The Effect of Soybean Protein on Bone Loss in a Rat Model of Postmenopausal Osteoporosis

Eric HARRISON,1 Andrew ADJEI,2 Clement AMEHO,3 Shigeru YAMAMOTO4 and Shinzo KONO1,*

1 Department of Adult Health, 2 Department of Bacteriology, and 3 Department of Pharmacology, Faculty of Medicine, University of the Ryukyus, Okinawa 903-0215, Japan
4 Department of Nutrition, Medical School, University of Tokushima, Tokushima 770-0042, Japan

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Summary This study was designed to investigate the modulatory effect of dietary soybean protein on the skeleton of an ovariectomized rat model with postmenopausal osteoporosis. Thirty-two female Sprague-Dawley rats were weight matched and divided into the following four experimental groups: Soy group, ovariectomized and fed soy protein diet; Estrogen group, ovariectomized, fed casein diet and injected with estrogen; Casein group, ovariectomized and fed casein diet; and Sham group, sham-operated and fed casein diet. The diets and estrogen were started two weeks after surgery, and continued for four weeks. Rats in the Sham, Soy and Estrogen groups had significantly higher (p<0.05) femur and tibia ash content than those in the Casein group. Accordingly, the calcium content of the tibia and femur were also significantly higher (p<0.05) in the Soy, Estrogen and Sham groups as compared to the Casein group. Serum total and bone-type alkaline phosphatase levels were both significantly lower (p<0.05) in the Estrogen and Sham groups in relation to the Soy and Casein groups. This study demonstrated that a 22% soybean protein diet could be just as effective as daily estrogen administration in suppressing bone loss due to ovariectomy. However, unlike estrogen, soy protein diet did not have any uterotrophic effect and did not decrease the markers of bone turnover measured, suggesting a possible difference in the mechanism of action.

Key Words soy protein, ovariectomy, estrogen, bone loss

Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue resulting in an increase in bone fragility and susceptibility to fractures (1). The fractures predominantly occur at

* To whom correspondence should be addressed.
the femoral neck, vertebra and lower forearm (2). Development of osteoporosis depends on peak bone mass achieved, rate of bone loss, maintenance of bone microarchitecture and duration of life. These are related to a composite mixture and inter-relationships of genetics, lifestyles, reproductive history, disease and its treatment, body weight and composition, and diet throughout life (3). Postmenopausal osteoporosis (PMO), resulting from the loss of estrogen at menopause, is associated with a rapid reduction of bone mass, leading to porotic bones prone to fractures.

Estrogen replacement can effectively prevent this rapid bone loss in postmenopausal women (4) and clinically relevant animal models (5), establishing a protective effect of estrogen on the skeleton. It is now well established that Estrogen Replacement Therapy (ERT) increases bone mineral density and decreases the risk of future bone fracture (6). To prevent postmenopausal bone loss, it is recommended that ERT be initiated soon after menopause and continued indefinitely (6), making estrogen replacement the cornerstone of preventive therapy for osteoporotic fractures. Existing data suggest that the beneficial skeletal effect of ERT can be maintained only as long as administration of the hormone is continued and that cessation of the therapy may result in a rapid loss of bone tissue to the level seen in untreated subjects (7). In addition, although the beneficial effects are clear, the overall value of ERT has been questioned due to estrogen-related side effects, many of which are related to hormonal stimulation of the reproductive tissues (8), including uterine stimulation and increased risk of endometrial cancer (9). As a result of these potential long-term risks of estrogen replacement, there is the need for alternative therapeutic measures that may be relatively risk free and equally beneficial.

Compounds in the diet that have properties similar to, or are antagonists of the physiologic estrogens may play a role in reducing the risk and/or extent of osteoporosis. Soybean is a rich source of phytoestrogens, which are non-steroidal estrogens of the isoflavone class (10). These compounds are structurally similar to the mammalian estrogen, estradiol. The principal compounds within these classes of phytoestrogens have been shown to have weak estrogenic activity, possess affinity for estrogen receptors and produce typical and predictable estrogenic responses when administered to animals, behaving as partial estrogen agonists and antagonists depending on the presence or absence of estrogens (11, 12). A few reports have indicated some beneficial effect of soybean diets on the skeleton of ovariectomized rats (13, 14). The ovariectomized rat model is suitable for studying problems that are relevant to postmenopausal bone loss (15) and has proven to be useful for investigating the cellular mechanisms of estrogen action on the skeleton (5, 16). Consequently, this study was designed to investigate the modulatory effect of dietary soybean protein on the skeleton of an ovariectomized rat model with PMO.

