We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,300

Open access books available

172,000

International authors and editors

190M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Phytochemicals in Soy and Their Health Effects*

Xianli Wu and Jie Kang

*USDA Arkansas Children's Nutrition Center,
Department of Physiology and Biophysics,
University of Arkansas for Medical Sciences,
USA*

1. Introduction

Consumption of soy foods has been associated, at least in part, with lower incidences of a number of chronic diseases indicated by epidemiological studies (1-4). Soy-based foods have been consumed in Asian countries such as China, Japan and Korea for many centuries. The lower rates of several chronic diseases in Asia, including cardiovascular diseases and certain types of cancer, have been partly attributed to consumption of large quantities of soy foods (5, 6).

Soy-based food was first introduced on a large scale to the general U.S. population as a source of high quality protein. A significant increase in soy food consumption during the last decade of the 20th century occurred because of the health benefits soy food might offer independent of their nutrient content (7). In the last few decades, extensive efforts have been made towards identifying bioactive components in soy foods that are responsible for the health benefits. Among them, isoflavones and soy proteins are the two major groups of components that have received the most attention (8-11). Isoflavones belong to a broad group of plant-derived compounds that have structural and functional similarities to estrogens, which has led to the term phytoestrogens (12, 13). Indeed, more than half of the soy-related papers are related to isoflavones (7). The analysis, bioavailability and the health effects of isoflavones have been extensively studied and frequently reviewed (12, 14-21). Consumption of isoflavones has been suggested to have multiple beneficial effects in a number of chronic diseases and medical conditions (4, 22, 23). However, accumulating evidence has also suggested that isoflavones only reflected certain aspects of the health effects associated with soy consumption. Other components in soy, such as soyasaponins, phytic acid or plant sterols, display a wide range of bioactivities, including anti-cancer, anti-oxidative, anti-viral, cardiovascular protective effects, and hepato-protective actions (24).

* Mention of trade names or commercial products in this publication is solely for the purpose of providing specific information and does not imply recommendation or endorsement by the U.S. Department of Agriculture.

contents of major phytochemicals from high to low in soybean are: phytic acid (1.0-2.2%) (25), sterols (0.23-0.46%) (26), saponins (0.17-6.16%) (27), isoflavones (0.1-0.3%) (23), and lignans (0.02%) (28). Secondly, the potential health effects of the major phytochemicals are outlined. For many years, the studies of health effects of soybean phytochemicals primarily focused on isoflavones. However, other phytochemicals in soy, such as soyasaponins, phytosterols, lignans, phytic acid, and oligosaccharides, have also been found to exert biological activities. These may contribute to overall health effects observed with soy consumption.

2.1 Isoflavones

2.1.1 Chemical characteristics of isoflavones

Isoflavones have been known to exist in plants for over 100 years. And soy, including the foods derived from this legume, is considered as a richest dietary source of isoflavones (7). Isoflavones (3-phenyl-4H-1-benzopyran-4-one) are a subclass of more ubiquitous flavonoids, while they differs from flavone (2-phenyl-4H-1-benzopyran-4-one) in that the phenyl group (B ring) is connected to position 3 instead of position 2 (**Figure 1**) (29). Soy mainly contains three isoflavones, namely daidzein (7,4'-dihydroxyisoflavone) (1), genistein (5,7,4'-trihydroxyisoflavone) (2) and glycitein (6-methoxy-7,4'-dihydroxyisoflavone) (3). Genistein and daidzein have been found in relatively high concentrations in soybean and most soy-based foods. In soybean and non-fermented soy foods, they are generally present as one of the following three β -glucoside conjugates: a) the corresponding glucosides: daidzin (daidzein 7-O- β -D-glucoside) (4), genistin (genistein 7-O- β -D-glucoside) (5) and glycitin (glycitein 7-O- β -D-glucoside) (6); b) the corresponding acetylglucosides: 6''-O-acetyldaidzin (7), 6''-O-acetylgenistin (8) and 6''-O-acetylglycitin (9); and c) the corresponding malonylglucosides: 6''-O-malonyldaidzin (10), 6''-O-malonylgenistin (11) and 6''-O-malonylglycitin (12) (29). In addition to β -glucoside conjugates, isoflavones conjugated with other sugar moieties, including 6''-O- β -D-arabinose-genistin (13) and 6''-O- β -D-xylose-genistin (14). Other isoflavones, including 2'',6''-O -diacetyloninin (15), and two dihydro-isoflavanones, dihydrodaidzin (16) and dihydrogenistin (17) were reported recently in the last ten years (30, 31).

2.1.2 Health effects of isoflavones

Health effects of isoflavones were initially thought to be related to their estrogenic activity (23). The molecular structures of isoflavones, especially genistein (2), are similar to that of 17 β -estradiol (**Figure 2**). Isoflavones can bind to both α and β isoforms of estrogen receptor (ER), but their binding affinity to ER β is about 20 times higher than that to ER α (11). However, compared to physiological estrogen such as 17 β -estradiol, isoflavones have approximately 100 times weaker affinities (32). Estrogen-like effects have been proposed as one of the major mechanism of action of isoflavone related to their health effects (8). A second mechanism of action of isoflavones, particularly of genistein, was discovered that genistein is a protein tyrosine kinase (PTK) inhibitor (8). Since then, isoflavones have been shown to affect a diverse array of intracellular signaling pathways (7). For instance, genistein and other isoflavones were found to interact with the peroxisome proliferator activated receptors, PPAR α/γ . These nuclear receptors are activated by fatty acids (PPAR α) and prostaglandins (PPAR γ) and serve as transcription factors (32). As polyphenols, isoflavones also have antioxidant activities,

which were proposed as another important mechanism of action of isoflavones. However, isoflavones are not strong antioxidant may not be able to scavenge oxidants directly. They therefore are considered as antioxidants because of their effects on gene expression of enzymes that enhance antioxidant defenses (32). In addition to what has been discussed above, several other mechanism have been proposed for the activities of isoflavones, including stimulation/inhibition of enzyme activities involved in steroid synthesis and metabolism, targeting thyroid peroxidase, and inhibiting cancer metastasis (32).

Fig. 2. The chemical structures of genistein and 17β-estradiol.

Consumption of isoflavones has been suggested to have multiple beneficial effects in a number of chronic diseases and medical conditions, including certain types of cancer (33-35), heart disease (36-38), bone functions (39-42) and most recently, prevention of obesity (43, 44). Many excellent reviews regarding the different aspects of health effects of soy isoflavone can be found in the literatures, thus, only a brief outline of the health effects of isoflavones is provided in this chapter.

2.1.2.1 Isoflavones and prevention of cancer

The incidences of breast and prostate cancers are much higher in the United States and European countries compared to Asian countries such as Japan and China. One of the major differences in diet between these populations is that the Japanese and the Chinese consume a traditional diet high in soy products (35). Epidemiological evidence together with preclinical data from animal and *in vitro* studies strongly supported a correlation between soy isoflavone consumption and protection towards breast and prostate cancers (45-47). However, clinical studies assessing soy consumption and risk of breast cancer have yielded inconsistent results. In a most recent meta-analysis of prospective studies suggested that soy isoflavones intake is associated with a significantly reduced risk of breast cancer incidence in Asian populations, but not in Western populations. Further studies are warranted to confirm the finding of an inverse association of soy consumption with risk of breast cancer recurrence (48).

Except for breast and prostate cancer, isoflavones also showed inhibitory effects on other hormone-related (e.g. endometrial, ovarian cancer) or hormone-independent cancers (e.g. leukemia and lung cancer) (49).

2.1.2.2 Isoflavones and prevention of cardiovascular diseases

A number of cardioprotective benefits have been attributed to dietary isoflavones including reduction in LDL cholesterol, inhibition of pro-inflammatory cytokines, cell adhesion

proteins and inducible nitric oxide production, potential reduction in the susceptibility of the LDL particle to oxidation, inhibition of platelet aggregation and an improvement in vascular reactivity (50). There are not randomized trials investigating the action of isoflavones on the incidence of clinical events. A few recent, well-designed studies have suggested an association of the ingestion of isoflavones with a reduction in the atherosclerotic burden, as indicated by the measurement of the intima-media thickness in carotid vessels (51).

2.1.2.3 Isoflavones and bone health

Observational studies have suggested that populations in Asia with a high dietary soy intake have a lower incidence of osteoporosis-related fractures when compared to Western populations. Isoflavones were suggested to prevent bone loss associated with menopause. Though extensive research using animal models has provided convincing data to indicate a significant improvement in bone mass or other end points following feeding with soyabean, results from intervention studies are still controversial (52). Additional research is needed to determine if isoflavones are an effective alternative to hormone replacement therapy for the prevention and treatment of osteoporosis (42).

2.1.2.4 Isoflavones and prevention of obesity

The prevalence of obesity and related diseases has increased rapidly in the Western world. Obesity is a disorder of energy balance and is associated with hyper-insulinemia, insulin resistance, and abnormalities in lipid metabolism, and it is one of the most important risk factors in the development of Type II diabetes, cardiovascular disease, atherosclerosis, and certain cancers (44). In recent years, evidence is emerging that soy isoflavones play a beneficial role in obesity and diabetes. Nutritional intervention studies in animals and humans indicate that consumption of soy isoflavones or soy protein containing isoflavones reduces body weight and fat mass by lowering plasma cholesterol and triglycerides as well as by other mechanisms (43, 44, 53). Though the published results suggest a beneficial effect of soy isoflavone on obesity in human, these results also suggest that the effect may be dependent on whether the isoflavones are consumed in combination with soy protein (44).

2.2 Soyasaponins and soyasapogenols

2.2.1 Chemical characteristics of soyasaponins and soyasapogenols

Saponins are sterol or triterpene glycosides that occur in a wide variety of plants. Soy-based foods are primary dietary sources of saponins (54). Chemical studies of saponins in soy track back to the 1930's (55, 56). From the 1980's to 1990's, a number of papers, especially those published by Japanese researchers, significantly enriched our knowledge about chemical structure and diversity of this type of compounds in soy (57-65).

Saponins in soy are often referred to soyasaponins. They differ from each other by the types of aglycones and the position where the sugar chain is attached. Generally, saponins are classified into four major groups, on the basis of their aglycone structures: group A, B, E and DDMP. Group A saponins have a hydroxyl group at the C-21 position, and group B saponins have a hydrogen atom at the same position. Group E saponins differ from group A and B by having a carbonyl group at C-22. Group B saponins may contain a DDMP (2,3-dihydro-2,5-dihydroxy-6-methyl-4H-pyran-4-one) moiety at C-22 position, which are

denoted as DDMP saponins (66) (**Figure 3**) . DDMP soyasaponins and the acetylated soyasaponins of group A are sometimes considered as the genuine forms of groups A and B in soybeans. Group E soyasaponins are also considered to be phyto-oxidation products of group B soyasaponins (62, 67, 68). All four groups of soyasaponins are glycosides of oleanan triterpene aglycones known as soyasapongenols. The oleanan aglycone contains one or more hydroxyl groups, and carboxylic groups and double bonds may also be present. The sugar moieties are generally attached at the C-3 position and sometimes at the C-22 position of the aglycones. Group A soyasaponins have two sugar chains, separately attached to C-3 and C-22 positions of soyasapogenol A, except for A3 (**33**), which has only one sugar chain at C-3 (**Table 1**). C-3 sugar chain consists of two or three sugar residues, starting with a glucoronyl residue (glcUA) (67). C-22 side chain consists of two sugar residues, starting with an anarabinosyl, and ending with a xylosyl or glycosyl residue (58, 63, 65, 69) (**Figure 3**). Group B soyasaponins have one sugar chain attached to the C-3 position of soyasapogenol B, with three exceptional compounds that have two sugar chains at C-3 and C-22 positions (**41-43**) (57, 59, 69-71) (**Figure 3**). Most recently, a new soyasaponin Bh (**40**) was identified to bear an unique five-membered ring containing a hemiacetal functionality (**Figure 3**) (72). Group E soyasaponins contain only one sugar chain at the C-3 position. They are considered to be formed by photo-oxidation at C-22 of group B (63, 69) (**Figure 3**). DDMP soyasaponins are categorized under B type soyasaponins by some researchers (27). Their structures were characterized as having DDMP group conjugated to group B at C-22 (67, 68, 73, 74) (**Figure 3**). Similar to B type soyasaponins, DDMP soyasaponins only contain one sugar chain attached to C-3 position. There are about 36 soyasaponins identified in soybean. Their structures and the related references are listed (**Tables 1-4**).

