
Soybean, Nutrition and Health

Sherif M. Hassan

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/54545>

1. Introduction

Soybean (*Glycine max* L.) is a species of legume native to East Asia, widely grown for its edible bean which has several uses. This chapter will focus on soybean nutrition and soy food products, and describe the main bioactive compounds in the soybean and their effects on human and animal health.

2. Soybean and nutrition

Soybean is recognized as an oil seed containing several useful nutrients including protein, carbohydrate, vitamins, and minerals. Dry soybean contain 36% protein, 19% oil, 35% carbohydrate (17% of which dietary fiber), 5% minerals and several other components including vitamins [1]. Tables 1 and 2 show the different nutrients content of soybean and its by-products [2]

Soybean protein is one of the least expensive sources of dietary protein [3]. Soybean protein is considered to be a good substituent for animal protein [4], and their nutritional profile except sulfur amino acids (methionine and cysteine) is almost similar to that of animal protein because soybean proteins contain most of the essential amino acids required for animal and human nutrition. Researches on rats indicated that the biological value of soy protein is similar to many animal proteins such as casein if enriched with the sulfur-containing amino acid methionine [5]. According to the standard for measuring protein quality, Protein Digestibility Corrected Amino Acid Score, soybean protein has a biological value of 74, whole soybeans 96, soybean milk 91, and eggs 97[6]. Soybeans contain two small storage proteins known as glycinin and beta-conglycinin.

Nutrient	Soybean				
	Flour	Protein concentrate	Seed heat processed	Meal solvent extracted	Seed without hulls, meal solvent extracted
Protein%	13.3	84.1	37.0	44.0	48.5
Fat%	1.6	0.4	18.0	0.8	1.0
Linoleic acid %	-	-	8.46	0.40	0.40
Crude fiber%	33.0	0.2	5.5	7.0	3.9
Calcium%	0.37	0.0	0.25	0.29	0.27
Total phosphorus%	0.19	0.80	0.58	0.65	0.62
Non phytate phosphorus %	-	0.32	-	0.27	0.22
Potassium %	1.50	0.18	1.61	2.00	1.98
Chlorine%	0.02	0.02	0.03	0.05	0.05
Iron (mg/kg)	-	130	80	120	170
Magnesium %	0.12	0.01	0.28	0.27	0.30
Manganese(mg/kg)	29	1	30	29	43
Sodium %	0.25	0.07	0.03	0.01	0.02
Sulfur %	0.06	0.71	0.22	0.43	0.44
Copper (mg/kg)	-	7	16	22	15
Selenium (mg/kg)	-	0.10	0.11	0.10	0.10
Zinc (mg/kg)	-	23	25	40	55
Biotein(mg/kg)	0.22	0.3	0.27	0.32	0.32
Choline(mg/kg)	640	2	2.860	2794	2731
Folacin (mg/kg)	0.30	2.5	4.2	1.3	1.3
Niacin(mg/kg)	24	6	22	29	22
Pantothenic acid (mg/kg)	13.0	4.2	11.0	16.0	15.0
Pyridoxine(mg/kg)	2.2	5.4	10.8	6.0	5.0
Riboflavin(mg/kg)	3.5	1.2	2.6	2.9	2.9
Thiamin(mg/kg)	2.2	0.2	11.0	4.5	3.2
Vitamin B12 (µg/kg)	-	-	-	-	-
Vitamin E (mg/kg)	-	-	40	2	3

Table 1. Shows composition of soybean and some soybean by-product.

Nutrient	Soybean				
	flour	Protein concentrate	Seed heat processed	Meal solvent extracted	Seed without hulls, meal solvent extracted
Arginine%	0.94	6.70	2.59	3.14	3.48
Glycine %	0.40	3.30	1.55	1.90	2.05
Serine%	-	5.30	1.87	2.29	2.48
Histidine%	0.18	2.10	0.99	1.17	1.28
Isoleucine%	0.40	4.60	1.56	1.96	2.12
Leucine %	0.57	6.60	2.75	3.39	3.74
Lysine%	0.48	5.50	2.25	2.69	2.96
Methionine%	0.10	0.81	0.53	0.62	0.67
Cystine%	0.21	0.49	0.54	0.66	0.72
Phenylalanine%	0.37	4.30	1.78	2.16	2.34
Tyrosine%	0.23	3.10	1.34	1.91	1.95
Threonine%	0.30	3.30	1.41	1.72	1.87
Tryptophan%	0.10	0.81	0.51	0.74	0.74
Valine%	0.37	4.40	1.65	2.07	2.22

Table 2. Shows amino acids contain of soybean and some soybean by-product.

On the other hand, Soy vegetable oil is another product of processing the soybean crop used in many industrial applications. Soybean oil contains about 15.65% saturated fatty acids, 22.78% monounsaturated fatty acids, and 57.74% polyunsaturated fatty acids (7% linolenic acid and 54% linoleic acid) [7]. Furthermore, soybeans contain several bioactive compounds such as isoflavones among other, which possess many beneficial effects on animal and human health [8].

Soybean is very important for vegetarians and vegans because of its rich in several beneficial nutrients. In addition, it can be prepared into a different type of fermented and non-fermented soy foods. Asians consume about 20–80 g daily of customary soy foods in many forms including soybean sprouts, toasted soy protein flours, soy milk, tofu and many more. Also fermented soy food products consumed include tempeh, miso, natto, soybean paste and soy sauce among other [9, 10]. This quantity intake of soy foods is equivalent daily to 25 and 100 mg total isoflavones [11] and between 8 and 50 g soy protein [12]. On the other hand, western people consume only about 1–3 g daily soy foods mostly as soy drinks, breakfast cereals, and soy burgers among other processed soy food forms [10].

Soybean is used as the raw material for oil milling, and the residue (soybean meal) can be mainly used as source of protein feedstuff for domestic animals including pig, chicken,

cattle, horse, sheep, and fish feed and many prepackaged meals as well [1]. It is widely used as a filler and source of protein in animal diets, including pig, chicken, cattle, horse, sheep, and fish feed [13]. In general, soybean meal is a great source of protein ranged from 44-49%, but methionine is usually the only limiting amino acid and contains some anti-nutritional factors such as trypsin inhibitor and hemagglutinins (lectins) which can be destroyed by heating and fermenting the soybean meal before use. Textured vegetable protein (TVP) is another soybean byproduct has been used for more than 50 years as inexpensively and safely extending ground beef up to 30% for hamburgers or veggie burgers, without reducing its nutritional value and in many poultry and dairy products (soy milk, margarine, soy ice cream, soy yogurt, soy cheese, and soy cream cheese). as well [1, 13, 14, 15]. The total estimates of feed consumed for broilers, turkeys, layers and associated breeders production over the world in 2006 was about 452 million tones [16]. This estimated value is calculated depending on poultry feeds containing about 30% soybean meal on average. Therefore, 136 million tones of soybean meal are used annually in poultry feeds. As a generalization, the numbers shown can be multiplied by 0.3 for an estimate of the needs of soybean meal. Soy-based infant formula (SBIF) is another soybean product that can be used for infants who are allergic to pasteurized cow milk proteins. It is sold in powdered, ready-to-feed, and concentrated liquid forms without side effects on human growth, development, or reproduction [17, 18, 19].