MATERIALS AND METHODS

Animals. Thirty-two female Sprague-Dawley rats (10 weeks old, 200–220 g)
were purchased from Kyudo Breeding Laboratories (Kumamoto, Japan) and used for the experiment. All the animals were kept in a constant temperature (25±2°C) and humidity (50-70%) room with a 12-h light period from 08:00 h to 20:00 h. Animal care was in compliance with applicable guidelines from the Ryukyus University Policy on Animal Care and Use. The animals were kept for one week before the onset of the experiment to acclimatize to our laboratory conditions. The rats were housed individually in rack-mounted wire cages. During this period, the rats were fed standard non-purified diet (Nihon Clea, Osaka, Japan). This standard rat diet contains 25.5% protein and 4.3% fat by weight. After the acclimatization period, the animals were weight matched and divided into the following four groups (n=8) according to dietary, surgical operation and estrogen treatment:

1. Soy group—ovariectomized, fed soy protein diet and injected with a vehicle;
2. Estrogen group—ovariectomized, fed casein diet and injected with estrogen;
3. Casein group—ovariectomized, fed casein diet and injected with a vehicle; and
4. Sham group—sham-operated, fed casein diet and injected with a vehicle.

Study protocol. After acclimatization, rats were ovariectomized or sham-operated and fed standard non-purified diet for two weeks. They were then given the experimental diets and injected with either estrogen or a vehicle for four weeks before being sacrificed and various analyses carried out.

Surgical operation. After the period of acclimatization, all the rats were anesthetized with an intraperitoneal injection of sodium pentobarbital (0.1 mL/100 g body weight). Rats in the Casein, Soy and Estrogen groups were ovariec-tomized via bilateral, paraspinal incisions. The uterus, with the ovary attached, was then exteriorized and the ovary removed after ligation of the uterine horn. Animals in the Sham group were subjected to a sham operation, in which the ovaries were exteriorized and then replaced. The success of ovariectomy was confirmed by failure to detect ovarian tissue, observation of marked atrophy of the uterine horns and reduction in the wet weight of the uterine tissue at necrospy.

Diet. Rats in the Sham, Casein and Estrogen groups were fed a 22% casein diet while rats in the Soy group received a 22% soybean protein diet (Table 1). These experimental diets were started two weeks after the surgery to allow for the development of moderate osteopenia, during which period all the animals were fed the non-purified standard diet. To prevent hyperphagia associated with ovariectomy, all the rats were pair-fed to the mean intake of those in the Sham group. This pair-feeding applied to both the non-purified and experimental diets. The animals were fed the experimental diets (which were isonitrogenous and isocaloric) for four weeks and then sacrificed. All the animals were allowed free access to drinking water for the duration of the whole experiment.

Estrogen injection. Two weeks after ovariectomy, rats in the Estrogen group received daily subcutaneous injections of 17β-estradiol at a dose of 10 μg/rat per
Table 1. Composition of experimental diets (%).

<table>
<thead>
<tr>
<th>Component</th>
<th>Casein</th>
<th>Soy protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casein</td>
<td>22.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Soy protein&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.0</td>
<td>22.0</td>
</tr>
<tr>
<td>Starch</td>
<td>43.3</td>
<td>43.3</td>
</tr>
<tr>
<td>Sucrose</td>
<td>21.7</td>
<td>21.7</td>
</tr>
<tr>
<td>Mineral mixture&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Vitamin mixture&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Cellulose</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Oil</td>
<td>5.0</td>
<td>5.0</td>
</tr>
</tbody>
</table>

<sup>a</sup> From Fuji Oil, Tokyo, Japan. Composition is as follows (%): crude protein, 90.5; water, 5.3; dry ash, 4.2.