NO.	name	C-3 sugar chain	C-22 sugar chain	molecular formula	ref
18	Aa (acetyl A ₄)	glc(1→2)gal(1→2)glcUA(1→3)	2,3,4-tri-O-acetyl-xyl(1→3)ara(1→22)	C ₆₄ H ₁₀₀ O ₃₁	65
19	Ab (acetyl A ₁)	glc(1→2)gal(1→2)glcUA(1→3)	2,3,4,6-tetra-O-acetyl-glc(1→3)ara(1→22)	C ₆₇ H ₁₀₄ O ₃₃	64
20	Ac	rha(1→2)gal(1→2)glcUA(1→3)	2,3,4,6-tetra-O-acetyl-glc(1→3)ara(1→22)	C ₆₇ H ₁₀₄ O ₃₂	63
21	Ad	glc(1→2)ara(1→2)glcUA(1→3)	2,3,4,6-tetra-O-acetyl-glc(1→3)ara(1→22)	C ₆₆ H ₁₀₂ O ₃₂	63
22	Ae (acetyl A ₅)	gal(1→2)glcUA(1→3)	2,3,4-tri-O-acetyl-xyl(1→3)ara(1→22)	C ₅₈ H ₉₀ O ₂₆	65
23	Af (acetyl A ₂)	gal(1→2)glcUA(1→3)	2,3,4,6-tetra-O-acetyl-glc(1→3)ara(1→22)	C ₆₁ H ₉₄ O ₂₈	64
24	Ag (acetyl A ₆)	ara(1→2)glcUA(1→3)	2,3,4-tri-O-acetyl-xyl(1→3)ara(1→22)	C ₅₇ H ₈₈ O ₂₅	65
25	Ah (acetyl A ₃)	ara(1→2)glcUA(1→3)	2,3,4,6-tetra-O-acetyl-glc(1→3)ara(1→22)	C ₆₀ H ₉₂ O ₂₇	64
26	Ax	glc(1→2)ara(1→2)glcUA(1→3)	2,3,4-tri-O-acetyl-xyl(1→3)ara(1→22)	C ₆₃ H ₉₈ O ₃₀	69
27	A ₁	glc(1→2)gal(1→2)glcUA(1→3)	glc(1→3)ara(1→22)	C ₅₉ H ₉₆ O ₂₉	64
28	A ₂	gal(1→2)glcUA(1→3)	glc(1→3)ara(1→22)	C ₅₃ H ₈₆ O ₂₄	64
29	A ₃	ara(1→2)glcUA(1→3)	glc(1→3)ara(1→22)	C ₅₂ H ₈₄ O ₂₃	64
30	A ₄	glc(1→2)gal(1→2)glcUA(1→3)	xyl(1→3)ara(1→22)	C ₅₈ H ₉₄ O ₂₈	64
31	A ₅	gal(1→2)glcUA(1→3)	xyl(1→3)ara(1→22)	C ₅₂ H ₈₄ O ₂₃	64
32	A ₆	ara(1→2)glcUA(1→3)	xyl(1→3)ara(1→22)	C ₅₁ H ₈₂ O ₂₂	64
33	A ₃	rha(1→2)gal(1→2)glcUA(1→3)		C ₄₈ H ₇₈ O ₁₉	58

Table 1. The structures and molecular formulas of group A soyasaponins

NO.	name	C-3 sugar chain	C-22 sugar chain	molecular formula	ref
34	soyasaponin Ba or V	glc(1→2)gal(1→2)glcUA(1→3)		C ₄₈ H ₇₈ O ₁₉	64
35	soyasaponin Bb or I	rha(1→2)gal(1→2)glcUA(1→3)		C ₄₈ H ₇₈ O ₁₈	59
36	soyasaponin Bc or II	rha(1→2)ara(1→2)glcUA(1→3)		C ₄₇ H ₇₆ O ₁₇	59
37	soyasaponin Bb' or III	gal(1→2)glcUA(1→3)		C ₄₂ H ₆₈ O ₁₄	59
38	soyasaponin Bc' or Bx	glc(1→2)ara(1→2)glcUA(1→3)		C ₄₇ H ₇₆ O ₁₈	69
39	soyasaponin IV	ara(1→2)glcUA(1→3)		C ₄₁ H ₆₆ O ₁₃	57
40	soyasaponin Bh	rha(1→2) gal(1→2)glcUA(1→3)		C ₄₈ H ₇₈ O ₁₉	72
41	3-O-{α-L-rhamnopyranosyl(1→2)-[β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl(1→2)]-β-D-glucuronopyranosyl}-22-O-[β-D-glucopyranosyl(1→2)-α-L-arabinopyranosyl]3β,22β,24-trihydroxyolean-12-ene	rha(1→2)[glc(1→3)gal(1→2)]glcUA(1→3)	glc(1→2)ar a(1→22)	C ₆₅ H ₁₀₆ O ₃₂	70
42	3-O-[α-L-rhamnopyranosyl(1→2)-β-D-galactopyranosyl(1→2)]- β-D-glucuronopyranosyl-22-O-[α-L-rhamnopyranosyl(1→2)- α-L-arabinopyranosyl]3β,22β,24-trihydroxyolean-12-ene	rha(1→2)gal(1→2)glcUA(1→3)	rha(1→2)ar a(1→22)	C ₅₉ H ₉₆ O ₂₆	71
43	3-O-[α-L-rhamnopyranosyl(1→2)-β-D-galactopyranosyl(1→2)]- β-D-glucuronopyranosyl-22-O-[α-L-rhamnopyranosyl(1→2)- β-D-glucopyranosyl]3β,22β,24-trihydroxyolean-12-ene	rha(1→2)gal(1→2)glcUA(1→3)	rha(1→2)gl c(1→22)	C ₆₀ H ₉₈ O ₂₇	71

Table 2. The structures and molecular formulas of group B soyasaponins

NO.	name	C-3 sugar chain	molecular formula	ref
44	soyasaponin Bd (sandosaponin A)	glc(1→2)gal(1→2)glcUA(1→3)	C ₄₈ H ₇₆ O ₁₉	63
45	soyasaponin Be (dehydrosoyasaponin I)	rha(1→2)gal(1→2)glcUA(1→3)	C ₄₈ H ₇₆ O ₁₈	63
46	soyasaponin Bf	glc(1→2)ara(1→2)glcUA(1→3)	C ₄₇ H ₇₄ O ₁₈	69
47	soyasaponin Bg	rha(1→2)ara-(1→2)glcUA(1→3)	C ₄₇ H ₇₄ O ₁₇	69

Table 3. The structures and molecular formulas of group E soyasaponins

NO.	name	C-3 sugar chain	C-22 DDMP	molecular formula	ref
48	soyasaponin αg	glc(1→2)gal(1→2)glcUA(1→3)	DDMP(22→2')	C ₅₄ H ₈₄ O ₂₂	68
49	soyasaponin αa	glc(1→2)ara(1→2)glcUA(1→3)	DDMP(22→2')	C ₅₃ H ₈₂ O ₂₁	74
50	soyasaponin βg or VI	rha(1→2)gal(1→2)glcUA(1→3)	DDMP(22→2')	C ₅₄ H ₈₄ O ₂₁	68
51	soyasaponin βa	rha(1→2)ara(1→2)glcUA(1→3)	DDMP(22→2')	C ₅₃ H ₈₂ O ₂₀	68
52	soyasaponin γg	gal(1→2)glcUA(1→3)	DDMP(22→2')	C ₄₈ H ₇₄ O ₁₇	68
53	soyasaponin γa	ara(1→2)glcUA(1→3)	DDMP(22→2')	C ₄₇ H ₇₂ O ₁₆	68

Table 4. The structures and molecular formulas of group DDMP soyasaponins

Fig. 3. The chemical structures of groups A, B, Bh, E and DDMP soyasaponins in soy.

Soyasapogenols are aglycones of soyasaponins. They can be obtained by acid or alkaline hydrolysis of soyasaponins. Though soyasapogenols don't exist in soy bean naturally, they may exist in certain soy products through food processing. Five soyasapogenols A (54), B (55), C (56), D (57) and E (58) have been found through hydrolysis of soyasaponins (59, 62, 75) (**Figure 4**). Among them, soyasapogenol A (54) has two hydroxyl groups at C-21 and C-22 position, which is considered as corresponding aglycones to bis-desmoside soyasaponin group A. Soyasapogenol B (55) has only one hydroxyl group at C-22 position. It is considered to be aglycone of both monodesmoside soyasaponin groups B and DDMP. Soyasapogenol E (58) is regarded as the corresponding aglycone to soyasaponin group E. Soyasapogenols C (56) and D (57) are considered by some researchers not to be genuine aglycones of soyasaponins, but as the acid hydrolysis products of soyasapogenol B (55) (76).

Fig. 4. The chemical structures of soyasapogenols A-E (hydrolysis products of soyasaponins).

2.2.2 Health effects of soyasaponins and soyasapogenols

Plant saponins as a whole have been reported to have a wide range of biological activities, which were summarized with a long list in a recent review (77). Soyasaponins and soyasapogenols have been reported to display diverse health effects (78), including anti-cancer, cardiovascular protective effects, anti-virus, hepatoprotective actions and antioxidant activities (24, 27, 79, 80). Their health effects largely depend on their chemical structures (81). Since this class of soy compounds are so poorly absorbed, their bioactivity maybe caused by indirect actions within the GI tract.

2.2.2.1 Anti-carcinogenic activities

Epidemiological studies have linked soy consumption to lower incidences of various types of cancer (82). As a group of major phytochemicals in soy, soyasaponins may be partially responsible (27). The evidence for soyasaponins having anti-carcinogenic effects in animal models is limited. Nevertheless, soyasaponins and soyasapogenols have been shown to have the anti-carcinogenic effects in a number of carcinoma cell lines. Before summarizing the data, we must keep in mind that since soy saponins are poorly absorbed, *in vitro* studies of these compounds in cell lines may not be able to provide much meaningful indication regarding their *in vivo* bioactivities.

