geographic and environmental conditions affect seed composition.

Finally, producing a soybean in which there is a decreased amount of proteins that are anti nutritional factors is a possible factor in improving protein quality [34]. This area has more of an impact on feed animals as soy is usually heated for human consumption, inactivating the protease inhibitors. Goyal [9] demonstrated that of 140 different genotypes of soybean, the range of Trypsin Inhibitor Activity (TIA) was 11.3-142.5 mg/g soybean powder. Soybean genotypes were placed in different clusters based on origin of the soybean and biochemical similarity. The average TIA of all 140 genotypes was 68.8 mg TIA/g soy powder, but of the 7 clusters, 3 clusters containing 55 genotypes had less than the average range of 20.6-51.4 mg TIA/g soy powder. Thus, those genotypes that demonstrate lower trypsin inhibitor activity may be appropriate for livestock in which raw/low heat treated soy is consumed.

There is a great body of work accomplished on improving protein quality and quantity and still much potential in this area [29,30]. Altering the protein content of the soybean for functional purposes is also a possible area of research [35].

Lipid

Soybean contributes to 28% of the world's edible oil [36,37], and is second in production of edible oils to palm oil. It should be noted that oils are produced from plant sources for other purposes than food such as detergents, candles, pharmaceuticals, and biofuels; considering these products, soy contributes to half of the world production of oil [37]. Edible oils from soybean are processed to create numerous food products such as salad dressings, margarines, and spreads. Oil comprises of 17-19% of soybean dry weight, of which most is polyunsaturated fatty acids [7,8,13,38,39]. Fatty acid profile will depend on the genotype [39], but in general, the majority of fatty acids consist of linoleic acid (53-54%). The oil is obtained from the bean by solvent extraction from the bean pod [40]. The lipid fraction is then processed and refined to remove impurities such as pigments, proteins, carbohydrates, and other chemicals that affect taste and appearance [37]. Within the lipid fraction exists phospholipids (collectively called lecithin) [41] and tocopherols [42]. A degumming process removes phospholipids. The tocopherols act as natural antioxidants, a positive role for soy oil since it is quite susceptible to oxidative rancidity [43,44].

The lipid content of soybeans in wild types is known for its high unsaturated fatty acid content [38]. Because of the high unsaturated fatty acid content in soy oil, it is considered to have a more beneficial lipid profile desired for human consumption. A higher unsaturated fatty acid intake is associated with lower risk of cardiovascular disease and, α-linolenic acid present in soy oil is a precursor of EPA and DHA, both of which are studied for their proposed benefit for cardiovascular and brain health.

One major advance in the production of soy oil has been the use of genetically modified soybeans to alter the fatty acid profile of the oil. High oleic acid soybeans have been genetically designed as a greater percentage of oleic acid can improve the oxidative stability of the oil [36]. DuPont developed a genetically modified high oleic acid soybean in the mid 1990's. Other high oleic acid lines, with greater than 80% to greater than 90% oleic acid (percentage of all fatty acids) were developed and approved for production and commercialization on a limited scale in 1998 and 2002 in the U.S. and Japan respectively [45].

A genome sequencing project, Qualisoy, was developed from the Better Bean Initiative. This program has worked to improve soybean lines with altered fatty acid compositions, protein compositions, and creation of specific varieties for tofu, soy drinks, or natto [6,45].

Currently there is need to provide a soy oil that provides necessary fatty acid profile for desirable cooking/processing qualities without trans fatty acids in view of the FDA's recent elimination of GRAS status for trans fats. The fatty acid profiles of soybean oils have high 18:2n-6 (~50%) and significant 18:3n-3 (~10%) contents, making the oil susceptible to oxidation. Partial hydrogenation produces trans isomers from the polyunsaturated fatty acids in soybean oil, lowering the total unsaturation and oxidation rates. While trans fatty acids are not found in non-processed soybean oils, trans isomers, mainly positional trans isomers, are formed in partially hydrogenated soybean oils at relatively high levels [46]. Geometrical isomers of 18:2n-6 and 18:3n-3 are found in deodorized oils at low total levels [47] but the relative amount of isomerization of 18:2n-6 and 18:3n-3 can be significant, depending on the time-temperature of deodorization [48]. There are genetically modified low linolenic acid soybeans that have no trans fats [49]. Fully hydrogenated soybean oil interesterified with soy oil blends have also been studied to create more stable oils [50]. Genetically modified high stearic acid soy oil may be a product in the future that allows for physical properties of saturated fats but without the negative effects on serum lipid profiles [6,45].

The lecithin that is isolated from the degumming process is used in food products as an emulsifier. Soy lecithin contains primarily phosphatidylcholine, phosphatidylethanolamine, and phosphatidylinositol, [51,52]. The composition of lecithin will depend on variety of the soybean and the extraction technique [53]. Estiasih [53] shows promising use of enzymatic hydrolysis of lecithin to alter the placement of fatty acids on the glycerol backbone and the phosphorous group to alter lecithin for specific food purposes.

Carbohydrates

The carbohydrate composition of the soybean consists primarily of fiber. The primary non-fiber carbohydrates in soy are the oligosaccharides, raffinose, stachyose and verbiscose. Raffinose is a trisaccharide of galactose, glucose and fructose, bound by 1 to 6 and 1 to 2 glycosidic linkages respectively and stachyose is tetrasaccharide of 2 galactoses, glucose, and fructose bound by 1 to 6, 1 to 6, and 1 to 2 glycosidic linkages respectively. Neither is digested in the small intestines as humans lack the enzyme α-galactosidase. Passed into the colon they serve as an energy substrate for colonic bacteria, producing hydrogen and methane, and hence flatulence. While discomforting, this role may allow them to serve as prebiotics for colonic bacteria, reducing the risk of colon cancer [54]. Interestingly, raffinose and stachyose and other oligosaccharides in plants are believed to play a role in antioxidant scavenging activity in plant tissue and may have potential as serving the same role for humans also [55]. Sucrose is the other nonstructural carbohydrate that is present to a relatively significant degree. The presence of sucrose provides some sweetness to processed soy products [12]. The content of these starches vary depending on genotype from 5.72-7.00% soluble sugars [56] and altering the oligosaccharides content is possible, but currently, cooking methodology and fermentation appear to best modulate oligosaccharides in soybean for human consumption.

