

An Overview of the Health Effects of Soyfoods and Soybean Isoflavones

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Introduction

The United States grows about 2 billion bushels of soybeans annually, approximately one-half of the world's total production. Most Americans consume insignificant amounts of soy protein, mainly only that which results from the consumption of foods to which small amounts of soy protein have been added for functional purposes. However, soyfoods have surged in popularity during the past decade. According to recent data, 27% of Americans use soy products at least once per week, up from 15% in 1998.¹ The increased popularity of soyfoods is due directly to evidence suggesting even modest amounts of soyfoods might play a role in reducing risk of several chronic diseases.

The soybean is truly unique, as it is the only food to contain nutritionally significant amounts of a chemical class of compounds called isoflavones. Research interest in isoflavones has increased exponentially over the past 10 years, which accounts for the recent creation of an online database of the isoflavone content of foods by the U.S. Department of Agriculture (<http://www.nal.usda.gov/fnic/>). Epidemiologic and clinical studies suggest the consumption of 30-90 mg of isoflavones/day may exert beneficial health effects.

Beyond isoflavones, the nutritional attributes of soy protein are also quite notable. Soy protein is of equal quality to animal protein as the recent decision by the United States Department of Agriculture allowing soy protein to completely replace (previously substitution was restricted to 30%) animal protein in the Federal School Lunch Program testifies.² Furthermore, in comparison to animal protein, soy protein may favorably affect renal function (isoflavones may also be beneficial in this regard),³ and as discussed below, decreases urinary calcium excretion⁴ and is hypocholesterolemic.⁵

Isoflavones – General Background

There are twelve different soybean isoflavone isomers. The primary isoflavones in soybeans are genistein (4', 5, 7-trihydroxyisoflavone) and daidzein (4', 7-dihydroxyisoflavone) and their respective β -glycosides, genistin and daidzin.⁶ The isoflavone content of raw soybeans is approximately 1.0 mg/g with a range of about 0.4 – 2.4 mg/g. One serving (e.g., 3-4 ounces of tofu or 1 cup soymilk) of a traditional soyfood provides about 20-35 mg of isoflavones.⁶ Native Japanese adults typically consume about 30-40 mg of isoflavones per day.⁷

Isoflavones have a similar spatial confirmation to mammalian estrogens and bind to estrogen receptors.⁸ Speculation that isoflavones may exert the same benefits of estrogen but without the disadvantages, has led many women to view soy as an alternative to

hormone replacement therapy. Isoflavones have traditionally been considered to be weak estrogens⁸ but it is really not possible to arrive at a general estimate of estrogenicity as this will vary greatly according to the assay employed. Importantly however, isoflavones have a much higher binding affinity for estrogen receptor beta (ER β) in comparison to estrogen receptor alpha (ER α).⁹ Furthermore, genistein was found to be over 1,000fold more potent at triggering transcriptional activity with ER β than ER α .¹⁰ This suggests, given the different tissue distributions of these receptors, that isoflavones are natural selective estrogen receptor modulators.¹¹

Clearly though, when evaluating the possible biological effects of isoflavones, it is necessary to look beyond the estrogen receptor. Genistein can influence signal transduction¹² by inhibiting the activity of many enzymes and cellular factors that control the growth of cells^{13, 14} and in some experimental systems, isoflavones exert antioxidant effects.¹⁵ These nonhormonal properties account for why genistein inhibits the growth of essentially all types of cancer cells in vitro.

Breast and Prostate Cancer

Initial enthusiasm for the anticancer effects of soy focused on protection against breast cancer because of the low breast cancer mortality rates in Asian countries and because weak estrogens (like isoflavones) have been postulated to exert antiestrogenic effects. Animal studies generally show that the addition of soy or isoflavones to a typical laboratory diet reduces the development of mammary cancer by 25-50%.^{16,17} In contrast, epidemiologic studies are generally not supportive of the notion that the adult consumption of soy reduces postmenopausal breast cancer risk.^{18,19} A particularly attractive hypothesis however, is that soy contributes to the low breast cancer incidence in Asia as a result of early consumption. Research shows that animals exposed to genistein when young develop approximately 50% fewer mammary tumors²⁰ and a recent epidemiologic study reported that adult women in China who were in the highest quintile (approximately 11 g soy protein/day) of soy intake as adolescents were 50% less likely to develop breast cancer as adults.²¹