<sup>b</sup> From Oriental Yeast, Tokyo, Japan. Composition is as follows (mg/kg): CaHPO₄·2H₂O, 7,280; KHPO₄, 12,800; NaH₂PO₄, 4,680; NaCl, 2,330; Ca lactate, 17,550; Fe citrate, 1,590; MgSO₄, 3,590; ZnCO₃, 55; MnSO₄·6H₂O, 60; CuSO₄·5H₂O, 15; KCl, 5.

<sup>c</sup> From Oriental Yeast. Composition is as follows (mg/kg): thiamine HCl, 12; riboflavin, 40; pyridoxine HCl, 8; vitamin B₁₂, 50; ascorbic acid, 300; d-biotin, 0.2; folic acid, 2; calcium pantothenate, 5; p-aminobenzoic acid, 50; niacin, 60; inositol, 60; choline chloride, 2,000; dl-α tocopherol acetate, 50; menadione, 52; retinyl acetate, 5,000; and ergocalciferol, 1,000.

Day. Estradiol (Sigma Chemical, St. Louis, MO, USA) was dissolved in a small volume of absolute ethanol (Nacalai Tesque, Kyoto, Japan) and mixed with corn oil (Fuji Oil, Tokyo, Japan) to a proportion of 95% corn oil and 5% ethanol. Animals in the Sham, Casein and Soy groups received daily subcutaneous injections of the corn oil–ethanol vehicle. All the rats were given 1 mL of the solution a day for a period of four weeks before they were sacrificed.

**Sample collection.** After four weeks on the experimental diets and subcutaneous injections, all the rats were deprived of food overnight (8:00 pm to 9:00 am) and anesthetised with intraperitoneal injection of sodium pentobarbital (0.1 mL/100 g body weight). Blood was collected by cardiac puncture. Serum was then separated and stored at −20°C for biochemical analyses. The adrenal glands, liver, kidneys, spleen and uterus were removed and weighed. The right femur and tibia were also dissected out and cleaned of all soft tissue.

**Analytical procedures**

Bone measurements: The wet weight of the femur and tibia were measured. Samples were also dried for 24 h at 100°C and the dry weights recorded. They were then ashed in a muffle furnace at 550–600°C for another 24 h and the ash weighed. The ash was pulverized into powder and hydrolyzed with 6 M HCl. Aliquots of the hydrolysate were then used for the determination of the calcium content. Calcium was determined by atomic absorption spectrophotometry (Hitachi, Model No. Z-6100).
Soy Protein and Bone Loss

Serum analyses: Serum calcium was determined with a commercial kit, Calcium-HR Test (Wako Pure Chemical Industries, Osaka, Japan) and serum inorganic phosphorus was also measured using a commercial kit, Phospha-HRII Test (Wako Pure Chemical Industries). Serum total alkaline phosphatase (T-Alp) was analyzed using a commercial kit, Rikitech-ALP Test (Boehringer Mannheim, Tokyo, Japan). Serum bone-type alkaline phosphatase (B-Alp) was estimated by heat inactivation as follows. The serum preparation was preheated at 56°C for 10 min and the ALP determined (with a Rikitech-ALP Test kit) to obtain the heat-stable ALP. The heat labile ALP level, representing the B-ALP level, was then calculated as the difference between the T-ALP and the heat-stable ALP levels.

Statistical analysis: The data were analyzed for differences between the means of the experimental groups using analysis of variance. Where differences were observed, Duncan's multiple range test was used to determine their significance. Differences were considered significant at \( p < 0.05 \).

RESULTS

Body weight and food intake

Rats in all four experimental groups had similar initial body weights. At the end of the experiment, however, the estrogen-treated rats had a significantly lower body weight \( (p < 0.05) \) than the Casein and Soy groups but not the sham-operated controls (Table 2). The mean daily food intake of all the animal was 14.2 g, since they were pair-fed. The differences in the final body weights of the groups were therefore not due to differences in amount of food ingested.

Organ weights

The weights of the spleen, kidneys, uterus, liver and adrenal glands of the groups are presented in Table 2. Ovariectomy resulted in the atrophy of the uterus which was reversed by estrogen treatment. The uterine weight of rats in the Casein and Soy groups remained significantly smaller \( (p < 0.05) \). The weight of both the spleen and kidneys showed no significant differences among the four experimental groups. Ovariectomy caused a significant decrease \( (p < 0.05) \) in the weight of the adrenal glands, which could not be reversed by estrogen treatment. Compared to the sham-operated controls, the Soy group had significantly smaller liver weights \( (p < 0.05) \). The Casein group also tended to have smaller liver weights compared to the Sham group, but the differences were not significant. Estrogen administration, however, resulted in a significant increase \( (p < 0.05) \) in liver weight.

