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Soy as a Functional Food

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1. Introduction

Soybean (*Glycine max*, L.) has been part of Southeast Asia culture for almost 2 millennia. However, only in the second half of the 19th century has it started being used in the Western world coinciding with the Chinese migration to the USA. Today, USA, South America, especially Brazil, and Northwestern Europe, account for almost 90% of the world total soybean production. At first, the nutrition value of soybean was attributed to its high quality protein content thus attracting considerable interest for its use in human diet. Nowadays, it is known that soybeans are a rich source of phytochemicals, and many of those compounds have important beneficial effects on human and animal health.
Among the important phytochemicals in soybeans for human health, phytoestrogens, mainly, isoflavones (genistein and daidzein) and lignans, are the most widely studied. Nevertheless, saponins and phytosterols have also been the subject of research on soybeans. This chapter will discuss these phytochemicals compounds, their chemical structures, and their relationship with the major biological functions, scientifically proved, and their health benefits.

2. Phytoestrogens

Phytoestrogens are non-steroidal compounds found in plants. They demonstrate estrogenic and/or antiestrogenic activity and constitute a diverse group of compounds that have similar chemical structures and biological activity of estrogens.
The phytoestrogens can be divided into four main classes: isoflavonoids, flavonoids, coumestrol and lignans. Nearly all food vegetables have phytoestrogens although the amount and concentration of the compounds vary significantly. Some vegetables are high in phytoestrogens content such as flaxseed, which are a rich source of lignans; soybeans and chickpeas have high concentrations of isoflavones. Lignans can also be found in cereals, vegetables, and fruits (Kuhnle et al., 2009), whereas isoflavone-containing foods, may be specially related and limited to grains and soy products such as tofu, soy beverages, soy flour, and soy flakes among others products, due to its high consumption. Discussions about the chemical structure and major properties such as the main biological functions will focus particularly on this type of phytoestrogen.

2.1 Chemical structure and properties of phytoestrogens

Phytoestrogens are intrinsic plant compounds and their contents depend on a number of factors including the cultivar, place of production, planting or harvesting season, or growth-related factors.

Among the phytoestrogens, isoflavones are found mostly in plants, especially in the glycosides forms and are biologically inactive. Soybeans are a main source of phytoestrogens in the human diet. Flavonoids are widely distributed throughout the plant kingdom and are found in many vegetables, grains, herbs, and green tea. As for the coumestrol, its only sources are alfalfa sprouts and a variety of bean seeds. Chemical structures of the four classes of phytoestrogens are shown in Figure 1.

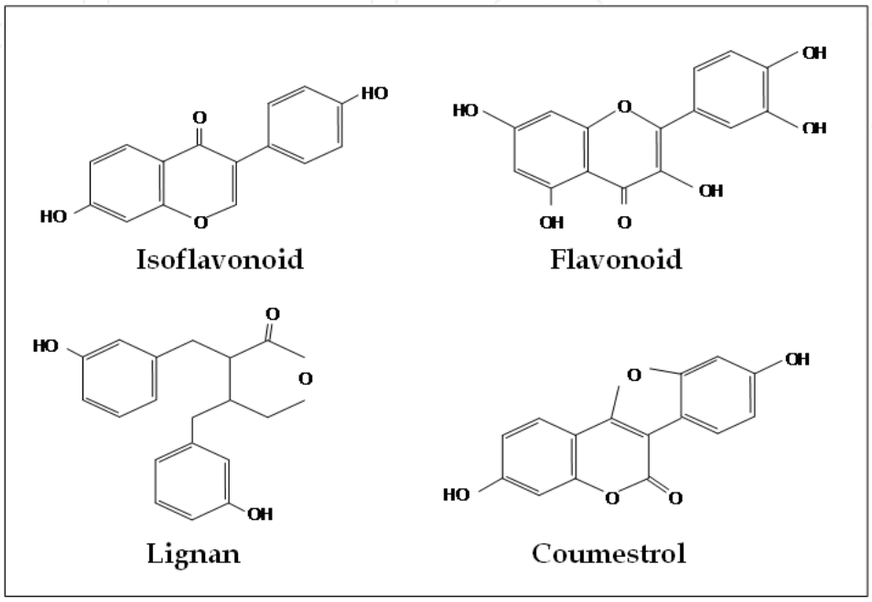

Fig. 1. Chemical structure of the major classes of phytoestrogens.

The contents of isoflavones in soybean and soy products have been extensively analyzed and studied. Those studies have demonstrated that the concentration and composition of isoflavones vary considerably, which can be explained by environmental and geographical conditions as well as by the level of industrial transformation. Daidzein, genistein, and glycitein are the most abundant isoflavones found in soy.

Isoflavones are naturally occurring compounds in foods as glycosides conjugated highly polar conjugated or non-conjugated form. For example, the textured soy protein and tofu have high contents of conjugated isoflavones such as daidzein and genistein, while fermented soy products such as miso, have approximately 90% of the isoflavones in non-conjugated form, mainly daidzein and genistein (Coward et al., 1993). Those chemical structures and their similarity with equol and estradiol (human estrogen) can be seen in Figure 2.

When ingested, phytoestrogens are metabolized by intestinal bacteria to equol (Cassidy, 1996; Setcehll et al., 1984). The metabolism of phytoestrogens in humans is probably facilitated and modulated by bacterial colonies; therefore, the colonic ecology might be associated with increased efficiency in conversion of dietary soy isoflavones to their bioactive form (Teas et al., 2009). After absorption, isoflavones undergo enterohepatic circulation and are primarily conjugated with glucuronic acid in the liver and then excreted in urine.

Numerous studies have shown that a number of factors influence the bioavailability of soy isoflavones. Xu et al. (1994) evaluated the bioavailability of daidzein and genistein from

soymilk and observed that daidzein was more bioavailable in adult women. The efficiency of absorption of soymilk isoflavones varies from 13% to 35% depending on individual gut microflora (Xu et al., 1995). Lampe et al., (1998) suggested that dietary fiber and other compounds in a diet rich in fibers might promote the growth and/or activity of bacterial colonies favorable to the conversion of daidzein to one of its catabolic products, equol, for a further absorption in the colon. Fermentation can reduce the isoflavones content in food products but increasing its bioavailability (Hutchins et al., 1995). Recently, it has been demonstrated in postmenopausal Japanese women that the bioavailability of isoflavones in fermented soy products rich in aglycones is much greater compared to the consumption of glucoside-rich non-fermented soybeans (Okabe et al., 2011).

