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Soy Protein Has a Greater Effect on Bone in Postmenopausal Women Not on Hormone Replacement Therapy, as Evidenced by Reducing Bone Resorption and Urinary Calcium Excretion

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Recent reports suggest that soy protein may reduce the risk of osteoporosis in peri- and postmenopausal women. The objective of this study was to examine whether soy supplementation exerts beneficial effects on serum and urinary biomarkers of bone metabolism in postmenopausal women, regardless of whether or not they are on hormone replacement therapy (HRT). A total of 71 women were randomly assigned to either soy protein (SP) or milk-based protein (MBP), 40 g daily for 3 months, in a double-blind parallel design. Forty-two women completed the study (20 on SP and 22 on MBP). Overall, both protein supplements positively influenced serum IGF-I, known to correlate with bone formation. However, SP had a more pronounced effect on IGF-I than MBP. Urinary deoxypyridinoline (Dpd) excretion, a specific biomarker of bone resorption, was significantly reduced by SP, but not by MBP when all women were included. Furthermore, women on MBP experienced a 33% increase in urinary calcium excretion, whereas SP did not have such an effect. To evaluate whether SP affects women differently on the basis of their HRT status, data from women on HRT (n = 22) and those not on HRT (n = 20) were analyzed separately. The subanalysis of the data indicated that SP had the greatest impact on serum IGF-I (an increase of 97%) in the women not on HRT. The changes in urinary Dpd due to SP were only observed in women not on HRT, indicating that the overall decrease in Dpd occurred with SP in the absence of HRT. These results indicate that soy protein may positively influence bone and calcium homeostasis in postmenopausal women, particularly those not on HRT. (*J Clin Endocrinol Metab* 88: 1048–1054, 2003)

THE POSTMENOPAUSAL PERIOD typically occupies one third of a woman's life (1) and places her at increased risk of osteoporosis (2). Although it is well documented that hormone replacement therapy (HRT) slows down the rate of bone turnover, especially bone resorption (3), on the basis of recent findings (4) its long-term use may not decrease fracture incidence. Other agents such as calcitonin and the bisphosphonate family are also effective antiresorptive agents (5). Despite the availability of drug therapies, there are a considerable number of women who would prefer dietary supplements as an alternative/adjunctive to conventional therapeutic options (6). Examples of these alternative therapies include the use of natural or plant-based substances such as soy isoflavones and other rich sources of phenolic compounds (5–7). Soy isoflavones, recently referred to as naturally occurring selective estrogen receptor modulators (SERMs; Refs. 8 and 9), may exert estrogen-like effects on selected tissues, *e.g.* bone, but not all tissues (8, 10). However, to what extent isoflavones behave like SERMs, *e.g.* raloxifene, remains to be illustrated.

A number of animal studies indicate that soy protein or its isoflavones, although maintaining the ovariectomy-induced elevated rate of bone formation, may simultaneously suppress the rate of bone resorption (11–13). Recently published human studies (14–16) have demonstrated the antiresorptive properties of soy or its isoflavones. These studies include both cross-sectional (16) and prospective (14) trials in which soy protein intake in postmenopausal women was associated with lower urinary specific markers of bone resorption, *e.g.* N-terminal cross-linked peptide (14) and deoxypyridinoline (Dpd; Ref. 16). Furthermore, clinical trials examining the effects of soy protein have found that daily intake of approximately 88 mg isoflavones in conjunction with 40 g soy protein for 6 months increased bone mineral density and bone mineral content in perimenopausal (17) and postmenopausal women who were not on HRT (14, 18).

The purpose of the present study was to examine the effects of soy protein on serum and urinary markers of bone turnover in postmenopausal women, with further analysis of data for women on HRT and women not on HRT.

Abbreviations: BSAP, Bone-specific alkaline phosphatase; Dpd, deoxypyridinoline; E_2, 17β-estradiol; HRT, hormone replacement therapy; MBP, milk-based protein; NTx, N-telopeptide; SERM, selective estrogen receptor modulator; SP, soy protein.