Femur and tibia weight

The wet and dry weights of both the femur and tibia of the experimental groups are shown in Table 3. Compared to the Sham group, ovariectomy caused a slight decrease in the wet weight of the tibia in the Casein group, which was prevented by the soy diet and estrogen treatment. Similar trends were observed in the dry Vol 44, No 2, 1998
Table 2. Body and organ weights of sham-operated and ovariectomized rats (g).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sham</th>
<th>Casein</th>
<th>Soy</th>
<th>Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial body weight</td>
<td>224.7±7.4</td>
<td>223.5±7.6</td>
<td>223.5±9.1</td>
<td>227.0±7.2</td>
</tr>
<tr>
<td>Final body weight</td>
<td>302.3±4.5</td>
<td>319.5±12.0*</td>
<td>317.7±12.5*</td>
<td>293.7±8.7†‡</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.55±0.09</td>
<td>0.59±0.03</td>
<td>0.58±0.02</td>
<td>0.56±0.06</td>
</tr>
<tr>
<td>Liver</td>
<td>7.6±0.54</td>
<td>7.0±0.52</td>
<td>6.4±0.34*</td>
<td>8.8±0.10*†‡</td>
</tr>
<tr>
<td>Kidneys</td>
<td>1.60±0.10</td>
<td>1.51±0.17</td>
<td>1.51±0.08</td>
<td>1.73±0.16</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.66±0.10</td>
<td>0.16±0.01*</td>
<td>0.16±0.03*</td>
<td>0.55±0.08*†‡</td>
</tr>
<tr>
<td>Adrenal gland</td>
<td>0.08±0.014</td>
<td>0.04±0.009*</td>
<td>0.05±0.014*</td>
<td>0.05±0.004*</td>
</tr>
</tbody>
</table>

Data are means±SD. Sham group, sham-operated and fed casein diet; Casein group, ovariectomized and fed casein diet; Soy group, ovariectomized and fed soy protein diet; Estrogen group, ovariectomized, fed casein diet and injected with estrogen.
* Significantly different from Sham group, p<0.05; † significantly different from Casein group, p<0.05; ‡ significantly different from Soy group, p<0.05.

Table 3. Femur and tibia weights of sham-operated and ovariectomized rats (g).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sham</th>
<th>Casein</th>
<th>Soy</th>
<th>Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibia (wt)</td>
<td>0.60±0.05</td>
<td>0.59±0.01</td>
<td>0.61±0.01</td>
<td>0.60±0.04</td>
</tr>
<tr>
<td>Femur (wt)</td>
<td>0.77±0.02</td>
<td>0.75±0.02</td>
<td>0.82±0.01*†</td>
<td>0.77±0.02‡</td>
</tr>
<tr>
<td>Tibia (dry)</td>
<td>0.44±0.03</td>
<td>0.43±0.01</td>
<td>0.45±0.01</td>
<td>0.46±0.01</td>
</tr>
<tr>
<td>Femur (dry)</td>
<td>0.55±0.04</td>
<td>0.53±0.03</td>
<td>0.55±0.02</td>
<td>0.57±0.03</td>
</tr>
</tbody>
</table>

Data are means±SD. Sham group, sham-operated and fed casein diet; Casein group, ovariectomized and fed casein diet; Soy group, ovariectomized and fed soy protein diet; Estrogen group, ovariectomized, fed casein diet and injected with estrogen.
* Significantly different from Sham group, p<0.05; † significantly different from Casein group, p<0.05; ‡ significantly different from Soy group, p<0.05.

weight of both the femur and tibia. The decrease in the wet weight of the femur was small after ovariectomy, but the feeding of soy protein diet resulted in a significant increase (p<0.05), whereas the increase after estrogen administration tended to be high.

Ash content of tibia and femur

The ash weight of both the tibia and femur showed similar trends (Fig. 1). Compared to the sham-operated controls, the ash weights in the Soy and Estrogen groups were not different. The rats in the Casein group, however, had significantly smaller tibia and femur ash weights (p<0.05).

