

## A Soy Isoflavone That Packs a Punch: Genistein

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Soybeans contains unique substances called isoflavones, most notably genistein and daidzein, which have been shown to block the buildup the dangerous type of testosterone (dihydrotestosterone) in the prostate gland linked to prostate enlargement and prostate cancer. Genistein does this by acting as a natural 5-alpha-reductase enzyme inhibitor, the enzyme that converts testosterone into dihydrotestosterone.

Soy isoflavones have also been shown to exert a multitude of other anti-cancer effects in the prevention of prostate and other types of cancer. This is especially true for the soy isoflavone known as genistein.

### An Important Soy Isoflavone

[Genistein](#) is the predominant isoflavone in the human diet and is derived primarily from soybeans, but is also found in other legumes, including peas, lentils and other bean varieties. A number of mechanisms have been proposed to explain the anticarcinogenic activity of genistein:<sup>1</sup>

- Inhibition of protein-tyrosine kinase, with the result of alleviating the growth of cancer cells by inhibiting PTK-mediated signaling mechanisms
- Inhibition of topoisomerases I and II and protein histidine kinase, which have antiproliferative or proapoptotic effects
- Antioxidant effects through inhibition of the expression of stress response-related genes
- Inhibition of nuclear factor kappa B (NF-kB) and Akt signaling pathways, both of which are important for cell survival
- Inhibition of angiogenesis
- Down-regulation of transforming growth factor-beta
- Inhibition of epidermal growth factor

Soy intake has also been shown to help lower LDL cholesterol by up to 8-10 percent (approximately), especially when substituted in the diet for high-fat animal products. This was confirmed in a comprehensive review article published in the *Journal of Nutrition* in 2010.<sup>2</sup>

### Genistein and Prediabetes Markers

[An important study](#) published in the *Journal Clinical Nutrition* in August 2018 showed supplementation with genistein (derived from soybeans) improved blood sugar regulation, lowered triglycerides and reduced inflammation in patients with prediabetes who also had fatty liver problems (NASH - non-alcoholic steatohepatitis). These patients all had high blood sugar, high triglyceride levels, and high levels of blood markers of inflammation and oxidative stress (serum malondialdehyde - MDA) at the outset of the study.

The double-blind clinical trial involved 82 subjects with prediabetes (metabolic disorder) and fatty liver problems ([NASH](#)), half of whom ingested 250 mg of genistein as a supplement for eight weeks, while the other half ingested a placebo. After eight weeks, the study clearly showed that the patients ingesting the genistein supplement had improved blood sugar regulation, lower

triglyceride levels, as well as lower markers of inflammation (TNF-alpha, IL-6) and less oxidative stress (serum malondialdehyde - MDA). They also had a reduction in waist-to-hip ratio circumference and a decrease in overall percentage body fat. These are impressive outcomes from simply ingesting 250 mg of genistein each day for only two months.<sup>3</sup>

This study is important because NASH is a chronic liver inflammation caused by fat accumulation in hepatocyte. NASH can progress to cirrhosis, hepatocellular carcinoma and eventually liver-related death. NASH is seen in the majority of patients who have central obesity and diabetes mellitus that share insulin resistance as a common feature; therefore, it is also considered as a liver manifestation of metabolic syndrome.

### Clinical Relevance

With the rising prevalence of obesity in the developed world, NASH is becoming an increasingly important global problem. Unfortunately, no therapy has been proven to be effective against NASH. Even though weight loss and lifestyle changes are the standard recommendations in overweight patients, they often fail and are unable to prevent NASH development. As such, supplementation with genistein may be an important intervention to reduce onset of NASH in patients with central obesity, metabolic syndrome and/or type 2 diabetes.

Animal studies have shown that the progression from steatosis to NASH results from increased oxidative stress due to lipid peroxidation. Increased oxidative stress, in turn, upregulates the action of inflammatory cytokines (TNF-alpha, NF-kappa beta, etc.) High levels of MDA are typically present in NASH as evidence of increased oxidative damage.

Genistein supplementation, by acting as an antioxidant, has been shown to decrease lipid peroxidation with resulting lower MDA serum levels and reduction in downstream inflammatory cytokines, which are related to degenerative hepatocyte changes associated with fatty liver problems (NASH).<sup>4</sup>

### Practice Pearls

Although many patients shy away from consuming soy foods and supplements, soy foods and the supplement genistein show impressive health attributes in many studies. It may not be necessary to ingest genistein supplements to improve various aspects of health and disease risk factors. Individuals can easily acquire 50-75 mg of soy isoflavones a day, on average, by regularly consuming soy and soy-based foods, such as edamame, roasted soy nuts, tofu, miso, tempeh, textured vegetable protein, soy cheeses and the like.

Using these foods to replace high-fat animal protein foods (red meat, pork, and dairy and goat-based cheeses) has been shown to improve blood cholesterol and is associated with a reduction in risk of certain cancers. For patients with central obesity, metabolic syndrome or type 2 diabetes who are highly prone to NASH and its serious health complications, ingesting a genistein supplement each day (250 mg) should also be considered as an intervention to help guard against NASH-related liver damage, according to the impressive 2018 study in the *Journal of Clinical Nutrition*.<sup>3</sup>

### References

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