There are several types commercially available of non fermented soy foods, including soy milk, infant formulas, tofu (soybean curd), soy sauce, soybean cake, tempeh, su-jae, and many more. However, fermented foods include soy sauce, fermented bean paste, natto, and tempeh, among others. Fermented soybean paste is native to the East and Southeast Asia countries such as Korea, China, Japan, Indonesia, and Vietnam [20]. Korean soy foods including kochujang (fermented red pepper paste with soybean flour) and long-term fermented soybean pastes (doenjang, chungkukjang, and chungkookjang) are now internationally accepted foods [20]. Furthermore, natto and miso are originally Japanese soy food types of chungkukjang and doenjang, respectively. China also has different fermented soybean products including doubanjiang, douche (sweet noodle sauce), tauchu (yellow soybean paste), and dajiang. Chungkukjang is a short-term fermented soy food similar to Japanese natto, whereas doenjang, kochujang, and kanjang (fermented soy sauce) undergo long term fermentation as do Chinese tauchu and Japanese miso.

In general, this fermentation of soy foods changes the physical and chemical properties of soy food products including the color, flavor and bioactive compounds content. These changes differ according to different production methods such as the conditions of fermentation, the additives, and the organisms used such as bacteria or yeasts during their manufacture. These changes differ as well as whether the soybeans are roasted as in chunjang or aged as in tauchu before being ground. In addition to physicochemical properties, the fermentation of these soybean products changes the bioactive components, such as isoflavonoids and peptides, in ways which may alter their nutritional and health effects.

Also, the nutritional value of cooked soybean depends on the pre-processing and the method of cooking such as boiling, frying, roasting, baking, and many more. The quality

and quantity of soybean components is considerably changed by physical and chemical or enzymatic processes during the producing of soy-based foods [21, 22, 23, 24, 25, 26]. Fermentation is a great processing method for improving nutritional and functional properties of soybeans due to the increased content of many bioactive compounds. On the other hand, the conformation of soy protein (glycinin) is easily altered by heat (steaming) and salt [27]. Many large molecules in raw soybean are broken down by enzymatic hydrolysis during fermentation to small molecules, which are responsible for producing new functional properties for the final products. For example, isoflavones, which are mostly present as 6-O-malonylglucoside and β -glycoside conjugates and associated with soybean proteins, are broken down by heat treatment and fermentation [28]. In general, the chemical profiles of various minor components related to health benefits and nutritional quality of products are also affected by fermentation [29]. It is usual to heat-treat legume components to denature the high levels of trypsin inhibitors soybean [30]. The digestibility of some soy foods are as follows: steamed soybeans 65.3%, tofu 92.7%, soy milk 92.6%, and soy protein isolate 93–97% [1].

3. Bioactive compounds of soybean

Many bioactive compounds are isolated from soybean and soy food products including isoflavones, peptides, flavonoids, phytic acid, soy lipids, soy phytoalexins, soyasaponins, lectins, hemagglutinin, soy toxins, and vitamins and more [31]. Flavonoids are low-molecular-weight polyphenolic compounds classified according to their chemical structure into flavonols, flavones, flavanones, isoflavones, catechins, anthocyanidins and chalcones [32]. Typical flavonoids are kaempferol, quercetin and rutin (the common glycoside of quercetin), belonging to the class of flavonols. Isoflavones (soy phytoestrogens) is a subgroup of flavonoids. The major isoflavones in soybean are genistein, daidzein, and glycitein, representing about 50, 40, and 10% of total isoflavone profiles, respectively. Soy isoflavones, daidzein and genistein, are present at high concentrations as a glycoside in many soybeans and soy food products such as miso, tofu, and soy milk. Soybeans contain 0.1 to 5 mg total isoflavones per gram, primarily genistein, daidzein, and glycitein, the three major isoflavonoids found in soybean and soy products [33]. These compounds are naturally present as the β -glucosides genistin, daidzin, and glycitin, representing 50% to 55%, 40% to 45%, and 5% to 10% of the total isoflavone content, respectively depending on the soy products [8]. Formononetin is another form of isoflavone found in soybeans and can be converted in the rumen (in sheep and cow) into a potent phytoestrogen called equol [34].

Recently, there has been increased interest in the potential health benefits of other bioactive polypeptides and proteins from soybean, including lectins (soy lectins are glycoprotein) and lunasin. Lunasin is a novel peptide originally isolated from soybean foods [35]. Lunasin concentration is ranged from 0.1 to 1.3 g/100 g flour [36, 37], and from 3.3 to 16.7 ng/mg seed [38]. Soybean phytosterols usually include four major or types: β -sitosterol, stigmasterol, campesterol, and brassicasterol, all of which make good raw materials for the production of steroid hormones. Triterpenoid saponins in the mature soybean are divided into two

groups; group A soy saponins have undesirable astringent taste, and group B soy saponins have the health promoting properties [39, 40]. Group A soy saponins are found only in soybean hypocotyls, while group B soy saponins are widely distributed in legume seeds in both hypocotyls (germ) and cotyledons [39]. Saponin concentrations in soybean seed are ranged from 0.5 to 6.5% [41, 42].

Soybeans also contain isoflavones called genistein and daidzein, which are one source of phytoestrogens in the human diet. Soybeans are a significant source of mammalian lignan precursor secoisolariciresinol containing 13–273 $\mu\text{g}/100\text{ g}$ dry weight [43]. Another phytoestrogen in the human diet with estrogen activity is coumestans, which are found in soybean sprouts. Coumestrol, an isoflavone coumarin derivative is the only coumestan in foods [44, 45]. Soybeans and processed soy foods are among the richest foods in total phytoestrogens present primarily in the form of the isoflavones daidzein and genistein [46].

4. Soybean and health

4.1. Beneficial effects of soybean

Recent research of the health effects of soy foods and soybean containing several bioactive compounds received significant attention to support the health improvements or health risks observed clinically or *in vitro* experiments in animal and human.

4.1.1. Effects on cancer

Recent studies suggested that soy food (soy milk) and soybean protein containing flavonoid genistein, Biochanin A, phytoestrogens (isoflavones) consumption is associated with lowered risks for several cancers including breast [11,47,48,49,50,51,52], prostate [53,54], endometrial [52,55], lung [56], colon [57], liver [58], and bladder [59] cancers.

Isoflavones (genistein) use both hormonal and non-hormonal action in the prevention of cancer, the hormonal action of isoflavones has been postulated to be through a number of pathways, which include the ability to inhibit many tyrosine kinases involved in regulation of cell growth, to enhance transformation growth factor- β which inhibits the cell cycle progression, as well as to influence the transcription factors that are involved in the expression of stress response-related genes involved in programmed cell death [60,61]. Other nonhormonal mechanisms by which isoflavones are believed to increase their anticarcinogenic effects are via their anti-oxidant, anti-proliferative, anti-angiogenic and anti-inflammatory properties [62].

On the other hand, soy proteins and peptides showed potential results in preventing the different stages of cancer including initiation, promotion, and progression [63]. They noted that Kunitz trypsin inhibitor (KTI), a protease inhibitor originally isolated from soybean, inhibited carcinogenesis due to its ability to suppress invasion and metastasis of cancer cells. Also, [64] found that soybean lectins and lunasin were able to possess cancer chemopreventive activity *in vitro*, *in vivo* (in human).

Cell culture experiments have demonstrated that a novel soybean seed peptide (lunasin) prevented mammalian cells transformation induced by chemical carcinogens without affecting morphology and proliferation of normal cells [65]. Lunasin purified from defatted soybean flour showed potent activity against human metastatic colon cancer cells. Lunasin caused cytotoxicity in four different human colon cancer cell lines [66]. It has been also demonstrated that lunasin causes a dose-dependent inhibition of the growth of estrogen independent for human breast cancer [67].