Functional food components

Isoflavones are found in significant concentration in the soybean, composing 0.05-0.5% of dry weight [57]. This has become an area of great interest due to correlations of isoflavones with health benefit which will be reviewed below. Isoflavones are a subgroup of polyphenols; the two major isoflavones found in soy are genistin and daidzin (aglycone forms are genistein and daidzein respectively) (Figure 1). Both have glucose moieties bound to them; during digestion glucosidase enzymes remove the glucose leaving aglycones which are absorbed into the lymphatic system [57]. Isoflavone content of the soybean varies according to soybean genotype and environmental conditions during growth of the plant [9,58-62]. Because genotype can influence the type and concentration of isoflavones, this is also an area of research in growing conditions for, breeding, and genetic engineering of the plant to produce high concentrations of isoflavones in the soybean [62].

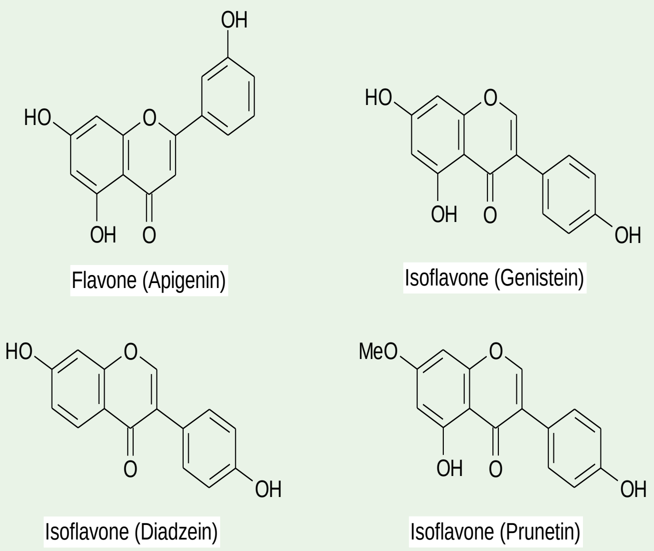

Figure 1: Structures of Flavone and the Isoflavones, Genistein, Diadzein, and Prunetin.

Saponins are triterpenoidal compounds that form water-soluble complexes with cholesterol, preventing its absorption. Soybean is a good source of this group of compounds also [63]. Saponin content varies largely depending on the genotype of the soybean from 11.0-35.6 mg/g seed [9].

Phytic acid is considered an anti nutritonal factor because it binds to important minerals, including calcium, iron, zinc, and copper, inhibiting their absorption. Soybean contains 1-1.5% (dry weight) phytic acid and the majority of the phosphorous in soy is bound to phytic acid [9].

Significance of Soy for Vegetarians

For many years, the soybean has been processed into a wide variety of food products, including soy oil, tofu, soymilk, tempeh, miso, soy sauce, lecithin, soy flour, texturized soy protein, soy protein concentrate and isolates, soy flour and soy protein based infant formula. Many of these food products are consumed in large quantities in Asian countries and indeed, correlations with decreased risk of certain diseases have prompted many studies on the relationship of soy products with health outcomes. Consumption of many of these products have increased in the U.S. since the 1990's [5] likely related to health claims that are allowed by the FDA for foods containing a minimum of 6gm soy protein per serving. Tucker [64] provides an interesting model demonstrating how increased soy intake could improve the nutrient intake profile of the U.S. population.

Soy products are not only convenient to consume, they are a good source of nutrients and are also used to make meat analogs. If used as a staple, consumption of one serving of soy products provides an intake of isoflavones equivalent to about 25-40 mg/day [65].

It has been observed that the intake of certain nutrients such as calcium, vitamin D, vitamin B12, and iron are generally below the dietary recommendations in some vegetarians [66]. Factors that have been indicated to reduce bioavailability of calcium include a high content of oxalate, phytate, and fiber in foods as seen in vegetarian and vegan diets [67]. This has, however, been controversial as calcium in soy is absorbed very well despite its high content of all these three nutrients. It has been reported that the bone mass density is similar in vegetarian as well as non-vegetarian adults. Studies have also reported that the absorption of calcium is better in vegans than vegetarians than omnivores [68].

Although anemia is rare in vegans, plasma levels of vitamin B12 are lower in vegetarians, especially vegans. Limited data suggests that the zinc content of diets of vegetarian and non-vegetarian children is similar, however, the bioavailability of zinc is lower on a vegetarian diet [69]. The absorption of zinc may be enhanced by simultaneously consuming protein foods rich in iron, such as nuts and legumes, and consuming fermented soy products as tempeh and miso [70].

It has been observed that the calcium intake of lacto-ovo-vegetarian pregnant women generally meets the RDA of calcium; however, the calcium intake of vegans is not adequate, and so such women must include additional sources of calcium, such as soy. Isoflavones in the soy products get easily transferred to fetus, but no significant correlation has been observed between cord blood isoflavone levels and estrogen metabolism in utero [71]. There is thus no valid reason to avoid soy products in pregnancy. Based on the amount of soy that is routinely consumed in many oriental countries, all pregnant women should be able to safely consume up to two to three servings of soy daily [72].

Soy formulas are recommended for infants with cow's milk allergy, lactose intolerance, or galactosemia [73]. Such formulas contain soy protein isolate, vegetable oils, and carbohydrate, and are fortified with iron, zinc, methionine, carnitine, and taurine [74]. Soy formulas have a higher content of calcium, phosphorus and protein content due to their lower bio-availability. Soy formulas elevate plasma isoflavone levels and are thus associated with a number of hormonal and non-hormonal effects [75]. Although infants fed soy formulas grow and develop normally, they are not recommended for preterm infants. In fact, no formulas are available for preterm vegan infants [76].