Calcium content of tibia and femur

The calcium contents of the femur in the Sham, Soy and Estrogen groups were
not different from each other, but they were all significantly higher \((p<0.05)\) than that in the Casein group (Fig. 2). Compared to the Sham group, the calcium contents of the tibia in the Soy and Estrogen groups were significantly higher \((p<0.05)\), while that of the Casein group was significantly lower \((p<0.05)\), as shown in Fig. 2.

**Serum assay**

Table 4 shows the serum calcium, phosphorus, T-Alp and B-Alp levels in the
Table 4. Serum calcium, phosphorus and alkaline phosphatase levels of sham-operated and ovariectomized rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sham</th>
<th>Casein</th>
<th>Soy</th>
<th>Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca (mg/100 mL)</td>
<td>10.73±0.35</td>
<td>10.40±0.28</td>
<td>10.00±0.27</td>
<td>11.57±0.21</td>
</tr>
<tr>
<td>P (mg/100 mL)</td>
<td>6.85±0.79</td>
<td>8.35±0.21</td>
<td>8.90±1.31</td>
<td>7.17±1.95</td>
</tr>
<tr>
<td>T-Alp (IU/L)</td>
<td>138.5±20.9</td>
<td>194.5±21.9*</td>
<td>196.0±28.4*</td>
<td>113.3±15.0*</td>
</tr>
<tr>
<td>B-Alp (IU/L)</td>
<td>94.0±9.8</td>
<td>122.0±11.3*</td>
<td>115.7±14.5*</td>
<td>57.0±5.6*</td>
</tr>
</tbody>
</table>

Data are means±SD. Sham group, sham-operated and fed casein diet; Casein group, ovariectomized and fed casein diet; Soy group, ovariectomized and fed soy protein diet; Estrogen group, ovariectomized, fed casein diet and injected with estrogen. * Significantly different from Sham group, p<0.05; † significantly different from Casein group, p<0.05; ‡ significantly different from Soy group, p<0.05.

four experimental groups. While there were no significant differences among the serum calcium and phosphorus levels, the T-Alp and B-Alp levels in the Sham and Estrogen groups were both significantly lower (p<0.05) than those in the Casein and Soy groups. The B-ALP level in the Sham group was however, significantly higher (p<0.05) than that in the Estrogen group.

DISCUSSION

This study has shown the effects of estrogen treatment and soybean protein diet on ovariectomized rats. The effects of ovariectomy on rat bone, organ weights and serum biochemical indices observed in this study have also been variously reported by other investigators (14, 17, 18). The beneficial effects of estrogen treatment are well documented by many researchers for both ovariectomized rats (5, 19, 20) and postmenopausal women (6, 21, 22). These and other similar findings form the basis for ERT. The positive effects of soybean diet on the skeleton of ovariectomized rats have also been reported by two other investigators (13, 14), where bone mineral density and bone strength were increased.

Postmenopausal bone loss is associated with a high bone turnover; both the resorption and formation of bone are increased, but resorption is relatively greater and the outcome is a net loss of bone. The accelerated loss is a result of declining ovarian function (23). This is similar in the ovariectomized rat because ovariectomy also causes a progressive loss of bone matrix. The characteristics of ovariectomy include high bone-turnover ratio with resorption exceeding formation; an initial rapid phase of bone resorption followed by a slower phase, and a significant loss of cancellous bone rather than cortical bone (15). In this study, bone loss was seen in the slight decrease in the dry and wet weights of the tibia and femur, together with the significant decrease in their ash and calcium contents, and the rise in the serum levels of both T-Alp and B-Alp, markers of bone turnover.