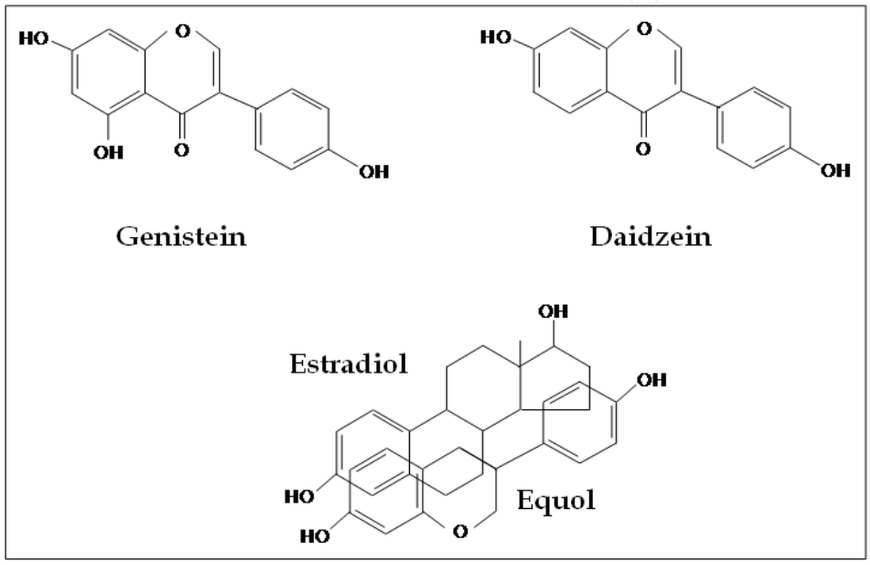

Fig. 2. Chemical structure of the major isoflavones found in soy and their similarity to equol and estradiol.

2.2 Mechanisms of action and biological functions

In recent years, it has been demonstrated that the phytoestrogens have multiple mechanisms of action. Such growing scientific evidence suggests that isoflavones are responsible for many of health benefits, which include the prevention and treatment of cardiovascular diseases, cancer, osteoporosis, and also for the relief of unpleasant pre- and post-menstrual symptoms.

2.2.1 Reduction in risk of coronary heart diseases

Coronary heart diseases are the leading cause of death especially in industrialized countries. High levels of total and LDL cholesterol are considered risk factors for these diseases. In humans, the consumption of 25g of soy protein per day may reduce the levels of total and LDL cholesterol

Preliminary results suggest that isoflavones, such as estrogens, may produce a cardioprotector effect directly on blood vessel walls and on other processes involved in the etiology of coronary heart diseases although the results are sometimes incompatible. Soy isoflavones act as potent antioxidants able to reduce the oxidation of LDL cholesterol and to induce vascular reactivity. The presence of modified LDL cholesterol in the blood vessel

walls contribute to the formation of atherosclerotic plaques and, according to studies in humans, soy isoflavones improve endothelial function and arterial relaxation.

Nagarajan (2010) suggested that soy isoflavones may inhibit the effect of endothelial cell activation associated to chronicle diseases such as atherosclerosis by blocking the activation of inflammatory cells and the adhesion to the vascular endothelium. This author concluded that the atherosclerotic protection of soy isoflavones is mediated through the regulation of monocyte activation (Figure 3). Another mechanism associated with soy isoflavones regarding cardiovascular health has been demonstrated by the reduction of vascular contraction through inhibition of the RhoA/Rho-kinase signaling pathway, which has a major role in muscle contraction (Seok et al., 2008).

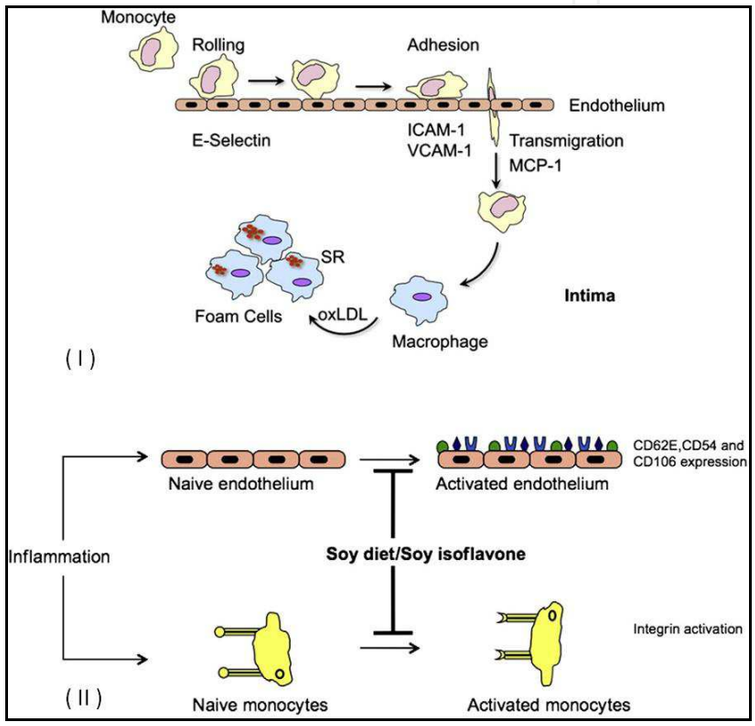

Fig. 3. (I) Inflammatory process associated with atherosclerosis. (II) Soy/isoflavone diet blocks endothelial and monocytes activation (Adapted from Nagarajan, 2010).

A prospective study carried out in Japan showed that the high consumption of isoflavones was associated with reduced risk of cerebral and myocardial infarctions in women, mainly in postmenopausal women, suggesting that the consumption of dietary isoflavones may be beneficial for the prevention of cardiovascular diseases (Kokubo et al., 2007).

Isoflavones may have inhibitory effects on the adipose tissue that could help prevent obesity-associated diseases by improving the plasma lipid profile. Nevertheless, *in vivo* studies, especially in humans, have demonstrated that the mechanisms of action of soy isoflavones seem to be dependent upon interactions between some other factors, such as the presence of soy protein and intestinal bacteria (Ørgaard & Jensen, 2008).

Cardiovascular health benefits of soy isoflavones are controversial. It has been suggested that a genistein supplemented diet (Villa et al., 2009) improves the glycemic and vascular reactivity indexes in postmenopausal women compared to the control. Nonetheless,

discrepancies in clinical studies may be associated with the differences in intestinal bacterial flora of subjects and, therefore, with the bioavailability of soy isoflavones metabolites, differences in dose-response effects, duration of isoflavones supplementation, and the limited number and metabolic status of subjects included in supplementation trials (Siow & Mann, 2010)

2.2.2 Anticancer effects

Most of the evidences of the phytoestrogens effects on humans are epidemiological and are based on the differences in the consumption of soy products in different areas of the world, considering soy products as the major source of isoflavones. A recent publication of a meta-analysis of a prospective study suggested that the consumption of isoflavones is associated with a reduced risk of breast cancer incidence in Asian populations (Dong & Qin, 2011). Accordingly, anticancer effects of soy isoflavones have been reported on prostate and colon cancer. The mechanisms that define the anticancer effects of isoflavones have also been reported in several studies that suggest various cellular pathways of the functional role as an anticancer agent.