Incorporating Soy in The Diet

To meet their daily requirements of calcium, vitamin D, vitamin B12, and zinc, vegans should emphasize consumption of soy products as tempeh, tofu, roasted soy nuts, edamame, calcium-fortified soymilk and soy-based meat analogs. Some examples of meals and snacks that offer complementary proteins for them include cereal with soymilk, rice pudding made with soymilk, textured soy protein taco with a corn tortilla, soy hot dog in a bun, and tofu salad instead of egg salad.

Some of the new soy products include soy nut butter, soy burgers, ground taco-burrito filler, sweet Italian sausage, soy sausage links, tofu cream cheese, veggie sour cream, soy yogurt, and soy ice cream. Soft or silken tofu can be blended and flavored to make puddings, smoothies, sauces, salad dressings and dips, while extra-firm tofu can be used in stir-fries or grilling. Up to a quarter of flour can easily be replaced with soy flour in recipes of muffins, bread, pancakes, biscuits etc.

To help vegan infants meet their protein needs, one can easily use well-mashed tofu and soy yogurt. However, soy should not be incorporated in the diet of an infant if allergy to soy is suspected.

The Use of Soy in Diet Therapy

Chronic Kidney Disease

Consumption of a vegetarian diet that includes soy protein reduces urinary protein excretion in nephrotic patients and those with advanced renal disease. Such diets that include soy protein also lower phosphorus intake and urinary phosphate excretion, which is advantageous for pre-dialysis and dialysis patients. Soy-based vegan diets appear to be nutritionally adequate for people with chronic kidney disease and are likely to slow progression of kidney disease [77]. Vegetarian diets may be especially important as kidney function declines with age [78].

Cardiovascular Disease

Factors that increase the risk for heart disease include consumption of trans fats, high Glycemic Index foods, and a Western dietary pattern. On the other hand, the factors that reduce the risk for heart disease include consumption of monounsaturated fatty acids, Mediterranean and prudent dietary patterns, nuts, avocados, soy foods, and high intake of anti-oxidants in fruits and vegetables. One may note that the fat content of soymilk is similar to that of reduced fat cow's milk [79]. Sacks (2006) provided an excellent review of research regarding soy protein and soy isoflavones to cardiovascular disease [80]. Soy isoflavones have been postulated to play a role in reducing LDL cholesterol levels and in reducing the susceptibility of LDL to oxidation [81]. A near vegan diet high in phytosterols, viscous fiber, nuts, and soy protein has been shown to be as effective as a low-saturated fat diet and a statin for lowering serum LDL-cholesterol levels [82].

Diabetes Mellitus

Vegetarians are less likely to develop Type 2 Diabetes due to the following reasons: higher fiber and lower saturated fat intake, a higher intake of lower-Glycemic Index foods such as nuts, legumes, fruits and vegetables, and lower rates of hypertension that prevent diabetic complications. Low-protein diets do not adversely affect kidney function. Soy protein may favorably affect renal function in diabetics [83]. In a study conducted by Vilegas, the risk of type 2 diabetes was 38% and 47% lower for those consuming a high intake of total legumes and soybeans, respectively, compared to their low intake [83].

Cancer

Soy isoflavones and soy foods have been shown to possess anti-cancer properties. A meta-analysis of eight studies (one cohort, and seven case controls) conducted in high-soy-consuming Asians showed a significant trend of increasing soy food intake with decreasing risk of breast cancer. In contrast, soy intake was unrelated to breast cancer risk in studies conducted in 11 low-soy-consuming Western populations [84]. One of the ways in which isoflavone genistein slows the growth of cancer cells is by inhibiting several enzymes involved in signal transduction, including tyrosine protein kinases [85], MAP kinase [86], and ribosomal S6 kinase [87]. Genistein also inhibits the activity of DNA topoisomerase II [88]. Peterson et al [89] reported that genistein increased the in-vitro concentrations of Transforming Growth Factor β (TGFβ). This last finding may be particularly important given the role that TGFβ may have in inhibiting the growth of cancer cells [90].

Besides isoflavones as daidzein and genistein, other phytochemicals present in soybeans such as phytosterols, phytates, saponins, protease inhibitors, and a variety of phenolic acids have also been shown to demonstrate anticarcinogenic activity [91]. Studies have reported that consumption of soy products in childhood is associated with a lower risk of breast cancer in adulthood [92]. However, it is still controversial if soy should be regarded as a cancer-protective agent, because not all research supports the protective value of soy towards breast cancer [93].

Isoflavones

Isoflavones are a class of polyphenol compounds that have reported biological activities and antioxidant properties [94-96]. They are called isoflavones because the B ring is attached to the adjacent carbon from a typical flavone structure (Figure 1). Although the flavones are widespread in plants, isoflavones are found in few plants, mainly in legumes such as soy (Glycine max) and chickpea (Cicer arietinum L), and in the tuber-producing vine, kudzu (Pueraria lobata) [97].

A great deal of attention has been focused on isoflavones because they have potential effects on cancer, cardiovascular diseases, osteoporosis and symptoms of menopause. Postmenopausal women have sharply increased incidences of hypercholesterolemia, coronary heart disease and risk of osteoporosis. Several excellent reviews have been published on isoflavones recently so this manuscript will focus on some of the more recent information [94-96].

Isoflavones are one of the main chemical classes that have been found to have estrogenic activity that are derived from plants. The estrogenic activity arises because structural similarity allows them to bind to estrogen receptors, resulting in antagonistic, agonistic or mixed effects at the receptor level. Because of this, they have been called phytoestrogens and much of the reported bioactivity focuses on their estrogenic or antagonistic effects.

Soy isoflavones exist as three main aglycone forms (Figure 1) but also as glucoside forms (the O-glucosides of aglucones diadzein, genistein and glycitenin are named diadzin, genistin, and glycitin). Analysis of isoflavones is complicated by the numerous possible forms present and because processing can affect levels and compositions of individual compounds [97]. Additionally, intestinal microflora metabolize isoflavones to forms equol, an isoflavandiol that may also be absorbed, have greater estrogenic activity and longer half life in humans [98]. Because intestinal microflora differ among people, some are able to produce much greater amounts of equol than others, making human experimentation challenging.