Most studies related to the anti-carcinogenic activities of soyasaponins and soyasapogenols have been performed in human colon cancer, liver cancer or breast cancer cell lines (83-88). The proposed mechanisms of anticarcinogenic properties of soyasaponins and soyasapogenols include direct cytotoxicity, induction of apoptosis, anti-estrogenic activity, inhibition of tumor cell metastasis, anti-mutagenic activity effect, bile acid binding action and normalization of carcinogen-induced cell proliferation (**Table 5**) (89). From these studies done in different cancer cell lines, we've learned that there are at least three major factors that may affect the observed effects of soyasaponins and soyasapogenols. The first factor is the testing materials. Some researchers used crude extracts while others used purified saponins. It is possible that components of the crude extract interact synergistically, thus inducing effects not observed with pure saponins. Therefore, investigations with purified saponins are indispensable for matching a result to the molecular action of a specific saponin (90). The second factor is the type of cell lines. It is clearly shown that different cancer cell lines respond differently to soy saponins. For instance, soyasaponin I (**35**) had no effect on HT-29 colon cell growth (81), but it can decrease the migratory ability of B16F10 melanoma cells (91). The third factor is the dose. In another study, soyasaponin III (**37**) showed significant growth suppression at the highest concentration tested (50 ppm), and no significant effects from concentrations 6 to 25 ppm.

2.2.2.2 Cardiovascular protective effects

Soyasaponins showed cardiovascular protective effects through several different mechanisms.

The hypocholesterolemic effects of soy saponins have long been recognized (92-95). Two mechanisms by which saponins can affect cholesterol metabolism were suggested (96): 1) some saponins with particularly defined structural characteristics form insoluble complexes with cholesterol. When this complex-forming process occurs in the gut, it inhibits intestinal absorption of both endogenous and exogenous cholesterol. 2) Saponins can interfere with the entero-hepatic circulation of bile acids by forming mixed micelles. The re-absorption of bile acids from the terminal ileum is effectively blocked (92).

In animal models, soyasaponins were found to significantly reduce serum total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), triglycerides (TG) concentrations, and to increase high-density lipoprotein-cholesterol (HDL-C) levels in rats (97). 24-Methylenecycloartanol (**59**), in combination with soysterol greatly reduced plasma cholesterol and enhanced cholesterol excretion in rats (98). Hamsters fed group B soyasaponins had significantly lower plasma TC (by 20%), non-HDL-C (by 33%), TG (by 18%)

materials	cell line	dose	observation	mechanism	ref
Total soyasaponins	Human HT-1080 fibrosarcoma cell	Inhibit the metastasis of HT-1080 cells dose-dependently (100-300 µg/ml) after 24 h.	Inhibit the invasion of HT-1080 cells through a Matrigel-coated membrane.	Suppress MMP-2 and MMP-9 productions and stimulate TIMP-2 secretion.	86
Total soyasaponins	Human HT-29 colon cancer cell	Decrease HT-29 cell growth in a dose dependent manner at concentrations of 150, 300, and 600 ppm after 72 h.	Decrease HT-29 cell growth.	Suppress inflammatory responses. COX-2 and PKC expressions were significantly down-regulated.	87
Total soyasaponins	Human HepG2 liver hepatoma cell	Inhibit AFB ₁ -DNA adduct formation in HepG2 liver hepatoma cells by 50.1 % at concentration of 30 µg/ml after 48 h.	Inhibit AFB ₁ -DNA adduct formation in HepG2 liver cells.	Induce membrane permeability change.	85
B-group soyasaponins	Human SNB 19 glioblastoma cell	Induce SNB 19 glioblastoma cell apoptosis dose-depently (25-75 µM) after 48 h.	Induce apoptosis in SNB 19 glioblastoma cells.	Stimulate cytochrome-c release and activate caspase cascade.	88
B-group soyasaponins	Human HCT-15 colon cancer cell	Suppress HCT-15 colon cancer cell proliferation dose-dependently at concentrations of 25-500 ppm, and induce macroautophagy at concentration of 100 ppm after 24 h	Suppress HCT-15 colon cancer cell proliferation and induce macroautophagy.	Delay S-phase cell cycle.	83
Soyasaponin I (35)	Highly metastatic B16F10 melanoma cell	Decrease migratory ability of B16F10 melanoma cell dose-dependently (25-75 µM) after 12 h.	Decrease the migratory ability of cells, enhance cell adhesion to extracellular matrix proteins.	Inhibit the expression of α-2,3-linked sialic acids of B16F10 melanoma cell.	91
Soyasaponin I (35)	Human MCF-7 breast cancer cell.	Significantly enhance MCF-7 cells to adhere the extracellular matrix at 50 µM after 24 h.	Enhance the adhesion of MCF-7 cells to the extracellular matrix proteins.	Alter MCF-7 breast cancer cell surface α2,3-sialylation pathway.	84
Soyasaponin III (37)	Human HT-29 colon cancer cell	37 and soyasapogenol B monoglucuronide show HT-29 colon cancer cell growth suppression at 50 ppm after 72 h.	They all suppress the growth of HT-29 colon cancer cell	The cell growth suppression of soyasaponins and soyasapogenols increased with increased lipophilicity.	81
Soyasapogenol B monoglucuronide					
Soyasapogenol A (54)		54 and 55 show a dose-dependent growth suppression from 6- 50 ppm after 72 h.			
Soyasapogenol B (55)					

Table 5. The anti-carcinogenic activities of soyasaponins and soyasapogenols

and a lower ratio of total to HDL cholesterol (by 13%) in hamsters fed group B soyasaponins, compared to those fed casein. Possible mechanisms involved greater excretion of fecal bile acids and neutral sterols (99).

The anti-thrombogenic action of soyasaponins was evaluated in a model of disseminated intravascular coagulation (DIC) induced by infusion of endotoxin or thrombin in rats. Total soyasaponins prevented the decrease of blood platelets and fibrinogen, and the increase of fibrin degradation products during DIC induced by infusion of endotoxin or thrombin in rats. *In vitro* experiments, total soyasaponins, soyasaponins I (35), II (36), A₁ (27), and A₂ (28) inhibited the conversion of fibrinogen to fibrin (100).

Total soyasaponins decreased elevated blood sugar and LPO levels, and reversed the decreased levels of SOD in streptozocin-induced diabetic rats (101). In an α -glucosidase inhibitory assay, groups B, E and DDMP soyasaponins were shown to have potent inhibitory activities with IC₅₀ values of 10-40 μ mol/L (102).

2.2.2.3 Anti-viral activities

Soyasapogenols A (54), B (55), E (58), and soyasaponin I (35), a major constituent of group B saponins, completely inhibited HIV-induced cytopathic effects 6 days after infection at concentration greater than 0.25 mg/mL, but had no direct effect on HIV reverse transcriptase activity. Soyasaponin I (35) also inhibited HIV-induced cell fusion in the MOLT-4 cell system (103).

Total soyasaponins showed significant inhibitory effect on the replication of HSV-1 and CoxB3. A soyasaponin cream was used in the treatment of patients suffering from herpes labialis. The treatment was found to be highly effective with a cure rate of 88.8% for the disease (104). Soyasaponin II (36) is more potent than soyasaponin I (35) as shown by a reduction of simplex virus type 1 (HSV-1) production. Soyasaponin II (36) was also found to inhibit the replication of human cytomegalovirus and influenza virus. This action was not due to inhibition of virus penetration and protein synthesis, but may involve a virucidal effect (105). In a structure-activity relationship study, the activity of soyasapogenol A (54) was less than 1/20 of that of soyasapogenol B (55), and the hydroxylation at C-21 seemed to reduce anti-HSV-1 activity (106).

2.2.2.4 Hepatoprotective actions

The group B soyasaponins I (35), II (36), III (37), and IV (38) all exhibit hepato-protective actions towards immunologically induced liver injury in primary cultured rat hepatocytes. The action of soyasaponin II (36) is almost comparable with that of soyasaponin I (35), whereas soyasaponins III (37) and IV (38) are more effective than soyasaponins I (35) and II (36). This suggests that the disaccharide group shows greater action than the trisaccharide group. Furthermore, the soyasaponins having a hexosyl unit shows a slightly greater action than that of the pentosyl unit in each disaccharide group or trisaccharide group. Structure-activity relationships suggest that the sugar moiety linked at C-3 may play an important role in hepato-protective actions of soyasaponins (107).

Also in *in vivo* experiments, total soyasaponins inhibit the elevation of liver transaminases when administered orally to rats with peroxidized corn oil. The liver injury caused by peroxidized salad oil is inhibited by the addition of soyasaponin A₁ (27) during peroxidation (108).

2.2.2.5 Antioxidant activities

One mg of DDMP saponin/mL scavenges superoxide at a degree equivalent to 17.1 units of superoxide dismutase/mL by the ESR spin trapping method. The scavenging superoxide activity of DDMP soyasaponins is caused by the DDMP moiety attached to the triterpene aglycon since soyasaponin I (35), which is derived from soyasaponin β g (50). Lack of this group didn't show the scavenging activity (109).

2.3 Triterpenes and sterols

2.3.1 Chemical characteristics of triterpenes and sterols

Triterpenes and sterols are found in soybean oil unsaponifiable matter. They are both present in minor quantities.

Three triterpenes have been identified in soy. They are 24-methylenecycloartenol (59) (98), cycloartenol (60) (98) and bacchara-12,21-dien-3 β -ol (61) (Figure 5) (110), respectively. Compounds 59 and 60 belong to the type of lanostane triterpene. In addition to having the basic structural characters of lanostane, they bear an extra tri-atomic ring in their structures that are formed by cyclization between methyl at C-18 and methine at C-9. Lanostane triterpenes in soy were believed to be the original materials for the biosynthesis of soy sterols. Bacchara-12,21-dien-3 β -ol (61) is a natural occurring of baccharane-type triterpene which has all six-membered tetracyclic skeleton, and its side chain is at position C-17. This type of triterpene is extremely rare in nature and no more than 20 compounds of this type have been separated and identified.

Cholesterol and thirteen so-called plant sterols or phytosterols were found in soybean seed or the shoots (111) (Figure 6). Unlike animals, plant membranes generally contain little or no cholesterol and instead contain several types of phytosterols. Phytosterols are also steroid alcohols, whose chemical structures are similar to that of cholesterol, but with the presence of one or two carbon, saturated or unsaturated, substituents in side chains at C-24 differing from that of cholesterol (62) (Figure 6) (26, 111). The most abundant phytosterols are sitosterol, campesterol and stigmasterol (112). Phytosterols identified from soy so far include cholesta-5,24-dien-3 β -ol (63), β -sitosterol (64) (113), stigmasterin (65) (24), sitostanol (66)(114), citrostadienol (67) (113), isofucosterol (68) (111), campesterol (69) (115), 24-epicampesterol (70) (115), 7-dehydrocampesterol (71) (115), campestanol (72) (111), obtusifoliol (73) (111), 24-methylenelophenol (74) (111), and 14 α -methyl-5 α -ergost-8-en-3 β -ol (75) (111). The most abundant soy phytoserol is β -sitosterol (64), followed by campesterol (69) (112). These sterols can be divided into four groups based on their backbones, cholesterol (62), cholesta (63), stigmasta (64-68) and ergosta (69-75) (Figure 6). Compounds 62 and 63 have the same backbone except for the type of bond between C-24 and C-25. The former is single bond while the latter is double bond (Figure 6). Stigmasta and ergosta also share similar structures with the only difference for stigmasta being that it has one more methyl group at C-28 (Figure 6). However, nutritionists prefer to divide the phytosterols into two categories of " Δ^5 -sterols", indicating a double bond at position C-5, and "stanol", indicating 5 α -reduction of that double bond (114). According to this principle, compounds 62-65 and 68-71 are Δ^5 -sterols; 66-67 and 72-75 are stanols (Figure 6).

Fig. 5. The chemical structures of triterpenes in soy.

2.3.2 Health effects of phytosterols

Phytosterols (not restricted to soy-based sources) that have long been known to reduce intestinal cholesterol absorption, lead to decreased blood LDL-cholesterol levels and lower cardiovascular disease risk. However, other biological activities for phytosterols have also been reported, including anti-cancer and immune modulatory effects.