4.1.2. Effect on hypercholesterolemia and cardiovascular diseases

Soy food and soybean protein containing isoflavones consumption lowered hypercholesterolemia [68, 69, 70, 71]. Many studies reported that soybean protein consumption lowered incidence of cardiovascular diseases [68]. Soy isoflavone suppress excessive stress-induced hyperactivity of the sympatho-adrenal system and thereby protect the cardiovascular system [72].

Several studies reported a relation between soybean protein consumption and the reduction in cardiovascular risk in laboratory animal's models by reducing plasma cholesterol levels [68, 69]. Reduction in the incidence of hypercholesterolemia and cardiovascular diseases in Asian countries depending on their diets rich in soy protein was reported [73]. Another study found that the substitution of the animal protein with soybean protein resulted in a significantly decrease in plasma cholesterol levels, mainly LDL (low-density lipoprotein) cholesterol [74]. In the same way, [69] showed that after replacing animal protein with soybean protein consumption for hypercholesterolemia persons resulted in a significant decrease of 9.3% of total plasma cholesterol, mainly 12.9% of LDL cholesterol level and 10.5% of triglycerides. The health beneficial effect for replacing animal protein with soy protein consumption showed the most effective in the highest hypercholesterolemic depend on the initial plasma cholesterol levels [70, 71] without or with the lowest effects in normocholesterolemic persons.

Several research attentions have been paid to the high dietary intake of isoflavones because of their potentially beneficial effects associated with a reduction in the risk of developing cardiovascular diseases. On the other hand, other studies conducted out to establish whether soybean protein and/or isoflavones could be responsible for the hypocholesterolemic effects of soybean diets and therefore their beneficial effects on cardiovascular disease. By studying the effect of soy bean protein and isoflavones, [75] reported that these major components of soybean flour (soybean proteins and soybean isoflavones) independently decreased serum cholesterol. Recent study reported that soybean protein containing isoflavones significantly reduced serum total cholesterol, LDL cholesterol, and triacylglycerol and significantly increased HDL (high-density lipoprotein) cholesterol, but the changes were related to the level and duration of intake, and gender and initial serum lipid concentrations of the persons [76].

Some studies have shown that soybean oil effective in lowering the serum cholesterol and LDL levels, and likely can be used as potential hypocholesterolemic agent if used as a dietary fat and ultimately help prevent atherosclerosis and heart diseases [77]. Soybean oil is a

rich source of vitamin E, which is essential to protect the body fat from oxidation and to scavenge the free radicals and therefore helps to prevent their potential effect upon chronic diseases such as coronary heart diseases and cancer [78]. The FDA granted the following health claim for soy: "25 grams of soy protein a day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease [79].

4.1.3. *Effect on osteoporosis and menopause*

Soy food and soybean isoflavones consumption lowered osteoporosis, improved bone health and other bone health problems [80, 81, 82]. In addition, consumption of soy foods may reduce the risk of osteoporosis and help alleviate hot flashes associated with menopausal symptoms which are major health concerns for women [83].

4.1.4. *Hypotensive activity*

Soy food kochujang extract consumption lowered hypertension [84]. The angiotensin I converting enzyme inhibitory peptide isolated from soybean hydrolysate and Korean soybean paste enhanced anti-hypertensive activity *in vivo* [85], causing a fall in blood pressure compared with thiazide diuretics or beta-blockers for mild essential hypertension [86].

4.1.5. *Effect on insulin secretion and energy metabolism*

Increasing the insulin secretion followed by glucose challenge was recorded when male monkeys fed soybean protein and isoflavones [87, 88]. Flavonoid genistein, tyrosine kinase inhibitor, inhibited insulin signaling pathways [60]. Dietary isoflavones induced alteration in energy metabolism in human [89]. They also noted an inhibition of glycolysis and a general shift in energy metabolism from carbohydrate to lipid metabolism due to isoflavone interference.

4.1.6. *Effect on blood pressure and endothelial function*

Reduction in the blood pressure via renin-angiotensin system activity (one of the most important blood pressure control systems in mammals) was recorded by feeding rats on diet containing commercial purified soybean saponin [90]. They found that soybean saponin inhibited renin activity *in vitro* and that oral administration of soybean saponin at 80 mg/kg of body weight daily to spontaneously hypertensive rats for 8 weeks significantly reduced blood pressure. In addition, [91] studied the effects of dietary intake of soybean protein and isoflavones on cardiovascular disease risk factors in high risk, 61 middle aged men in Scotland. For five weeks, half the men fed diets containing at least 20 g of soybean protein and 80 mg of isoflavones daily. The effects of isoflavones on blood pressure, cholesterol levels, and urinary excretion were measured, and then compared to those of the remaining men who were fed placebo diet containing olive oil. Men that fed soybean in their diet showed significant decrease in both diastolic and systolic blood pressure. In addition, [92] found that feeding soy nut significantly decreased systolic and diastolic pressure in hypertensive postmenopausal women. On the other hand, [93] found no effect of soybean protein with isofla-

vones on blood pressure in hypertensive persons. Soy protein and soy isoflavones intake improved endothelial function and the flow-induced dilatation in postmenopausal hypercholesterolemia women by raising the levels of endothelial nitric oxide synthase (eNOS), a regulator of the cardiovascular function [94, 95, 96, 97]. Furthermore, chronic administration of genistein increased the levels of NOS in spontaneously hypertensive rats [98, 99].

4.1.7. Effects on platelet aggregation and fibrinolytic activity

The effect of genistein, a protein tyrosine kinase inhibitor on platelet aggregation was exhibited [100,101]. Nattokinase, a strong fibrinolytic enzyme, in the vegetable cheese natto (a popular soybean fermented Japanese food) showed approximately fourtimes stronger activity than plasmin in the clot lysis assay [102]. However, intraduodenal administration natto-kinase decreased fibrinogen plasma levels in rats [103,104] and in humans [105]. In addition, soybean protein and peptides exhibited anti-fatigue activity helping in performing exercise and delaying fatigue [106], antioxidant [107,108], anti-aging, skin moisturizing, anti-solar, cleansing, and hair-promoting agent [109].

The beneficial effect of Soy isoflavonne (daidzein) on human health extends to the prevention of cancer [110], cardiovascular disease [111]. Also, soybean isoflavones (genistein, daidzein, and their beta glycoside conjugates) showed antitumor [112], estrogenic [113], antifungal activities [114]. Soy isoflavonne (daidzein) stimulates catecholamine synthesis at low concentrations [115]. However, daidzein at high concentrations (1-100 μM) inhibited catecholamine synthesis and secretion induced by stress or emotional excitation. Recent studies recoded an improvement in cognitive function, particularly verbal memory [116] and in frontal lobe function [117] with the use of soy supplements. Glyceollins molecules are also found in the soybean and exhibited an antifungal activity against *Aspergillus sojae*, the fungal ferment used to produce soy sauce [118]. They are phytoalexins with an antiestrogenic activity [119].