Soy derived isoflavones have been shown to have a wide range of effects on human health, including ameliorating symptoms of menopause, osteoporosis, cancer and heart disease. Reported positive effects are not limited to women; as a dihydrotestosterone blocker, equol may have positive effects on male pattern baldness as well as lowering incidence of prostate cancer [94-96].

One of the difficulties in the interpretation of studies on soy isoflavones and health is that different forms of soy or soy extracts have different levels of concentration and doses [99]. Processing and fermentation of soy products reduce the isoflavone levels significantly. It is important to measure all of the isoflavone forms in foods or supplements. Fermentation results in more aglycone forms as a result of hydrolysis during fermentation, and thermal processing by extrusion results in more acetyl forms compared to malonyl forms [94-96,98].

A randomized double-blind study (n experimental = 30, n control = 31) on the supplementation of diets of post menopausal women with soy providing 54 mg of isoflavones per day was conducted over 8 weeks [100]. The study focused on blood pressure, circulating hormonal levels and symptoms as measured using the Blatt-Kupperman index (a measure of menopausal symptoms including depression, fatigue, hot flashes, joint or muscle pain, paresthia, insomnia, mood swings, vertigo, headache, palpitation). No significant change was observed in diastolic or systolic blood pressure in the isoflavone treatment group, but there was a significant improvement in menopause symptom severity and intensity, as determined using the Blatt-Kupperman index. This is in agreement with other studies that have shown isoflavones can help reduce symptoms of menopause. Levels of the circulating hormones, follicular stimulating hormone and luteinizing hormone, decreased after isoflavone supplementation, but estradiol levels increased. The supplementation of soy isoflavones (40-80 mg/day) was studied for hot flashes and night sweats in African post-menopausal women [101]. Although this was not a double blind, placebo controlled study, results indicated that the incidence of night sweats and hot flashes decreased significantly after 4 months. These studies underline the positive effects of soy isoflavones on menopause symptoms.

Soy isoflavones are known to have antioxidant effects in vivo and in vitro and the impact of soy isoflavone extract supplementation on hypoxia and fatigue was studied in mice [102]. Soy isoflavones improved serum lactate and urea levels and extended survival under hypoxia and sodium nitrite toxicity conditions. The supplementation levels were quite high (200-600 mg/kg) and the isoflavone extract was only characterized by genistein and diadzein concentrations; the other isoflavone/forms known to exist in soy were not reported. Isoflavone extracts are not all equal, and some commercial isoflavone extracts have been reported to contain mycotoxins and pesticides [103]. Nonetheless, these contaminants are likely found only in low concentrations and the main problem with interpretation across experiments is the incomplete characterization of the isoflavone profiles of samples provided.

One of the results of the estrogen deficiency that occurs after menopause is increased oxidative stress and insulin resistance. In ovariectomized rats, supplementation with 150 mg soy isoflavones/day for 12 weeks resulted in lower oxidative stress and improved measures of glucose intolerance and insulin resistance [104]. Soy isoflavones also improved symptoms in rats fed a high-fat diet, which exacerbates metabolic problems associated with estrogen loss. Soy milk consumption was studied as a means of reducing markers of inflammation and oxidative stress in women with rheumatoid arthritis in a randomized, cross-over trial [105]. Treatment phases were 4 weeks, with a 2 weeks washout and an additional 4 weeks on the crossed diet. Soy milk consumption resulted in lower levels of serum TNF-α (Tumor Necrosis Factor Alpha) and CRP (C-reactive protein), indicating reduced inflammation, although there was no difference in blood malonaldehyde (a measure of polyunsaturated fatty acid oxidation) levels after soy milk consumption.

Asthma is a complex disease and some studies have shown a potentially positive effect of soy isoflavones on severity of symptoms. A randomized, double-blind, placebo-controlled study was conducted of soy isoflavone supplementation in patients with poorly-controlled asthma who were taking a controller medication [106]. The isoflavone pill supplements contained 49 mg total isoflavones, with around 32 mg as aglycone form. The concentration of genistein in plasma increased significantly (4.87 ng/ml compared to 37.67 ng/ml) after isoflavone consumption, but there were no significant differences in measures of lung function or clinical measures of disease. The study authors concluded that soy isoflavone supplements have little value for patients with poorly controlled asthma who were currently taking a controller medication.

A wide range of studies have shown the potential value of soy isoflavones in reducing risk of a wide range of cancers [94-96], including prostate, stomach, lung, breast or colorectal. Conversely, some studies have reported proliferative effects at low concentrations [94]. Because of the differences in intestinal metabolism of isoflavones and the importance of metabolic products such as equol, significant differences in responses among people within a population are expected. Studies on the fermentation of a soymilk beverage as a means of metabolizing isoflavones and producing a beverage with enhanced sensory acceptability has been reviewed recently [107]. Fermentation can change absorption efficiency and the combination of probiotic bacteria and isoflavones may provide positive, complementary effects. Soy isoflavone intake is associated with lower risk of breast cancer among different populations, including Caucasian and African-American women in North America [108]. However, not all studies on cancers have shown such positive effects. In some studies, isoflavones have been shown to enhance growth of estrogen-dependent breast cancer tumors [109]. A recent study was conducted on the effect of soy isoflavone consumption on breast cancer with bone metastasis [110]. Authors studied purified genistein, diadzein, (-)-equol, and a mixture of soy isoflavones, so differential effects can be attributed to specific compounds. Their results indicated that soy isoflavones enhanced growth of bone micro-tumors and increased metastatic tumor formation in lungs.

Many post menopausal women report problems with cognitive functions (such as concentration) and memory. A study of 90 women for 6 months was conducted to determine if a supplement of 60 mg soy isoflavones/day can improve cognitive functions [110]. Some, but not all, measures of cognitive function were improved by isoflavone treatment. For example, the isoflavone group performed better on verbal fluency tests, but there was no improvement in immediate memory, storage capacity and recovery or memory test of word list.

