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PHYTOESTROGENS IN POSTMENOPAUSAL WOMEN – Effects on Climacteric Symptoms, Reproductive Organs, and Markers of Bone and Vascular Health

ABSTRACT

Isoflavonoids are phytoestrogens present in soybeans concomitantly with soy protein, and they resemble estradiol in structure and manner of action. Isoflavones such as genistein and daidzein bind weakly to estrogen receptor α and more strongly to estrogen receptor β, and as this binding is tissue-specific, they possess organ-specific estrogenic and antiestrogenic effects. A high intake of dietary phytoestrogens has been suggested to account for the lower rates of climacteric complaints, cardiovascular diseases, breast and endometrial cancers, and osteoporosis-related fractures in Asian than in Western countries. We examined the effects of isolated isoflavones on menopausal symptoms, quality of life, working capacity, vaginal and endometrial epithelium, and markers of bone and vascular health in symptomatic postmenopausal women with a history of breast cancer in a randomized placebo-controlled crossover trial involving 64 women, who used both phytoestrogen (114 mg isoflavonoids/day) and placebo for 3 months. Fifty-six women completed the 8-month study.

The phytoestrogen regimen raised the circulating levels of isoflavonoids (daidzein, genistein, equol) 19- to 100-fold, but it failed to improve climacteric symptoms. The parameters reflecting quality of life such as working capacity and mood changes were unaffected by phytoestrogen. In addition, isoflavonoids caused no changes in circulating concentrations of follicle-stimulating hormone, luteinizing hormone, estradiol, or sex hormone-binding globulin. Twenty-five of 56 women (44.6%) preferred the phytoestrogen regimen as compared with 15 (26.8%) who preferred the placebo ($p > 0.05$), and 16 (28.6%) reported no preference.

Isoflavonoids did not relieve vaginal dryness nor did they improve the maturation index of vaginal epithelium. Moreover, they caused no changes in endometrial thickness, histology, and expression of estrogen and progesterone receptors and the proliferation marker Ki-67.

Markers of bone resorption (deoxypyridinoline, pyridinoline and N-terminal cross-linked telopeptide of type I collagen) were reduced during isoflavonoid use, compared with the placebo. The fall in deoxypyridinoline was significant (5%; $p = 0.022$) and the falls in levels of

pyridinoline (9%; $p = 0.084$) and N-terminal cross-linked telopeptide of type I collagen (7%; $p = 0.082$) showed a trend towards significance. These changes may imply a mild useful effect of isoflavonoids on bone, although bone formation markers (bone-specific alkaline phosphatase and amino-(N-)terminal and carboxy-(C-)terminal procollagen type I) were not affected by isoflavonoids.

Isoflavonoids did not affect the concentrations of lipids or lipoproteins (total cholesterol, high- and low-density lipoprotein cholesterol, triglycerides, apolipoproteins B and A1, and lipoprotein (a)), or insulin sensitivity, as assessed by an oral 2-h glucose tolerance test (75 g). Changes in the levels of ghrelin were significantly different during the isoflavonoid (-7.1 ± 151 μmol/L) and placebo regimens (+47.9 ± 198 μmol/L) ($p = 0.048$). The levels of C-reactive protein and nitrate were not affected by isoflavonoids, but the levels of E-selectin were reduced by 4.0% (= 2.9 ng/mL) ($p = 0.031$) during isoflavonoid use; however no difference in these three markers between the study groups was seen at three months. These neutral effects on vascular surrogate markers fail to support a vasoprotective role of isoflavonoids.

In conclusion, pure isoflavonoids (114 mg for three months) did not have estrogen-like effects in postmenopausal women, except for mild inhibition of bone resorption. Thus, their use for the treatment of menopausal symptoms cannot be supported by our data.

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