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## Soy and Soy Extract

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### General Features

Soybeans contain a variety of biologically active components that are associated with the prevention of certain cancers, detoxification, bone density support, cholesterol lowering and cardiovascular health, prevention of prostate enlargement and antioxidant function.

### Principle Active Constituents

Some of their more potent bioactive constituents include:

- Isoflavonoids
- Saponins
- Phenolic acids
- Coumarins
- Protease inhibitors
- Phytic acid<sup>1,2,3,4</sup>

### Clinical Application and Mechanism of Action

#### 1. Reproductive Cancers

Of the above bioactive constituents, isoflavones and protease inhibitors have been studied most thoroughly for their anti-cancer effects. Soy isoflavones may reduce risk of breast, prostate and other hormone-dependent cancers. The low breast cancer mortality rates in Asian countries and the putative anti-estrogen effects of isoflavones support this contention. Strong evidence for the prevention of prostate cancer may explain, in part, the 80 percent lower incidence of prostate cancer in Asia compared to Canada, the United States and other western countries, that do not include Soy as a common dietary staple.

Soy and Soy isoflavones have been shown to decrease reproductive organ cancers in animal-based studies. Human research also suggests a protective role of Soy against cancer, however, the data is currently insufficient to make formalized recommendations.

There are literally hundreds of in vitro studies showing that genistein (a predominant Soy isoflavone) inhibits the growth of a wide range of both hormone-dependent and hormone-independent cancer cells, including breast, prostate, colon and skin cells.

In vitro, genistein also inhibits the metastatic activity of both breast and prostate cancer cells independent of the effects on cell growth.

Genistein is known to inhibit several enzymes involved in signal transduction, including tyrosine protein kinase, MAP kinase, ribosomal S6 kinase, and DNA topoisomerase II. Genistein also increases the concentration of transforming growth factor B (TGF-B).

Together these biological mechanisms account for the ability of genistein to arrest cancer cell growth.

These findings may have important implications, as the breast cancer rate in Japan is only about one-quarter of that of the United States. Similar data exists for prostate and colon cancer incidence.

In vitro, genistein inhibits the growth of both androgen-dependent and androgen-independent prostate cancer cells. Genistein has also been shown to inhibit the 5-alpha reductase enzyme that is strongly linked to prostate enlargement (benign prostatic hyperplasia) and prostate cancer metastasis. The 5-alpha reductase enzyme converts testosterone to dihydrotestosterone (DHT). DHT build up encourages more rapid prostate cell proliferation leading to prostate enlargement and fuels the proliferation and spread of existing prostate cancer.

Increased Soy intake in men under clinical trial conditions demonstrates a reduction in DHT metabolites in the blood, indicating that Soy consumption reduces DHT production in men.

Soy isoflavones concentrate in prostate fluid and increased isoflavone intake has been linked to significant apoptosis (programmed cell death) of prostate cancer cells (adenocarcinoma) in a patient taking 160 mg of isoflavone content per day, one week before prostate surgery.<sup>1</sup>

Genistein also inhibits angiogenesis, the growth of new blood vessels that contribute to the spread of cancer.<sup>5</sup>

## **2. Menopausal Symptoms and Female Bone Health**

After menopause Soy isoflavones and other phytoestrogens can provide sufficient estrogenic activity as to reduce hot flashes and other menopausal symptoms, as well as help to support bone density. Soy intervention trials have shown a reduction in hot flashes by up to 40 percent in various studies.<sup>1,6,7,8</sup>

Soy constituents (especially diadzein and genistein) have been linked to favourable effects on bone density in postmenopausal women and in animal experimental studies, often using ovariectomized rats.

Dailais et al found that early postmenopausal women had a 5 percent increase in bone mineral content compared with baseline values after only 3 months of consuming Soy flour. Ipriflavone, a semisynthetic compound similar to the Soy isoflavone, diadzein, has been shown to increase bone density in postmenopausal women, at a dosage of 200 mg, three times daily.<sup>1</sup> It is approved in Japan, Hungary and Italy as a drug for the treatment and prevention of osteoporosis.<sup>1,9</sup>

## **3. Cholesterol-Lowering and Cardiovascular Health**

Soy isoflavones appear to have favourable effects on vascular function and lipid metabolism. Soy isoflavones, structurally similar to estrogens, interact with estrogen receptors and appear to increase LDL-receptor formation. In turn this helps the body clear LDL-cholesterol and VLDL-cholesterol from the bloodstream.<sup>2</sup> The meta-analysis of 38 controlled studies demonstrated that an average intake of 47 gm per day of Soy protein was associated with a 9.3 percent lowering of cholesterol, 12.7 percent lowering of LDL-cholesterol, 10.5 percent lowering of triglycerides and a 2.4 percent elevation of HDL-cholesterol.<sup>10</sup>