The relationship between intake of soy products and osteoporosis is complex and may involve not just isoflavones, but also the high calcium and protein contents of some soy products [94]. Epidemiological studies suggest that soy isoflavones would be more beneficial in preventing osteoporosis than its reversal [96]. Long term studies have reported no negative effects of soy isoflavone consumption (80 or 120 mg/day) on endometrial thickness, reported adverse effects, or thyroid function, underlining the safety of long-term use of soy isoflavone supplements [111].

Kawasaki disease is a serious inflammatory disease of children that is particularly common in Asian countries. There is some evidence that soy consumption may be associated with increased incidence of Kawasaki disease, and that this is associated with soy isoflavones, particularly genistein [112]. Genistein is thought to affect function of Fc γ receptors, disrupting the inflammatory response. At this point, the relative importance of diet and genetics is unclear.

Conclusion

Soy research has many exciting advances as breeding and genetic modifications are allowing for higher protein beans and desirable fatty acids profiles for food use and for health. Soybean products are useful not only for the vegetarian, but also for other aspect of diet therapy. As a component of soy, isoflavones potentially have a wide range of positive effects on human health. Their complexity of structure and intestinal metabolism creates difficulties in the interpretation and comparison of experiments, but clearly there are many positive human health effects of isoflavones derived from soy.

References

1. Hymowitz T. Soybeans: The Success Story Advances in New Crops, Edited by Jules Janick and James Simon, Timber Press, Portland, Oregon, 1990; 159-163.
2. Hymowitz, Shurtleff T, Debunking WR. Soybean myths and legends in the popular and historical literature. Crop Sci. 2005; 45: 473-476.
3. Singh RJ, Hymowitz T. Soybean genetic resources and crop improvement. Genome. 1999; 42: 605-616.
4. USDA. World Agricultural Supply and Demand Estimates. 2015.
5. Soyfoods Association of North America. Soy Products Sales and Trends. 2014.
6. Wilson RF. Outlook for soybeans and soybean products in 21st century markets. Lipid Technol. 2010; 22: 199-202.
7. Yaklich RW. beta-Conglycinin and glycinin in high-protein soybean seeds. J Agric Food Chem. 2001; 49: 729-735.
8. Krishnan HB, Natarajan SS, Mahmoud AA, Nelson RL. Identification of glycinin and beta-conglycinin subunits that contribute to the increased protein content of high-protein soybean lines. J Agric Food Chem. 2007; 55: 1839-1845.
9. Goyal R, Sharma S, Gill BS. Variability in the nutrients, antinutrients and other bioactive compounds in soybean (Glycine max (L.) Merrill) gentoypes. J Food Legumes. 2012; 25: 314-320.
10. Natarajan S, Luthria D, Bae H, Lakshman D, Mitra A. Transgenic soybeans and soybean protein analysis: an overview. J Agric Food Chem. 2013; 61: 11736-11743.
11. Sharma S, Goyal R, Barwal S. Domestic processing effects of physiochemical, nutritional and anti-nutritional attributes in soybean (Glycine max L. Merill). Internat Food Res J. 2013; 20: 3203-3209.
12. Medic J, Atkinson C, Hurburgh CR. Current knowledge in soybean composition. J Am Oil Chem Soc. 2014; 91: 363-384.
13. Natarajan SS, Xu C, Bae H, Caperna TJ, Garrett WM. Characterization of storage proteins in wild (Glycine soja) and cultivated (Glycine max) soybean seeds using proteomic analysis. J Agric Food Chem. 2006; 54: 3114-3120.
14. Wang T, Qin GX, Sun ZW, Zhao Y. Advances of research on glycinin and Î²-conglycinin: a review of two major soybean allergenic proteins. Crit Rev Food Sci Nutr. 2014; 54: 850-862.
15. Bennett JO, Krishnan AH, Wiebold WJ, Krishnan HB. Positional effect on protein and oil content and composition of soybeans. J Agric Food Chem. 2003; 51: 6882-6886.
16. Krishnan HB, Bennett JO, Kim WS, Krishnan AH, Mawhinney TP. Nitrogen lowers the sulfur amino acid content of soybean (Glycine max [L.] Merr.) by regulating the accumulation of Bowman-Birk protease inhibitor. J Agric Food Chem. 2005; 53: 6347-6354.
17. Krishnan HB, Kim WS, Jang S, Kerley MS. All three subunits of soybean beta-conglycinin are potential food allergens. J Agric Food Chem. 2009; 57: 938-943.
18. Xu C, Caperna T, Garrett WM, Cregan P, Bae H, Luthria D, et al. Proteomic analysis of the distribution of the major seed allergens in wild, landrace, ancestral, and modern soybean genotypes. J Sci Food Agric. 2007; 87: 2511-2518.
19. Liener IE. Legume toxins in relation to protein digestibility – a review. J Food Sci. 1974; 41: 1076-1081.

20. Pusztai A, King TP, Clarke EM. Recent advances in the study of the nutritional toxicity of kidney bean (Phaseolus vulgaris) lectins in rats. Toxicon. 1982; 20: 195-197.

21. Higuchi M, Suga M, Iwai K. Participation of lectin in biological effects of raw winged bean seeds on rats. Agric Biol Chem. 1983; 47: 1879-1886.

22. Gupta YP. Anti-nutritional and toxic factors in food legumes: a review. Plant Foods Hum Nutr. 1987; 37: 201-228.

23. Kunitz M. CRYSTALLIZATION OF A TRYPSIN INHIBITOR FROM SOYBEAN. Science. 1945; 101: 668-669.

24. Birk Y. The Bowman-Birk inhibitor. Trypsin- and chymotrypsin-inhibitor from soybeans. Int J Pept Protein Res. 1985; 25: 113-131.

25. Guillamón E, Pedrosa MM, Burbano C, Cuadrado C, de Cortez Sanchez M, Muzquiz M. The trypsin inhibitors present in seed of different grain legume species and cultivar. Food Chem. 2008; 107: 68-74.

26. Haines PC, Lyman RL. Relationship of pancreatic enzyme secretion to growth inhibition in rats fed soybean trypsin inhibitor. J Nutr. 1974; 74: 445-452.