4.2. Harmful effects

Despite the several beneficial effects documented of soybean consumption, there are some controversial effects claimed in recent studies on animal and human health. Soybean contains several naturally occurring compounds that are toxic to humans and animals such as the trypsin (a serine protease found in the digestive system) inhibitors, phytic acid, toxic components such as lectins and hemagglutinins, some metalloprotein such as soyatoxin and many more other biological of soyatoxin. Some studies reported high levels of protease or trypsin inhibitors (1-5% of total protein) in legume seeds such as soybean [120]. *In vivo* studies using rat, high levels of exposure to trypsin inhibitors isolated from raw soy flour cause pancreatic cancer whereas moderate levels cause the rat pancreas to be more susceptible to cancer-causing agents. However, the US FDA concluded that low levels of soybean protease (trypsin) inhibitors cause no threat to human health. For human consumption, soybeans must be cooked with "wet" heat to destroy the trypsin inhibitors (serine protease inhibitors). Raw soybeans, including the immature green form, are toxic to humans, swine, chickens, and in fact, all monogastric animals [121]. Tofu intake was associated with worse memory,

but tempeh (a fermented soy product) intake was associated with better memory [122]. Isoflavones might increase breast cancer risk in healthy women or worsen the prognosis of breast cancer patients [123].

Soy compounds	Biological properties	Selected references
Genistein, daidzein, lectins and lunasin	Anticancer	[11, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 62, 63, 65, 66, 67, 110, 113]
Isoflavones and oil	Hypercholesterolemia	[68, 69, 70, 71, 73, 74, 75, 76, 77]
Daidzein and oil	Cardiovascular diseases	[68, 72, 73, 77, 78, 79, 91, 111]
Isoflavones	Osteoporosis and menopause	[80, 81, 82, 83]
Genistein	Hypertensive	[84, 85, 86, 98, 99]
Genistein	Insulin secretion and energy metabolism	[60, 87, 88, 89]
Saponin and genistein	Blood pressure and endothelial function	[90, 91, 92, 94, 95, 96, 97, 98, 99]
Genistein	Plate aggregation and fibrinolytic activity	[100, 101, 102, 103, 104, 105]
Genistein	Antioxidant	[107, 108]
Protein and peptides	Anti aging	[109]
Protein and peptides	Anti-fatigue	[106]
Genistein	Anti-flammation	[62]
Genistein, daidzein and Glyceollins	Antifungal	[114, 118]
Genistein, daidzein and Glyceollins	Estrogenic activity	[113, 119]
Daidzein	Catecholamine synthesis	[115]
Genistein	Anti-angiogenic	[62]

Table 3. Summarizes some beneficial effects of some soybean compounds on animal and human health

Phytic acid is also criticized for reducing vital minerals due to its chelating effect, especially for diets already low in minerals [124]. Phytic acid present in soybean seeds binds to minerals and metals to form phytate (chelated forms of phytic acid with magnesium, calcium, iron, and zinc). Phytate is not digestible and impermeable molecules through cell membranes for humans or nonruminant animals. In addition, phytic acid prevents the body to use many essential minerals such as magnesium, calcium, iron and especially zinc. Unfermented soy products contain high levels of lectins/hemagglutinins. Hemagglutinin makes red blood cells unable to absorb oxygen. However, the soybean fermentation process deactivates soybean hemagglutinins and makes the amounts of lectins present in soybeans inconsiderable. However, some dried soybean products may still contain a large amount of active

or toxic lectins. These lectins are believed to cause allergic in a human body. Recently, a metalloprotein named soyatoxin exhibiting toxicity to mice (LD_{50} 7-8 mg/kg mouse upon intraperitoneal injection) was identified. Regardless of the beneficial effect of genistein, there are some controversies about safety and harmful effect of soybean food supplementation rich in genistein. Some studies reported that genistein is not safe and has harmful effects on human health. Consumption of genistein-rich soy food and supplements during pregnancy has been suggested to raise the risk of infant leukemias [125]. In addition, some researches showing stimulatory effect of genistein on proliferation of some breast cancer cells lines increase the concerning problem about the safety of genistein intake for breast cancer women [126]. Recent study reported that administration 56g soy protein powder daily caused a reduction in serum testosterone up to 4% in four weeks in a test group of 12 healthy males [127]. Finally, allergy to soy is common, and the food is listed with other foods. Only a few reported studies have attempted to confirm allergy to soy by direct challenge with the food under controlled conditions [127]. Table (3) shows several beneficial effects reported of some soybean compounds on animal and human health.

Acknowledgements

This work was supported by a grant from the Deanship of Scientific Research, King Faisal University, Kingdom of Arabia Saudi. The authors have no conflict of interest for the information presented in this review.

Author details

Sherif M. Hassan

College of Agricultural and Food Sciences, King Faisal University, Kingdom of Saudi Arabia

References

- [1] Liu K.S. Chemistry and Nutritional Value of Soybean Components. In: Soybean: Chemistry, Technology, and Utilization. New York: Chapman & Hall; 1997.p25-113.
- [2] Composition of Feedstuffs Used in Poultry Diets. In: National Research Council (NRC). Washington, DC: National Academy of Sciences; 1994.p61-68.
- [3] Derbyshire, E, Wright DJ, Boulter D. Review: Legumin and vicilin, storage proteins of legume seeds. *Phytochemistry* 1976;15:3.
- [4] Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris-Etherton P, Winston M. "Soy Protein, Isoflavones, and Cardiovascular Health. An American Heart Association Sci-

- ence Advisory for Professionals from the Nutrition Committee". *Circulation* 2006;113(7):1034–1044.
- [5] Hajos G, Gelencsér E, Grant G, Bardocz S, Sakhri M, Duguid TJ, Newman AM, Pusztai A. Effects of Proteolytic Modification and Methionine Enrichment On the Nutritional Value of Soya Albumins For Rats. *The Journal of Nutritional Biochemistry* 1996;7:481-487.
- [6] FAO/WHO (1989). Protein Quality Evaluation: Report of the Joint FAO/WHO Expert Consultation. Bethesda, MD (USA): Food and Agriculture Organization of the United Nations (Food and Nutrition Paper) 1989:51.
- [7] Wolke RL "Where There's Smoke, There's a Fryer". *The Washington Post*.2007.
- [8] Young VR. Soy Protein in Relation to Human Protein and Amino Acid Nutrition. *Journal of American Dietetic Association* 1991;91:828-835.
- [9] Wang H, Murphy, P. Isoflavone content in commercial soybean foods. *Journal of Agricultural and Food Chemistry* 1994;42(8):1666-1673.
- [10] Fournier DB, Erdman JW, Gordon GB. Soy, its components, and cancer prevention: a review of the in vitro, animal, and human data. *Cancer Epidemiology, Biomarkers and Prevention* 1998;7(11):1055–1065.
- [11] Messina M, McCaskill-Stevens W, Lampe JW. Addressing the soy and breast cancer relationship: review, commentary, and workshop proceedings. *Journal of the National Cancer Institute* 2006;98:1275-1284.
- [12] Erdman JrJ, Jadger T, Lampe J, Setchell KDR, Messina M. Not all soy products are created equal: caution needed in interpretation of research results. *The Journal of Nutrition* 2004;134(5):S1229–S1233.
- [13] Riaz, MN. *Soy Applications in Food*. Boca Raton, Florida: CRC Press;2006.
- [14] Hoogenkamp HW. *Soy Protein and Formulated Meat Products*. Wallingford, Oxon, UK: CABI Publishing; 2005:14.
- [15] Joseph GE. *Soy Protein Products*. AOCS Publishing. 2001.
- [16] Leesons S., Summers J. *Commercial Poultry Nutrition*. Guelph, Ontario, Canada: Nottingham University Press; 2005.
- [17] Giampietro PG, Bruno G, Furcolo G, Casati A, Brunetti E, Spadoni GL, Galli E. Soy Protein Formulas in Children: No Hormonal Effects in Long-term Feeding. *Journal of Pediatric Endocrinology and Metabolism* 2004;17(2):191–196.
- [18] Strom BL. "Exposure to Soy-Based Formula in Infancy and Endocrinological and Reproductive Outcomes in Young Adulthood". *The Journal of the American Medical Association* 2001;286(7):807–814.
- [19] Merritt RJ, Jenks BH. Safety of Soy-Based Infant Formulas Containing Isoflavones: The Clinical Evidence. *The Journal of Nutrition*2004;134(5):1220S–1224S.