Studies have demonstrated that isoflavones prevent the growth of a variety of cells including those that are not hormone-dependent, these effects are based on the capacity of isoflavones to inhibit the activity of enzymes that control cell growth. Recently, it has been proved that dietary genistein may reduce breast cancer progression via transcriptional regulation of Rho GTPases and PAK (Martínez-Montemayor et al., 2010). Genistein acts as an inhibitor of the tyrosine-kinase activity, essential enzyme in the biological control of cell growth and differentiation.

Another mechanism proposed for the anticancer activity of isoflavones was demonstrated by the inhibition of angiogenesis. Guo et al. (2007) found that soy isoflavones may inhibit prostate tumor angiogenesis through the suppression of vascular endothelial growth factor signaling pathways between tumor cells and vascular endothelial cells. Similar results were found by Su et al., (2005) in human bladder cancer cells lines. These authors demonstrated that isoflavones did not exhibit toxicity to normal bladder cells due to their angiogenic inhibitor effects.

In prostate cancer cell lines has been observed that genistein significantly decreased reactive oxygen species levels and induce the expression of antioxidant enzymes such as manganese, superoxide dismutase and catalase through AMP-activated protein kinase (AMPK) activation and increase PTEN expression (phosphatase and tensin homolog deleted from chromosome 10) (Park et al., 2010).

Based on *in vitro* studies, it has been proposed that isoflavones antagonize tumor cell growth in different cell lines by inhibiting cell cycle and inducing apoptosis. Studies have showed that isoflavones act in the activation of apoptotic pathways. Isoflavones may to induce the formation of Smad-DNA complexes and phosphorylation of Smad2 and Smad3 indicating increased TGF-β1 signaling, which has been associated with proapoptotic and antimitotic activities inducing the death of tumor cells (Davis et al., 2008; Yu et al., 2005).

2.2.3 Pre- and post- menopausal effects

Experimental and epidemiological evidences support the hypothesis that phytoestrogens have estrogenic and antiestrogenic effects in women. The biological effect varies according

to the woman's biological phase. Hence in premenopausal women, the phytoestrogens act as antiestrogens when the estrogen levels are high, and they act as estrogen in postmenopausal women when the estrogen levels are low (Messina, 2000).

2.2.3.1 Premenopause

Studies of controlled intervention in premenopausal women suggest that phytoestrogens diet may produce estrogenic effects (Cassidy et al., 1994, 1995). The interest in soy's hormonal effects on premenopausal women is based on potential antiestrogenic benefits evidenced in hormone-dependent cancers, such as breast cancer. Hence, frequent assays measure the plasma concentration of reproductive hormones and the menstrual cycle. A reduced risk of breast cancer is associated to a longer menstrual cycle, reduced estrogens, increase in sex hormone-binding globulin, and increase urinary excretion ratio of 2- to 16α-hidroxy estrogens (Kurzer, 2002). In a randomized study with 40 premenopausal women was demonstrated that a soy diet slightly increased menstrual cycle length by 1.8±0.7 days and significantly increased urinary isoflavonoid excretion compared to women fed a control diet (Brown et al., 2002). In similar study, Hooper et al. (2009) found that the consumption of isoflavone-rich soy products significantly reduced concentrations of FSH and LH hormones that regulate the development, growth, puberty maturation, and reproduction processes in premenopausal women. Menstrual cycle length was increased by 1.05 days.

A recently published study, carried out in 73,223 premenopausal Chinese women demonstrated that the consumption of soy protein or isoflavones was inversely associated with the risk of breast cancer, and the association was highly statistically significant (P for trend < 0.001)). Women who frequently consume a high amount of soy foods during adolescence and adulthood had a very low risk of developing breast cancer (Lee et al., 2009).

A daily intake of soy textured protein containing 45mg of isoflavones alters the menstrual cycle in healthy premenopausal women by prolonging its length, especially in the follicular phase. This effect was not observed with soy protein free of isoflavones, supporting the evidence that soy phytoestrogens act as an endocrine regulator. Similar effects of phytoestrogens on the menstrual cycle have been reported in other studies; nonetheless Phipps et al (1993) reported an increase in the length of the luteal phase. This result is not so easy to explain since changes in the luteal phase length are associated almost exclusively with changes in the follicular phase. The luteal phase is extremely constant and difficult to modify (Ferin et al., 1993).

2.2.3.2 Postmenopause

Epidemiological and clinical data indicate that postmenopausal estrogen therapy provides protection against cardiovascular diseases, reduces osteoporosis, improves the cognitive function, and relieves the menopausal symptoms related to the major loss of ovarian estrogen (Col et al., 1997). Alternative sources of exogenous estrogen have been extensively investigated due to a possible increased risk of breast cancer associated with hormonal replacement therapy (Brechkwoldt et al., 1995). Various studies have focused on verifying the potential of soy isoflavones as a source of exogenous estrogen.

During menopause, the ovarian production of estrogens decreases. A reduction of estrogen levels in the blood leads a series of characteristic symptoms of menopause, such as hot flashes, insomnia, excessive sweating, headaches, mood swings, nervous tension, irritability, depression and vaginal dryness and pain. A group of 145 postmenopausal women was fed a diet rich in phytoestrogens (soy and flaxseed) and a control diet for 12 weeks. The subgroup

of women fed a phytoestrogen diet presented a significant lower incidence of hot flashes and vaginal dryness and an increase in the serial phytoestrogen concentrations (Brzezinski et al., 1997).
A study involving 51 perimenopausal women who were fed a rich diet supplemented with isoflavones presented menopausal symptoms relief, reduction in the blood pressure, and improvements in the lipoprotein profile (Washburn et al., 1999). Similarly, a double-blind study involving 40 women who received daily doses of 100mg of isoflavones reported a decrease in menopausal symptoms and in the plasma levels of total and LDL cholesterol, which are risk factors for cardiovascular diseases (Han et al., 2002). Similar results were found in a study involving 58 postmenopausal women who consumed 45g of soy flour or 45g of wheat flour. Those who consumed the soy flour presented a significant reduction of hot flash (Warren et al., 2002).