27. DiPietro CM, Liener IE. Heat inactivation of the Kunitz and Bowman-Birk soybean protease inhibitors. J Agric Food Chem. 1989; 37: 39-44.

28. LIENER IE. Inactivation studies on the soybean hemagglutinin. J Biol Chem. 1958; 233: 401-405.

29. Sebolt AM, Shoemaker RC, Diers BW. Analysis of a quantitative trait locus allele from wild soybean that increases seed protein concentration in soybean. Crop Sci. 2000; 40: 1438-1444.

30. Mahmoud AA, Natarajan SS, Bennett JO, Mawhinney TP, Wiebold WJ. Effect of six decades of selective breeding on soybean protein composition and quality: a biochemical and molecular analysis. J Agric Food Chem. 2006; 54: 3916-3922.

31. Krishnan HB, Kim W, Oehrle NW, Alaswad AA, Baxter I, Wiebold WJ, et al. Introgression of leginsulin, a cysteine-rich protein, and high-protein trait from an Asian soybean plant introduction genotype into a North American experimental soybean line. J Agric Food Chem. 2015; 63:2862-2869.

32. Kim W, Chronis D, Juergens M, Schroeder AC, Hyun SW, Jez JM, et al. Transgenic soybean plants overexpressing O-acetylserine sulfhydrylase accumulate enhanced levels of cysteine and Bowman-Birk protease inhibitor in seeds. Planta. 2012; 235: 13-23.

33. Nordlee JA, Taylor SL, Townsend JA, Thomas LA, Bush RK. Identification of a Brazil-nut allergen in transgenic soybeans. N Engl J Med. 1996; 334: 688-692.

34. Gillman JD, Kim WS, Krishnan HB. Identification of a new soybean kunitz trypsin inhibitor mutation and its effect on bowman-birk protease inhibitor content in soybean seed. J Agric Food Chem. 2015; 63: 1352-1359.

35. Wang TL, Domoney C, Hedley CL, Casey R, Grusak MA. Can we improve the nutritional quality of legume seeds?Plant Physiol. 2003; 131: 886-891.

36. Kim H, Ha B, Ha K, Chae J, Park J, Kim M, et al. Comparison of a high oleic acid soybean line to cultivated cultivars for seed yield, protein and oil concentrations. Euphytica. 2015; 201: 285-292.

37. Foster R, Williamson CS, Lunn J. Culinary oils and their health effects. Nutr Bulletin. 2009; 34: 4-47.

38. Hammond EG, Chen AH, Tandy DC, Duff HG, Hastert RC, Gavin AM, et al. The raw materials of the fats and oil industry. Wan PJ, editor. In: Introduction to Fats and Oils Technology. AOCS Champagne IL. 1991.

39. Sharma S, Kaur M, Goyal R, Gill BS. Physical characteristics and nutritional composition of some new soybean (Glycine max (L.) Merrill) genotypes. J Food Sci Technol. 2014; 51: 551-557.

40. Towa LT, Kapchie VN, Wang G, Hauck C, Wang T, Murphy PA. Quantity and quality of free oil recovered from enzymatically disrupted soybean oleosomes. J Am Oil Chem Soc. 2011; 88: 1581-1591.

41. Cherry JP, Kramer WH. Lecithins: Sources, Manufacture and Uses. BF Szuhaj, editor. In: Plant sources of lecithin. American Oil Chemists Society Champaign. 1989; 16-31.

42. Carpenter AP. Determination of tocopherols in vegetable oils. J Am Oil Chem Soc. 1979; 56: 668-671.

43. Evans JC, Kodali DR, Addis PB. Optimal tocopherol concentration to inhibit soybean oil oxidation. J Am Oil Chem Soc. 2002; 79: 47-51.

44. Choe E, Min DB. Mechanisms and factors for edible oil oxidation. Comp Rev Food Sci Food Safety. 2006; 5:169-186.

45. Debruyne I. Novel soybean oil products for a healthier nutrition – recent developments, market introduction and targeted commercialization. Lipid Technol. 2007; 19: 128-131.

46. Karabulut I, Kayahan M, Yaprak. Determination of changes in some physical and chemical properties of soybean oil during hydrogenation. Food Chem. 2003; 81: 453-456.

47. O'Keefe SF, Gaskins-Wright S, Wiley V, Chen I-C. Levels of trans geometrical isomers of essential fatty acids in some unhydrogenated U.S. vegetable oils. J. Food Lipids. 1994; 1: 165-176.

48. O'Keefe SF, Wright D, Wiley V. Effect of temperature on linolenic acid loss and 18:3 cct formation in soybean oil. J Amer Oil Chem Soc. 1993; 70: 915-917.

49. Tarrago-Trani MT, Phillips KM, Lemar LE, Holden JM. New and existing oils and fats used in products with reduced trans-fatty acid content. J Amer Diet Asso. 2006; 106: 867-880.

50. Ribeiro APB, Grimaldi R, Gioielli LA, Gonçalves LAG. Zero trans fats from soybean oil and fully hydrogenated soybean oil: physio-chemical properties and food applications. Food Res Internat. 2009; 42: 401-410.

51. Wu Y, Wang T. Fractionation of crude soybean lecithin with aqueous ethanol. J Am Oil Chem Soc. 2004; 81: 697-704.

52. Ceci LN, Constenla DT, Crapiste GH. Oil recovery and lecithin production using water degumming sludge of crude soybean oils. J Sci Food Agric. 2008; 88: 2460-2466.

53. Estiasih T, Ahadi K, Ginting E, Priyanto AD. Modification of soy crude lecithin by partial enzymatic hydrolysis using phospholipase A. Internat Food Res J. 2013; 20: 843-849.

54. Di Bartolomeo F, Startek JB, Van den Ende W. Prebiotics to fight diseases: reality or fiction? Phytother Res. 2013; 27: 1457-1473.