Fig. 6. The chemical structures of sterols in soy.

2.3.2.1 Phytosterols and cholesterol absorption

In the 1950's, phytosterols from soybeans were found to lower serum cholesterol level (116). Since then, the cholesterol-lowering effects of phytosterols have been extensively demonstrated in both humans and animals (117-120). A meta-analysis of 41 clinical trials showed that intake of 2 g/d of stanols or sterols reduced low-density lipoprotein (LDL) by 10%, with little additional reduction at higher doses (121). The U.S. National Cholesterol Education Program has recommended adding 2.0 g/day of phytosterols to the diet of adults to reduce LDL cholesterol and coronary heart disease risk (122).

Because phytosterols are not systemically absorbed, they are thought to act primarily in the intestinal lumen. As cholesterol analogs phytosterols compete for cholesterol in absorptive micelles resulting in reduced solubility of cholesterol (118). However, recent evidence suggests that the mechanism of action of phytosterols may be more complicated than originally thought (119, 123). As summarized in a recent review (123), since phytosterols/phytostanols do not need to be present in the intestinal lumen simultaneously with cholesterol to inhibit its absorption (120), other studies have suggested that phytosterols/phytostanols may exert an unknown molecular action inside enterocytes and hepatocytes. In line with this, injected phytosterols/phytostanols reduced plasma cholesterol levels in hamsters (124). To gain insight into the phytosterol/phytostanol effects on circulating cholesterol concentration via mechanisms independent of the luminal incorporation of cholesterol into mixed micelles, the effects of these plant compounds on intestinal LXR-mediated targets involved in sterol absorption have been evaluated. Conclusive studies using ABCA1 and ABCG5/G8-deficient mice demonstrated that the phytosterol-mediated inhibition of intestinal cholesterol absorption is independent of these ATP-binding cassette (ABC) transporters. Other reports have raised questions as to whether phytosterols/phytostanols regulate cholesterol metabolism in intestinal and hepatic cells through independent-LXR pathways. A number of studies have proposed a phytosterol/phytostanol action on cholesterol esterification and lipoprotein assembly (ACAT, apoB), cholesterol internalisation (NPC1L1, ANXA2), cholesterol synthesis (HMG-CoA reductase, C-24-reductase) and removal of apoB100-containing lipoproteins (LDLr). However, the impact of phytosterol/phytostanol intake on these physiological processes *in vivo* remains unclear (123).

In one study specifically using soybean-derived phytosterols (125), it was found that consumption of phytosterol-supplemented ground beef lowered plasma TC and LDL-cholesterol concentrations and TC:HDL cholesterol from baseline by 9.3%, 14.6%, and 9.1%, respectively.

2.3.2.2 Anti-cancer effects of phytosterols

In addition to their cholesterol-lowering actions, mounting evidence suggests that phytosterols possess anti-cancer effects against a number of different types of cancers (126-132). Phytosterols seem to act through multiple mechanisms of action, including inhibition of carcinogen production, cancer-cell growth, angiogenesis, invasion and metastasis, and through the promotion of apoptosis of cancerous cells. Phytosterol consumption may also increase the activity of antioxidant enzymes and thereby reduce oxidative stress. In addition to altering cell-membrane structure and function, phytosterols probably promote apoptosis by lowering blood cholesterol levels (127).

2.3.2.3. Physterols and immune function

Several reports in the literature suggest that phytosterols may have some immunological activity as highlighted in animal models of inflammation or even in *in vitro* and *in vivo* models of cancer (colorectal and breast cancer). Their direct immune modulatory activity on human lymphocytes has been proven, and the mechanism of action in cancer cells has been elucidated (133, 134).

2.4 Lignans

2.4.1 Chemical characteristics of lignans

In addition to isoflavones, lignans are considered another main group of phytoestrogens in soy, based on their chemical structures. Lignans are defined as dimeric phenylpropanoid (C6-C3) compounds, mostly linked at 8-8' (Figure 7) (135, 136). They are seven lignans identified from soy, namely, anhydrosecoisolariciresinol (76), isolariciresinol (77), secoisolariciresinol (78), matairesinol (79), lariciresinol (80), pinorensinol (81) and syringaresinol (82) (Figure 7) (28, 137).

2.4.2 Health effects of lignans

2.4.2.1 Antioxidant activity

Pinorensinol (81) has been reported frequently as an antioxidant, using thiocyanate antioxidant, Cu²⁺-induced low density lipoprotein oxidation, lipid peroxidation in rat liver, DPPH radical, and peroxy radical assays (138). Syringaresinol (82) has also been demonstrated as antioxidative in Cu²⁺-induced low density lipoprotein oxidation and DPPH radical assays (138). Lariciresinol (80) has a high radical scavenging capacity compared to the well-known antioxidant Trolox. The trapping capacity (mmoles peroxy radicals scavenged per gram of compound) of lariciresinol (80) (7.3 mmol/g) is higher than that of trolox (6.8 mmol/g) (139). Secoisolariciresinol (78) showed strong antioxidant activity against DPPH with an IC₅₀ of 0.017±0.001 mM. It is about two times stronger than the standard antioxidant, 2,6-di-(*tert*-butyl)-4-methylphenol (BHT), IC₅₀ 0.031±0.001 mM (140). Isolariciresinol (77) showed 86.2 % inhibition of lipid peroxidation (LPO) at 25 µg/ml (141).

2.4.2.2 Anticancer activity

Estrogenic enterolignans, END or ENL are the major metabolites of lignans in the mammalian gut. Because estrogens were linked to some cancers, especially breast cancer, enterolignans could affect some cancer risk. To our knowledge, the estrogenic or anti-estrogenic effects of enterolignans in humans are not very clear (142). For example, while weak estrogenic activity of ENL was demonstrated the anti-estrogenic activity of ENL was disclosed through depression of estrogen-stimulated rat uterine RNA synthesis (143).

The lignan ENL was found to have a bi-phasic effect on DNA synthesis in human breast cancer MCF-7 cells, showing induction at 10-50 µM and inhibition at higher concentrations, with an IC₅₀ of 82.0 µM (144). END and ENL are weak and moderate inhibitors of aromatase enzyme activity in a pre-adipose cell culture system (143). In human colon tumor cell

Fig. 7. The chemical structures of lignans in soy.

lines (LS174T, Caco-2, HCT-15, T-84), the same concentration of END and ENL (100 μ M) significantly reduce the proliferation of all cell lines, though ENL was more than twice as effective as END (145).

2.5 Phytate

2.5.1 Chemical characteristics of phytate

Phytate (**83**), the salt of phytic acid (myo-inositol-(1,2,3,4,5,6)hexakisphosphate, IP-6, InsP-6) (**Figure 8**), is a naturally occurring polyphosphorylated carbohydrate. It is widely distributed in the plant kingdom. Phytate serves as a storage form of phosphorous and minerals and contains ~75% of total phosphorous of the kernels (25). It is the major source of phosphorus in soy (79). Phytate is considered as a strong chelator of important minerals such as calcium, magnesium, iron, and zinc, and can contribute to mineral deficiencies in people. However, recent studies demonstrate that this “antinutrient” effect of IP6 is only manifested when large quantities of IP6 are consumed in combination with an oligoelements-poor diet (146).

83

Fig. 8. The chemical structures of phytic acid in soy.

2.5.2 Health effects of phytic acid

2.5.2.1 Anti-cancer activities

Phytic acid (**83**) plays an important role in signal transduction, cell proliferation and differentiation (147). Recently phytic acid (**83**) has received much attention for its role in cancer prevention and control of experimental tumor growth, progression, and metastasis (148). A great majority of the studies were done in animals and showed that phytic acid had anti-neoplastic properties in breast, colon, liver, leukemia, prostate, sarcomas, and skin cancer (149, 150). The results and proposed mechanism of anti-carcinogenic activities of IP6 in various cell lines are summarized in **Table 6** (151-154).

In animal studies, phytic acid can increase blood NK cell activity in DMH-induced colon tumors in rats, suppress rhabdomyosarcoma cell growth in a xeno-grafted nude mouse model (155), inhibit tumor growth and metastasis in rats (156), prolong survival of tumor-bearing mice, and reduce the numbers of pulmonary metastases (157). Phytic acid can also inhibit DMBA-induced mouse skin tumor development and this inhibitory effect is likely, by modulating proliferation, differentiation, or apoptosis (158).

2.5.2.2 Other health effects

For a long time IP6 has been recognized as a natural antioxidant. In addition, IP6 possesses other significant benefits for human health, such as the ability to enhance the immune

cell line	dose	observation	mechanism	ref
Human Caco-2 colon cancer cell	Decrease the expression of TNF- α and TNFII in a dose dependent manner (1, 2.5 and 5 mM) after 12 h.	Decrease the expression of TNF- α and TNFII in Caco-2 cells.	Regulate cytokine production including TNF- α , to modulate immune response and cell death activation.	147
Human HT-29 colon cancer cell	Inhibit proliferation of HT-29 cells at 8 mmol/L and 13 mmol/L after 12 h.	Inhibit proliferation of HT-29 cells	Affect special cell cycle regulators, reduce over-expression of mutant P53, and prevent PCNA-dependent cellular proliferation.	154
Human MCF-7/Adr MDA-MB 231 and MCF-7 breast cancer cells	MCF-7/Adr - IC ₅₀ 1.26 mM MDA-MB 231- IC ₅₀ 1.32 mM MCF-7- IC ₅₀ 4.18 mM after 96 h.	Inhibit the growth of three breast cancer cells	Change cell cycle distribution	153
Human HepG2 liver hepatoma cell	Inhibit the growth of HepG2 liver hepatoma cell in a dose-dependent fashion (0.25-5 mM) after 6 days.	Inhibit the growth of HepG2 liver hepatoma cell	Modulate cell signal transduction pathways	155
Human LNCaP prostate cancer cell	Inhibit the growth of LNCaP prostate cancer cell dose dependently (0.5-4 mM) after 24 h.	Inhibit the growth of LNCaP prostate cancer cell	Inhibit Akt activation, cause CDKI accumulation and induce LNCaP cell cycle arrest.	151
Human DU145 prostate cancer cell	Inhibit the growth of DU145 prostate cancer cell dose dependently (0.25-2 mM) after 24 h.	Inhibit the growth of DU145 prostate cancer cell	Induce G1 arrest in DU145 cell cycle progression.	152

Table 6. The anti-carcinogenic activities of IP

system, prevent pathological calcification and kidney stone formation, lower elevated serum cholesterol, and to reduce pathological platelet activity (148). IP6 inhibited the replication of HIV-1 in a T cell line and in a freshly isolated strain in peripheral blood mononuclear cells, possibly acting on HIV-1 early replicative stage (149)

Fig. 9. The chemical structures of cinnamic acid ester glycosides in soy.

2.6 Cinnamic acid ester glycosides

2.6.1 Chemical characteristics of cinnamic acid ester glycosides

Two cinnamic acid ester glycosides were isolated by Hosny et al from soybean molasses, which is a by-product of aqueous alcohol soy protein concentrate production (70). They were identified as 1-*O*-(*E*)-feruloyl[α -L-arabinofuranosyl-(1 $\rightarrow$ 3)][β -D-glucopyranosyl(1 $\rightarrow$ 6)] β -D-glucopyranose (84) and 1-*O*-(*E*)-3,4,5-trimethoxycinnamoyl[α -L-arabinofuranosyl(1 $\rightarrow$ 3)][glucopyranosyl(1 $\rightarrow$ 6)] β -D-glucopyranose (85) (Figure 9).