- [20] Kwon DY, Daily JW, Kim HJ, Park S. Antidiabetic Effects of Fermented Soybean Products on Type 2 Diabetes. *Nutrition Research* 2010;30:1-13.
- [21] Park JS, Lee MY, Kim JS, Lee TS. Compositions of Nitrogen Compound and Amino acid in Soybean Paste (Doenjang) Prepared with Different Microbial Sources. *Korean Journal of Food Science and Technology* 1994; 26:609-615.
- [22] Garcia MC, Torre M, Marina ML, Laborda F. Composition and Characterization of Soybean and Related Products. *Critical Reviews in Food Science and Nutrition* 1997;37:361-391
- [23] Nakajima N, Nozaki N, Ishihara K, Ishikawa A, Tsuji H. Analysis of Isoflavone Content in Tempeh, a Fermented Soybean, and Preparation of a New Isoflavone enriched Tempeh. *Journal of Bioscience and Bioengineering* 2005;100: 685-687.
- [24] Yamabe, S, Kobayashi-Hattori, K, Kaneko, K, Endo, K, Takita, T. Effect of Soybean Varieties on the Content and Composition of Isoflavone in Rice-koji Miso. *Food Chemistry* 2007;100:369-374.
- [25] Jang CH, Park CS, Lim JK, Kim JH, Kwon DY, Kim YS, Shin DH, Kim JS. Metabolism of Isoflavone Derivatives during Manufacturing of Traditional Meju and Doenjang. *Food Science and Biotechnology* 2008; 17:442-445.
- [26] Baek LM, Park LY, Park KS, Lee SH. Effect of Starter Cultures on the Fermentative Characteristics of Cheonggukjang. *Korean Journal of Food Science and Technology* 2008;40:400-405.
- [27] Kim KS, Kim S, Yang HJ, Kwon DY. Changes of Glycinin Conformation due to pH, Heat and Salt Determined by Differential Scanning Calorimetry and Circular Dichroism. *International Journal of Food Science and Technology* 2004;39:385-393.
- [28] Choi HK, Yoon JH, Kim YS, Kwon DY. Metabolomic Profiling of Cheonggukjang during Fermentation by ¹H NMR Spectrometry and Principal Components Analysis. *Process Biochemistry* 2007;42:263-266
- [29] Kim, NY, Song EJ, Kwon DY, Kim HP, Heo MY. Antioxidant and Antigenotoxic Activities of Korean Fermented Soybean. *Food and Chemical Toxicology* 2008; 46:1184-1189.
- [30] Teakle R., Jensen J. *Heliothis punctiger*. In: Singh R., Moore R. (ed.) *Handbook of Insect Rearing*. Amsterdam: Elsevier; 1985.p312 – 322.
- [31] Davis J, Iqbal MJ, Steinle J, Oitker J, Higginbotham DA, Peterson RG. Soy Protein Influences the Development of the Metabolic Syndrome in Male Obese ZDFxSHHF Rats. *Hormone and Metabolic Research* 2007;37:316-325.
- [32] Rice-Evans C. Flavonoid antioxidants. *Current Medicinal Chemistry* 2001; 8(7): 797-807.

- [33] Park OJ, Surh Y-H. Chemopreventive potential of epigallocatechin gallate and genistein: evidence from epidemiological and laboratory studies. *Toxicology Letters* 2004; 150(1):43-56.
- [34] Tolleson WH, Doerge DR, Churchwell MI, Marques MM, Roberts DW. Metabolism of Biochanin A and Formononetin by Human Liver Microsomes in Vitro. *Journal of Agricultural and Food Chemistry* 2002;50(17):4783-4790.
- [35] Galvez AF, Revilla MJR, de Lumen BO. A novel methionine-rich protein from soybean cotyledon: cloning and characterization of cDNA (accession No. AF005030). *Plant Register #PGR97-103. Plant Physiology* 1997;114:1567-1569.
- [36] de Mejia EG, Vasconez M, de Lumen BO, Nelson R. Lunasin concentration in different soybean genotypes, commercial soy protein, and isoflavone products. *Journal of Agricultural and Food Chemistry* 2004;52(19):5882-5887.
- [37] Wang W, Dia VP, Vasconez M, Nelson RL, de Mejia EG. Analysis of soybean protein-derived peptides and the effect of cultivar, environmental conditions, and processing on lunasin concentration in soybean and soy products. *Journal of AOAC International* 2008;91(4):936-946.
- [38] de Mejia EG., Dia VP. Chemistry and biological properties of soybean peptides and proteins. In: Cadwallader K. et al. (ed.) *Chemistry, Texture and Flavor of Soy*. USA: American Chemical Society; 2010b.p133-154. Available from <http://pubs.acs.org>.
- [39] Shiraiwa M, Harada K, Okubo K. Composition and structure of group B saponin in soybean seed. *Agricultural and biological chemistry* 1991;55:911-917.
- [40] Kuduo S, Tonomura M, Tsukamoto C. Isolation and structure elucidation of DDMP-conjugated soyasaponins as genuine saponins from soybean seeds. *Bioscience, Biotechnology, and Biochemistry*. 1993;57:546-550.
- [41] Ireland, PA, Dziedzic SZ, Kearsley MW. Saponin content of soya and some commercial soya products by means of high-performance liquid chromatography of the saponin. *Journal of the Science of Food and Agriculture* 1986;37:694-698.
- [42] Berhow MA, Kong SB, Vermillion KE, Duval SM. Complete quantification of group A and group B soyasaponins in soybeans. *Journal of Agricultural and Food Chemistry* 2006;54:2035-2044.
- [43] Adlercreutz H, Mazur W, Bartels P, Elomaa V, Watanabe S, Wähälä K, Landström M, Lundin E, Bergh A, Damber JE, Aman P, Widmark A, Johansson A, Zhang JX, Hallmans G. "Phytoestrogens and Prostate Disease". *The Journal of Nutrition* 2000;130(3): 658S-659S.
- [44] De Kleijn MJ, Van Der Schouw YT, Wilson PW, Grobbee DE, Jacques PF. Dietary Intake of Phytoestrogens is Associated With a Favorable Metabolic Cardiovascular Risk Profile in Postmenopausal U.S. Women: The Framingham Study. *The Journal of Nutrition* 2002;132(2):276-282.