55. Van den Ende W. Multifunctional fructans and raffinose family oligosaccharides. Front Plant Sci. 2013; 4: 247.

56. Rani V, Grewal RB. Carbohydrate profile dietary fibre, antinutrients and invitro digestibility of nine cultivars of soybean (Glycine maxL.) Merr. Legume Res. 2009; 32: 31-35.

57. Tepavcevic V, Cvejic J, Poša M, Popovic J. Isoflavone content and composition in soybean. Tzi-Bun Ng, editor. In: Soybean – Biochemistry, Chemistry and Physiology. 2011.

58. Wang C, Sherrard M, Pagadala S, Wixon R, Scott RA. Isoflavone content among maturity group 0 to II soybeans. J Am Oil Chem Soc. 2000; 77: 483-487.

59. TepavceviÄ‡ V, AtanackoviÄ‡ M, MiladinoviÄ‡ J, MalenciÄ‡ D, PopoviÄ‡ J. Isoflavone composition, total polyphenolic content, and antioxidant activity in soybeans of different origin. J Med Food. 2010; 13: 657-664.

60. SJ, Yan W, Ahn JK, Chung IM. Effects of year, site, genotype and their interactions on various soybean isoflavones. Field Crops Research. 2003; 81: 181-192.

61. Hoeck JA, Fehr WR, Murphy PA, Welke GA. Influence of genotype and environment on isoflavones contents of soybean. Crop Sci. 2014; 40: 48-51.

62. Bi Y, Li W, Xiao J, Lin H, Liu M. Heterosis and combining ability estimates in isoflavone content using different parental soybean accessions: wild

soybean, a valuable germplasm for soybean breeding. PLoS One. 2015; 10: e0114827.

63. Fenwick DF, Oakenfull D. Saponin content of soya beans and some commercial soya bean products. J Sci Food Agric. 1981; 32: 273-278.

64. Tucker KL, Qiao N, Maras JE. Simulation with soy replacement showed that increased soy intake could contribute to improved nutrient intake profiles in the U.S. population. J Nutr. 2010; 140: 2296S-2301S.

65. Messina MJ. Legumes and soybeans: overview of their nutritional profiles and health effects. Am J Clin Nutr. 1999; 70: 439S-450S.

66. Farmer B. Nutritional adequacy of plant-based diets for weight management: observations from the NHANES. Am J Clin Nutr. 2014; 100 Suppl 1: 365S-8S.

67. Platel K, Srinivasan K. Bioavailability of Micronutrients from Plant Foods: An Update. Crit Rev Food Sci Nutr. 2015;.

68. Mangels AR. Bone nutrients for vegetarians. Am J Clin Nutr. 2014; 100 Suppl 1: 469S-75S.

69. Ezmirly M, Phelps J, Crook T, Hakkak R. Comparison of Selected Micronutrient Intakes Between Vegans and Omnivores Using Dietary Reference Intakes. FASEB J. 2015; 29S: 587-615.

70. Hsiao AK-F, Lyons-Wall PM. Soy consumption in Taiwanese children in Taipei. J Nutr. 2004; 134: 1248S.

71. Kaludjerovic J, Ward WE. Soy: Animal Studies, Spanning the Lifespan. Bioactive Food as Dietary Interventions for the Aging Population: Bioactive Foods in Chronic Disease States. 2012; 383.

72. Nagata C, Iwasa S, Shiraki M, Ueno T, Uchiyama S, Urata K, et al. Associations among maternal soy intake, isoflavone levels in urine and blood samples, and maternal and umbilical hormone concentrations (Japan). Cancer Causes Control. 2006; 17: 1107-1113.

73. Tzifi F, Grammeniatis V, Papadopoulos M. Soy- and rice-based formula and infant allergic to cow's milk. Endocr Metab Immune Disord Drug Targets. 2014; 14: 38-46.

74. Belamarich PF, Bochner RE, Racine AD. A Critical Review of the Marketing Claims of Infant Formula Products in the United States. Clin Pediatr (Phila). 2015;.

75. Setchell KDR, Zimmer-Nechemias L, Cai J, Heubi J. Exposure of infants to phytoestrogens from soy infant formulas. Lancet. 1997; 350:23-27.

76. Valentine C. Protein Nutrition for the Preterm Infant. Nutr Infancy. Humana Press. 2013; 157-167.

77. D'Amico G, Gentile MG, Manna G, Fellin G, Ciceri R. Effect of vegetarian soy diet on hyperlipidaemia in nephrotic syndrome. Lancet. 1992; 339: 1131-1134.

78. Bernstein AM, Treyzon L, Li Z. Are highprotein, vegetable-based diets safe for kidney function? A review of the literature. J Am Diet Assoc. 2007; 107: 644-650.

79. Haub MD, Wells AM, Campbell WW. Beef and soy-based food supplements differentially affect serum lipoprotein-lipid profiles because of changes in carbohydrate intake and novel nutrient intake ratios in older men who resistive train. Metabolism. 2005; 54:769-774.

80. Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris-Etherton P, Winston M. Soy protein, isoflavones, and cardiovascular health An American Heart Association science advisory for professionals from the nutrition committee. Circulation. 2006; 113: 1034-1044.

81. Rimbach G, Boesch-Saadatmandi C, Frank J, Fuchs D, Wenzel U, Daniel H, et al. Dietary isoflavones in the prevention of cardiovascular disease—A molecular perspective. Food Chem Toxicol. 2008; 46: 1308-1319.

82. Jenkins DJ, Kendall CW, Marchie A, Faulkner DA, Wong JM, de Souza R, et al. Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. Am J Clin Nutr. 2005; 81: 380-387.

83. Villegas R, Gao YT, Yang G, Li HL, Elasy TA. Legume and soy food intake and the incidence of type 2 diabetes in the Shanghai Women's Health Study. Am J Clin Nutr. 2008; 87: 162-167.

84. Wu AH, Yu MC, Tseng CC, Pike MC. Epidemiology of soy exposures and breast cancer risk. Br J Cancer. 2008; 98: 9-14.

85. Akiyama T, Ishida J, Nakagawa S, Ogawara H, Watanabe S, Itoh N, et al. Genistein, a specific inhibitor of tyrosine-specific protein kinases. J Biol Chem 1987; 262: 5592-5595.

