Provocative relation between soy and bone maintenance\textsuperscript{1,2}

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There has been a substantial increase in research on the potential health aspects of soy protein and soy phytoestrogens since the publication of the Proceedings of the First International Symposium on the Role of Soy in Preventing and Treating Chronic Disease in 1995 (1). The data showing a significant reduction in serum cholesterol with soy protein consumption were strong enough that in October 1999 the Food and Drug Administration approved a health claim for food labels on products that contain ≥6.25 g soy protein/serving. Other soy and health relations are less clear.

The effects of soy and soy phytoestrogens on bone maintenance are under active evaluation. Trials with ovariectomized rats suggested that soy with isoflavones compared with ethanol-washed soy (essentially devoid of isoflavones) prevents the bone loss associated with the reduction of endogenous estrogen that occurs with menopause (2). In contrast, supplementation of surgically postmenopausal cynomolgus monkeys with conjugated equine estrogens prevented bone loss, but soy did not (3).

In the first published human trial, we found that supplementing postmenopausal woman for 6 mo with 40 g soy protein/d containing 90 but not 45 mg isoflavones/d (aglycone units) significantly increased bone mineral content (BMC) and bone mineral density (BMD) of the lumbar spine but not of other bone sites (4). In this issue of the Journal, Alekel et al (5) give the results of a second 6-mo feeding trial with soy that specifically evaluated the effects of soy with isoflavones (80 mg/d) and with isoflavones reduced to 4.4 mg/d on bone sparing in perimenopausal

\begin{table}[h]
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\begin{tabular}{|l|c|c|c|c|c|c|}
\hline
\textbf{Measure} & \textbf{Alekel et al} & \textbf{Potter et al} \\
\hline
\multicolumn{3}{|c|}{\textbf{Control}} & \textbf{SPI} & \textbf{ISP (45)} & \textbf{ISP (90)} \\
\hline
Isoflavones (mg/d) & 0 & 4.4 & 80.4 & 0 & 45 & 90 \\
\hline
Bone sparing of BMC and BMD & & & & & & \\
Lumbar spine & No & No & Yes & No & No & Yes \\
Total body & — & — & — & No & No & No \\
Proximal femur & — & — & — & No & No & No \\
Femoral neck & — & — & — & No & No & No \\
Ward’s triangle & — & — & — & No & No & No \\
\hline
Menopausal status & Perimenopausal & Postmenopausal & & & & \\
\hline
Study length (wk) & 24 & 24 & & & & \\
\hline
Average BMI & 24 & 28 & & & & \\
\hline
Subjects per group & 21–24 & 22 & & & & \\
\hline
Average calcium intake (mg/d) & 844 & 939 & & & & \\
\hline
Calcium in test protein (mg/d) & 650 & 650 & & & & \\
\hline
Weight gain & All groups & No & & & & \\
\hline
\end{tabular}
\caption{Comparison of studies by Alekel et al and Potter et al\textsuperscript{1}}
\end{table}

\textsuperscript{1}SPI, isoflavone-poor soy protein isolate; SPI+, isoflavone-rich soy protein isolate; ISP (45), 45-mg isoflavone supplement; ISP (90), 90-mg isoflavone supplement; BMC, bone mineral content; BMD, bone mineral density; —, variable not tested; no, no significant change from baseline; yes, significant bone sparing, \(P < 0.05\).

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As noted by Alekel et al (5), 24 wk is a short time for a dietary study of bone loss because the bone remodeling cycle ranges up to 80 wk in length (7). It would be premature to assume that soy with isoflavones has a significant long-term bone-sparing effect or that soy reduces bone fractures of the spine. Studies of 2 or 3 y in length are necessary to test for long-term bone-sparing effects. However, these 2 published studies along with results from trials with ipriflavone (8), a synthetic isoflavone, on vertebral bone loss provide strong support for longer studies. It is interesting that one of the metabolites of ipriflavone is daidzein, one of the isoflavones in soy (9).

Note that the spine was the bone site affected by soy with isoflavones (Table 1). Results from the Postmenopausal Estrogen/Progestin Interventions Trial (10) showed a greater responsiveness to various estrogen treatments in the spine than in the hip. Duan et al (11) suggested that hormone replacement therapy may be a more effective means of reducing the risk of spine than of hip fractures. Trabecular bone is known to have a higher turnover rate than does cortical bone. Thus, the lumbar spine, which is relatively high in trabecular bone, should be more sensitive to compounds that are thought to affect remodeling, such as estrogens and phytoestrogens.

In a recent editorial focused on the potential role of soy phytoestrogens in postmenopausal women, Clarkson (3) concluded that the effects of soy or phytoestrogen supplements on postmenopausal bone loss were uncertain. Messina (9) labeled the relation between isoflavones and bone health as “provocative.” We feel that the positive effects in these 2 trials warrant further long-term studies. It would be a great benefit to peri- and postmenopausal women if soy with isoflavones alone or with other therapy were shown to attenuate bone loss in the spine, providing these women with an alternative approach to hormone therapy for maintaining bone.

REFERENCES