3. Constituents formed during processing

Food processing may dramatically change the compositions and relative contents of the constituents in soy products and artificial compounds may also occur (159). The processing of foods can improve nutrition, quality, and safety; though processing could also lead to the formation of anti-nutritional and toxic compounds. These multi-faceted consequences of food processing result from molecular interactions among nutrients and with other food ingredients, both natural and added (160).

Some components isolated from soy products such as soy sauce and fermented products do not occur naturally in the soybean. And the types of these compounds vary among different soy products based upon processing methods. These compounds may be formed by 1) soybean processing or fermentation; 2) compounds from other ingredients of soy products; 3) compounds from reactions of components in soybean and/or other ingredients during processing. Even though these compounds are not found naturally in soybean, they do exist widely in various soy products and may contribute to important beneficial or detrimental biological effects associated with soy consumption. Unfortunately, the key role of these compounds is largely ignored.

In Japan, soybeans molasses and soy fermented with *Bacillus subtilis* (*natto*) are very popular daily foodstuffs (161). Six isoflavones which differ from that isolated from soy were generated by this process. They are glycitein 7-*O*- β -D-(2'',4'',6''-*O*-triacetyl)glucopyranoside (86), 8-(γ -hydroxy- γ,γ -dimethylpropyl)genistin (87), 5-hydroxy-8-(γ -hydroxy- γ,γ -dimethylpropyl)-3',4'-dimethoxyisoflavone-7-*O*- β -D-glucopyranoside (88), 6''-*O*-succinyldaidzin (89), 6''-*O*-succinylgenistin (90), and 6''-*O*-succinylglycitin (91) (161, 162) (Figure 10).

Another group of well-known compounds formed during food processing in soy is The Maillard reaction products (163, 164). The Maillard reaction is the heat-induced reaction of amino groups of amino acids, peptides, and proteins with carbonyl groups of reducing sugars such as glucose, that results in the concurrent formation of so-called Maillard browning products and acrylamide (165). In the past, extensive work has been done on Maillard reaction products in food products including several excellent reviews (160, 164-167). Five Maillard reaction products, fructose-lysine (92), fructose-alanine (93), fructose-valine (94), fructose-leucine (95) and fructose-isoleucine (96) (Figure 11) were isolated from soy sauce and miso (168, 169).

Other groups of compounds may also be found in different soy products. Guided by platelet aggregation analysis, two anti-platelet alkaloids, 1-methyl-1,2,3,4-tetrahydro- β -carboline (97) and 1-methyl- β -carboline (98), were obtained from soy sauce. These two compounds inhibited the maximal aggregation response induced by epinephrine, platelet-activating

86. glycitein 7-O-β-D-(2'',4'',6''-O-triacetyl)glucopyranoside

87. $R_1 = H, R_2 = OH$ 8-(γ-hydroxy-γ,γ-dimethylpropyl)genistin

88. $R_1 = R_2 = OCH_3$ 5-hydroxy-8-(γ-hydroxy-γ,γ-dimethylpropyl)-3',4'-dimethoxyisoflavone-7-O-β-D-glucopyranoside

89. $R_1 = R_2 = H, R_3 = CH_2CH_2COOH$ 6''-O-succinyldaidzin

90. $R_1 = OH, R_2 = H, R_3 = CH_2CH_2COOH$ 6''-O-succinylgenistin

91. $R_1 = H, R_2 = OCH_3, R_3 = CH_2CH_2COOH$ 6''-O-succinyglycitin

Fig. 10. The chemical structures of new isoflavones generated during food processing in soy products.

Fig. 11. The chemical structures of other components generated during food processing in soy products.

factor, collagen, adenosine 5'-diphosphate, and thrombin, respectively (170). Compound **97** had much greater inhibitory effect than that of **98** on platelet aggregation. Three other alkaloids, asperparalines A (**99**), B (**100**) and C (**101**) were found from okara (the insoluble residue of whole soybean) fermented with *Aspergillus japonicus* JV-23 (**Figure 11**) (171). Since soybean does not contain alkaloids, these compounds were likely brought into the soy products from other sources.

A series of aromatic compounds were isolated from soy sauce and miso (a traditional Japanese seasoning produced by fermented soybeans) (172-174). Their structures were identified as 4-hydroxy-2-ethyl-5-methyl-3(2H)-furanone (HEMF; **102**), 4-hydroxy-5-ethyl-2-methyl-3(2H)-furanone (**103**), 2,5-dimethyl-4-hydroxy-3(2H)-furanone (DMHF; **104**) and 3-hydroxy-2-methyl-4H-pyran-4-one (maltol; **105**) (**Figure 11**). They are considered to form the base of the sweet aroma of miso. All of these compounds were most likely generated during soy processing and/or fermentation.

Processing may also significantly elevate or reduce certain naturally occurring soybean components. For instance, a remarkable increase in folate content was found after fermentation, 5.2-fold and 1.7-fold higher than that of the boiled soybeans and soybean seeds, respectively (175). Thus, we must be aware that the composition of soybean products may differ substantially from the native soybean.

4. Conclusion

The soy bean has been used as a human food source of high quality protein and other nutrients for hundreds of years and is currently a major source of protein in commercial food products for the beef, pork and chicken industry. This chapter summarizes our current knowledge about chemical structures and health effects of the major phytochemicals in soy. Clearly, the observed health effects from soy or soy-based foods (other than those attributed to nutrients like protein) are not solely from the actions of certain individual or types of compounds, but rather are due to the mixed effects of different compounds. Additive, synergistic, and/or antagonistic effects of different soy components combine to provide a final effect of soy foods and these effects may also be altered by phytochemicals from other non-soy foods in the meal. In order to fully understand the mechanism of health effects of soy, it is important to identify the genuine bioactive compounds in soy.

5. References

- [1] Anderson, J. W.; Johnstone, B. M.; Cook-Newell, M. E., Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 1995, 333, 276-82.
- [2] Boyapati, S. M.; Shu, X. O.; Ruan, Z. X.; Dai, Q.; Cai, Q.; Gao, Y. T.; Zheng, W., Soyfood intake and breast cancer survival: a followup of the Shanghai Breast Cancer Study. *Breast Cancer Res Treat* 2005, 92, 11-7.
- [3] Toyomura, K.; Kono, S., Soybeans, Soy Foods, Isoflavones and Risk of Colorectal Cancer: a Review of Experimental and Epidemiological Data. *Asian Pac J Cancer Prev* 2002, 3, 125-132.
- [4] Zhou, J. R., Soy and the prevention of lifestyle-related diseases. *Clin Exp Pharmacol Physiol* 2004, 31 Suppl 2, S14-9.
- [5] Wu, A. H.; Ziegler, R. G.; Nomura, A. M.; West, D. W.; Kolonel, L. N.; Horn-Ross, P. L.; Hoover, R. N.; Pike, M. C., Soy intake and risk of breast cancer in Asians and Asian Americans. *Am J Clin Nutr* 1998, 68, 1437S-1443S.
- [6] Messina, M., Modern applications for an ancient bean: soybeans and the prevention and treatment of chronic disease. *J Nutr* 1995, 125, 567S-569S.
- [7] Messina, M., A brief historical overview of the past two decades of soy and isoflavone research. *J Nutr* 2010, 140, 1350S-4S.
- [8] Barnes, S.; Boersma, B.; Patel, R.; Kirk, M.; Darley-USmar, V. M.; Kim, H.; Xu, J., Isoflavonoids and chronic disease: mechanisms of action. *Biofactors* 2000, 12, 209-15.
- [9] Friedman, M.; Brandon, D. L., Nutritional and health benefits of soy proteins. *J Agric Food Chem* 2001, 49, 1069-86.
- [10] Omoni, A. O.; Aluko, R. E., Soybean foods and their benefits: potential mechanisms of action. *Nutr Rev* 2005, 63, 272-83.
- [11] Xiao, C. W., Health effects of soy protein and isoflavones in humans. *J Nutr* 2008, 138, 1244S-9S.

- [12] Setchell, K. D., Phytoestrogens: the biochemistry, physiology, and implications for human health of soy isoflavones. *Am J Clin Nutr* 1998, 68, 1333S-1346S.
- [13] Cabot, W., Phytoestrogens. *J Am Acad Orthop Surg* 2003, 11, 153-6.
- [14] Goldwyn, S.; Lazinsky, A.; Wei, H., Promotion of health by soy isoflavones: efficacy, benefit and safety concerns. *Drug Metabol Drug Interact* 2000, 17, 261-89.
- [15] Ren, M. Q.; Kuhn, G.; Wegner, J.; Chen, J., Isoflavones, substances with multi-biological and clinical properties. *Eur J Nutr* 2001, 40, 135-46.
- [16] Delmonte, P.; Rader, J. I., Analysis of isoflavones in foods and dietary supplements. *J AOAC Int* 2006, 89, 1138-46.
- [17] Messina, M.; Kucuk, O.; Lampe, J. W., An overview of the health effects of isoflavones with an emphasis on prostate cancer risk and prostate-specific antigen levels. *J AOAC Int* 2006, 89, 1121-34.
- [18] Vacek, J.; Klejdus, B.; Lojkova, L.; Kuban, V., Current trends in isolation, separation, determination and identification of isoflavones: a review. *J Sep Sci* 2008, 31, 2054-67.
- [19] Larkin, T.; Price, W. E.; Astheimer, L., The key importance of soy isoflavone bioavailability to understanding health benefits. *Crit Rev Food Sci Nutr* 2008, 48, 538-52.
- [20] Dentith, S.; Lockwood, B., Development of techniques for the analysis of isoflavones in soy foods and nutraceuticals. *Curr Opin Clin Nutr Metab Care* 2008, 11, 242-7.
- [21] Mortensen, A.; Kulling, S. E.; Schwartz, H.; Rowland, I.; Ruefer, C. E.; Rimbach, G.; Cassidy, A.; Magee, P.; Millar, J.; Hall, W. L.; Birkved, F. K.; Sorensen, I. K.; Sontag, G., Analytical and compositional aspects of isoflavones in food and their biological effects. *Mol Nutr Food Res* 2009, 53.
- [22] Badger, T. M.; Ronis, M. J.; Hakkak, R.; Rowlands, J. C.; Korourian, S., The health consequences of early soy consumption. *J Nutr* 2002, 132, 559S-565S.
- [23] Messina, M. J., Legumes and soybeans: overview of their nutritional profiles and health effects. *Am J Clin Nutr* 1999, 70, 439S-450S.
- [24] Rochfort, S.; Panozzo, J., Phytochemicals for health, the role of pulses. *J Agric Food Chem* 2007, 55, 7981-7994.
- [25] Schlemmer, U.; Frolich, W.; Prieto, R. M.; Grases, F., Phytate in foods and significance for humans: food sources, intake, processing, bioavailability, protective role and analysis. *Mol Nutr Food Res* 2009, 53 Suppl 2, S330-75.
- [26] Piironen, V.; Lindsay, D. G.; Miettinen, T. A.; Toivo, J.; Lampi, A.-M., Plant sterols: biosynthesis, biological function and their importance to human nutrition. *J Sci Food Agric* 2000, 80, 939-966.
- [27] Lin, J.; Wang, C., Soybean saponins: chemistry, analysis, and potential of health effects. In *Soybeans as Functional Foods and Ingredients*, 2004; pp 73-100.
- [28] Penalvo, J. L.; Heinonen, S.-M.; Nurmi, T.; Deyama, T.; Nishibe, S.; Adlercreutz, H., Plant lignans in soy-based health supplements. *J Agric Food Chem* 2004, 52, 4133-4138.
- [29] Wang, H.; Murphy, P. A., Isoflavone content in commercial soybean foods. *J Agric Food Chem* 1994, 42, 1666-1673.
- [30] Hosny, M.; Rosazza, J. P., New isoflavone and triterpene glycosides from soybeans. *J Nat Prod* 2002, 65, 805-13.
- [31] Xu, D.-P.; Xiao, K.; Gu, W.-Y.; Ding, X.-L., Isolation of a new isoflavone from soybean germ. *Zhongcaoyao* 2003, 34, 1065-1067.