Genistein also inhibits thrombin formation and platelet activation in vitro and Soy isoflavones act as antioxidants, which may help prevent LDL-cholesterol oxidation in the bloodstream. All of these factors help to support the positive influence that Soy has on cardiovascular health.<sup>2</sup>

## **4. Detoxification**

Soy and Soy Extract have been shown to induce phase II detoxification enzymes such as Quinone reductase, Glutathione-S transferase and uridine-S-diphosphate glucuronodlyl transferase. These enzymes function to detoxify and destroy electrophilic (free radicals) metabolites, formed during phase I detoxification activity. This function may also explain some of Soy's anti-cancer effects.<sup>3</sup>

#### Supplementation Studies and Clinical Application

Clinical studies are underway to help determine the ideal Soy or Soy Extract intake level that may help prevent cancer, cardiovascular disease, prostate enlargement, osteoporosis and to help manage menopausal symptoms. Societies demonstrating the best health effects and the early intervention trials from human studies suggest that a Soy intake yielding 50-100 mg per day of Soy isoflavones provides a level of intake associated with the above mentioned benefits according to recent reviews.<sup>1,11</sup>

#### Dosage and Standardized Grade

Soy or Soy Extract intake yielding 50 - 100 mg of isoflavones per day support the following applications:

- General health support
- Menopausal symptom management
- Bone density support
- Cholesterol and triglyceride lowering and cardiovascular system support
- Enhancement of phase II detoxification and liver support<sup>1, 2, 6, 7, 8, 10</sup>

#### Adverse Side Effects, Toxicity and Contraindications

Soy products and cooked soybeans are safe at a wide range of intakes. A small percentage of people have allergies to soybeans and thus should avoid Soy products.

#### Drug-Nutrient Interactions

Simultaneous intake of Soy or Soy Extract with estrogen replacement, the birth control pill (oral contraceptives) or thyroid hormone may decrease the absorption of these drugs. It is best not to take these drugs at the same time as Soy foods or Soy Extract supplements. Due to the coumarin content of Soy it may potentiate the effects of warfarin,<sup>12</sup> however, no reports of bleeding disorders have been documented in patients using Soy products and anti-coagulants, concurrently.

Estrogen-containing drugs and Tamoxifen: There is uncertainty at this time as to the interaction of soy phytoestrogens with oral contraceptives, hormone replacement therapy, and the use of the drug tamoxifen, which is used to help prevent a recurrence of cancer in women who previously had estrogen-receptor positive breast cancer. To date, no human studies have revealed a negative interaction in this regard. Although some researchers caution against combining these interventions, there is evidence to support the intake of soy and possibly other phytoestrogens in these cases. Isoflavones are a form of "selective estrogen receptor modulator (modifier), which preferentially activate the beta estrogen receptor on reproductive and other tissues, while having little affinity for alpha estrogen receptors on these tissues (this is similar to the effect of Tamoxifen, which is used to help prevent recurrence of estrogen receptor-positive breast cancer). Over-stimulation of alpha receptors from estradiol and estrone (two of the body's natural estrogens that are found in estrogen-containing drugs) tends

to result in more rapid cell division and increased risk of breast cancer. Due to their greater affinity for beta receptors, isoflavones tend to slow the proliferation rate of breast cells, and breast cancer cells, in the presence of the body's own estrogens. As such, isoflavones demonstrate, in experimental and animal models, features suggesting a potential to prevent breast cancer and other reproductive cancers, and may also be useful in containing or controlling existing cancers in certain cases. Intensive investigation is underway at this time to determine if this latter application is valid. Until this is clearly established, women should not take soy isoflavone supplements of any kind to help treat existing reproductive cancer or to help block recurrence of a reproductive cancer, without the consent of her attending physician.<sup>13,14,15</sup>

#### ***Pregnancy and Lactation***

*During pregnancy and lactation, the only supplements that are considered safe include standard prenatal vitamin and mineral supplements. All other supplements or dose alterations may pose a threat to the developing fetus and there is generally insufficient evidence at this time to determine an absolute level of safety for most dietary supplements other than a prenatal supplement. Any supplementation practices beyond a prenatal supplement should involve the cooperation of the attending physician (e.g., magnesium and the treatment of preeclampsia.)*

#### ***References: Pregnancy and Lactation***

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