2.2.4 Osteoporosis

By the time a woman reaches menopause, her bone density (peak bone density is reached at approximately 30 years of age) decreases rapidly along with a reduction in estrogen in the plasma. If the estrogen replacement treatment starts before the onset of menopause, it is possible to prevent bone density loss as well as the risk of cardiovascular diseases in postmenopausal women. However, estrogen hormone replacement can also cause an increase in the risk of endometrial and breast cancer.
The possibility that soy phytoestrogens may offer a natural alternative to the conventional hormone therapy for the prevention of bone loss has fostered research in animals and humans. Animal studies have used ovariectomized rats, although this is not an ideal model that simulates the influence of ovarian hormones on the reproductive physiology and bone loss in postmenopausal women; the findings are encouraging in terms of the protective effects of phytoestrogens. The consumption of soy isoflavone has demonstrated a significantly decreased in the number of osteoclasts and an inhibition of bone resorption after ovariectomy in this type of animals (Uchida et al., 2010). Analogously, it has been observed in ovariectomized rats, a reduction of urinary excretion levels of deoxypyridinoline, a specific biomarker of bone resorption, after the consumption of isoflavones with supplemental calcium (Breitman et al., 2003). Another study in rats demonstrated that genistein and moderate physical exercises prevented body weight gain and bone loss (Wu et al., 2004).
Epidemiologic studies have showed a lower incidence of osteoporosis in populations consuming diets high in soy, such as Asians, when compared to western populations. Hip fracture is 50-60% less frequent among Asian compared to western women although this benefit gradually disappears as Asians adapt a western lifestyle (Adlercreutz & Mazur, 1997; Roos et al., 1991, as cited in Lagari & Levis, 2010).

3. Saponins

In addition to the usual investigations on isoflavones as one of the main soy bioactive compounds, there has been a growing interest for investigating the functionality of soy saponins and their health benefits.
Saponins (from the Latin "*sapo*") constitute a vast group of glycosides that form foamy solutions in water exhibiting hemolytic and toxic effects in fish and invertebrates (Oleszek,

2000; Tsukamoto & Yoshiki, 2006). They are the major active constituents of many roots and corks that have been used by primitive people as a soap substitute (Fieser & Fieser, 1959).
Saponins are usually located in the seed, hulls, leaves, stems, and roots of plants (Carlson, 2009), and many of those compounds occur naturally even within a single vegetable species. Among the legumes, soy is one the main sources of saponins in the human diet (Lin & Wang, 2004).
Saponins have an antifungal activity and a major role in defenses against predators in plants. This function has been traditionally associated with an anti-nutritional factor in foods containing saponins, besides having limited their application due to their bitter taste. However, recent studies have demonstrated the role of these compounds in the prevention and control of chronic degenerative diseases.

3.1 Chemical structure and properties of saponins

Saponins are compounds that have amphiphilic structure, i.e. having polar and non-polar fractions. The polar fraction is represented by one or more hydrophilic sugars chains linked to hydrophobic aglycon, triterpen or steroidal called sapogenin.
Sapogenins are composed of carbon atoms in the form of fused rings. The sugars are in the form of oligosaccharides, linear or branched chains, although monosaccharides can also occur, such as the case of glucose and galactose. Both polar and non-polar groups are responsible for the beneficial biological effects.
The structure of saponins from different plant sources varies depending on the types and amount of sugars as well as the composition of the steroid ring (Rao & Sung, 1995). In vegetables, steroidal saponins are mainly found in monocotyledons, and triterpene saponins are predominately present in dicotyledons such as leguminous plants, in which soy is considered as one of their major food sources (Güçlü-Üstündağ & Mazza, 2007). Galactose, arabinose, rhamnose, glucose, glucuronic acid, and fructose are the most common sugars in saponin structures, and five sapogenins have been identified in soybeans (Figure 4). Soy saponins are usually classified into three groups: A, B, and E (Lin & Wang, 2004) suggesting that saponins group E are formed from group B saponins during extraction and analysis when the 22-hydroxyl group is oxidized to a ketone (Berhow et al., 2006).
As in most vegetables, the concentration of soy saponins depends on many factors, including the cultivar, age, physiological stage, geographical location, processing, and storage. Similarly, there are qualitative and quantitative variation also exists between plant parts (Oleszek, 2000).
The contents of saponins in soybeans can vary among the different genotypes. In a study conducted in the USA, 21 lines of soybean grown in five different environments were evaluated. The contents of saponins found were between 2209 and 5830 $\mu g.g^{-1}$ among the different lines and locations (MacDonald et al., 2005). The saponin content in the grain varies, and the highest amount is found in the hypocotyl, where there is a 4-fold accumulation compared to that of cotyledon and pod shell (Shimoyamada et al., 1990).
Saponins are thermal sensitive, and several studies have evaluated the characteristics and stability of saponins in a number of soy products. During processing and storage of soybeans, chemical modification of saponins can occur resulting in a change in the total content, composition, and properties/biological activity and properties, which may or may not be desirable (Güçlü-Üstündağ & Mazza, 2007).

The cooking process of legumes as soybean reduces the amount of saponins by 7-53% (Shi et al., 2004). Soy-based foods have different amounts of saponins; usually low values compared to those of raw soybeans. Soybean flour, soy protein isolate, lecithin, and tofu present reduced content of saponins, 50, 25, 73, and 37%, respectively, compared to that of the whole soybeans (Fenwick & Oakenfull, 1981). Soy-based foods obtained by ethanol processes, such as concentrated proteins, for example, present low content of saponins due to their solubility in alcohol (Murphy et al., 2008).

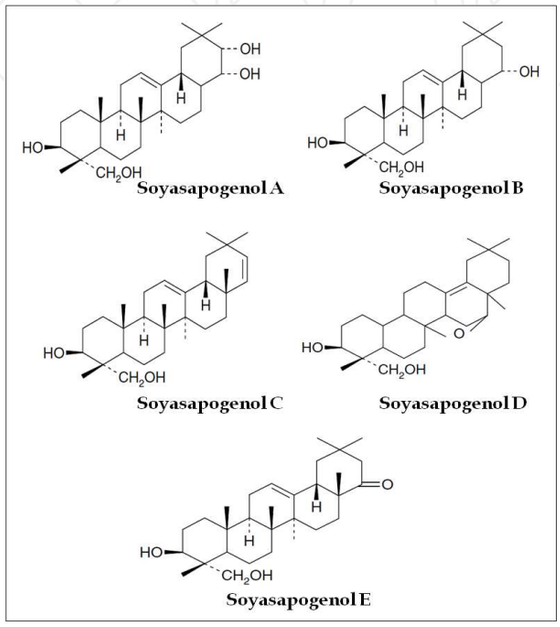

Fig. 4. Structures of five types of sapogenins identified in soybeans (Adapted from de Lin & Wang, 2004).

