SOY ISOFLAVONES

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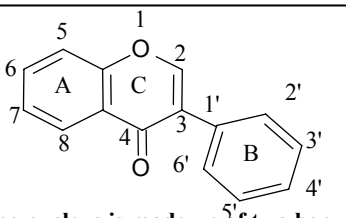
The soybean (*Glycine max L.*) has been an integral part of the diet of the people of Southeast Asia for centuries. A rich source of protein (constituting about 20-60 percent of the dietary daily protein intake in Southeast Asia)), soy foods such as soy milk, tofu, fermented soy products (soy bean paste, miso and tempeh) and soy flour have gained increasing acceptance in Western cultures as well. In recent years, the focus has shifted to their diverse health benefits. The medicinal uses of soy were first documented in the Materia Medica of the Chinese emperor Shen Nung in 2838 BC.

The phytonutrients in soyfoods known as "isoflavones" are proven to be useful in the management of a number of chronic health conditions. The major compounds responsible for the health benefits of soy are polyphenolics belonging to the class of bioflavonoids. Bioflavonoids are ubiquitous compounds in the vegetable kingdom, present in the cells involved in photosynthesis. Over 4000 of these compounds have been identified from both higher and lower plants and the list constantly expands. Bioflavonoids have an important influence on the color and flavor of the vegetables, fruits and beverages such as tea and wine. Two classes of pharmacologically important bioflavonoids have been identified: the flavonoids and the isoflavonoids, which differ in structural configuration, as shown in Figure 1.



The basic flavone nucleus is made up of two benzene rings A and B, linked through a heterocyclic pyran ring C.

Flavonoids : B ring is in the'2' position (such as green tea catechins)

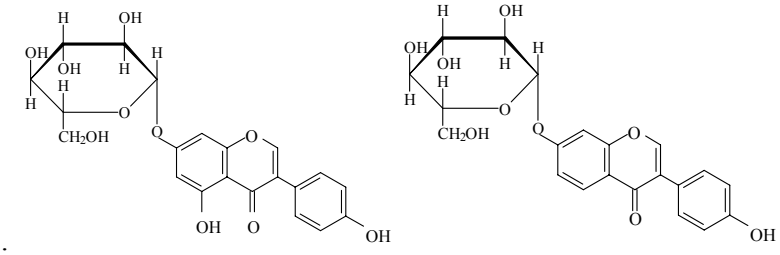
Isoflavonoids : B ring is in the '3' position (such as soy isoflavones)

Figure 1: Soy isoflavones defined

Soy Isoflavones in health and nutrition

Isoflavones are classified as "phytoestrogens" or plant derived estrogens. These compounds are structurally similar to the female hormone estradiol. Isoflavones are therefore important complementary estrogens and a useful and safe alternative to estrogen replacement therapy in post-menopausal women. The major isoflavones in soybean are genistein, daidzein and glycitein, of which genistein is the most beneficial component.

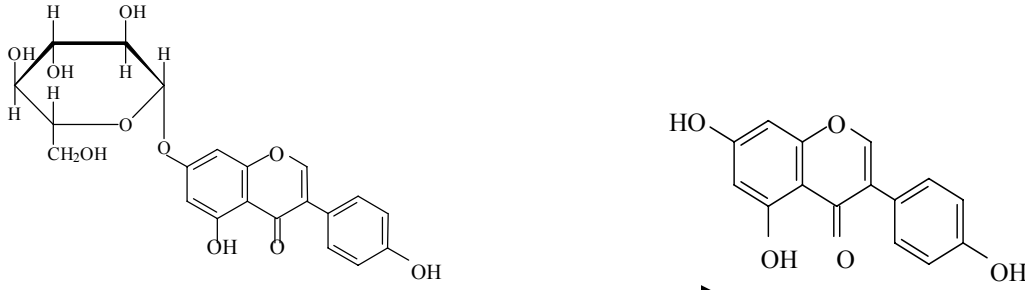
In whole soy foods, the isoflavones are present in inactive precursor forms - "beta-glucosides" consisting of the isoflavone components (aglycones) each bound covalently to a sugar (glucose) molecule. Thus genistein is present as genistin, daidzein as daidzin and glycitein as glycitin. Genistin forms about 60 percent of the total isoflavone precursors in soybean, daidzin about 30 percent and glycitin about 8 percent. When soyfoods are consumed, the glucosides are broken down by the bacteria in the gut during the digestive processes and yield the aglycones, the biologically active isoflavones. Figure 2 shows the chemical structures of the major soy isoflavone glucosides.