Subjects and Methods

Subjects

A total of 71 postmenopausal women were recruited for this study irrespective of their HRT status, ethnic, and racial backgrounds. Subjects were excluded if they had gastrointestinal disorders, cancer, diabetes,

hypo- or hyperthyroidism, liver or kidney problems, pelvic inflammatory disease, or endometrial polyps, and if they were heavy smokers (>1 pack/d). The mean age of study participants was 62.4 ± 2.4 yr for the soy protein (SP) group and 61.8 ± 2.4 yr for the milk-based protein (MBP) group. The study participants were asked to sign a consent form after receiving oral and written descriptions of the study. A complete medical and diet history was obtained from all subjects before initiating the treatments. Subjects were recruited by advertisement at-large in the city of Stillwater, Oklahoma, and the surrounding communities. The study protocol was approved by the Institutional Review Board at Oklahoma State University.

Study design

Study participants were randomly assigned to consume 40 g of either supplemental SP or MBP (control) daily for 3 months in a double-blind, controlled parallel design. Randomization was performed for all subjects regardless of HRT use. The protein supplements were provided to study participants in two packages, each containing 29 g of a powdered-unflavored drink-mix (Protein Technologies International, St. Louis, MO) to be consumed daily. The composition of the protein supplements is presented in Table 1. The supplements were distributed to the subjects in monthly rations. Subjects were asked to return any unused supplement and mark their calendar daily as a part of monitoring compliance. The free-living study participants were informed of the additional amount of dietary protein they were receiving and were advised to make reasonable substitutions, otherwise continue to consume their habitual diet, and maintain their usual physical activity.

Dietary assessment and anthropometric measurements

For each subject, medical and nutrition history was obtained at the beginning of the study. Anthropometric data were assessed at baseline and at the end of the study and are presented in Table 2. One-week food frequency questionnaires were obtained via interview by a registered dietitian at the beginning and at the end of the 3-month treatment period (Table 3). Nutrient analysis was performed using food analysis software (Food Processor version 7.50, ESHA Research, Salem, OR).

Blood and urine collection

A venous blood sample was obtained after an overnight fast from each subject before and after the treatment period for various analyses. Samples were centrifuged at 2000 × *g* for 15 min at 4 C, and serum was separated and stored at −80 C until analyzed. Each subject collected a 24-h urine specimen, excluding the first morning void, before and after the treatment period. Urine volume was recorded, and aliquots were stored at −20 C for later analysis.

Analytical methods

Blood analyses. Serum bone-specific alkaline phosphatase (BSAP) activity, a specific marker of bone formation (19), was quantified by immunoassay in a microtiter format (Metra Biosystems, Mountain View, CA). Serum 17β-estradiol (E_2) was determined using RIA kits from Diagnostic Systems Laboratories Inc. (Webster, TX). IGF-I was extracted from serum using the acid-ethanol extraction procedure and kits from Nichols Institute Diagnostics (San Juan Capistrano, CA), following the manufacturer's procedures. The intra- and interassay coefficients of variation were 9.7% and 3.9% for BSAP, 6.5% and 7.6% for E_2, and 3.0% and 8.4% for IGF-I.

Urinary analyses. Urinary creatinine was measured colorimetrically with a commercially available kit from Roche Diagnostic Systems, Inc. (Montclair, NJ) using a Cobas Fara II clinical analyzer. Urinary Dpd excretion, a specific marker of bone resorption, was measured by competitive enzyme immunoassay in a microassay stripwell format (Quidel Corporation, Mountain View, CA; Ref. 20). Urinary calcium excretion was measured using a kit from Sigma (St. Louis, MO). The intra- and interassay coefficients of variation were 1.7% and 6.3% for creatinine and 4.3% and 4.6% for Dpd.