3.2 Mecahisms of action and biological functions

Due to recent advances in analysis and purification techniques of saponins, several studies have evaluated the functionality of these compounds influenced by the genetic polymorphism of their different structures (Tsukamoto & Yoshiki, 2006). Hence, saponins have been reported to possess a wide range of biological activities (Güçlü-Üstündağ and Mazza, 2007), mainly anticancer, antioxidant, hypocholesterolemic, and antiviral effects.

3.2.1 Anticancer and antioxidant effects

The biological oxidation caused by reactive oxygen species (ROSs) and free radicals is involved in biological processes such as aging and degenerative diseases such as cancer. The etiology and pathogenesis of cancer are multifactorial and involve multiple steps that culminate into complex disarray of cell signaling.

Today, there are no clinical studies evaluating the activity of saponins as an anticancer or antioxidant agent, and even considering the scanty experimental research in animals, information is still insufficient to provide pertinent conclusions. Most studies in the literature are limited to *in vitro* analysis with cell lines of colon, liver, and breast cancer, and several mechanisms of action are proposed, among which include direct cytotoxicity,

induction of apoptosis, antiestrogenic activity, inhibition of tumor cell metastasis, antimutagenic activity effect, bile acid binding action, and normalization of carcinogen-induced cell proliferation (Kang et al., 2010). Saponins (such as diosgenin, Figure 5) have been demonstrated to target multiple cellular and molecular pathways in their functional role as cancer chemopreventive agents.

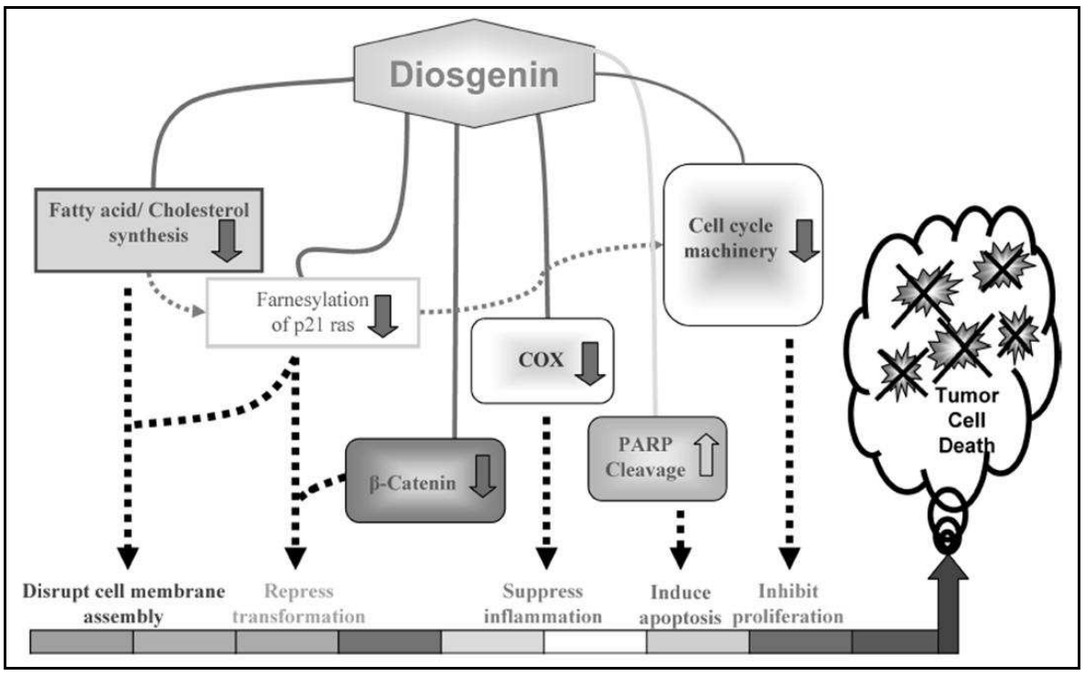

Fig. 5. Schematic representation of plausible mechanism of action(s) of diosgenin (saponin) at the cellular level as a cancer chemopreventive agent (Adapted from Raju & Mehta, 2009)

Soy saponins help preventing the development and reducing the number of tumors in rats (Konoshima & Takasaki, 2000). More recently, the effect of soy saponins on human colon cancer cells was evaluated leading to the conclusion that these compounds may be effective in preventing colon cancer by affecting cell morphology, cell growth, and cell proliferation enzymes. In this study, the saponins affected the cell growth in two different ways; by increasing the alkaline phosphatase activity while reducing protein kinase C activity to induce cell differentiation, or by inducing type II autophagic death (Tsai et al., 2010).

The antioxidant activity of saponins is also related to their capacity to bind to cholesterol and prevent cholesterol oxidation. Group B saponins, abundant in soy, linked with 2, 3-dihydro-2,5-dihydroxy-6-methyl-4H-pyran-4-one (DDMP) group, are responsible for preventing lipid peroxidation or degeneration of DNA and protecting proteins from free radical attack (Ruiz et al., 1996; Shi et al., 2004; Yoshiki et al., 1994).

In addition to preventing cholesterol oxidation by the action of free radicals, group A and B saponins have antioxidant effects on rat liver microsome through the inhibition of lipid peroxidation (Nishida et al., 1993). Recently, a group of researchers isolated type I soy saponins, one of the main groups occurring in soybeans, showing that it presents a free radical scavenging activity comparable to that of α-tocopherol inhibiting lipid peroxidation. In this study was also demonstrated that the treatment with soy saponins increases the

superoxide dismutase and catalase activity, essential for the control of free radicals (Lee et al., 2010). Similarly, mice fed a soy extract rich in saponins exhibited a better profile of the antioxidants system with significant increase of superoxide dismutase, glutathione peroxidase, and glutathione S-transferase activities (Yang et al., 2011).
Saponins may have a synergistic antioxidative effect in the presence of hydrogen donors such as phenol compounds. Iron and copper ions generate hydroxyl radicals through the Fenton reaction to facilitate biological oxidation. Saponins may also have a preventive antioxidant that prevents active oxygen from being generated during the chelation of these metal ions (Tsukamoto and Yoshiki, 2006).