- [45] Valsta LM, Kilkkinen A, Mazur W, Nurmi T, Lampi A-M, Ovaskainen M-L, Korhonen T, Adlercreutz H, Pietinen P. Phyto-oestrogen Database of Foods and Average Intake in Finland. *British Journal of Nutrition* 2003;89 (5):S31-S38.
- [46] Thompson, Lilian U.; Boucher, Beatrice A.; Liu, Zhen; Cotterchio, Michelle; Kreiger N. Phytoestrogen Content of Foods Consumed in Canada, Including Isoflavones, Lignans, and Coumestan". *Nutrition and Cancer* 2006;54 (2): 184-201.
- [47] Peterson G, Barnes S Genistein and Biochanin A. Inhibit the Growth of Human Prostate Cancer Cells but not Epidermal Growth Factor Receptor Autophosphorylation. *Prostate* 1993;22:335-345.
- [48] Wu AH, Ziegler RG, Horn-Ross PL, Nomura AMY, West DW, Kolonel LN, Rosenthal JF, Hoover RN, Pike MC. Tofu and risk of breast cancer in Asian-Americans. *Cancer Epidemiological Biomarkers Preview* 1996;5(11):901-906.
- [49] Wu AH, Ziegler RG, Nomura AM, West DW, Kolonel LN, Horn-Ross PL, Hoover RN, Pike MC. Soy intake and risk of breast cancer in Asians and Asian Americans. *The American Journal of Clinical Nutrition* 1998;68:1437S-1443S.
- [50] Zheng W, Dai Q, Custer LJ, Shu XO, Wen WQ, Jin F, Franke AA. Urinary excretion of isoflavonoids and the risk of breast cancer. *Cancer Epidemiology Biomarkers & Prevention* 1999;8(1):35-40.
- [51] Boyapati SM, Shu XO, Ruan ZX, Dai Q, Cai Q, Gao YT, Zheng W. Soyfood intake and breast cancer survival: a followup of the Shanghai Breast Cancer Study. *Breast Cancer Res Treat* 2005;92:11-17.
- [52] Lof M, Weiderpass E. Epidemiological evidence suggests that dietary phytoestrogens intake is associated with reduced risk of breast, endometrial and prostate cancers. *Nutrition Research* 2006; 26(12):609-619.
- [53] Peterson G, Barnes S. Genistein Inhibition of the Growth of Human Breast Cancer Cells: Independence from Estrogen Receptors and the Multi-drug Resistance Gene. *Biochemical and Biophysical Research Communications* 1991; 179: 661-667.
- [54] Jacobsen BK, Knutsen SF, Fraser GE. Does high soy milk intake reduce prostate cancer incidence? The Adventist health study (United States). *Cancer Causes Control* 1998; 9(6):553-557.
- [55] Goodman MT, Wilkens LR, Hankin JH, Lyu LC, Wu AH, Kolonel LN. Association of soy and fiber consumption with the risk of endometrial cancer. *American Journal of Epidemiology* 1997;146(4):294-306.
- [56] Swanson CA, Mao BL, Li JY, Lubin JH, Yao SX, Wang JZ, Cai SK, Hou Y, Luo QS, Blot WJ. Dietary determinants of lung-cancer risk - results from a case-control study in Yunnan province, China. *International Journal of Cancer* 1992;50(6):876-880.

- [57] Azuma N, Machida K, Saeki T, Kanamoto R, Iwami K. Preventive effect of soybean resistant proteins against experimental tumorigenesis in rat colon. *Journal of Nutritional Science and Vitaminology* 2000;46(1):23–29.
- [58] Kanamoto R, Azuma N, Miyamoto T, Saeki T, Tsuchihashi Y, Iwami K. Soybean resistant proteins interrupt an enterohepatic circulation of bile acids and suppress liver tumorigenesis induced by azoxymethane and dietary deoxycholate in rats. *Bio-science, Biotechnology, and Biochemistry* 2001; 65(4):999–1002.
- [59] Sun CL, Yuan JM, Arakawa K, Low SH, Lee HP, Yu MC. Dietary soy and increased risk of bladder cancer: The Singapore Chinese health study. *Cancer Epidemiological Biomarkers Preview* 2002;11(12):1674-1677.
- [60] Akiyama T, Ishida J, Nakagawa S, Ogawara H, Watanabe S, Itoh N, Shibuya M, Fukami Y. Genistein a specific inhibitor of tyrosine-specific protein kinases. *The Journal of Biological Chemistry* 1987;262:5592-5595.
- [61] Zhou Y, Lee AS. Mechanism for the suppression of the mammalian stress response by genistein, an anticancer phytoestrogen from soy. *Journal of National Cancer Institute* 1998;9(5):381–388.
- [62] Gilani G.S., Anderson J.J.B., editor. *Phytoestrogens and Health*. IL, USA: AOCS Press; 2002.
- [63] de Mejia EG, Dia VP. The role of nutraceutical proteins and peptides in apoptosis, angiogenesis, and metastasis of cancer cells. *Cancer Metastasis Review* 2010a; 29(3): 511-528.
- [64] de Mejia EG, Bradford T, Hasler C The anticarcinogenic potential of soybean lectin and lunasin. *Nutrition Reviews* 2003;61(7):239-246.
- [65] Galvez A.F, Chen N, Macasieb J, de Lumen BO. Chemopreventive property of a soybean peptide (Lunasin) that binds to deacetylated histones and inhibit acetylation. *Cancer Research* 2001; 61(20):7473-7478.
- [66] Dia VP, and de Mejia EG. Lunasin induces apoptosis and modifies the expression of genes associated with extracellular matrix and cell adhesion in human metastatic colon cancer cells. *Molecular Nutrition and Food Research* 2011;55(4): 623-634.
- [67] Hsieh C-C, Hernandez-Ledesma B, de Lumen BO. Lunasin, a novel seed peptide, sensitizes human breast cancer MDA-MB-231 cells to aspirin-arrested cell cycle and induced-apoptosis. *Chemico-Biological Interactions* 2010;186(2):127-134.
- [68] Carroll KK. Hypercholesterolemia and atherosclerosis: effects of dietary protein. *Fed Proc* 1982;41:2792-2796.
- [69] Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. *The New England Journal of Medicine* 1995;333:276-282.