Genistin **Daidzin**

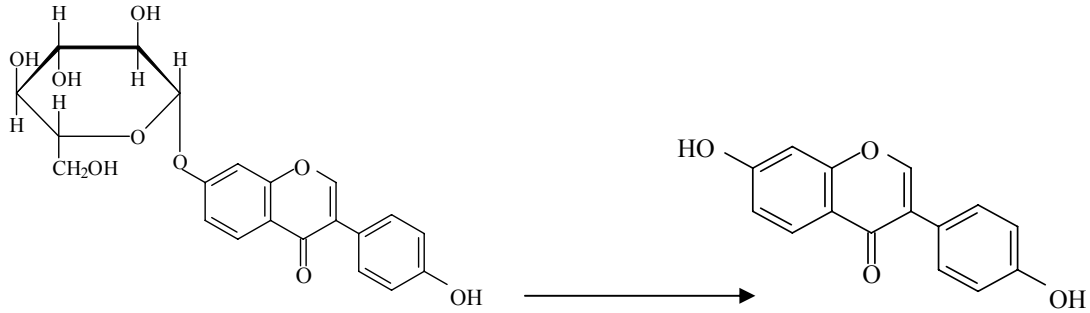
Figure 2: The major soy isoflavone glucosides

Processing of soybeans into soyfoods causes some loss of isoflavones. Defatted soy flour retains much of the isoflavones content, as isoflavones are associated with the soy protein fraction and not with the oil. As isoflavones are soluble in alcohol, soy protein concentrates washed with alcohol lose a major portion of their isoflavones content. The alcohol extract is therefore rich in isoflavones and may be used to prepare a soy concentrate containing 10 to 30 percent of isoflavones, standardized in terms of the aglycones. If the standardization were in terms of the glucosides, the same extracts would be reported to contain 16 to 48 percent isoflavones. The major isoflavone precursors genistin and daidzin, should yield about 62.5 percent of genistein, and 61.08 percent of daidzein respectively, based on molecular weights. However, the actual amount of genistin, for example, which is converted to genistein in the body (Figure 3), depends upon several factors and varies from individual to individual. A lot depends upon the initial content of isoflavones in the soybean itself. Studies reveal that soy isoflavones content varies from 0.5 to 2.0 mg/g of soy protein, depending on the variety of soybean and the growing conditions.



Genistin **Genistein**

Converted by gut microflora-
Sugar molecule removed



Converted by gut microflora-
Sugar molecule removed

Daidzin **Daidzein**

Figure 3 The breakdown of soy isoflavone glucosides in the body.

As indicated in Figure 3, the conversion of inactive precursor to the biologically active form is crucial in providing the reported health benefits of isoflavones. It is reported that on the average, the bioavailability of soy isoflavones varies from 13-35 percent depending upon the individual gut microflora[1]. It may be inferred that soy isoflavones supplied in the aglycone form (such as genistein and daidzein) would be more bioavailable as the conversion step is eliminated. This conversion of the glucosidic isoflavones can be effectively done during processing of soy powder.

The estimated daily intake of soy isoflavones based on soy food consumption is about 50 mg/person in Japan while in countries where soyfoods are not consumed traditionally, the dietary levels are much lower. Soy isoflavones taken as dietary supplements are particularly beneficial to health, in view of recent research data:

1. Soy isoflavones as anticancer agents:

- Epidemiological evidence suggests that the low incidence of breast cancer in certain women of oriental origin is related to the consumption of a diet rich in soy isoflavones [2,3].
- Genistein and certain other flavonoid substances have growth inhibiting activity on tumor cells *in vitro*, protect animals from experimentally induced mammary tumors and inhibit neo-angiogenesis[4].
- Soy isoflavones have been shown to inhibit several of the key enzymes thought to be involved in carcinogenesis[5].

The cancer protective effects of soy isoflavones may be mediated through a number of different mechanisms. The antioxidant properties of soy isoflavones may have an important role in the prevention of cancer[6]. The estrogenic[2]/anti-estrogenic[7] properties and its reported ability to inhibit the action of key enzymes such as tyrosine kinase[8], could be relevant as well. A recent randomized crossover study performed in 12 healthy postmenopausal women revealed that soy isoflavones consumption decreased the urinary excretion of estradiol, estrone, estriol and total estrogens as well as the excretion of the hypothesized genotoxic estrogen metabolites 16alpha-hydroxyestrone, 4-hydroxyestrone and 4-hydroxyestradiol, significantly as compared to the non-isoflavones diet. There was a significant increase in the ratio 2-hydroxyestrone/16-alphahydroxyestrone and a decrease in the genotoxic/total estrogens ratio, suggesting that soy isoflavone consumption may exert cancer-preventive effects by decreasing estrogen synthesis and altering the metabolic process towards the production of non-genotoxic metabolites[9].

Asian men, who consume a low fat/high fiber soy-based diet, have a lower incidence of prostate cancer than men from North America and Europe. One study postulates that dietary isoflavones could influence both endocrine and growth factor signaling pathways, thereby offering protection against prostate cancer[10].

2. Soy isoflavones in the management of the symptoms of menopause:

The major health benefits of diets supplemented with soy isoflavones have been observed in menopausal and post-menopausal women. Soy isoflavones were found to play a potential role in the prevention of osteoporosis[11,12] and cardiovascular disorders[13]. These conditions often accompany menopause in women. Genistein is thought to offer protection against osteoporosis by inhibiting bone degradation[11] and prevent cardiovascular disease by helping to lower both blood cholesterol and blood pressure[14].

Soy isoflavones are therefore a potential alternative to estrogen replacement therapy, the conventional approach to the management of menopause in women[11]. The initial interest in soy isoflavones was generated by the epidemiological observation that Asian females who typically consume a soy-rich diet have a lower incidence of the symptoms of menopause as compared to Western women. For example, it is reported that the occurrence of hot flashes varies in menopausal women in China and Singapore is 14 percent as compared to 70 to 80 percent in

women in Europe[15]. Recent clinical studies have confirmed the beneficial effects of soy in this context. In one study, hot flashes were decreased by 45 percent in women given soy powder, as compared to 30 percent reduction in women receiving a placebo[16]. In a study on postmenopausal women, 104 subjects were given daily dietary levels of soy protein isolate containing 76 milligrams of isoflavones or a placebo for 12 weeks. The results showed a significant decrease in the number of hot flashes in women on soy supplementation as compared to the women receiving the placebo. A 26 percent reduction in the mean number of hot flashes was observed by week three, a 33 percent reduction by week four and a 45 percent reduction by the end of the study[17].

Consumption of soy phytochemicals may also help to prevent osteoporosis[18]. The role of isoflavones in the prevention of bone loss associated with menopause is based on the effects of estrogen on bone remodeling. As soy isoflavones are similar to estrogens in structure, they attach to the specific receptor sites for estrogens and provide beneficial effects. A recent preclinical study revealed that genistein had a marked inhibitory effect on osteoclast-like cell formation in mouse marrow cultures[19]. This finding substantiates the role of soy isoflavones in maintaining the balance between osteoclastic activity, which facilitates breakdown of old bone tissue, and osteoblastic activity, which potentiates new bone formation.

3. Soy isoflavones in cardiovascular health

Coronary heart disease represents one of the major clinical consequences of postmenopausal estrogen deficiency. Figure 4 summarizes the results of two experiments in which groups of atherosclerotic monkeys were treated with CEE (conjugated equine estrogen only, conventional combined hormone replacement therapy viz CEE+MPA (medroxyprogesterone acetate) or SBE (soybean isoflavones). These data suggest that the effect of SBE is superior to combined hormone therapy in the management of postmenopausal coronary heart disease[20].

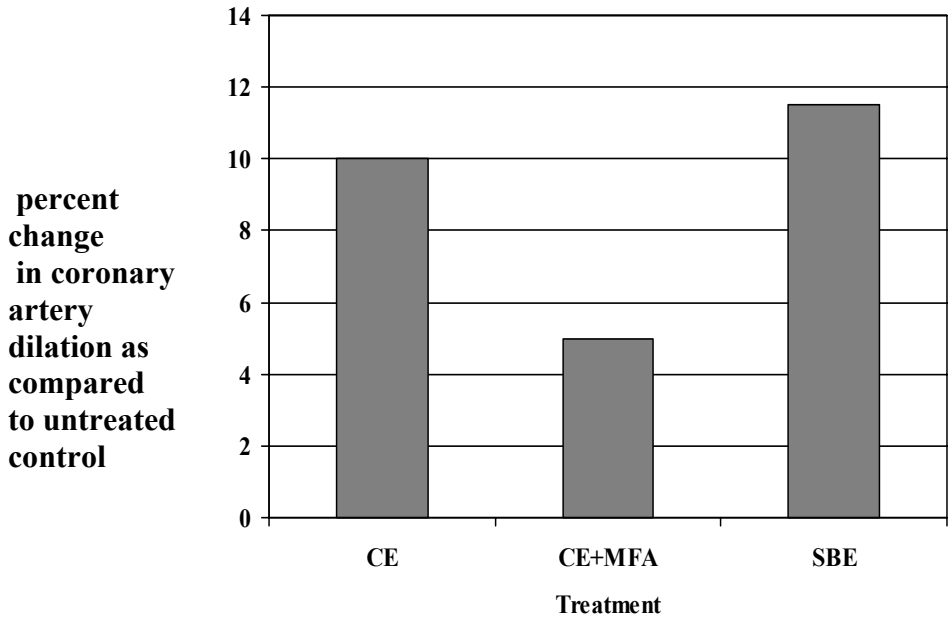


Figure 4: Effects of CEE, combined hormone replacement therapy dietary soybean isoflavones on coronary artery reactivity in atherosclerotic female monkeys.

A study performed on 21 women who were given 80 mg of soy isoflavones per day revealed a marked improvement in arterial elasticity (25 percent) as compared to untreated

controls. In this trial, the levels of plasma lipids remained unaffected[21]. However, in a randomized double-blind crossover trial in which 51 normal (nonhypercholesterolemic, nonhypertensive) perimenopausal women were given either a diet with 20 g of soy protein containing 34 mg of isoflavones or a carbohydrate placebo diet, the soy supplemented group showed significant improvements in lipid and lipoprotein levels, blood pressure and reduction in the severity of menopausal symptoms, as compared to the group receiving the placebo carbohydrate diet[22].

Soy isoflavones are thus a potential therapeutic alternative to conventional measures used to alleviate the symptoms of menopause. In view of their safety, evidenced by the long food use of soy, and efficacy as validated by clinical trials, soy isoflavones represent an effective option to estrogen replacement therapy. Through stabilization of circulating estrogen levels, soy isoflavones reduce the need for conventional drugs in the management of menopausal symptoms and other hormone-related conditions, thereby lessening the risk of side effects associated with the long-term use of hormone replacement therapy. Dietary supplements containing soy isoflavones are becoming increasingly popular. These products offer a convenient and effective means to obtain the rich health benefits of soy.

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