TABLE 1. Analytical composition of SP and MBP used in the study

Component	SP	MBP
Protein (g)	40	40
Carbohydrates (g)	6	6
Total fat (g)	2	<1
Vitamins		
Vitamin A (IU)	1000	1000
Vitamin C (mg)	4.8	4.8
Vitamin D (IU)	200	200
Minerals		
Calcium (mg)	1400	1400
Iron (mg)	7.2	0
Magnesium (mg)	80	80
Phosphorus (mg)	1000	1000
Zinc (mg)	1.8	1.8
Total isoflavones (mg)	88.4	0.0

Statistical analyses

All data were analyzed using ANOVA methods with PROC MIXED in PC SAS (version 8.2, SAS Institute, Inc., Cary, NC). A three-way ANOVA model was fit, using HRT, soy treatment, and time as factors. Each factor has two levels. Because each subject was measured before and after treatment, a repeated measures analysis was used, with HRT and soy treatment as the main unit factors and time as the within-subject factor. The primary objective was to assess the effects of treatment over time, so the interaction of soy treatment with time was tested (interaction will measure the consistency of treatment differences over time). This interaction is calculated for both cases of HRT and averaged over HRT. A SLICE option in PROC MIXED was used to test soy treatment by time interaction for both levels of HRT. If the interaction was significant due to a soy treatment improvement, then that indicated an improvement over time relative to the nonsoy group. Data are reported as least squares mean ± SE. Unless otherwise indicated, a P value less than 0.05 was regarded as significant.

Results

Baseline characteristics, anthropometric measurements, and dietary intakes

Forty-two of 71 women completed the study, an attrition rate of approximately 41%. Reasons for attrition included lack of palatability of the powdered protein supplements (seven and six women in MBP and SP treatment groups, respectively), time constraints preventing adherence with study protocol (five and seven women in MBP and SP treatment groups, respectively), gastrointestinal disturbances (one and two women in MBP and SP treatment groups, respectively), and personal reasons preventing compliance with study protocol (one woman in SP treatment group). Baseline characteristic data for women who completed the study are presented in Table 2. Baseline characteristics did not differ for women receiving the soy protein regimen and those receiving the control regimen.

Those who finished the study adhered to their regimens as indicated by self-monitoring checklists provided to them and by returning any unconsumed supplement packets on a monthly basis. Daily nutrient intake as assessed by 1-wk food frequency questionnaires for subjects in both treatment groups were similar before and after the 3-month treatment period (Table 3).

Serum and urinary parameters

In assessing the effect of treatment with SP or MBP, we first analyzed the differences between baseline and final in each

TABLE 2. Subject characteristics at baseline and after a 3-month supplementation

	SP (n = 20)			MBP (n = 22)		
	Baseline	Final	*P*	Baseline	Final	*P*
Age (yr)	62.4 ± 2.4			61.8 ± 2.4		
Height (m)	1.63 ± 0.02			1.64 ± 0.02		
Weight (kg)	84.5 ± 4.6	84.7 ± 4.6	0.7385	87.3 ± 4.4	88.3 ± 4.4	0.0718
BMI (kg/m^2)	31.8 ± 1.8	31.9 ± 1.8	0.6134	32.6 ± 1.7	32.9 ± 1.7	0.0910
Waist/hip ratio	0.85 ± 0.02	0.86 ± 0.02	0.2164	0.86 ± 0.02	0.87 ± 0.02	0.3866
Body fat (%)	40.7 ± 1.7	39.4 ± 1.7	0.0532	41.9 ± 1.5	40.9 ± 1.5	0.0783

Values are least square means ± SE.

TABLE 3. Daily nutrient dietary intake calculated from 7-d food frequency questionnaires obtained from study participants before and after the 3-month dietary intervention[a]

	SP (n = 20)		MBP (n = 22)	
	Baseline	Final	Baseline	Final
Total energy (kcal)	1,343 ± 119	1,432 ± 79	1,598 ± 103	1,626 ± 169
Macronutrients				
Protein (g)	60 ± 6	61 ± 4	75 ± 9	68 ± 5
Carbohydrates (g)	181 ± 18	200 ± 10	196 ± 16	213 ± 22
Total fat (g)	46 ± 4	46 ± 4	60 ± 6	59 ± 8
Vitamins				
Vitamin A (IU)	13,512 ± 2,382	16,945 ± 2,826	10,108 ± 2,033	11,650 ± 1,549
Vitamin C (mg)	104 ± 14	131 ± 18	93 ± 11	127 ± 16
Vitamin D (IU)[b]	168 ± 28	152 ± 23	164 ± 33	173 ± 26
Vitamin E (IU)	7.8 ± 0.7	8.3 ± 0.7	21.2 ± 12.9	9.9 ± 2.3
Vitamin K (μg)	119 ± 24	139 ± 28	81 ± 15	95 ± 17
Minerals				
Calcium (mg)[b]	842 ± 112	786 ± 97	752 ± 96	826 ± 134
Iron (mg)	11.5 ± 1.3	10.8 ± 0.9	11.6 ± 1.0	11.3 ± 0.7
Magnesium (mg)	280 ± 31	246 ± 16	254 ± 14	281 ± 30
Phosphorus (mg)	1,201 ± 152	1,097 ± 94	1,201 ± 99	1,157 ± 103
Potassium (mg)	2,796 ± 308	2,788 ± 168	2,661 ± 191	3,064 ± 362
Zinc (mg)	8.58 ± 0.95	8.24 ± 0.57	9.48 ± 0.75	9.04 ± 0.62