- [70] Crouse JR III, Morgan T, Terry JG, Ellis J, Vitolins M, Burke GL. A randomized trial comparing the effect of casein with that of soy protein containing varying amounts of isoflavones on plasma concentrations of lipids and lipoproteins. *Archives of Internal Medicine* 1999;159:2070-2076.
- [71] Jenkins DJ, Kendall CW, Jackson CJ, Connelly PW, Parker T, Faulkner D, Vidgen E, Cunnane SC, Leiter LA, Josse RG. Effects of high- and low isoflavone soyfoods on blood lipids, oxidized LDL, homocysteine, and blood pressure in hyperlipidemic men and women. *The American Journal of Clinical Nutrition* 2002; 76:365-372.
- [72] Yanagihara N, Toyohira Y, Shinohara Y. Insights into the pharmacological potentials of estrogens and phytoestrogens on catecholamine signaling. *Annals of the New York Academy of Sciences* 2008;1129: 96-104.
- [73] Keys A. *Seven Countries: A Multivariate Analysis of Death and Coronary Heart Disease*. Cambridge, Massachusetts: Harvard University Press;1980.
- [74] Descovich GC, Ceredi C, Gaddi A, Benassi MS, Mannino G, Colombo L, Cattin L, Fontana G, Senin U, Mannarino E, Caruzzo C, Bertelli E, Fragiaco C, Nosedà G, Sirtori M, Sirtori CR. Multicentre study of soybean protein diet for outpatient hypercholesterolaemic patients. *Lancet* 1980;2:709-712.
- [75] Potter SM, Baum JA, Teng H, Stillman RJ, Shay NF, Erdman Jr JW. Soy protein and isoflavones: their effects on blood lipids and bone density in postmenopausal women, *The American Journal of Clinical Nutrition* 1998;68 (Suppl):1375S-1379S.
- [76] Zhan S, Ho SC. Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile. *The American Journal of Clinical Nutrition* 2005;81:397-408.
- [77] Kummerow FA, Mahfouz MM, Zhou Q. Trans fatty acids in partially hydrogenated soybean oil inhibit prostacyclin release by endothelial cells in presence of high level of linoleic acid, *Prostaglandins & other Lipid Mediators* 2007;84(3-4):138-153.
- [78] Lu C, Liu Y. Interaction of lipoic acid radical cations with vitamins C and E analogue and hydroxycinnamic acid derivatives. *Archives of Biochemistry and Biophysics* 2002;406:78-84.
- [79] Henkel J. Soy:Health Claims for Soy Protein, Question About Other Components. *FDA Consumer (Food and Drug Administration)* 2000;34 (3): 18-20.
- [80] Toda T, Uesugi T, Hirai K, Nukaya H, Tsuji K, Ishida H. New 6-O-acyl isoflavone Glycosides from Soybeans Fermented with *Bacillus subtilis* (natto). I. 6-O-succinylated Isoflavone Glycosides and Their Preventive Effects on Bone Loss in Ovariectomized Rats Fed a Calcium-Deficient Diet. *Biological & Pharmaceutical Bulletin* 1999a; 22(11):1193-1201.
- [81] Toda T, Uesugi T, Hirai K, Nukaya H, Tsuji K, Ishida H. New 6-O-acyl isoflavone glycosides from soybeans fermented with *Bacillus subtilis* (natto). I. 6-O-succinylated isoflavone glycosides and their preventive effects on bone loss in ovariectomized rats fed a calcium-deficient diet, *Biological & Pharmaceutical Bulletin* 1999b22:1193-1201.

- [82] Messina M, Messina V. Soyfoods, soybean isoflavones, and bone health: a brief overview. *Journal of Renal Nutrition* 2000;10:63-68.
- [83] Persky VW, Turyk ME, Wang L, Freels S, Chatterton RJ, Barnes S, Erdman JJ, Sepkovic DW, Bradlow HL, Potter S. Effect of soy protein on endogenous hormones in postmenopausal women. *American Society for Clinical Nutrition* 2002;75(1):145-153.
- [84] Kim SJ, Jung KO, Park KY. Inhibitory Effect of Kochujang Extracts on Chemically Induced Mutagenesis. *Journal of Food Science and Nutrition* 1999; 4:38-42.
- [85] Ahn SW, Kim KM, Yu KW, Noh DO, Suh HJ. Isolation of angiotensin I converting enzyme inhibitory peptide from soybean hydrolysate. *Food Science Biotechnology* 2000;9(3):378-381.
- [86] Pool JL, Smith SG, Nelson EB, Taylor AA, Gomez HJ. Angiotensin converting enzyme inhibitors compared with thiazide diuretics or beta-blockers as monotherapy for treatment of mild essential hypertension. *Current Opinion Cardiology* 1989;4:11-15.
- [87] Sites CK, Cooper BC, Toth MJ, Gastaldelli A, Arabshahi A, Barnes S. Effect of Daily Supplement of Soy Protein on Body Composition and Insulin Secretion in Postmenopausal Women. *Fertility and Sterility* 2007; 88:1609-1617.
- [88] Wagner JD, Zhang L, Shadoan MK, Kavanagh K, Chen H, Tresnasari K, Kaplan JR, Adams MR. Effects of soy protein and isoflavones on insulin resistance and adiponectin in male monkeys. *Metabolism* 2008;57:S24-S31.
- [89] Solanky KS, Bailey NJ, Beckwith-Hall BM, Bingham S, Davis A, Holmes E, Nicholson JK, Cassidy A. Biofluid 1H NMR-based metabolomic techniques in nutrition research - metabolic effects of dietary isoflavones in humans. *The Journal of Nutritional Biochemistry* 2005;16:236-244.
- [90] Hiwatashi K, Shirakawa H, Hori K, Yoshiki Y, Suzuki N, Hokari M, Komai M, Takahashi S. Reduction of blood pressure by soybean saponins, rennin inhibitors from soybean, in spontaneously hypertensive rats. *Bioscience, Biotechnology, and Biochemistry* 2010;74:2310-2312.
- [91] Sagara M, Kanda T, Njeleker M, Teramoto T, Armitage L, Birt N, Birt C, Yamori Y. Effects of dietary intake of soy protein and isoflavones on cardiovascular disease risk factors in high risk, middle-aged men in Scotland. *Journal of the American College of Nutrition* 2004; 23:85-91.
- [92] Welty, FK, Lee, KS, Lew, NS, Zhou, JR. Effect of soy nuts on blood pressure and lipid levels in hypertensive, prehypertensive, and normotensive postmenopausal women. *Archives of Internal Medicine* 2007;167:1060-1067.
- [93] Teede HJ, Giannopoulos D, Dalais, FS, Hodgson, J, McGrath, BP. Randomised, controlled, cross-over trial of soy protein with isoflavones on blood pressure and arterial function in hypertensive subjects. *Journal of the American College of Nutrition* 2006;25:533-540.

- [94] Cuevas AM, Iribarra VL, Castillo OA, Yanez MD, Germain AM. Isolated soy protein improves endothelial function in postmenopausal hypercholesterolemic women. *European Journal of Clinical Nutrition* 2003;57:889-894.
- [95] Lissin LW, Oka R, Lakshmi S, Cooke JP. Isoflavones improve vascular reactivity in post-menopausal women with hypercholesterolemia. *Vascular Medicine* 2004;9:26-30.
- [96] Colacurci N, Chiantera A, Fornaro F, de NV, Manzella D, Arciello A, Chiantera V, Improta L, Paolisso G. Effects of soy isoflavones on endothelial function in healthy postmenopausal women. *Menopause* 2005;12:299-307.
- [97] Hall WL, Formanuk NL, Harnpanich D, Cheung M, Talbot D, Chowienczyk PJ, Sanders TA. A meal enriched with soy isoflavones increases nitric oxidemediated vasodilation in healthy postmenopausal women. *Journal of Nutrition* 2008;138:1288-1292.
- [98] Vera R, Sanchez M, Galisteo M, Villar IC, Jimenez R, Zarzuelo A, Perez-Vizcaino F, Duarte J. Chronic administration of genistein improves endothelial dysfunction in spontaneously hypertensive rats: involvement of eNOS, caveolin and calmodulin expression and NADPH oxidase activity. *Clinical Science* 2007;112:183-191.
- [99] Si H, Liu, D. Genistein, a soy phytoestrogen, upregulates the expression of human endothelial nitric oxide synthase and lowers blood pressure in spontaneously hypertensive rats. *Journal of Nutrition* 2008;138:297-304.
- [100] Nakashima S, Koike T, Nozawa Y. Genistein, a protein tyrosine kinase inhibitor, inhibits thromboxane A2-mediated human platelet responses. *Molecular Pharmacology* 1991;39:475-480.
- [101] McNicol A. The effects of genistein on platelet function are due to thromboxane receptor antagonism rather than inhibition of tyrosine kinase. *Prostaglandins Leukot Essent Fatty Acids* 1993;48:379-384.
- [102] Fujita M, Nomura K, Hong K, Ito Y, Asada A, Nishimuro S. Purification and characterization of a strong fibrinolytic enzyme (nattokinase) in the vegetable cheese natto, a popular soybean fermented food in Japan. *Biochemical and Biophysical Research Communications* 1993;197:1340-1347.
- [103] Fujita M, Hong K, Ito Y, Fujii R, Kariya K. Nishimuro Shrombolytic effect of nattokinase on a chemically induced thrombosis model in rat. *Biological & Pharmaceutical Bulletin* 1995;18:1387-1391.
- [104] Suzuki Y, Kondo K, Matsumoto Y, Zhao BQ, Otsuguro K, Maeda T, Tsukamoto Y, Urano T, Umemura K. Dietary supplementation of fermented soybean, natto, suppresses intimal thickening and modulates the lysis of mural thrombi after endothelial injury in rat femoral artery. *Life Sciences* 2003;73:1289-1298.