3.2.2 Hypocholesterolemic effects

The amphiphilic nature of saponins can explain the hypocholesterolemic activity of these compounds. This activity has been attributed to saponins for years (Sautier et al., 1979; Sidhu & Oakenfull, 1986), and, in general, is associated with their ability to interfere with cholesterol absorption through possible mechanisms of action such as the formation of insoluble complexes with cholesterol, affectation micelle formation, interference with bile acid metabolism, and/or the perturbation the unstirred water layer or brush border membrane characteristics of enterocytes due to their detergent-like properties (Cohn et al., 2010).
Afrose et al. (2010) demonstrated the hypocholesterolemic effects of saponins in laying hens suggesting that the reductions in the levels of serum and egg cholesterol are caused by the suppression of cholesterol synthesis and the promotion of cholesterol catabolism in the liver. In another study, Zhao et al., (2008) proved these effects in hamsters fed a diet supplemented with saponins, but they attributed the results to the substantial increase in fecal cholesterol loss and not to the reduction of cholesterol absorption or synthesis.

3.2.3 Antiviral effects

A glycoside saponin, glycyrrhizin, found in some roots, exhibited suppressive effects on the replication *in vitro* of HIV (Ito et al., 1988). Due to its structural similarity to soy saponins, several studies have investigated the antiviral effects of this compound on soybeans.
Soybean saponins have been evaluated for their antiviral activity against *in vitro* HIV demonstrating that group B soy saponin inhibits HIV-induced cytopathic effects and virus-specific antigen expressions (Nakashima et al., 1989). The antiviral functions of soy saponins was also demonstrated in the herpes simplex virus type 1 (Hayashi et al., 1997; Ikeda et al., 2005).
Group B saponins with arabinose as the second sugar has an inhibitory effect on human cytomegalovirus (HCMV), influenza A virus, and human immunodeficiency virus type 1. The antivirus effect of soy saponins is not limited to inhibit cell permeability and protein synthesis but also exhibit virus inactivation activity (Tsukamoto and Yoshiki, 2006).

4. Phytosterols

Phytosterols are compounds found in plants that have important functions, especially in the structure of cell membranes and in cellulose biosynthesis. Studies have suggested that due to structural and functional analogy of phytosterols and phytostanols with cholesterol, they

have properties to compete for incorporation into micelles inhibiting cholesterol absorption in the intestine and enhancing its elimination in the feces.
Phytosterols, also called plant sterols, are found naturally in plants (Schneider et al., 2009; Harrabi, 2008) in small quantities. Their hypocholesterolemic properties come from their structural similarity to cholesterol (Kaloustian et al., 2008).
Since the 1950s, beneficial effects of plant sterols have been observed due to decreases in the plasma cholesterol levels and a significant reduction in the incidence of atherosclerosis in chick fed a soybean diet; therefore, it is possible that some soy sterols interfere with cholesterol absorption in the intestine (Peterson et al., 1952). Since that time, there have been studies in animals and humans demonstrating the effects of these compounds on the reduction of plasma cholesterol.

4.1 Chemical structure and properties of phytosterols

Phytosterols are steroid alcohols derived from plants with resemblance to cholesterol, the predominant sterol found in animals, and also are similar in functions to cholesterol, especially in terms of structure and functions of cell membranes. These compounds are members of the triterpen family and, unlike cholesterol, include a methyl or ethyl group at carbon 24 (AbuMweis & Jones, 2008; Palou et al., 2005, Piironen et al., 2000).
Phytostanols are formed from the saturation of the double bond at carbon-5, and they do not occur very frequently in nature. The term plant sterols is usually used to refer to phytosterols and phytostanols. A phytosterol can be converted to its similar phytostanol by enzyme activity in plants, *in vivo,* or by industrial hydrogenation.
More than 200 phytosterols have been identified in the plant kingdom, and many are found in edible foodstuffs (Bradford & Awad, 2007). Their nomenclature is rather confusing due to the partial approval of international norms defined by the International Union of Pure and Applied Chemistry (IUPAC) and the International Union of Biochemistry (IUB) (Moreau et al., 2002).
The most common and widely studied phytosterols are sitosterol or *β*-sitosterol estigmasterol and campesterol. Other relevant phytosterols that can be found in plants in minor amounts are brassicasterol, Δ^5-avenasterol, sitostanol and campestanol (Fernandes & Cabral, 2007). Figure 6 shows the chemical structures of the common phytosterols and phytostanols and their similarity to animal cholesterol.
In addition to the free form, phytosterols can be found as conjugated or esterified compounds, in which the 3β-hidroxyl group is esterified to fatty acids, glycosides, or phenolic compounds with different chemical, technological, and nutritional properties (Figure 7). The occurrence of these classes varies between the foods and parts of these foods (Palou et al., 2005; Piironen & Lampi, 2004). Vegetable oils are, in general, rich in free phytosterols and their fatty acid esters (Piironen & Lampi, 2004) although there is a great variability in the contents of free and esterified phytosterols in many types of oils and fats (Phillips et al., 2002). Nuts also contain high amounts of phytosterols (Piironen & Lampi, 2004). Due to the wide variety of soy-based food products for human consumption, it is considered an important dietary source of phytosterol, and it can contribute significantly to the consumption of those products. A study involving 510 soybean cultivars showed that the content of phytosterols ranged from 202 and 843 μg.g-1. The highest amounts are found in soybeans with high lipid content. β-sitosterol, campesterol, and estigmasterol were the main phytosterols found in the grain at the proportions of 43-67%, 17-34%, and 10-30%, respectively (Yamaya et al., 2007). Germinated soybeans have higher levels of phytosterols,

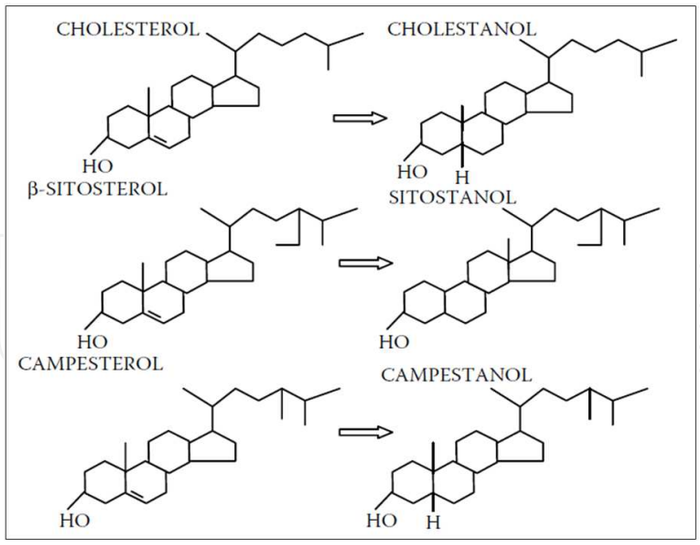

Fig. 6. Chemical structures of cholesterol, phytosterols and their saturated derivatives (Adapted from Yankah, 2006).

