



## SOY FOODS AND OSTEOPOROSIS

For many years, soy foods have been considered controversial. This initial impression may be because they were termed phytoestrogens. Suddenly there were concerns that babies having soy milk would become feminized. Then there was the concern that they may cause cancer.

This article will explain what soy is, where it comes from, the best sources and its safety and benefits. By the time you have finished reading, you will have more confidence about what it's all about with soy.

Food like soy beans, chickpeas and other legumes contain a plant chemical called isoflavones. Soy beans contain the most isoflavones as well as the individual isoflavones that give health benefits – genistein and daidzein are the main ones, with a lesser one – glycitein. Isoflavones are in turn, members of the flavinoid family which are in turn, members of the polyphenol family. These are just terms that are used in biochemistry that you may find helpful when reading about other plant molecules in the future.

Other isoflavone containing foods include lentils, kidney beans, lima beans, broad beans and chick peas. This could be why the vegetarian and Mediterranean diets may give health benefits.

Isoflavones have numerous health qualities that I will describe later. But first, what happens to them in the body? Once in the gut, genistein and daidzein are further transformed into other molecules by bacteria – this can vary from person to person.

The way isoflavones act in the body to give health benefits could include the following:

- Antioxidant – inhibits NF $\kappa$ B activation and production of TNF- $\alpha$ , IL-1, IL-6
- Inhibits free radical formation and lipid peroxidation
- Induces apoptosis of osteoclasts
- Increases intestinal calcium absorption
- Inhibition of angiogenesis
- Inhibition of protein tyrosine kinase ( genistein)
- Inhibits topoisomerase I and II
- Inhibits aromatase, 5 $\alpha$ -reductase, 17 $\beta$ -hydroxysteroid dehydrogenase
- Binds progesterone, androgen, oxytocin, and peroxisome proliferator activator receptors
- Binds to ER receptors with greater affinity than ER $\beta$  than ER $\alpha$
- Alter Receptor Activator of NK B –Receptor Activator of NK Ligand –Osteoprotegerin pathway ( increase OPG and decrease RANKL)

- Encouraging cells to die when they are supposed to (called apoptosis) by causing DNA strand breakage
- Modulates IGF-1 and IGBP3
- Inhibition of P-form phenolsulfotransferase ( PST) – mediated sulfation
- Inhibiting the enzyme 5 alpha reductase – this helps prevent excessive production of dihydrotestosterone which causes excess hair in women and prostate problems in men
- Inhibiting thrombin ( blood clot factor) formation and increased platelet activity
- Increases LDL cholesterol receptor activity

Health benefits of soy have included: reduction of breast and prostate cancer recurrence, reduction of blood pressure, atherosclerosis, heart disease, stroke and type 2 diabetes. In this article, I will describe how soy helps prevent and maintain bones.

Bone density enhancement is especially present in post-menopausal women. Fifty percent of women, and one in 8 men will experience an osteoporosis related fracture. Bone loss becomes rapid just before and between 5-7 years after menopause where women may lose up to 20 % of their bone mass. Japanese women eat 50-100 times more than Western women and have been found to have better preserved bones.

Eating protein is thought to cause a loss of calcium from the bones, mainly because animal protein contains sulfur containing amino acids – methionine and cysteine. Eating more plant proteins like soy does not cause this problem because there are no sulphur containing amino acids – this is one way it preserves bone.

Estrogen influences the action of bone cells. After menopause, the osteoclasts (bone cells that break down bone), become more active than osteoblasts (cells that build up bone). Before menopause, Estrogen acts to suppress osteoclasts but once menopause occurs, this action is lost.

Furthermore, studies on Isoflavones show that they act on both osteoclasts and osteoblasts. Daidzein stimulates osteoblast activity. Genistein inhibits osteoclasts.

