Isoflavones (Dietary Phytoestrogens)

Background

- Phytoestrogens are a class of compounds derived from plants with estrogenic effects.
- Isoflavones are the class of phytoestrogens which have been most studied.
- Soy and flaxseed are the foods that contain the highest concentrations of isoflavones. Although soy and flaxseed also contain other phytoestrogens such as lignans and coumestans, their effects are less well-studied.
- Red clover is the most common herbal source of isoflavones.
- Black cohosh is another herb used for hot flashes. Most authorities consider black cohosh to be a phytoestrogen, but its exact mechanism of action is controversial.

History

- Plants containing isoflavones have been used in Asia for thousands of years for the management of female reproductive conditions.
- High dietary intake of soy in Japan, China and Korea may account for the lower prevalence of menopausal symptoms reported by women living in these countries. (The average daily intake of isoflavones in these countries is more than 50 times that in the U.S.)

Most studied uses

Menopausal symptoms, hyperlipidemia.

Other common uses

Prevention and treatment of osteoporosis, prevention of cancer.

Summary of the evidence

- Isoflavones from soy may be beneficial for the treatment of hot flashes, but trials have had conflicting results. More data supports the use of soy from dietary sources than from concentrated supplements.
- There is no data that isoflavones from red clover are effective for hot flashes.
- There is a fair amount of evidence that substituting soy protein for animal protein may reduce total and LDL cholesterol.
- The safety of high doses of isoflavones and other phytoestrogens in patients with breast cancer is uncertain.

Pharmacology

- Intestinal bacteria convert conjugated isoflavones to active unconjugated isoflavones such as genistein, daidzein and equol.
- Dietary isoflavones have a high bioavailability and circulate in the blood in both conjugated and free forms. Some are excreted in the bile via enterohepatic pathways, but most are excreted in the urine, with a half-life of approximately 24 hours.

Mechanism of action

- Isoflavones bind to estrogen receptors in the brain, breast, bone, cardiovascular, endometrium and other hormonally responsive tissues in humans.
- They appear to act as selective estrogen receptor modulators (SERMs), having both agonist and antagonist effects on the estrogen receptor.
- Different isoflavones vary in their affinity, effect, and potency.
- In general, isoflavones have a lower ability to bind to human estrogen receptors than estradiol, and demonstrate lower potency.

Clinical studies

- An exhaustive review of the literature (Kronenberg 2002) found 11 clinical trials that have examined soy or isoflavone supplementation for hot flashes. These studies had conflicting results, however, probably due to heterogeneous data collection instruments used, small numbers of patients, and a wide range of products tested.
- A meta-analysis (Anderson 1995) documented the lipid lowering effects of soy. There have been no clinical trials, however, to evaluate whether soy decreases cardiovascular events or mortality.
- In a study of isoflavones from red clover (Tice 2003), 252 participants were randomly assigned to red clover extract (82 mg or 57 mg per day) vs. placebo and followed for 12 weeks. Reductions in the number of hot flashes per day were similar for the three groups (5.1 vs. 5.4 vs. 5.0) as were changes in quality-of-life scores.

Adverse effects

- Rarely, high quantities of soy or isolated isoflavones cause constipation, bloating, or nausea.

Contraindications/cautions

- Caution should be used in patients with breast cancer given that there is in vitro data demonstrating breast cell proliferation.
- Caution in patients with asthma or allergic rhinitis (possible risk of soy hull allergy).

Important drug/herb interactions

- Possible inhibition of tamoxifen efficacy.

Formulation and dosage

- The most studied doses of isoflavones have been 50-150 mg per day.
- Typically, one must ingest about a gram of soy protein to get one mg of isoflavones.

References

1. Kronenberg F, Fugh-Berman A. Complementary and alternative medicine for menopausal symptoms: A review of randomized, controlled trials. Ann Int Med 2002;137:805-13.
2. Anderson, JW, Johnstone BM, Look-Newell ME. Meta-analysis of the effects of soy protein intake on serum lipids. N Engl J Med 1995; 333:276-82.
3. Tice JA, et al. Phytoestrogen supplements for the treatment of hot flashes: the Isoflavone Clover Extract (ICE) Study: a randomized controlled trial. JAMA. 2003;290(2):207-14

For Additional Information

1. Natural Medicines Comprehensive Database. Available through UW Healthlinks.
2. About Herbs. http://www.fammed.washington.edu/predoctoral/CAM/sites.html.
3. Herbmed.org for more general background.
4. For information about the quality of specific brands, check Consumerlabs.com.