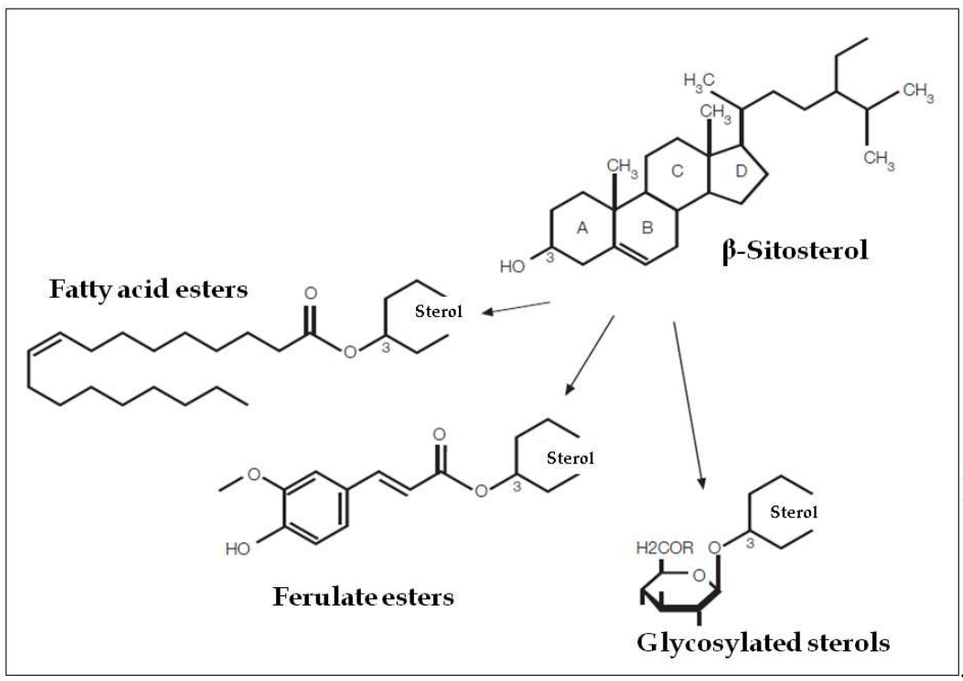

Fig. 7. Modification of 3β-OH group in phytosterols (Adapted from de Palou et al., 2005).

finding that has been corroborated recently in a study involving soybeans with 7 days of germination with phytosterol contents of 1004 and 1987 $\mu g.g^{-1}$; the predominant phytosterol found was β-sitosterol (Shi et al., 2010).

Soy germ is rich in phytosterols. Therefore, the soybean oil produced is an important source of these compounds in countries where it is highly consumed. Studies cited by Piironen et al., (2000) indicated that the contents of phytosterols in raw soybean oil vary between 2,290

and 4,490 μg.g^{-1} and between 2,210 and 3,280 μg.g^{-1} in refined soybean oil. This type of oil showed lower loss of phytosterols in a continuous frying system compared with corn and sunflower oils (Winkler et al., 2007).

4.2 Mechanisms of action and biological functions

The intake of free phytosterols, especially β-sitosterol and the esterified sources, has demonstrated properties of reducing serum cholesterol in animals and humans studies.
According to the World Health Organization criteria, this biological function is fairly convincing, but further studies are necessary to demonstrate that this reduction is associated to the prevention of cardiovascular diseases. Other biological activities have also been attributed to the action of phytosterols such as antioxidant activity, cancer prevention, and immune system improvement. Nevertheless, those studies are considered insufficient to corroborate these hypotheses (de Jong et al., 2008).

4.2.1 Hypocholesterolemic effects

The functions of phytosterol in plants are similar to those of cholesterol in animals. They have an important role in the structure of the vegetable cell membranes acting as regulators of membrane fluidity and permeability by affecting the proteins associated to membranes (Alignan et al., 2009; Piironen et al., 2000; Roche et al., 2008). In addition to this structural function, phytosterols also act as precursors of a group of factors related to the growth of the plant. They act in the biosynthesis of cellulose and as substrates for secondary vegetable products such as alkaloids, cardenolides, and saponins (Palou et al., 2005; Peng et al., 2002; Piironen et al., 2000; Read & Bacic, 2002;). Phytosterols can also act as biogenetic precursors of a number of metabolites including plant steroid hormones, such as brassinosteroids and are involved in embryogenesis (Alignan et al., 2009; Breinhölder et al., 2002; Schaller, 2003).
Scientific evidences demonstrate that phytosterols interfere in the reduction of cholesterol absorption stimulating a subsequent synthesis of the endogenous cholesterol. This leads a reduction in the plasma cholesterol levels and an increase elimination of cholesterol in the feces. The way by which phytosterols reduce cholesterol absorption has not been defined yet; however, there are evidences that indicate that the phytosterols compete with cholesterol for the micelles of absorption in the intestine.
Studies have demonstrated serum cholesterol-lowering effect of phytosterols when consumed at levels of 1.5-2 g per day (Piironen & Lampi, 2004). An increase in the rate of endogenous cholesterol synthesis caused by the action of phytosterols leads to an increase LDL-receptor activity in the liver and an increase of the number of LDL receptors in order to capture the cholesterol from these lipoproteins for the bile acid synthesis thus increasing elimination of LDL from circulation. Finally, the levels of LDL cholesterol, and therefore, total cholesterol in humans decrease without affecting the levels of HDL cholesterol and triglycerides (Palou et al., 2005).
The contents of phytosterols in soy and its products are relatively too low to cause relevant effects in the reduction of cholesterol levels, which has attracted the interest of industries in the development and improvement of soy-based products.
A clinical study on the consumption of a soy drink enriched with 2.6 g of phytosterol was conducted in 50 subjects (19 men and 31 women) for eight weeks, aged between 19 and 65 years with moderate hypercholesterolemia. The study found that the regular consumption of 200 ml of soy drink enriched with plant sterols reduces significantly the level of LDL

cholesterol by approximately 0.29 mmol.L^{-1} or 7% compared to baseline. The reduction in the levels of total, LDL and non-HDL cholesterol were significant greater than in the placebo group. Nevertheless, HDL cholesterol and triglycerides were not affected by the consumption of the drink, which was sensorally accepted by the subjects (Weidner et al., 2008).

Accordingly, many studies have demonstrated and corroborated the effectiveness of phytosterols enriching various foods; margarine (AbuMweis et al., 2008), juices (Devaraj et al., 2003), milk (Plana et al., 2008; Hansel et al., 2007), and yogurt (Plat et al., 2009), evaluating cholesterol-lowering effect when consumed in the recommended dose.

