Women’s Health Update
by Tori Hudson, ND
womanstime@aol.com

Soy as a Prevention Strategy for Osteoporosis

The potential for soy protein or soy isoflavones to alter bone metabolism and bone resorption is currently contradictory and inconclusive. The lack of agreement in the literature is thought to be related to variations in study design. These variations include dosage and form of soy products studied (soy protein isolate, whole soy foods, or extracted soy isoflavones), menopausal status of the women studied (perimenopausal, early menopausal, or late postmenopausal), duration of the various trials, and tests used to assess bone density and bone metabolism. All of these different approaches and study designs make it very difficult to determine the effectiveness of soy for bone health, and make the decision to include soy in a protocol for supporting bone health more difficult for the practitioner.

Soybeans contain a class of compounds called phytoestrogens, comprising mostly genistein, daidzein, and glycitein, all of which have a biochemical structure similar to 17 beta-estradiol. The binding of isoflavones to estrogen receptors is preferential for the estrogen receptor beta and thus indicates that soy isoflavones act as selective estrogen modulators. Daidzein is similar in shape to a drug called Iprifiavone, which is used in Europe to treat osteoporosis. In the US, Iprifiavone is available as a nutritional supplement.

Bone mineral density (BMD) is the gold standard for determining fracture risk due to nontraumatic events. Bone turnover is an independent predictor of fracture risk.

While research on the effects of soy on bone metabolism has been inconsistent, many positive studies do exist that suggest a role for soy in slowing bone turnover and increasing bone density in women. Soy appears to have an estrogenic effect on bone in some experimental evaluations. The bone density of ovariectomized rats was evaluated in a study in which soy replaced casein in the diet and compared with another group that received estrogen. The addition of soy inhibited bone loss, although not to the same extent as was achieved with the estrogen treatment. Another study of ovariectomized rats also reported a positive effect of genistein in maintaining bone. These authors also reported that genistein suppresses osteoclasts, the cells responsible for bone resorption, both in the test tube and in vivo. Arjmandi also did a double-blind, randomized, controlled trial using 40g of soy-protein containing isoflavones over 3 months in postmenopausal women. Bone resorption was decreased, when compared to milk protein.

Several human studies have provided further insight into the possible role of soy in our bone health. A study conducted at the University of Illinois found that menopausal women had an increase in mineral levels and density in their lumbar spines after taking 55 to 90 mg of soy isoflavones for six months. The placebo group showed the lowest bone density and the greatest bone loss, while the estrogen group showed the highest bone density and the slowest bone loss. What was surprising was that the isoflavone diet was effective in preventing bone loss in the fourth lumbar vertebra and, although less so, in the right hip. Soy isoflavones seem to have more of an effect on trabecular bone (predominant in the spine) than on cortical bone (predominant in the hip). The soy did not show as great an ability in preventing bone loss as the estrogen group, but the positive effect it showed is encouraging.

An analysis of the relationship of soy isoflavone intake and bone mineral density was conducted from the Study of Women’s Health Across the Nation, a US cohort study of women aged 42 to 52 years. For African-American and Caucasian women, median intakes of genistein were too low to pursue analyses. For Chinese women, no association between genistein and bone mineral density was found. Premenopausal (but not perimenopausal) Japanese women

<table>
<thead>
<tr>
<th>Calcium Content Of Selected Soy Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soy Product</td>
</tr>
<tr>
<td>tofu, firm</td>
</tr>
<tr>
<td>tofu, regular</td>
</tr>
<tr>
<td>soy milk, calcium-fortified</td>
</tr>
<tr>
<td>soy milk</td>
</tr>
<tr>
<td>soybeans, roasted</td>
</tr>
<tr>
<td>soybeans, boiled</td>
</tr>
<tr>
<td>tempeh</td>
</tr>
</tbody>
</table>
whose intakes were greater had a higher bone density of the spine and femoral neck. The mean spinal bone density of those women in the highest group was 7.7% greater than that of women in the lowest group. Bone density of the femoral neck was 12% greater in the highest intake group versus the lowest.