- [32] Barnes, S., The biochemistry, chemistry and physiology of the isoflavones in soybeans and their food products. *Lymphat Res Biol* 2010, 8, 89-98.
- [33] Adlercreutz, H., Phyto-oestrogens and cancer. *Lancet Oncol* 2002, 3, 364-73.
- [34] Ganry, O., Phytoestrogen and breast cancer prevention. *Eur J Cancer Prev* 2002, 11, 519-22.
- [35] Sarkar, F. H.; Li, Y., Soy isoflavones and cancer prevention. *Cancer Invest* 2003, 21, 744-57.
- [36] Clair, R. S.; Anthony, M., Soy, isoflavones and atherosclerosis. *Handb Exp Pharmacol* 2005, 301-23.
- [37] Clarkson, T. B., Soy, soy phytoestrogens and cardiovascular disease. *J Nutr* 2002, 132, 566S-569S.
- [38] Anthony, M. S.; Clarkson, T. B.; Williams, J. K., Effects of soy isoflavones on atherosclerosis: potential mechanisms. *Am J Clin Nutr* 1998, 68, 1390S-1393S.
- [39] Zhang, Y.; Chen, W. F.; Lai, W. P.; Wong, M. S., Soy isoflavones and their bone protective effects. *Inflammopharmacology* 2008, 16, 213-5.
- [40] Messina, M.; Ho, S.; Alekel, D. L., Skeletal benefits of soy isoflavones: a review of the clinical trial and epidemiologic data. *Curr Opin Clin Nutr Metab Care* 2004, 7, 649-58.
- [41] Setchell, K. D.; Lydeking-Olsen, E., Dietary phytoestrogens and their effect on bone: evidence from in vitro and in vivo, human observational, and dietary intervention studies. *Am J Clin Nutr* 2003, 78, 593S-609S.
- [42] Brynin, R., Soy and its isoflavones: a review of their effects on bone density. *Altern Med Rev* 2002, 7, 317-27.
- [43] Bhatena, S. J.; Velasquez, M. T., Beneficial role of dietary phytoestrogens in obesity and diabetes. *Am J Clin Nutr* 2002, 76, 1191-201.
- [44] Orgaard, A.; Jensen, L., The effects of soy isoflavones on obesity. *Exp Biol Med (Maywood)* 2008, 233, 1066-80.
- [45] Steiner, C.; Arnould, S.; Scalbert, A.; Manach, C., Isoflavones and the prevention of breast and prostate cancer: new perspectives opened by nutrigenomics. *Br J Nutr* 2008, 99 E Suppl 1, ES78-108.
- [46] Jian, L., Soy, isoflavones, and prostate cancer. *Mol Nutr Food Res* 2009, 53.
- [47] Messina, M. J.; Wood, C. E., Soy isoflavones, estrogen therapy, and breast cancer risk: analysis and commentary. *Nutr J* 2008, 7, 17.
- [48] Dong, J. Y.; Qin, L. Q., Soy isoflavones consumption and risk of breast cancer incidence or recurrence: a meta-analysis of prospective studies. *Breast Cancer Res Treat* 2011, 125, 315-23.
- [49] Sarkar, F. H.; Li, Y., Isoflavones, soybean phytoestrogens, and cancer. In *Nutrition and Cancer Prevention*, Awad, A. B.; Bradford, P. G., Eds. CRC Press: Boca Raton, 2006; pp 295-312.
- [50] Rimbach, G.; Boesch-Saadatmandi, C.; Frank, J.; Fuchs, D.; Wenzel, U.; Daniel, H.; Hall, W. L.; Weinberg, P. D., Dietary isoflavones in the prevention of cardiovascular disease--a molecular perspective. *Food Chem Toxicol* 2008, 46, 1308-19.
- [51] Cano, A.; Garcia-Perez, M. A.; Tarin, J. J., Isoflavones and cardiovascular disease. *Maturitas* 2010, 67, 219-26.
- [52] Lagari, V. S.; Levis, S., Phytoestrogens and bone health. *Curr Opin Endocrinol Diabetes Obes* 2010, 17, 546-53.

- [53] Velasquez, M. T.; Bhathena, S. J., Role of dietary soy protein in obesity. *Int J Med Sci* 2007, 4, 72-82.
- [54] Oakenfull, D., Saponins in food – A review *Food Chem* 1981, 7, 19-40.
- [55] Sumiki, Y., Studies on the saponin of soy bean. I. *Bull Agric Chem Soc Jap* 1929, 5, 27-32.
- [56] Sumiki, Y., The saponin of soy bean. II. *Bull Agric Chem Soc Jap* 1930, 6, 49-51.
- [57] Burrows, J. C.; Price, K. R.; Fenwick, R. G., Soyasaponin IV, an additional monodesmosidic saponin isolated from soyabean *Phytochemistry* 1987, 26, 1214-1215.
- [58] Curl, C. L.; Price, K. R.; Fenwick, G. R., Soyasaponin A3, a new monodesmosidic saponin isolated from the seeds of *Glycine max*. *J Nat Prod* 1988, 51, 122-124.
- [59] Kitagawa, I.; Saito, M.; Taniyama, T.; Yoshikawa, M., Saponin and sapogenol. XXXVIII. Structure of soyasaponin A2, a bisdesmoside of soyasapogenol A, from soybean, the seeds of *Glycine max* Merrill. *Chem Pharm Bull* 1985, 33, 598-608.
- [60] Kitagawa, I.; Saito, M.; Taniyama, T.; Yoshikawa, M., Saponin and sapogenol. XXXIX. Structure of soyasaponin A1, a bisdesmoside of soyasapogenol A, from soybean, the seeds of *Glycine max* Merrill. *Chem Pharm Bull* 1985, 33, 1069-76.
- [61] Kitagawa, I.; Taniyama, T.; Nagahama, Y.; Okubo, K.; Yamauchi, F.; Yoshikawa, M., Saponin and sapogenol. XLII. Structures of acetyl-soyasaponins A1, A2, and A3, astringent partially acetylated bisdesmosides of soyasapogenol A, from American soybean, the seeds of *Glycine max* Merrill. *Chem Pharm Bull* 1988, 36, 2819-28.
- [62] Kitagawa, I.; Wang, H. K.; Taniyama, T.; Yoshikawa, M., Saponin and sapogenol. XLI. : Reinvestigation of the structures of soyasapogenols A, B, and E, oleanene-sapogenols from soybean. Structures of soyasaponins I, II, and III. *Chem Pharm Bull* 1988, 36, 153-161.
- [63] Shiraiwa, M.; Harada, K.; Okubo, K., Composition and structure of "group B saponin" in soybean seed. *Agric Biol Chem* 1991, 55, 911-917.
- [64] Taniyama, T.; Nagahama, Y.; Yoshikawa, M.; Kitagawa, I., Saponin and sapogenol. XLIII. Acetyl-soyasaponins A4, A5, and A6, new astringent bisdesmosides of soyasapogenol A, from Japanese soybean, the seeds of *Glycine max* Merrill. *Chem Pharm Bull* 1988, 36, 2829-39.
- [65] Taniyama, T.; Yoshikawa, M.; Kitagawa, I., Saponin and sapogenol. XLIV. Soyasaponin composition in soybeans of various origins and soyasaponin content in various organs of soybean. Structure of soyasaponin V from soybean hypocotyl. *Yakugaku Zasshi* 1988, 108, 562-571.
- [66] Heng, L.; Vincken, J. P.; Hoppe, K.; van Koningsveld, G. A.; Decroos, K.; Gruppen, H.; van Boekel, M. A. J. S.; Voragen, A. G. J., Stability of pea DDMP saponin and the mechanism of its decomposition. *Food Chem* 2006, 99, 326-334.
- [67] Decroos, K.; Vincken, J. P.; Heng, L.; Bakker, R.; Gruppen, H.; Verstraete, W., Simultaneous quantification of differently glycosylated, acetylated, and 2,3-dihydro-2,5-dihydroxy-6-methyl-4H-pyran-4-one-conjugated soyasaponins using reversed-phase high-performance liquid chromatography with evaporative light scattering detection. *J Chromatogr A* 2005, 1072, 185-193.
- [68] Kudou, S.; Tonomura, M.; Tsukamoto, C.; Uchida, T.; Sakabe, T.; Tamura, N.; Okubo, K., Isolation and structural elucidation of DDMP-conjugated soyasaponins

- as genuine saponins from soybean seeds. *Biosci Biotechnol Biochem* 1993, 57, 546-550.
- [69] Tsukamoto, C.; Kikuchi, A.; Harada, K.; Kitamura, K.; Okubo, k., Genetic and chemical polymorphisms of saponins in soybean seed. *Phytochemistry* 1993, 34, 1351-1356.
- [70] Hosny, M.; Rosazza, J. P. N., Novel isoflavone, cinnamic acid, and triterpenoid glycosides in soybean molasses *J Nat Prod* 1999, 62, 853 -858.
- [71] Hosny, M.; Rosazza, J. P. N., New isoflavone and triterpene glycosides from soybeans *J Nat Prod* 2002, 65, 805-813.
- [72] Ali, Z.; Khan, S. I.; Khan, I. A., Soyasaponin Bh, a Triterpene Saponin Containing a Unique Hemiacetal-Functional Five-Membered Ring from Glycine max (Soybeans). *Planta Med* 2009, 75, 371-374.
- [73] Quan, J. S.; Shen, M. H.; Zhang, S., Protective effects of soybean isoflavones and soy saponins on oxidation of lipoproteins. *Shipin Kexue* 2003, 24, 121-123.
- [74] Okubo, K., Physiological function of soybean glycosides, especially DDMP saponin. *Daizu Tanpakushitsu Kenkyu* 1993, 14, 108-111.
- [75] Willner, E. D.; Gestetner, B.; Lavie, D.; Birk, Y.; Bondi, A., Soybean saponins. *J Chem Soc, Suppl.* 1964, 1, 5885-8.
- [76] Hu, X. Y.; Wang, X. G., Prospect of soya-sapnins (I) - the distribution, structure and characteristics. *Chin Oils Fats* 2001, 26, 29-33.
- [77] Guclu-Ustundag, O.; Mazza, G., Saponins: properties, applications and processing. *Crit Rev Food Sci Nutr* 2007, 47, 231-58.
- [78] Lee, Y. B.; Lee, H. J.; Kim, C. H.; Lee, S. B.; Sohn, H. S., Soy isoflavones and soyasaponins: characteristics and physiological functions. *Agric Chem Biotechnol* 2005, 48, 49-57.
- [79] Jiang, H. Y.; Lv, F. J.; Tai, J. Q., Bioactive components of soybean and their function. *Soybean Sci* 2000, 19, 160-164.
- [80] Lv, F. X.; Lu, Z. X., Research process of bioactive substances in soybean. *Food Sci Technol* 2001, 5, 69-71.
- [81] Gurfinkel, D. M.; Rao, A. V., Soyasaponins: the relationship between chemical structure and colon anticarcinogenic activity. *Nutr Cancer* 2003, 47, 24-33.
- [82] Persky, V.; Van Horn, L., Epidemiology of soy and cancer: perspectives and directions. *J Nutr* 1995, 125, 709S-712S.
- [83] Ellington, A. A.; Berhow, M.; Singletary, K. W., Induction of macroautophagy in human colon cancer cells by soybean B-group triterpenoid saponins. *Carcinogenesis* 2005, 26, 159-67.
- [84] Hsu, C. C.; Lin, T. W.; Chang, W. W.; Wu, C. Y.; Lo, W. H.; Wang, P. H.; Tsai, Y. C., Soyasaponin-I-modified invasive behavior of cancer by changing cell surface sialic acids. *Gynecol Oncol* 2005, 96, 415-22.
- [85] Jun, H. S.; Kim, S. E.; Sung, M. K., Protective effect of soybean saponins and major antioxidants against aflatoxin B1-induced mutagenicity and DNA-adduct formation. *J Med Food* 2002, 5, 235-240.
- [86] Kang, J. H.; Han, I. H.; Sung, M. K.; Yoo, H.; Kim, Y. G.; Kim, J. S.; Kawada, T.; Yu, R., Soybean saponin inhibits tumor cell metastasis by modulating expressions of MMP-2, MMP-9 and TIMP- 2. *Cancer Lett* 2008, 261, 84-92.

