

Guest Editorial (President ASPIRE)

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PHYTOESTROGENS—WHAT IS THE CURRENT EVIDENCE?

Foods phytoestrogen molecules can be divided into major chemical classes—isoﬂavones and coumestans. The isoﬂavones are found predominantly in soybeans, whereas coumestans are produced primarily by clovers and some legumes. Genistein is a phytoestrogen found in leguminase. These molecules function as antioxidant in plants, but in mammalian tissues these natural products act as agonists or partial agonist of estrogens. Isoﬂavones including daidzin, diadzein, genistein and genistin are present in soybean at a comparatively higher concentration.

Though hormone replacement therapy has clear bone related benefits but because of the associated risks, the compliance is generally poor. It has both stimulatory effect on the bone formation and also inhibits osteoblastic bone resorption by causing apoptosis of mature osteoclasts and by preventing the formation and differentiation of osteoclast like cells.

Genistein has been shown to have a strong inhibitory effect on protein tyrosine kinases.^{1,2}

Dietary fiber intake has been positively correlated with urinary excretion of phytoestrogens and concentration of sex hormone binding globulin.¹

Phytoestrogens and Breast Cancer

Women with prior early stage breast cancer and vasomotor symptoms have been benefitted with phytoestrogens in a cross-sectional study.¹ Soy food consumption is associated with lower risk of breast and endometrial cancer in observational studies.²

Phytoestrogens and Vasomotor Symptoms

Meta-analysis revealed that isoﬂavones reduced hot flash severity by 26% compared with placebo isoﬂavone supplement containing 18.8 mg of genistein were more than twice as potent at reducing hot flash frequency than lower genistein supplement.¹ One study found that 40 mg/day of S-equol had a greater reduction in hot flush frequency compared to isoﬂavones ($p = 0.021$). S-equol ≥ 20 mg/day, alleviates hot flushes to a greater extent than soy isoﬂavones in those women who experience more than eight hot flashes/day.³

According to the position statement of North American Menopausal Society lower vasomotor symptoms (VMS) were reported by the use of soy isoﬂavone supplements.

Perimenopausal women have VMS comparable to postmenopausal women. The effect has not been reported for perimenopausal women. It has largely only related to reducing VMS in those who have them rather preventing them⁴ and it can cause cell cycle arrest and apoptosis in leukemic cells⁵ such a cellular mechanism may be important in the prevention of cancers. Isoﬂavones as a food factor are a useful tool in the prevention of and therapy for osteoporosis.

ACTION OF ISOFLAVONE ON OSTEOLASTIC BONE FORMATION-

The antiestrogen tamoxifen was shown to completely block the genistein induced increase in bone components although tamoxifen itself had no effects on these components. These findings suggest that the anabolic effect of genistein on bone metabolism is partly mediated through estrogen like action.⁶ Presumably, genistein binds to the receptor of estrogen in osteoblastic cell.⁷

EFFECT OF PHYTOESTROGENS ON BONE MINERAL DENSITY

In Asian population where diet is rich in soy, ratio of hip fracture are substantially lower than in people in United States. But after adjustment for height and weight, the bone mineral density in Asian is comparable to that in Whites. Postmenopausal women consuming 90 mg isoﬂavones/day for 24 weeks resulted in a significant increase in lumbar spine bone mineral content and bone marrow density. Similarly 57 mg of red clover isoﬂavones or 85.5 mg isoﬂavones/day for 6 months resulted in an increase in bone mineral density of proximal radius and ulna.

Effects of soy on markers of bone turnover have been studied in various studies. Soy rich diet result in significant increase in serum osteocalcin concentration and decrease in urinary N-telopeptide excretion. Bone resorption marker pyridinolone has been found to be reduced after 4 weeks of isoflavone supplement in perimenopausal women. But other studies have reported little or no effect of soy protein on markers of bone turnover. In a double blind randomized placebo controlled trial participant were green isoflavones supplement containing daily dose of 26 mg biochamin A, 16 mg formononetin, 1 mg genistein and 0.5 mg daidzein for 1 year. The results showed that there were no significant effect on hip or bone mineral content or bone mineral density, markers of bone resorption but markers of bone formation were significantly increased (bone specific alkaline phosphatase and N-propeptide collagen type 1) in women taking the isoflavones supplement *vs* placebo. This suggests that rather than increasing peak bone mass in young premenopausal women, isoflavones may be attenuating the age related bone loss. The exact mechanism of action of soy isoflavones on bone is still to be understood. It is hypothesized that their action are mediated via estrogen receptors.

Rates of hip fracture in Asian populations, whose traditional diets rich in soy, are substantially lower than those in Whites residing in the United States. However, bone mineral density in Asian population is comparable to that in White populations, after adjustment for height and weight. Nevertheless, data from animal experiments provided evidence that soy protein can attenuate menopausal bone loss.⁸

Red clover isoflavones supplement providing 57 or 85.5 mg isoflavones/day for 6 months resulted in an increase in bone marrow density of the proximal radius and ulna. In postmenopausal women, diet rich in soy foods resulted in significant increases in serum osteocalcin concentration and decrease in urinary N-telopeptide excretion. In perimenopausal women, a 4 weeks intervention with an isoflavones extract resulted in a significant reduction in the bone resorption marker pyridinolone.

The efficacy of isoflavone on bone has not been proven and the clinical picture of cardiovascular benefits of soy is still evolving. Younger postmenopausal women derive more cognitive benefit than older women.²

Lipid lowering effects of soy isoflavones have been conflicting.

CONCLUSION

Supplemental intake of dietary isoflavone has many health benefits. For the prevention of bone loss with increasing age soyabean foods containing isoflavones are a good choice. Further research is required to clearly define the effects of isoflavones.

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