Other positive studies on soy and bone density also give some credence to the role of soy and bone health. In a study estimating the daily intakes of soy isoflavones in the diets of 478 postmenopausal Japanese women who reported soy consumption, high consumption of soy products was associated with increased bone mass.9

A recent meta-analysis further increases our optimism about using soy to inhibit bone resorption. Nine studies with a total of 432 menopausal women were evaluated in this meta-analysis.10 Amount of soy intake varied amongst the nine studies from 37 to 118 mg of isoflavones per day. Testing for urinary peptides (deoxypyridinoline), a marker of bone turnover, demonstrated that those who consumed isoflavones had a decrease in these biomarkers of -2.08 nmol/mmol when compared with those who did not consume isoflavones. In five of the studies where isolated soy protein was used, there was no significant effect on urinary deoxypyridinoline. In the current analysis, a significant reduction in urinary deoxypyridinoline was not observed in those studies with isoflavones of less than 90 mg/day. In a review of the research in 2003, the author concluded that 90 mg of isoflavones per day is required to achieve benefits to bone health. In contrast to the positive studies, several clinical trials using a variety of soy protein isolate formulations found no clinically important effects of soy on bone metabolism and bone turnover markers.12-14 Further inconsistent research can be seen with several clinical trials using soy protein or isoflavones demonstrating a positive effect on BMD,15-19 while others have not had positive findings.20,21

I mentioned variations in dosing, duration, soy formulations used, and different study populations as possible reasons for inconsistent results on the effects of soy isoflavones on bone turnover and bone density. But another significant consideration may be due to how the isoflavones are metabolized in the gut. In the meta-analysis mentioned above that analyzed nine studies,10 the significant effects on urinary peptides occurred in Asian women but not Caucasian women. This may be due to the conversion by intestinal flora of daidzein into its active metabolite equol, and by the fact that only one-third of Caucasian women can metabolize isoflavones into equol, whereas more than half of Asian women possess this ability.

Soy isoflavones may also have more of an effect in postmenopausal women than in pre- or perimenopausal women. In one study, taking 53.3 mg of isoflavones per day was associated with an increase in bone density in postmenopausal women, but not premenopausal women.22

A nutritional influence of soy foods that may be overlooked is the amount of calcium in some of these foods or in diets that contain soy foods. A diet that includes greater amounts of soy products can account for a meaningful amount of calcium, and some soy foods can offer as much, or more, calcium than a serving of dairy products.

With the inconsistent research, it is difficult to draw confident conclusions about the role of soy in bone health. My clinical advice is to increase soy foods as part of a regular diet in prevention strategies for all pre-, peri- and postmenopausal women. For all women who have significant risk factors for osteoporosis, I would also recommend soy supplementation so that their total daily soy isoflavone intake would deliver approximately 90 mg of soy isoflavones per day. For treatment of peri- and postmenopausal women who already have osteoporosis, I would not consider soy an adequate treatment alone. For these women who already have osteoporosis, I am in favor of proven conventional therapies to reduce fracture risk in addition to the 90 mg per day of soy isoflavones and typical supplementation, including calcium, vitamin D, and other potential nutrients (vitamin K, boron, magnesium, manganese, and more), as well as dietary and exercise advice.

Notes
Nutritional Influences on Illness continued from page 120

Vitamin E: While it is not known how to increase lens SOD activity directly, animal work suggests that vitamin E deficiency decreases the levels of both SOD and glutathione reductase in the lens. Although there is evidence that long-term vitamin E supplementation is inversely associated with the mean 5-year change in lens nuclear density, two randomized trials found vitamin E supplementation to be ineffective.18

Zinc: Superoxide dismutase requires zinc for its activity. When zinc levels in lenses with mature senile cataract were compared with those in lenses with traumatic cataract, those with senile cataract had lower levels.19 Some studies, however, have found lens zinc levels to be higher in patients with senile cataract, possibly secondary to disturbed glucose utilization in the lens due to loss of activity of key zinc-dependent enzymes.20-22

Zinc supplementation improves the impaired glucose metabolism occurring in old age, and a rabbit study found that zinc stimulates mitotic activity of the lens epithelium.22,23 Therefore, zinc supplementation may theoretically be beneficial for both prevention and treatment of senile cataract.

Thus, as is the case with other antioxidant nutrients, randomized trials have yet to offer evidence that combating cataract by aiding the lens’ antioxidant enzyme systems is an effective intervention.18

Dr. Werbach cautions that the nutritional treatment of illness should be supervised by physicians or practitioners whose training prepares them to recognize serious illness and to integrate nutritional interventions safely into the treatment plan.

Notes