Estrogen deficiency in menopause causes increased levels of TNF- $\beta$  which is a cytokine (a messenger) that causes bone dissolving. Estrogen deficiency, such as that occurs during menopause, results in an increase in the levels of tumor necrosis factor  $\beta$  (TNF- $\beta$ ), a

cytokine that is involved in many changes of aging including bone resorption. The discovery of new members of the TNF super family led to an increased understanding of what happens during estrogen-repleted and estrogen-depleted states. Osteoblasts express the receptor activator of nuclear factor- $\kappa$ B ligand (RANKL). RANKL is involved in osteoclast differentiation in a paracrine manner by binding to its receptor, which is located on the osteoclast membrane. Osteoblasts also secrete osteoprotegerin (OPG), a decoy factor that neutralizes the actions of RANKL. Estrogen increases the production of OPG and hence decreases the activity of RANKL. Recently, genistein has been found to increase the production of OPG from osteoblasts, providing a further mechanism for the bone-sparing effects of isoflavones.

Interleukin (IL)-6 is a proinflammatory cytokine that has been shown to increase in chronic inflammation, diabetes mellitus, cardiovascular disease, rheumatoid arthritis, Alzheimer's disease, osteoporosis, aging, and some cancers. The expression of IL-6 is thought to occur via the transcription factor nuclear factor  $\kappa$ B (NF- $\kappa$ B). Isoflavones have been shown to inhibit NF- $\kappa$ B activation and indirectly inhibit IL-6 production in osteoporosis, arthritis, and some cancers such as breast, prostate, lymphoma, and pancreas. In addition to coupled osteoblast-osteoclast activities, isoflavones seem to act independently on osteoclasts via nonestrogenic mechanisms because there are no estrogen receptors in the nuclei of osteoclasts. Isoflavones act on osteoclasts by inhibition of tyrosine kinase as previously mentioned, inhibition of topoisomerase I and II, and induction of apoptosis. Other postulated mechanisms of action for isoflavones include inhibition of angiogenesis, inhibition of free radical formation, stimulation of antioxidant enzymes, reduction of lipid peroxidation, and inhibition of aromatase, 5 $\beta$ -reductase,[38] and 17 $\beta$ -hydroxysteroid dehydrogenase enzymes. Although the mechanisms of isoflavones are still not completely known, evidence from these in vitro studies suggests that they act in multiple ways, via genomic and nongenomic pathways and via both osteoblasts and osteoclasts, to maintain bone mass.

Both estrogen and genistein decreased bone resorption markers. However, increases in bone formation markers were observed only with genistein. This effect of genistein is consistent with the results of in vitro studies suggesting an anabolic role of soy isoflavones on osteoblasts. To date, there is only one study examining the association between soy intake and the risk of fracture. The Shanghai Women's Health Study is a population-based, prospective cohort study of 75,000 Chinese women aged 40 to 70 years. The inverse association was more pronounced among women with early menopause. In one study, women who consumed the most soy had an approximately 35% decreased risk of fractures compared with women who consumed the least soy. The benefit was greatest in women within 10 years of menopause with a reduction in hot flushes.

## Which foods have the most beneficial isoflavones?

- Soybeans contain 2-5mg isoflavones
- Dehulling, flaking and defatting to produce isolated soy protein reduces the isoflavone content
- Textured soy protein and soy flour contain 5mg isoflavone per gram of protein
- Soy milk and tofu contain 2mg isoflavone per gram of protein
- Non-fermented soy foods like roasted soy beans and soy beverage powders contain 2-3 times the amount of isoflavones compared with fermented soy foods like tempeh, miso and fermented bean curd.
- The baking of soy flour does not lower its isoflavone content.

## Safety of soy

Soy foods have been consumed in large amounts for decades in Asia without ill effect. However, taking isoflavones have not been studied enough. It is therefore best to take soy as a food for its benefits until there is more information.

## References

1. Medscape, 2012 - <http://www.medscape.com/viewarticle/580688>
2. Atmaca, A., Kleerekoper, M., Bayraktar, M., Kucuk, O. (2008). Soy isoflavones in the management of postmenopausal osteoporosis. *Menopause*, 15(4), 748-757.