- [105] Hsia CH, Shen MC, Lin JS, Wen YK, Hwang KL, Cham TM, Yang NC. Nattokinase decreases plasma levels of fibrinogen, factor VII, and factor VIII in human subjects. *Nutrition Research* 2009;29:190-196.
- [106] Marquezi ML, Roschel HA, Costa ADS, Sawada LA, Lancha AH. Effect of aspartate and asparagine supplementation on fatigue determinants in intense exercise. *International Journal of Sport Nutrition and Exercise Metabolism* 2003;13(1):65-67.
- [107] Chen HM, Muramoto K, Yamauchi F, Fujimoto K, Nokihara K. Antioxidative properties of histidine-containing peptides designed from peptide fragments found in the digests of a soybean protein. *Journal of Agricultural and Food Chemistry* 1998; 46(1): 49-53.
- [108] Tsai P, Huang P. Effects of isoflavones containing soy protein isolate compared with fish protein on serum lipids and susceptibility of low density lipoprotein and liver lipids to in vitro oxidation in hamsters. *The Journal of Nutritional Biochemistry* 1999;10(11):631-637.
- [109] Sudel KM, Venzke K, Mielke H, Breitenbach U, Mundt C, Jaspers S, Koop U, Sauer- mann K, Knussman-Hartig E, Moll I, Gercken G, Young AR, Stab F, Wenck H, Gallinat S. Novel aspects of intrinsic and extrinsic aging of human skin: beneficial effects of soy extract. *Photochemistry and Photobiology* 2005;81(3), 581-587.
- [110] Birt DF, Hendrich S, Wang W. Dietary agents in cancer prevention: flavonoids and isoflavonoids. *Pharmacology & therapeutics* 2001;90(2-3):157-177.
- [111] Rimbach G, Boesch-Saadatmandi C, Frank J, Fuchs D, Wenzel U, Daniel H, Hall WL, Weinberg PD. Dietary isoflavones in the prevention of cardiovascular disease - A molecular perspective. *Food and Chemical Toxicology* 2008;46(4):1308-1319.
- [112] Coward L, Barnes N, Setchell K, Barnes S. Genistein, daidzein, and their beta glyco- side conjugates: antitumor isoflavones in soybean food from American and Asian di- ets. *Journal of Agricultural Food Chemistry* 1993; 41(11):1961-1967.
- [113] Doerge DR, Sheehan DM. Goitrogenic and Estrogenic Activity of Soy Isoflavones, *Environmental Health Perspectives Supplements* 2002;110(3):349-353.
- [114] Weidenboerner, M, Hindorf, H, Jha, HC, Tsotsonos, P, Egge, H. Antifungal Activity of Isoflavonoids in Different Reduced Stages on *Rhizoctonia solani* and *Sclerotium rolfsii*. *Phytochemistry* 1990;29(3):801-803.
- [115] Liu M, Yanagihara N, Toyohira Y, Tsutsui M, Ueno, S, Shinohara Y. Dual effects of daidzein, a soy isoflavone, on catecholamine synthesis and secretion in cultured bo- vine adrenal medullary cells. *Endocrinol* 2007;148:5348-5354.
- [116] Kritz-Silverstein D, Von Mühlen D, Barrett-Connor E, Bressel MA. Isoflavones and Cognitive Function in Older Women: The Soy and Postmenopausal Health in Aging (SOPHIA) Study. *Menopause* 2003;10(3):196-202.

- [117] File SE, Hartley DE, Elsabagh S, Duffy R, Wiseman H. Cognitive Improvement After 6 Weeks of Soy Supplements in Postmenopausal Women is Limited to Frontal Lobe Function. *Menopause* 2005;12(2):193–201.
- [118] Kim HJ, Suh H-J, Lee CH, Kim JH, Kang SC, Park S, Kim J-S. Antifungal Activity of Glyceollins Isolated From Soybean Elicited with *Aspergillus Sojae*. *Journal of Agricultural and Food Chemistry* 2010;58 (17): 9483–9487.
- [119] Tilghman SL, Boué SM, Burow ME. Glyceollins, a Novel Class of Antiestrogenic Phytoalexins. *Molecular and Cellular Pharmacology* 2010;2(4):155–160.
- [120] Sastry M, Murray D. The contribution of trypsin inhibitors to the nutritional value of chickpea seed protein. *Journal of Science Food and Agriculture* 1987;40: 253 – 261.
- [121] Circle SJ, Smith AH. Soybeans: chemistry and technology. Westport, Conn: Avi Pub. Co.; 1972.
- [122] Hogervorst E, Sadjimim T, Yesufu A, Kreager P, Rahardjo TB. High Tofu Intake is Associated with Worse Memory in Elderly Indonesian Men and Women". *Dementia and Geriatric Cognitive Disorders* 2008;26 (1): 50–57.
- [123] Messina MJ, Loprinzi CL. Soy for breast cancer survivors: a critical review of the literature. *The Journal of Nutrition* 2001;131(11):3095–3108.
- [124] National Research Council (NRC), Committee on Food Protection, Food and Nutrition Board "Phytates". *Toxicants Occurring Naturally in Foods*. Washington, DC: National Academy of Sciences; 1973.p363–371.
- [125] Hengstler JG, Heimerdinger CK, Schiffer IB, Gebhard S, Sagemuller J, Tanner B, Bolt HM, Oesch F Dietary topoisomerase II-poisons: contribution of soy products to infant leukemia? *Experimental and Clinical Sciences International online journal for advances in science Journal* 2002;1:8-14.
- [126] Lavigne JA, Takahashi Y, Chandramouli GVR, Liu H, Perkins SN, Hursting SD, Wang TTY Concentration-dependent effects of genistein on global gene expression in MCF-7 breast cancer cells: an oligo microarray study. *Breast Cancer Research and Treatment* 2008;110(1):85-98.
- [127] Goodin S, Shen F, Shih WJ, Dave N, Kane MP, Medina P, Lambert GH, Aisner J, Gallo M, DiPaola RS Clinical and Biological Activity of Soy Protein Powder Supplementation in Healthy Male Volunteers. *Cancer Epidemiology Biomarkers & Prevention* 2007;16 (4): 829–833.
- [128] Cantani A, Lucenti P Natural History of Soy Allergy and/or Intolerance in Children, and Clinical Use of Soy-protein Formulas. *Pediatric Journal of Allergy and Clinical Immunology* 1997;8 (2):59–74.