The precise mechanism of action of estrogen in the treatment of PMO has not
been well elucidated, but the major therapeutic effect of estrogen replacement is to inhibit bone resorption (24). This decrease in bone turnover may be due to the inhibition of the action or recruitment of osteoclasts (25), with the initial response to estrogen being reduced resorption of bone followed sometime later by reduced bone formation as the ongoing remodelling cycles are completed and fewer new cycles are begun. However, evidence is now available indicating that there are estrogen receptors in normal human osteoblast-like cells (26). This means that since estrogen is the major hormone responsible for the maintenance of bone mass, the presence of specific estrogen receptors on osteoblasts could suggest that estrogen acts directly on human bone cells through a classical estrogen receptor-mediated mechanism. It has also been observed that estrogen stimulates the proliferation of osteoblast-like cells without the mediation of other added hormones in vivo (16) and in cell cultures (27). The identification of estrogen receptors in avian osteoclasts (28) also suggests that estrogen has the ability to directly affect osteoclast activity. Alternatively, some other findings suggest that 17β-estradiol may have an indirect effect on osteoclasts by controlling the production of various cytokines in osteoblasts and monocytes (26, 29, 30). These cytokines have been shown to play an important role in osteoclastic bone resorption and osteoclastogenesis (29, 31). These observations provide a powerful tool for studying the exact role and mechanism of action of estrogen in the pathogenesis of estrogen-deficiency bone loss and ERT.

The view that estrogen prevents ovarian hormone-deficiency bone loss by decreasing bone turnover was confirmed in this study by our observation that 17β-estradiol treatment caused: a marked reduction in the serum T-Alp and B-Alp levels, a significant increase in bone ash and calcium contents, and a slight increase in both the wet and dry weights of the bones measured. Estradiol injection also had varying effects on organ weights. Estrogen is known to act on the pituitary gland to stimulate the somatotrophs and lactotrophs (32, 33) and in the feedback regulation of gonadotrophins (34), thus it remains an open question (requiring investigating into) whether the changes in organ weights due to estrogen administration have any physiological implications. Since the maintenance of calcium homeostasis is important in the treatment of metabolic bone diseases, serum calcium must be assessed along with other biochemical markers. The levels of serum calcium observed in this study (no significant differences among the groups) underscore the fact that serum calcium poorly reflects an altered state of calcium homeostasis because they are maintained within the normal range by various homeostatic mechanisms.

Concentrations of estrogenic isoflavones in most soybean protein products reach levels of 0.1–0.2% (35), the major substances being daidzein and genistein (36). The isoflavone content of the soybean protein used in this study was 0.18% (daidzein, 0.06% and genistein, 0.12%). After the ingestion of soy protein, intestinal flora can convert the soy isoflavones to equol (37), a more potent estrogenic isoflavone that is absorbed along with the unconverted genistein and daidzein.
Equol possesses weak estrogenic activity, in the order of $10^{-3}$ times that of estradiol (38), while that of genistein is about $10^{-3}$ to $10^{-5}$ that of estradiol (39). Phytoestrogens have also been reported to produce uterotrophic effects in animals (40), but this was not observed in our study or that of other researchers (14). This lack of uterotrophic activity could, however, be beneficial in reducing the risk of endometrial cancer associated with ERT. The effects of soy isoflavones also differed from that of estrogen with regard to the markers of bone turnover (serum T-Alp and B-Alp) measured in this experiment. Although there was a significant decrease with estrogen treatment, there was no response after a diet of soy protein. A similar result was obtained by Arjmandi et al (14). This suggests that the mechanism of action of estradiol and isoflavones in soybeans may differ in relation to their skeletal effects. The difference between our study and that of Arjmandi et al is in the dosage of estradiol given and the period between surgery and commencement of treatment. We injected a higher dose and started treatment two weeks after surgery (to allow for the development of moderate osteopenia), while they started treatment from the day of surgery. The results obtained are similar however, suggesting that soy protein diet may not only be effective in the prevention but also in the treatment of estrogen-deficiency bone loss. Bone histomorphometric studies are needed to address and confirm this observation. Apart from isoflavones, other components of soybean, like peptides, have also been implicated in increasing the bone mineral density and bone strength of ovariectomised rats by other researchers (13). The authors suggested that the skeletal effects were possibly due to the acceleration of intestinal calcium absorption by the peptides in soybean. They, however, concluded that further studies are required to identify which peptides or amino acid sequences are involved and precisely how bone metabolism is affected.

In conclusion, this study has demonstrated that a soybean protein diet could be just as effective as daily estradiol administration in suppressing bone loss due to ovariectomy, and that the results provide support for soy diet as a potentially effective alternative to ERT for the maintenance of postmenopausal bone mass and protection against and treatment of PMO.

REFERENCES

Soy Protein and Bone Loss