[a] Values are least square means ± SE; analyses do not include nutrients and calcium from the protein supplements provided to the study participants. There were no statistically significant differences observed between baseline values of the two treatment groups and between baseline and corresponding final values.

[b] Each protein supplement provided 1400 mg calcium and 200 IU vitamin D.

TABLE 4. Effect of a 3-month SP or MBP daily supplementation on serum and urine parameters in all postmenopausal women

	SP (n = 20)			MBP (n = 22)			Time × treat
	Baseline	Final	*P*	Baseline	Final	*P*	*P*
Serum							
BSAP (μkat/liter)	0.438 ± 0.032	0.412 ± 0.032	0.1394	0.381 ± 0.031	0.348 ± 0.031	0.0493	0.7601
E_2 (pg/ml)	51.5 ± 22.4	66.6 ± 23.1	0.3428	84.8 ± 21.5	95.0 ± 22.2	0.5135	0.8292
IGF-I (nmol/liter)	12.42 ± 1.91	20.94 ± 1.98	<0.0001	14.02 ± 1.87	19.12 ± 1.87	0.0045	0.1718
Urine							
Dpd (nmol/mol creatinine)	9.62 ± 0.76	7.19 ± 0.74	0.0115	7.66 ± 0.69	6.79 ± 0.69	0.3055	0.2164
Calcium (mmol/mmol creatinine)	0.52 ± 0.06	0.55 ± 0.06	0.5456	0.42 ± 0.06	0.56 ± 0.06	0.0018	0.0694
Phosphorous (mmol/mmol creatinine)	2.83 ± 0.22	2.92 ± 0.22	0.6761	2.72 ± 0.20	3.09 ± 0.20	0.0794	0.3542
Magnesium (mmol/mmol creatinine)	0.53 ± 0.05	0.53 ± 0.05	0.9305	0.47 ± 0.05	0.58 ± 0.05	0.0630	0.2205

Values are least square means ± SE.

group. As expected, both protein supplements significantly increased serum levels of IGF-I (Table 4). Although SP supplementation did not alter serum levels of BSAP, MBP significantly ($P < 0.05$) suppressed its levels. Urinary Dpd levels were only significantly lowered in those who consumed SP. Subjects in the MBP group experienced a 33% increase ($P < 0.002$) in urinary calcium excretion with similar trends for phosphorus and magnesium, whereas SP had no such effect. Soy protein supplementation had no effect on serum levels of E_2, indicating its lack of apparent estrogenicity.

To evaluate the possible influence of HRT, subanalysis of the data were performed within each treatment group for those who were on HRT (Table 5) or those who were not on HRT (Table 6). When comparisons were made for

TABLE 5. Effect of a 3-month SP or MBP daily supplementation on serum and urine parameters in postmenopausal women on HRT