- [87] Kim, H. Y.; Yu, R.; Kim, J. S.; Kim, Y. K.; Sung, M. K., Antiproliferative crude soy saponin extract modulates the expression of IkappaB α , protein kinase C, and cyclooxygenase-2 in human colon cancer cells. *Cancer Lett* 2004, 210, 1-6.
- [88] Yanamandra, N.; Berhow, M. A.; Konduri, S.; Dinh, D. H.; Olivero, W. C.; Nicolson, G. L.; Rao, J. S., Triterpenoids from *Glycine max* decrease invasiveness and induce caspase-mediated cell death in human SNB19 glioma cells. *Clin Exp Metastasis* 2003, 20, 375-383.
- [89] Rao, A. V.; Sung, M. K., Saponins as anticarcinogens. *J Nutr* 1995, 125, 717-724.
- [90] Bachran, C.; Bachran, S.; Sutherland, M.; Bachran, D.; Fuchs, H., Saponins in tumor therapy. *Mini Rev Med Chem* 2008, 8, 575-84.
- [91] Chang, W. W.; Yu, C. Y.; Lin, T. W.; Wang, P. H.; Tsai, Y. C., Soyasaponin I decreases the expression of alpha2,3-linked sialic acid on the cell surface and suppresses the metastatic potential of B16F10 melanoma cells. *Biochem Biophys Res Commun* 2006, 341, 614-9.
- [92] Oakenfull, D.; Sidhu, G. S., Could saponins be a useful treatment for hypercholesterolaemia? *Eur J Clin Nutr* 1990, 44, 79-88.
- [93] Oakenfull, D. G.; Topping, D. L., Saponins and plasma cholesterol. *Atherosclerosis* 1983, 48, 301-3.
- [94] Potter, J. D.; Topping, D. L.; Oakenfull, D., Soy, saponins, and plasma cholesterol. *Lancet* 1979, 1, 223.
- [95] Topping, D. L.; Trimble, R. P.; Illman, R. J.; Potter, J. D.; Oakenfull, D. G., Prevention of dietary hypercholesterolemia in the rat by soy flour high and low in saponins. *Nutr Rep Int* 1980, 22, 513-19.
- [96] Oakenfull, D., Soy protein, saponins and plasma cholesterol. *J Nutr* 2001, 131, 2971-2.
- [97] Xiao, J. X.; Peng, G. H.; Zhang, S. H., Prevention effects of soyasaponins on hyperlipidemia mice and its molecular mechanism. *Acta Nutr Sin* 2005, 27, 147-150.
- [98] Kiribuchi, M.; Miura, K.; Tokuda, S.; Kaneda, T., Hypocholesterolemic effect of triterpene alcohols with soysterol on plasma cholesterol in rats. *J Nutr Sci Vitaminol* 1983, 29, 35-43.
- [99] Lee, S. O.; Simons, A. L.; Murphy, P. A.; Hendrich, S., Soyasaponins lowered plasma cholesterol and increased fecal bile acids in female golden Syrian hamsters. *Exp Biol Med* 2005, 230, 472-478.
- [100] Kubo, M.; Matsuda, H.; Tani, T.; Namba, K.; Arichi, S.; Kitagawa, I., Effects of soyasaponin on experimental disseminated intravascular coagulation. I. *Chem Pharm Bull* 1984, 32, 1467-1471.
- [101] Wang, Y. P.; Wu, J. X.; Zhang, F. L.; Wang, X. R., Effect of soyasaponin and ginsenoside (stem-leave saponin) on SOD and LPO in diabetic rats. *J Baiqiuen Med Univ* 1993, 19, 122-123.
- [102] Quan, J. S.; Yin, X. Z.; Tanaka, M.; Kanazawa, T., The hypoglycemic effects of soybean hypocotyl extract in diabetic rats and their mechanism. *Acta Nutr Sin* 2004, 26, 207-210.
- [103] Okubo, K.; Kudou, S.; Uchida, T.; Yoshiki, Y.; Yoshikoshi, M.; Tonomura, M., Soybean saponin and isoflavonoids: structure and antiviral activity against human immunodeficiency virus in vitro. *ACS Symposium Series* 1994, 546, 330-339.

- [104] Li, J. B.; Hu, J. S.; Cheng, B. H.; Wang, X. G.; An, Z. Y.; Wei, Y. D., Inhibitory effect of total soyasaponin on virus replication and its clinical application. *Chin J Exp Clin Virol* 1995, 9, 111-114.
- [105] Hayashi, K.; Hayashi, H.; Hiraoka, N.; Ikeshiro, Y., Inhibitory activity of soyasaponin II on virus replication in vitro. *Planta Med* 1997, 63, 102-105.
- [106] Ikeda, T.; Yokomizo, K.; Okawa, M.; Tsuchihashi, R.; Kinjo, J.; Nohara, T.; Uyeda, M., Anti-herpes virus type 1 activity of oleanane-type triterpenoids. *Biol Pharm Bull* 2005, 28, 1779-81.
- [107] Kinjo, J.; Imagire, M.; Udayama, M.; Arao, T.; Nohara, T., Structure-hepatoprotective relationships study of soyasaponins I-IV having soyasapogenol B as aglycone. *Planta Med* 1998, 64, 233-236.
- [108] Ohominami, H.; Okuda, H.; Yoshikawa, M.; Kitagawa, I., Effect of soyasaponins on lipid metabolism. *Wakanyaku Shinpojumu* 1981, 14, 157-162.
- [109] Yoshiki, Y.; Okubo, K., Active oxygen scavenging activity of DDMP (2,3-dihydro-2,5-dihydroxy-6-methyl-4H-pyran-4-one) saponin in soybean seed. *Biosci Biotechnol Biochem* 1995, 59, 1556-1557.
- [110] Akihisa, T.; Kimura, Y.; Tamura, T., Bacchara-12,21-dien-3 β -ol from the seeds of *Glycine max* *Phytochemistry* 1994, 37, 1413-1415
- [111] Marshall, J. A.; Dennis, A. L.; Kumazawa, T.; Haynes, A. M.; Nes, W. D., Soybean sterol composition and utilization by *Phytophthora sojae*. *Phytochemistry* 2001, 58, 423-428.
- [112] van Ee, J. H., Soy constituents: modes of action in low-density lipoprotein management. *Nutr Rev* 2009, 67, 222-34.
- [113] Garbuzov, A. G.; Medvedev, F. A.; Levachev, M. M., Change in the composition of soybean oil sterols after heat treatment. *Voprosy pitaniya* 1986, 67-69.
- [114] Ostlund, R. E., Jr., Phytosterols in human nutrition. *Annu Rev Nutr* 2002, 22, 533-49.
- [115] Kircher, H. W.; Rosenstein, F. U., Purification of campesterol and preparation of 7-dehydro- campesterol, 7-campestenol, and campestanol. *Lipids* 1974, 9, 333-337.
- [116] Peterson, D. W., Plant sterols and tissue cholesterol levels. *Am J Clin Nutr* 1958, 6, 644-9.
- [117] Lin, X.; Ma, L.; Racette, S. B.; Spearie, C. L. A.; Ostlund, R. E., Jr., Phytosterol glycosides reduce cholesterol absorption in humans. *Am. J. Physiol.* 2009, 296, G931-G935.
- [118] Ostlund, R. E., Jr., Phytosterols, cholesterol absorption and healthy diets. *Lipids* 2007, 42, 41-5.
- [119] Ostlund, R. E., Jr., Phytosterols and cholesterol metabolism. *Curr Opin Lipidol* 2004, 15, 37-41.
- [120] Moghadasian, M. H.; Frohlich, J. J., Effects of dietary phytosterols on cholesterol metabolism and atherosclerosis: clinical and experimental evidence. *Am J Med* 1999, 107, 588-94.
- [121] Katan, M. B.; Grundy, S. M.; Jones, P.; Law, M.; Miettinen, T.; Paoletti, R., Efficacy and safety of plant stanols and sterols in the management of blood cholesterol levels. *Mayo Clin Proc* 2003, 78, 965-78.
- [122] Adults, E. P. o. D. E. a. T. o. H. B. C. i., Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *Jama* 2001, 285, 2486-97.

- [123] Calpe-Berdiel, L.; Escola-Gil, J. C.; Blanco-Vaca, F., New insights into the molecular actions of plant sterols and stanols in cholesterol metabolism. *Atherosclerosis* 2009, 203, 18-31.
- [124] Vanstone, C. A.; Raeini-Sarjaz, M.; Jones, P. J., Injected phytosterols/stanols suppress plasma cholesterol levels in hamsters. *J Nutr Biochem* 2001, 12, 565-574.
- [125] Matvienko, O. A.; Lewis, D. S.; Swanson, M.; Arndt, B.; Rainwater, D. L.; Stewart, J.; Alekel, D. L., A single daily dose of soybean phytosterols in ground beef decreases serum total cholesterol and LDL cholesterol in young, mildly hypercholesterolemic men. *Am J Clin Nutr* 2002, 76, 57-64.
- [126] Zhao, Y.; Chang, S. K.; Qu, G.; Li, T.; Cui, H., Beta-sitosterol inhibits cell growth and induces apoptosis in SGC-7901 human stomach cancer cells. *J Agric Food Chem* 2009, 57, 5211-8.
- [127] Woyengo, T. A.; Ramprasath, V. R.; Jones, P. J., Anticancer effects of phytosterols. *Eur J Clin Nutr* 2009, 63, 813-20.
- [128] Bradford, P. G.; Awad, A. B., Phytosterols as anticancer compounds. *Mol Nutr Food Res* 2007, 51, 161-70.
- [129] Awad, A. B.; Williams, H.; Fink, C. S., Phytosterols reduce in vitro metastatic ability of MDA-MB-231 human breast cancer cells. *Nutr Cancer* 2001, 40, 157-64.
- [130] Awad, A. B.; Fink, C. S., Phytosterols as anticancer dietary components: evidence and mechanism of action. *J Nutr* 2000, 130, 2127-30.
- [131] Awad, A. B.; von Holtz, R. L.; Cone, J. P.; Fink, C. S.; Chen, Y. C., beta-Sitosterol inhibits growth of HT-29 human colon cancer cells by activating the sphingomyelin cycle. *Anticancer Res* 1998, 18, 471-3.
- [132] Philpotts, M., Phytochemicals for cancer prevention. *Lippincott Health Promot Lett* 1997, 2, 7, 10.
- [133] Bouic, P. J., The role of phytosterols and phytosterolins in immune modulation: a review of the past 10 years. *Curr Opin Clin Nutr Metab Care* 2001, 4, 471-5.
- [134] Bouic, P. J.; Lamprecht, J. H., Plant sterols and sterolins: a review of their immune-modulating properties. *Altern Med Rev* 1999, 4, 170-7.
- [135] Dixon, R. A., Phytoestrogens. *Annu Rev Plant Biol* 2004, 55, 225-261.
- [136] Kurzer, M. S.; Xu, X., Dietary phytoestrogens. *Annu Rev Nutr* 1997, 17, 353-81.
- [137] Mazur, W. M.; Duke, J. A.; Wahala, K.; Rasku, S.; Adlercreutz, H., Isoflavonoids and lignans in legumes: nutritional and health aspects in humans. *J Nutr Biochem* 1998, 9, 193-200.
- [138] Chin, Y. W.; Chai, H. B.; Keller, W. J.; Kinghorn, A. D., Lignans and other constituents of the fruits of *Euterpe oleracea* (Acai) with antioxidant and cytoprotective activities. *J Agric Food Chem* 2008, 56, 7759-64.
- [139] Willfor, S. M.; Ahotupa, M. O.; Hemming, J. E.; Reunanen, M. H.; Eklund, P. C.; Sjöholm, R. E.; Eckerman, C. S.; Pohjamo, S. P.; Holmbom, B. R., Antioxidant activity of knotwood extracts and phenolic compounds of selected tree species. *J Agric Food Chem* 2003, 51, 7600-6.
- [140] Sutthivaiyakit, S.; Nakorn, N. N.; Kraus, W.; Sutthivaiyakit, P., A novel 29-nor-3,4-seco-friedelane triterpene and a new guaiane sesquiterpene from the roots of *Phyllanthus oxyphyllus*. *Tetrahedron* 2003, 59, 9991-9995.