Like breast cancer, prostate cancer mortality rates in Asia are very low relative to the West.²² Current thinking is that one or more factors in low-risk countries such as Japan, retard the progression of prostate cancer from the more latent forms and/or delay the onset of prostate cancer. An international group of experts recently concluded that soybean isoflavones are likely one of those factors in the Japanese diet.²³ In support of this conclusion are data showing that when mice are implanted with prostate cancer cells, isoflavone administration inhibits tumor growth in a dose-dependent manner.²⁴ There are multiple mechanisms by which soy/isoflavones can reduce prostate cancer risk, including both hormonal and non-hormonal mechanisms.²⁵ Although the epidemiologic data on soy and prostate cancer are limited, two studies found that daily soy consumption was associated with a 65-70% reduction in prostate cancer risk.^{26, 27}

Coronary Heart Disease (CHD)

The cholesterol-lowering effects of soy protein have been demonstrated in humans for nearly 40 years. However, it was the publication of a meta-analysis in 1995, which summarized these data, that finally alerted the nutrition and medical communities to the existence of this research.²⁸ Largely on the basis of the meta-analysis, the U.S. Food and Drug Administration approved a health claim for soy protein. The health claim is based on the premise that 25 g of soy protein consumed through the day will significantly lower cholesterol levels.²⁹ Products must contain at least 6.25 g soy protein per serving to qualify for the health claim. The meta-analysis found that the average reduction in low-density-lipoprotein

cholesterol in response to soy protein was 12.9%. However, cholesterol reduction is inversely related to initial cholesterol levels; consequently, people with moderately elevated cholesterol (220-260 mg/dl) can expect decreases of approximately 5-10%.

Although elevated cholesterol is a well-recognized risk factor for CHD, arguably, the effects of isoflavones on other CHD risk factors such as arterial compliance, cholesterol oxidation, and smooth muscle cell proliferation, may prove to be of more value than the cholesterol-lowering effects of soy protein. Preliminary data suggest that isoflavones, like estrogen, may exert cardioprotective effects via direct effects on coronary vessels and other physiological processes involved in the etiology of heart disease.³⁰⁻³²

Osteoporosis

The estrogenic properties of soybean isoflavones and the reported efficacy of the synthetic isoflavone, ipriflavone,³³ for retarding bone loss, provided the basis for initial speculation that soy might favorably affect bone health as the benefits of estrogen are well established.³⁴ Most studies have demonstrated that soy or isoflavones favorably affect markers of bone turnover and/or bone mineral density in ovariectomized rodents.³⁵ Human studies are limited, but several have found that soy protein retards spinal bone loss or favorably affects markers of bone turnover, in perimenopausal and postmenopausal women.^{36, 37}

In addition to the direct effects of isoflavones, soy protein has been shown to decrease urinary calcium excretion when substituted for a similar amount of animal protein.^{4, 38} Thus, there are two separate mechanisms by which soyfoods may improve bone health. The protein effect is attributed to the lower sulfur amino acid content of soy protein. Since net calcium absorption is only approximately 10%, substituting 15 g of soy protein for animal protein may decrease dietary calcium requirements by 50 – 100 mg.

Menopausal Symptoms

The first published speculation that soy might relieve menopausal symptoms was based on the weak estrogenic effects of isoflavones and the low incidence of hot flashes in Japan.^{39, 40} Recent data indicate that women of Chinese and Japanese ancestry residing in the United States are also much less likely to report experiencing hot flashes compared to Caucasian women.⁴¹ However, clinical studies have produced mixed results, with some studies showing no effects⁴² and others showing modest beneficial effects.⁴³ Since

hot flashes are personally experienced and effects should be apparent within a few weeks, recommendations for women to try soy for relief of hot flashes can be justified in spite of the mixed data.

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