	SP (n = 20)			MBP (n = 22)			Time × treat
	Baseline	Final	*P*	Baseline	Final	*P*	*P*
Serum							
BSAP (μkat/liter)	0.354 ± 0.024	0.324 ± 0.032	0.2444	0.363 ± 0.033	0.338 ± 0.027	0.2872	0.4481
E_2 (pg/ml)	93.4 ± 16.8	116.9 ± 28.1	0.3335	122.84 ± 28.7	158.3 ± 48.38	0.6299	0.3990
IGF-I (nmol/liter)	13.43 ± 2.50	19.85 ± 3.72	0.0221	15.49 ± 1.85	21.21 ± 2.56	0.0147	0.0101
Urine							
Dpd (nmol/mol creatinine)	7.60 ± 1.11	6.84 ± 0.94	0.5719	6.68 ± 0.55	6.46 ± 0.55	0.8489	0.8738
Calcium (mmol/mmol creatinine)	0.50 ± 0.09	0.47 ± 0.09	0.6285	0.42 ± 0.05	0.57 ± 0.06	0.0119	0.0806
Phosphorous (mmol/mmol creatinine)	2.44 ± 0.36	2.33 ± 0.17	0.7213	2.97 ± 0.21	3.32 ± 0.23	0.2157	0.0715
Magnesium (mmol/mmol creatinine)	0.61 ± 0.11	0.49 ± 0.04	0.0682	0.41 ± 0.04	0.57 ± 0.05	0.0285	0.0306

Values are least square means ± SE.

TABLE 6. Effect of a 3-month SP or MBP daily supplementation on serum and urine parameters in postmenopausal women not on HRT

	SP (n = 20)			MBP (n = 22)			Time × treat
	Baseline	Final	*P*	Baseline	Final	*P*	*P*
Serum							
BSAP (μkat/liter)	0.523 ± 0.042	0.499 ± 0.045	0.3501	0.404 ± 0.06	0.360 ± 0.044	0.0910	0.0427
E_2 (pg/ml)	35.6 ± 6.4	61.7 ± 16.9	0.7793	45.9 ± 13.9	93.2 ± 44.4	0.6596	0.9610
IGF-I (nmol/liter)	11.40 ± 2.15	22.45 ± 4.16	0.0001	12.06 ± 1.25	16.33 ± 3.18	0.1062	0.0005
Urine							
Dpd (nmol/mol creatinine)	11.24 ± 1.89	7.49 ± 0.38	0.0041	8.85 ± 1.14	7.19 ± 0.69	0.1829	0.009
Calcium (mmol/mmol creatinine)	0.55 ± 0.14	0.63 ± 0.14	0.1859	0.42 ± 0.05	0.55 ± 0.07	0.0472	0.0974
Phosphorous (mmol/mmol creatinine)	3.23 ± 0.27	3.52 ± 0.45	0.3502	2.41 ± 0.24	2.81 ± 0.18	0.2183	0.0644
Magnesium (mmol/mmol creatinine)	0.43 ± 0.03	0.57 ± 0.08	0.0581	0.54 ± 0.07	0.59 ± 0.04	0.5665	0.1952

Values are least square means ± SE.

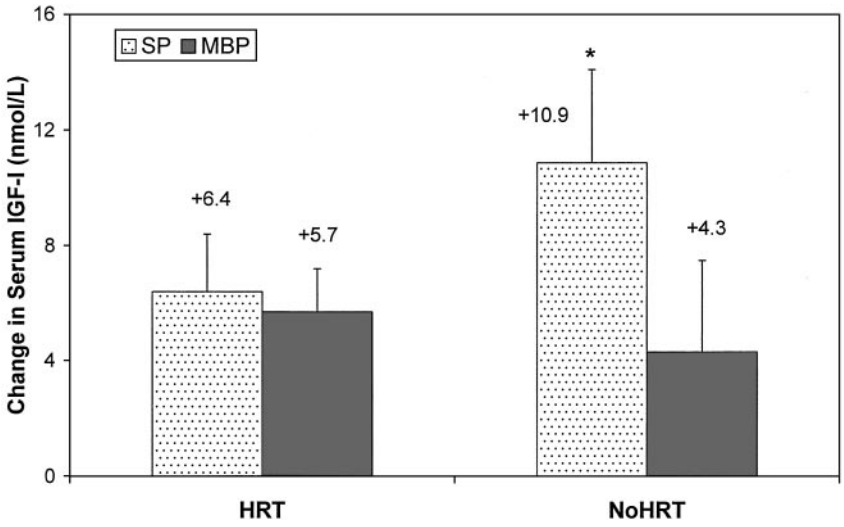

FIG. 1. Mean changes from baseline values in serum IGF-I concentrations after 3 months of SP or MBP supplementation in women on HRT and not on HRT (noHRT). *, In the noHRT group, the change in IGF-I concentration was significantly ($P < 0.05$) higher in women on SP compared with those on MBP.

women within the HRT and no-HRT groups, baseline values did not differ for the SP and MBP treatments. Similar to the overall findings, serum IGF-I levels were increased by both protein supplements; however, soy protein had a more pronounced effect in increasing serum IGF-I levels in women who were not on HRT (Fig. 1). Despite the increase in IGF-I concentrations, serum BSAP levels were not significantly influenced by any of the treatments.

In terms of the antiresorptive properties of soy, the subanalysis of the data clearly indicated that soy with its isoflavones significantly ($P < 0.01$) suppressed urinary Dpd in women who were not on HRT (Fig. 2). Additionally, MBP increased ($P < 0.05$) urinary excretion of calcium irrespective of hormonal status, whereas soy had no such negative effect. The data show that there may be an interaction between soy protein, urinary magnesium loss, and HRT. In women on HRT, urinary magnesium excretion was significantly elevated in those consuming MBP, whereas SP reduced ($P = 0.068$) its loss. In contrast, in women not on HRT, SP not only failed to lower magnesium excretion, but also tended ($P = 0.058$) to increase its urinary loss, whereas MBP had no such effect.

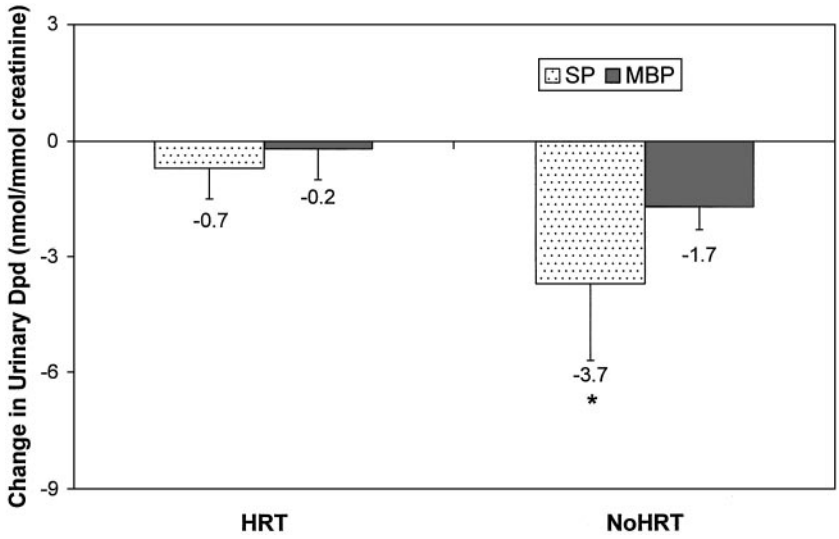

FIG. 2. Mean changes from baseline values in urinary Dpd concentrations after 3 months of SP or MBP supplementation in women on HRT and not on HRT (noHRT). *, In the noHRT group, the change in Dpd concentration was significantly ($P < 0.05$) lower in women on SP compared with those on MBP.

Discussion

This study intended to elucidate whether soy protein positively influences postmenopausal women's bone health as assessed by bone biochemical markers, regardless of HRT status. To answer this question, the data were first analyzed for all women on soy for the overall effect and subsequently were examined for the differences in the effectiveness for women on HRT or not on HRT. Based on the findings of this study, soy protein appeared to exert its bone protective effects mainly by suppressing the rate of bone resorption, while at the same time maintaining or enhancing the rate of bone formation.

When all women in the present study were considered, the overall findings indicated that soy protein was effective in reducing the rate of bone resorption as evidenced by suppressed urinary Dpd excretion. These findings are in agreement with those from a limited number of human trials (14–16) and animal studies (11–13). In a cross-sectional study by Horiuchi *et al.* (16), soy protein intake in Japanese postmenopausal women was associated with significantly lower urinary Dpd excretion. In another cross-sectional study by Kritz-Silverstein and Goodman-Gruen (15), postmenopausal women in southern California with the highest daily intake of dietary genistin had 18% lower N-telopeptide (NTx) excretion than women who did not consume genistin. The results of a prospective study by Scheiber *et al.* (14) also indicated a significant reduction of urinary NTx excretion in postmenopausal women who consumed soy foods providing 60 mg isoflavones for 3 months.