Recently, a meta-analysis of 84 clinical trials was conducted evaluating the effect of the enrichment of foods with phytosterols on subjects with hypercholesterolemia. The combined results of all studies grouped indicated that the reductions in the levels of LDL cholesterol were of 0.34 mmol.L^{-1} or 8.8% compared with control, for a mean daily dose of 2.15 g phytosterol. This study evaluated the impacts of subject baseline characteristics of the grouped studies through regression analysis suggesting that groups higher baseline LDL cholesterol resulted in greater absolute LDL cholesterol reductions, which could indicate the effectiveness of those foods in subjects with hypercholesterolemia (Demonty et al., 2009). Figure 8 shows the dose/response relationship in the reduction of LDL cholesterol levels in the grouped studies.

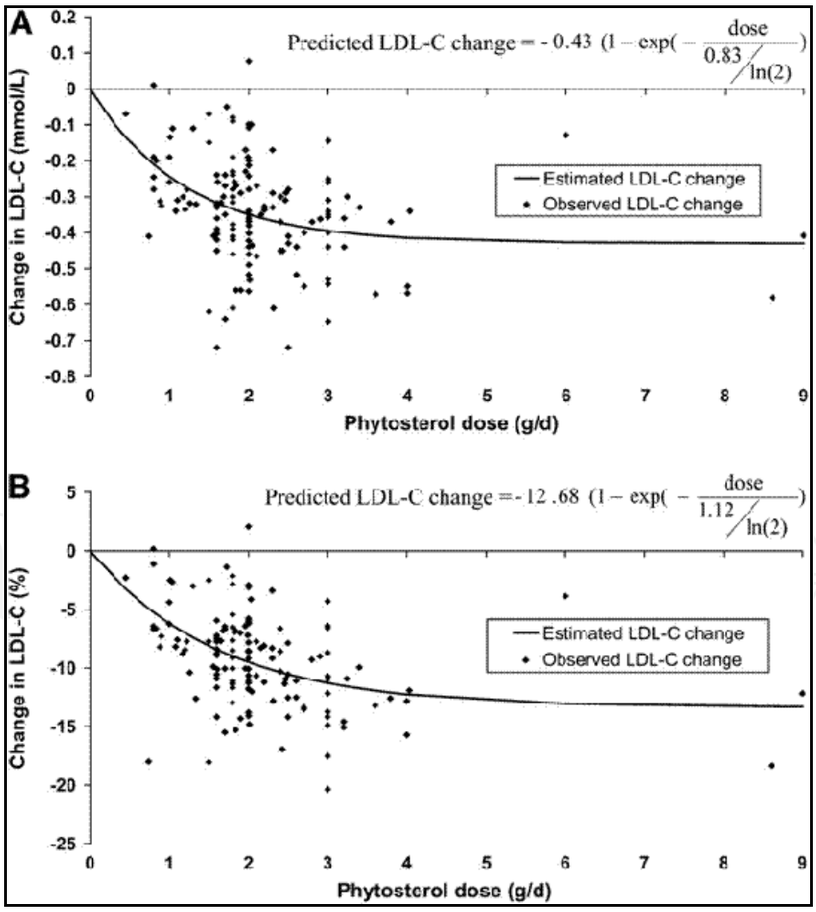

Fig. 8. Dose-response relationship for the absolute (A) and relative (B) LDL cholesterol-lowering effect of phytosterols (Adapted from Demonty et al., 2009).

Soy-based products have high potential for phytosterols enrichment. Soy is considered a very important food due to its countless benefits, and its phytosterols and high quality protein can produce a synergic effect, which also has proved to reduce the levels of LDL and total cholesterol.

4.2.2 Antioxidant effects

Some studies suggest the hypothesis that phytosterols have antioxidant activity and may help the prevention of certain types of cancer (Awad et al., 2001; Normén & Andersson, 2004; Wang et al., 2002). Nonetheless, the information available is still insufficient to corroborate those findings.

In a study in mice was founded that phytosterols modulated and reduced the growth of tumors in ovariectomized female athymic (Ju et al., 2004). On the other hand, oxidant effects of phytosterols on biomarkers, such as DNA or lipid peroxidation, were not found in clinical studies (de Jong et al., 2008). The discrepancies between the results are frequently found in the literature.

Emerging evidence supports the inhibitory actions of phytosterols on lung, stomach, ovarian and breast cancer, through multiple mechanisms of action, including inhibition of carcinogen production, cancer-cell growth, angiogenesis, invasion, metastasis and apoptosis. Phytosterol consumption may also increase the activity of antioxidant enzymes and thereby reduce oxidative stress (Woyengo et al. , 2009).

5. Conclusions

Soy is considered a rich source of proteins and lipids and contains other bioactive compounds such as isoflavones, saponins, and phytosterols. Such diversity in compounds makes it difficult to attribute an exclusive beneficial biological function to a single compound after consuming soy-based food products. For example, cholesterol-lowering effects are associated to the consumption of soy protein, but are also associated to phytosterols, isoflavones, and even saponins. Highlight the synergistic multicomponent effects of soy on biological functions would be a recommendation for further studies, as well as studies of the mechanism of action and new biomarkers for to prove the effectiveness of soy bioactive compounds in preventing and treating several symptoms and/or pathologies.

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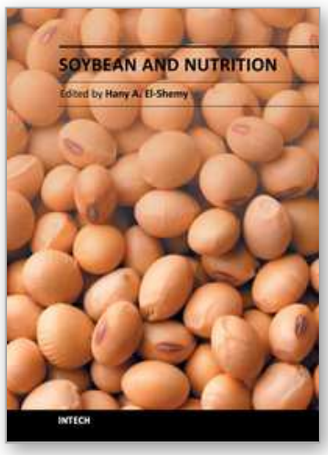

Soybean and Nutrition

Edited by Prof. Hany El-Shemy

ISBN 978-953-307-536-5

Hard cover, 476 pages

Publisher InTech

Published online 12, September, 2011

Published in print edition September, 2011

Worldwide, soybean seed proteins represent a major source of amino acids for human and animal nutrition. Soybean seeds are an important and economical source of protein in the diet of many developed and developing countries. Soy is a complete protein and soy-foods are rich in vitamins and minerals. Soybean protein provides all the essential amino acids in the amounts needed for human health. Recent research suggests that soy may also lower risk of prostate, colon and breast cancers as well as osteoporosis and other bone health problems and alleviate hot flashes associated with menopause. This volume is expected to be useful for student, researchers and public who are interested in soybean.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Jocelem Mastrodi Salgado and Carlos M. Donado-Pestana (2011). Soy as a Functional Food, Soybean and Nutrition, Prof. Hany El-Shemy (Ed.), ISBN: 978-953-307-536-5, InTech, Available from: http://www.intechopen.com/books/soybean-and-nutrition/soy-as-a-functional-food

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