- [141] Mulabagal, V.; Subbaraju, G. V.; Ramani, M. V.; DeWitt, D. L.; Nair, M. G., Lipid peroxidation, cyclooxygenase enzyme and tumor cell proliferation inhibitory lignans from *Justicia* species. *Nat Prod Commun* 2008, 3, 1793-1798.
- [142] Carreau, C.; Flouriot, G.; Bennetau-Pelissero, C.; Potier, M., Enterodiol and enterolactone, two major diet-derived polyphenol metabolites have different impact on ERalpha transcriptional activation in human breast cancer cells. *J Steroid Biochem Mol Biol* 2008, 110, 176-85.
- [143] Wang, L. Q., Mammalian phytoestrogens: enterodiol and enterolactone. *J Chromatogr B Analyt Technol Biomed Life Sci* 2002, 777, 289-309.
- [144] Wang, C.; Kurzer, M. S., Phytoestrogen concentration determines effects on DNA synthesis in human breast cancer cells. *Nutr Cancer* 1997, 28, 236-47.
- [145] Sung, M. K.; Lautens, M.; Thompson, L. U., Mammalian lignans inhibit the growth of estrogen-independent human colon tumor cells. *Anticancer Res* 1998, 18, 1405-8.
- [146] Grases, F.; Simonet, B. M.; Vucenik, I.; Prieto, R. M.; Costa-Bauza, A.; March, J. G.; Shamsuddin, A. M., Absorption and excretion of orally administered inositol hexaphosphate (IP(6) or phytate) in humans. *Biofactors* 2001, 15, 53-61.
- [147] Cholewa, K.; Parfiniewicz, B.; Bednarek, I.; Swiatkowska, L.; Jezienicka, E.; Kierot, J.; Weglarz, L., The influence of phytic acid on TNF-alpha and its receptors genes' expression in colon cancer Caco-2 cells. *Acta Pol Pharm* 2008, 65, 75-9.
- [148] Vucenik, I.; Shamsuddin, A. M., Protection against cancer by dietary IP6 and inositol. *Nutr Cancer* 2006, 55, 109-25.
- [149] Otake, T.; Mori, H.; Morimoto, M.; Miyano, K.; Ueba, N.; Oishi, I.; Kunita, N.; Kurimura, T., Anti-HIV-1 activity of myo-inositol hexaphosphoric acid (IP6) and myo-inositol hexasulfate (IS6). *Anticancer Res* 1999, 19, 3723-6.
- [150] Fox, C. H.; Eberl, M., Phytic acid (IP6), novel broad spectrum anti-neoplastic agent: a systematic review. *Complementary thera Med* 2002, 10, 229-234.
- [151] Agarwal, C.; Dhanalakshmi, S.; Singh, R. P.; Agarwal, R., Inositol hexaphosphate inhibits growth and induces G1 arrest and apoptotic death of androgen-dependent human prostate carcinoma LNCaP cells. *Neoplasia* 2004, 6, 646-59.
- [152] Singh, R. P.; Agarwal, C.; Agarwal, R., Inositol hexaphosphate inhibits growth, and induces G1 arrest and apoptotic death of prostate carcinoma DU145 cells: modulation of CDKI-CDK-cyclin and pRb-related protein-E2F complexes. *Carcinogenesis* 2003, 24, 555-63.
- [153] Tantivejkul, K.; Vucenik, I.; Eiseman, J.; Shamsuddin, A. M., Inositol hexaphosphate (IP6) enhances the anti-proliferative effects of adriamycin and tamoxifen in breast cancer. *Breast Cancer Res Treat* 2003, 79, 301-312.
- [154] Tian, Y.; Song, Y., Effects of inositol hexaphosphate on proliferation of HT-29 human colon carcinoma cell line. *World J Gastroenterol* 2006, 12, 4137-4142.
- [155] Vucenik, I.; Kalebic, T.; Tantivejkul, K.; Shamsuddin, A. M., Novel anticancer function of inositol hexaphosphate: inhibition of human rhabdomyosarcoma in vitro and in vivo. *Anticancer Res* 1998, 18, 1377-1384.
- [156] Zhang, Z.; Song, Y.; Wang, X. L., Inositol hexaphosphate-induced enhancement of natural killer cell activity correlates with suppression of colon carcinogenesis in rats. *World J Gastroenterol* 2005, 11, 5044-5046.

- [157] Vucenik, I.; Tomazic, V. J.; Fabian, D.; Shamsuddin, A. M., Antitumor activity of phytic acid (inositol hexaphosphate) in murine transplanted and metastatic fibrosarcoma, a pilot study. *Cancer Lett* 1992, 65, 9-13.
- [158] Gupta, K. P.; Singh, J.; Bharathi, R., Suppression of DMBA-induced mouse skin tumor development by inositol hexaphosphate and its mode of action. *Nutr Cancer* 2003, 46, 66-72.
- [159] Anderson, R. L.; Wolf, W. J., Compositional changes in trypsin inhibitors, phytic acid, saponins and isoflavones related to soybean processing. *J Nutr* 1995, 125, 581S-588S.
- [160] Friedman, M., Nutritional consequences of food processing. *Forum Nutr* 2003, 56, 350-2.
- [161] 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. *Biol Pharm Bull* 1999, 22, 1193-201.
- [162] Hosny, M.; Rosazza, J. P., Novel isoflavone, cinnamic acid, and triterpenoid glycosides in soybean molasses. *J Nat Prod* 1999, 62, 853-8.
- [163] Molnar-Perl, I.; Pinter-Szakacs, M., Monitoring of Maillard reactions in soy products. *Z Lebensm Unters Forsch* 1986, 183, 18-25.
- [164] Csaky, I.; Fekete, S., Soybean: feed quality and safety. Part 1: biologically active components. A review. *Acta Vet Hung* 2004, 52, 299-313.
- [165] Friedman, M., Biological effects of Maillard browning products that may affect acrylamide safety in food: biological effects of Maillard products. *Adv Exp Med Biol* 2005, 561, 135-56.
- [166] Silvan, J. M.; van de Lagemaat, J.; Olano, A.; Del Castillo, M. D., Analysis and biological properties of amino acid derivatives formed by Maillard reaction in foods. *J Pharm Biomed Anal* 2006, 41, 1543-51.
- [167] Dyer, D. G.; Blackledge, J. A.; Katz, B. M.; Hull, C. J.; Adkisson, H. D.; Thorpe, S. R.; Lyons, T. J.; Baynes, J. W., The Maillard reaction in vivo. *Z Ernahrungswiss* 1991, 30, 29-45.
- [168] Nunomura, N.; Sasaki, M.; Asao, Y.; Yokotsuka, T., Studies on flavor components in shoyu. II. Isolation and identification of 4-hydroxy-2(or 5)-ethyl-5(or 2)-methyl-3(2H)-furanone, as a flavor component in shoyu (soy sauce). *Agric Biol Chem* 1976, 40, 491-5.
- [169] Hashiba, H., Isolation and identification of Amadori compounds from miso, white wine and sake. *Agr Biol Chem* 1978, 42, 1727-1731.
- [170] Tsuchiya, H.; Sato, M.; Watanabe, I., Antiplatelet activity of soy sauce as functional seasoning. *J Agric Food Chem* 1999, 47, 4167-74.
- [171] Hayashi, H.; Nishimoto, Y.; Akiyama, K.; Nozaki, H., New paralytic alkaloids, asperparalines A, B and C, from *Aspergillus japonicus* JV-23. *Biosci Biotechnol Biochem* 2000, 64, 111-115.
- [172] Sugawara, E., Relation between the aroma components and palatability of miso. *Nippon Kasei Gakkaishi* 1992, 43, 635-642.
- [173] Sugawara, E.; Saiga, S.; Kobayashi, A., Relations between aroma components and sensory evaluation of miso. *Nippon Shokuhin Kogyo Gakkaishi* 1992, 39, 1098-1104.

- [174] Wang, H.; Jenner, A. M.; Lee, C. Y.; Shui, G.; Tang, S. Y.; Whiteman, M.; Wenk, M. R.; Halliwell, B., The identification of antioxidants in dark soy sauce. *Free Radic Res* 2007, 41, 479-88.
- [175] Ginting, E.; Arcot, J., High-performance liquid chromatographic determination of naturally occurring folates during tempe preparation. *J Agric Food Chem* 2004, 52, 7752-8.

IntechOpen

IntechOpen

Phytochemicals - Bioactivities and Impact on Health

Edited by Prof. Iraj Rasooli

ISBN 978-953-307-424-5

Hard cover, 388 pages

Publisher InTech

Published online 22, December, 2011

Published in print edition December, 2011

Among the thousands of naturally occurring constituents so far identified in plants and exhibiting a long history of safe use, there are none that pose - or reasonably might be expected to pose - a significant risk to human health at current low levels of intake when used as flavoring substances. Due to their natural origin, environmental and genetic factors will influence the chemical composition of the plant essential oils. Factors such as species and subspecies, geographical location, harvest time, plant part used and method of isolation all affect chemical composition of the crude material separated from the plant. The screening of plant extracts and natural products for antioxidative and antimicrobial activity has revealed the potential of higher plants as a source of new agents, to serve the processing of natural products.

How to reference

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

Xianli Wu and Jie Kang (2011). Phytochemicals in Soy and Their Health Effects, *Phytochemicals - Bioactivities and Impact on Health*, Prof. Iraj Rasooli (Ed.), ISBN: 978-953-307-424-5, InTech, Available from: <http://www.intechopen.com/books/phytochemicals-bioactivities-and-impact-on-health/phytochemicals-in-soy-and-their-health-effects>

INTeCH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2011 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](https://creativecommons.org/licenses/by/3.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen