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The Healthful Versatility of Soy © VR

By Yousry Naguib, PhD

Soy has become a hot nutritional supplement following the announcement in July 2002 by the National Institutes of Health that it had called off a study of a hormone-replacement therapy drug used by millions of menopausal women. This drug was unexpectedly found to increase the risk of heart disease, stroke and breast cancer. This news is prompting women to seek natural alternative therapy, including soy supplementation.

In 1999, the U.S. Food and Drug Administration (FDA) announced that eating 25 grams of soy protein a day lowers the risk of coronary heart disease, and ruled that any food containing at least 6.25 grams of soy protein per serving can carry a healthy-heart label.

Soy contains high levels of the isoflavones, also known as phytoestrogens: genistein and daidzein, and their glycosides (with a sugar moiety) genistin and daidzin. These phytoestrogens are believed to be the active components that ease the symptoms of menopause: night sweats, hot flashes, and thinning bones. Soy has also been indicated in various studies to combat cancer, diabetes, osteoporosis, gastrointestinal disorders, and cardiovascular diseases.

Bioavailability

In one human study, ingestion of 40 grams of isoflavone-rich vegetables for a period of five days raised the amount of isoflavones in the urine 1,000 times.

In a recent study, researchers reported that the bioavailability of isoflavones glycosides requires first the hydrolysis of the sugar moiety by intestinal beta-glucosidase enzymes to the corresponding sugar free form (aglycon) before uptake to the peripheral circulation.

Fermented soy foods, such as miso and natto, contain mostly the better-absorbed genistein, which is produced during fermentation by the natural microbes that act as fermenting agents and also cleave genistin's sugar moiety, converting it to genistein.

Natto is produced by adding the bacteria *Bacillus natto* to cooked soybeans, and contains five times more genistein than either tofu or soy milk.

Cardiovascular Health

The National Cholesterol Education Program Adult Treatment Panel recommends reductions in saturated fats and cholesterol and therapeutic dietary options for lowering LDL-cholesterol, with inclusion of plant stanols/sterols (2 g per day) and increased soluble fiber (10 to 25 g daily), in addition to foods with cardio-protective effects such as soy, nuts, legumes, and garlic. It has long been recognized that rates of coronary heart disease are lower in Japan, where soy consumption is common, than in Western countries.

The health benefit of soy products in cardiovascular health stems from their ability to lower total cholesterol and low-density lipoprotein (bad cholesterol) levels in serum, reduce their susceptibility to oxidation, and inhibit platelet aggregation.

Compared with soy protein from which most of the phytoestrogens have been extracted, soy protein with intact phytoestrogens increases HDL-cholesterol but does not influence LDL-cholesterol. In a randomized crossover trial, 22 healthy young normal-lipidemic subjects (five men and 17 women) consumed diets providing 56 or 2 mg isoflavones per day for 17 days. Plasma isoflavone concentrations were significantly greater after the high isoflavones diet than after the low isoflavones diet.

In another study, 41 hyper-lipidemic men and postmenopausal women received either a low-fat control diet or a soy diet high in isoflavones (73 mg) or a soy diet low in isoflavones (10 mg) daily for one month. Compared with the control diet, both soy diets resulted in significantly lower cholesterol and cardiovascular disease risk, but no significant differences were seen between the high- and low-isoflavone soy diets.

Women's Health

Currently, there is an interest among postmenopausal women to treat problems associated with menopause, such as hot flashes, headaches, and joint pain, with natural products as opposed to synthetic hormones. Indeed, clinical research showed isoflavones reduced the incidence of hot flashes in menopausal women. These compounds may be designated as healthy alternatives to hormone replacement therapy.

Soy contains bioactive isoflavone compounds, called phyto-

estrogens, which mimic estrogen and are thus capable of alleviating postmenopausal symptoms. The anti-estrogenic effects of these isoflavones are ascribed to their ability to bind estrogen receptor sites thereby making the receptors unavailable for binding by the natural, more potent estrogens of the body.

The anti-estrogenic effect of genistein in reducing menopausal flashes was demonstrated in a 12-week, double-blind, placebo-controlled, randomized study involving 104 women. Those who received a daily diet containing 76 mg of soy isoflavones providing 40 mg genistein experienced a 45 percent reduction of hot flashes. The study concluded that soy protein when added to a daily diet can substantially reduce the frequency of hot flashes in postmenopausal women.

A Japanese study of 284 women aged 40 to 59 years showed that consumption of fermented soy products significantly reduced hot flashes as compared to the control group.

In a double-blind, randomized study, postmenopausal women given 400 mg per day of a standardized soy extract, corresponding to 50 mg per day of isoflavones for six weeks, showed a significant reduction in the number of hot flashes per week. The study concluded that the particular soy compound is safe and efficacious in relieving hot flashes.