86. Thorburn J, Thorburn A. The tyrosine kinase inhibitor, genistein, prevents α-adrenergic-induced cardiac muscle cell hypertrophy by inhibiting activation of the Ras-MAP kinase signaling pathway. Biochem Biophys Res Commun. 1994; 202: 1586-1591.

87. Linassier C, Pierre M, Le Peco J-B, Pierre J. Mechanism of action in NIH-3T3 cells of genistein, an inhibitor of EGF receptor tyrosine kinase activity. Biochem Pharmacol. 1990; 39: 187-193.

88. Constantinou A, Kiguchi K, Huberman E. Induction of differentiation and DNA strand breakage in human HL-60 and K-562 leukemia cells by genistein. Cancer Res. 1990; 50: 2618-2624.

89. Peterson TG, Kim H, Barnes S. Genistein may inhibit the growth of human mammary epithelial (HME) cells by augmenting transforming growth factor beta (TGFβ) signaling. Am J Clin Nutr. 1998; 68: 1527S (abstr)

90. Markowitz SD, Roberts AB. Tumor suppressor activity of the TGF-β pathway in human cancers. Cytokine Growth Factor Rev. 1996; 7: 93-102.

91. Messina MJ, Barnes S. The role of soy products in reducing risk of cancer. J Natl Cancer Inst. 1991; 83: 541-546.

92. Korde LA, Wu AH, Fears T, Nomura AM, West DW. Childhood soy intake and breast cancer risk in Asian American women. Cancer Epidemiol Biomarkers Prev. 2009; 18: 1050-1059.

93. Messina MJ, Loprinzi CL. Soy for breast cancer survivors: A critical review of the literature. J Nutr. 2001; 131: 3095S-3108S.

94. Hendrich S, Murphy P. Isoflavones: Source and Metabolism. Wildman REC, editor. In: Ch 4 in "Handbook of Nutraceuticals", CRC Press, Baca Raton FL. 2000; 55-75.

95. Kurzer MS, Xu X. Dietary phytoestrogens. Annu Rev Nutr. 1997; 17: 353-381.

96. Murphy PA, Hendrich S. Phytoestrogens in foods. Advances in Food and Nutrition Research. 2002; 44: 196-246.

97. Wu QL, Yang YH, Simon J. Chemical profiling and quantitation of isoflavone phytoestrogens in kudzu using LC/UV/MSD. American Journal of Analytical Chemistry. 2011; 2: 665-674.

98. Yuan JP, Wang JH, Liu X. Metabolism of dietary soy isoflavones to equol by human intestinal microflora--implications for health. Mol Nutr Food Res. 2007; 51: 765-781.

99. Wang HJ, Murphy PA. Isoflavone content in commercial soy foods. Journal of Agricultural and Food Chemistry. 1994; 42: 1666-1673.

100. Husain D, Khanna K, Puri S, Haghighizadeh M. Supplementation of soy isoflavones improved sex hormones, blood pressure, and postmenopausal symptoms. J Am Coll Nutr. 2015; 34: 42-48.

101. Mbu RE, Abauleth YR, Koffi A, Keita N, Dolo A, Lankoande J. Effects of dietary supplementation of soy isoflavones on hot flashes and night sweats in African menopausal women. Open Journal of Obstetrics and Gynecology. 2014; 4: 42-46.

102. Li X, Qi B. Anti-fatigue and anti-hypoxia effects of soy isoflavones. Applied Mechanics and Materials. 2015; 737: 332-335.

103. Martínez-Domínguez G, Romero-González R, Arrebola FJ, Frenich AG. Multi-class determination of pesticides and mycotoxins in isoflavones supplements obtained from soy by liquid chromatography coupled to Orbitrap high resolution mass spectrometry. Food Control. 2016; 59: 218-224.

104. Sankar P, Zachariah B, Vickneshwaran V, Jacob SE, Sridhar MG. Amelioration of oxidative stress and insulin resistance by soy isoflavones (from Glycine max) in ovariectomized Wistar rats fed with high fat diet: the molecular mechanisms. Exp Gerontol. 2015; 63: 67-75.

105. Mohammad-Shahi M, Mowla K, Haidari F, Zarei M, Choghakhori R. Soy milk consumption, markers of inflammation and oxidative stress in women with rheumatoid arthritis: a randomized cross-over clinical trial. Nutrition & Dietetics. 2015.

106. Smith LJ, Kalhan R, Wise RA, Sugar EA, Lima JJ. Effect of a soy isoflavone supplement on lung function and clinical outcomes in patients with poorly controlled asthma: a randomized clinical trial. JAMA. 2015; 313: 2033-2043.

107. Takagi A, Kano M, Kaga C. Possibility of breast cancer prevention: use of soy isoflavones and fermented soy beverage produced using probiotics. Int J Mol Sci. 2015; 16: 10907-10920.

108. Jaceldo-Siegl K, Gatto N, Beeson L, Fraser G. Intake of soy isoflavones reduces breast cancer incidence among Western women in North America. The FASEB Journal. 2015; 28: S406.

109. Yang X, Belosay A, Hartman JA, Song H, Zhang Y, Wang W, et al. Dietary soy isoflavones increase metastasis to lungs in an experimental model of breast cancer with bone micro-tumors. Clinical and Experimental Metastasis. 2015; 32: 323-333.

110. Vieira LHL, de Araújo TRE, Haidar MA, Silva I. Prospective memory assessment, before and after the use of concentrated extract of soy, in postmenopausal women complaining of memory impairment. Neuroscience & Medicine. 2013; 4: 217-222.

111. Alekel DL, Genschel U, Koehler KJ, Hofmann H, Van Loan MD. Soy Isoflavones for Reducing Bone Loss Study: effects of a 3-year trial on hormones, adverse events, and endometrial thickness in postmenopausal women. Menopause. 2015; 22: 185-197.

112. Portman MA. Kawasaki disease and soy: potential role for isoflavone interaction with FcÎ³ receptors. Pediatr Res. 2013; 73: 130-134.