In contrast to the findings of the present study and those of other investigators (14–16), the results of a clinical trial by Wangen *et al.* (21) showed that soy isoflavones in the context of soy protein had no effect on biomarkers of bone turnover in postmenopausal women. However, in their study (21), all subjects were consuming soy protein so that conclusions were based on comparing soy protein with normal and added isoflavones to that of soy protein with minimal isoflavone content rather than a nonsoy protein control. To date, the existing clinical trials have exclusively looked at soy protein or whole soy consumption on bone; hence, it is too early to credit the positive effects of soy protein on bone solely to its isoflavones. If isoflavones act similarly to synthetic SERMs (8, 9), it is reasonable to assume that the isoflavones in soy protein, in part, are responsible for the observed reduction in markers of bone resorption.

Recent reports have indicated that soy protein supplementation may exert positive effects on calcium homeostasis as indicated by significantly reduced urinary calcium excretion in postmenopausal women (22, 23). Similarly, in the present study, subjects who consumed soy protein did not experience a significant increase in urinary calcium loss, whereas urinary calcium excretion was higher in those who received MBP. This calcium-conserving property of soy has been attributed to the lower levels of sulfur-containing amino acids in soy protein (24–26). Additionally, intestinal calcium absorption declines in ovarian hormone deficiency (27, 28), which may contribute to accelerated bone loss (27–30). In this respect, similar to estrogen (31, 32), soy isoflavones may enhance intestinal calcium absorption and further improve calcium homeostasis (7, 26, 33). Furthermore, in the present study conservatory trends were also observed with magnesium and phosphorus homeostasis, both of which are important in the maintenance of skeletal health.

Soy protein, with its nonprotein constituents, when given in conjunction with calcium not only suppresses bone resorption, but simultaneously may have the ability to enhance the rate of bone formation. In this study, although both protein sources elevated serum IGF-I levels, soy protein had a more pronounced effect in increasing serum IGF-I by 69%, compared with a 36% increase with MBP. Although the role of circulating IGF-I in bone is unclear, IGF-I has been reported to directly stimulate collagen synthesis *in vitro* by osteoblastic cells (34) and may mediate the anabolic action of parathyroid hormone on bone (35). Serum IGF-I concentrations have also been reported to correlate positively with bone mass in premenopausal (36), perimenopausal (37), and postmenopausal

(38) women. In support of the notion that soy protein with its isoflavones may have an anabolic effect, isoflavones have been shown to stimulate osteoblastic activity through activation of estrogen receptors and increase bone alkaline phosphatase activity (39). However, our findings that soy protein has the ability to increase serum IGF-I but not circulating levels of BSAP is paradoxical, making the bone-forming ability of soy protein questionable at the present time.

The subanalysis of the data in this study, however, revealed that soy protein is only effective in reducing the bone resorption marker, Dpd, in the absence of HRT. These findings seem logical because HRT has already substantially suppressed bone resorption and further reduction should not be expected. The ineffectiveness of soy protein to reduce bone resorption in the presence of estrogen has also been observed by Alekel *et al.* (17) in perimenopausal women. In that study (17), soy protein did not alter urinary NTx excretion, which is similar to our observation in postmenopausal women on HRT. Therefore, the efficacy of soy protein or its isoflavones in preventing bone loss or improving bone health may vary, depending on estrogen status of women.

In summary, our findings suggest that women who are not on HRT may greatly benefit from consuming soy products. This conclusion is based on our observations that soy supplementation not only reduced bone resorption, as assessed by urinary Dpd, but also did not exert a negative effect on calcium, magnesium, and phosphorus homeostasis. Although the aforementioned findings plus the stimulatory effect of soy protein on IGF-I are suggestive of the bone protective effects of soy protein, it is noteworthy that the conclusions derived from this study are based on biochemical parameters associated with bone metabolism. Consequently, these conclusions need to be substantiated by longer-term clinical studies in which the effects of soy protein supplementation on bone mineral density, bone mineral content, and fracture risk can be evaluated.

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