Cancer Prevention

Epidemiological studies have indicated that high dietary intake of soybeans by Chinese and Japanese is associated with lower incidence of cancers, particularly breast and prostate. The incidence rates of these types of cancers is higher in Western countries, where consumption of soy foods is low as compared to Eastern countries. Asians consume about 10 to 35 g of soy foods daily per capita, which translates to a daily dose of 25 to 100 mg isoflavones.

On the other hand, Western populations ingest only a few milligrams or less of isoflavones per day. A recent survey showed the average intake of total isoflavones to be 15 mg/day, of which 7 mg is genistein, 6 mg is daidzein, and 2 mg is glycitein.

The consumption of soy has also been linked to the prevention of colorectal, lung, and gastric cancers. The compounds genistein, daidzein, and lignans in soy products have been shown to exhibit anticancer effects. Genistein has been recognized as the most potent of these compounds in inhibiting various processes in the development of cancer including cell proliferation and transformation, and to inhibit

the process of angiogenesis (the process of growth of new blood vessels into tissue). Genistein has also been shown to decrease the amount of reactive oxygen species produced by tumor cells.

In a recent study, postmenopausal women received a soy diet with either 73 mg or 10 mg isoflavones daily for one month. The women on a high isoflavone soy diet showed increased serum concentrations of pro-inflammatory cytokine interleukin-6 (IL-6). This finding indicates that soy isoflavones may enhance the immune response, and hence may explain the lower incidence of certain cancers in population with high soy intakes.

Because of the similar chemical structure of these isoflavones and the hormone estradiol, it was hypothesized that these compounds may be related to the risk of breast cancer. However, a recent study showed that individuals with the highest levels of daidzein, glycitein and total isoflavonoids in their urine samples had about half the cancer risk than did those with the lowest isoflavone levels. The study concluded that high intake of soy foods may reduce the risk of breast cancer.

Clinical studies also appear to support these epidemiological observations. In a case-control study, women with newly diagnosed early breast cancer with a high intake of isoflavones had a substantial reduction in breast cancer risk.

A recent review published in Journal of Nutrition also reported that isoflavone supplements do not affect breast tissue density in pre-menopausal women and may decrease density in postmenopausal women. These effects are opposite of those of hormone replacement therapy. The study suggested that breast cancer patients might enjoy soy products.

In a recent study, pre-menopausal women free of breast cancer were randomly assigned to receive either a dietary supplement of isoflavones (40 mg per day) or a placebo for 12 weeks. The hormone estradiol and its metabolite estrone (anticipated to be a carcinogen) decreased significantly in the isoflavone group as compared to the placebo. The study suggested that increased isoflavone intake affects estrogen metabolism, thereby demonstrating a potential to reduce the risk of breast cancer.

Bone Health

Soy isoflavones have also been found to promote healthy bones. Although calcium is the primary dietary factor that dictates the course of osteoporosis, other variables, including

estrogen deficiency, exercise and protein composition of the diet, influence the overall maintenance of healthy bones. Diminished levels of estrogens due to menopause, lack of exercise, and excessive protein intake all exert deleterious effects on bone integrity.

To reduce these negative effects, the use of soy protein in combination with calcium has been suggested as an advantageous way to promote calcium uptake and bone strength. An animal study concluded that supplementation with genistein prevents the tearing down of bone, while simultaneously encouraging bone mineralization.

Preliminary human studies show that isoflavones are able to increase bone density in postmenopausal women. Menopausal hormone decline contributes significantly to the risk of osteoporosis. Hormone replacement therapy (HRT) with estrogen or a combination of estrogen and progestins has been recommended for treating osteoporosis.

In recent years, isoflavones have emerged as a natural alternative to HRT, for treating osteoporosis. Genistein is the main isoflavone present in soy that appears to bind to the estrogen receptor, and in animal studies it appears to be effective in preventing bone loss caused by estrogen deficiency.

In a recent study, 23 healthy postmenopausal women were randomly assigned to receive either 62 mg isoflavones or placebo daily for four weeks. Both excretion of bone loss markers, and total serum cholesterol and LDL-cholesterol (bad cholesterol) were reduced significantly in the isoflavones group. The study concluded that soy isoflavone supplementation has the potential to reduce the risk of postmenopausal osteoporosis and cardiovascular disease in women.

Safety

The safety of purified isoflavones (genistein, daidzein, glycitein) was demonstrated in a recent clinical study involving 30 healthy men. Ingestion of purified genistein, daidzein, and glycitein in a single dose exceeding normal dietary intake manifold resulted in rapid clearance from plasma and excretion in urine. It is suggested to limit soy intake to 100 mg of isoflavones daily.

Summary

Soy contains bioactive components that have been shown to help reduce the risk of cardiovascular diseases, breast cancer, prostate cancer, and to fight osteoporosis by stimulating bone

formation. Soy isoflavones may also relieve menopausal symptoms such as night sweats, hot flashes, and thinning bones. **VR**

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