Soy and Breast Cancer

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Perhaps no other food has been surround by as much controversy as soy, especially for the women who have or have had breast cancer. Part of the confusion is that women and often even their physicians think that there is estrogen in soy. However, there is not. Soy does contain a group of compounds called phytoestrogens. The phytoestrogens in soy are called isoflavones and the dominant isoflavones are genistein and daidzein. These are not estrogen, but have the ability to bind to estrogen receptors and exert some weak estrogen-like effects on some cells, and perhaps surprisingly, weak anti-estrogen effects on other cells. While different from estrogen, they can exert estrogen-like effects in tissues such as bones,[1,2] but do not have estrogen like effects on the lining of the uterus and unlike estrogen,[3,4] do not increase serum triglyceride levels.[5]

What has been confusing is how do the soy isoflavones function in the breast? The potential antiestrogenic effects of isoflavones provide a possible mechanism for the possible protective effects of soy consumption against breast cancer. The problem is that it is not clearly evident that soyfoods exert antiestrogenic effects on breast tissue, although there are several mechanisms by which protective effects can occur. The isoflavone, genistein, does inhibit several key enzymes which are responsible for the inhibitory effects of isoflavones on cancer cells in laboratory studies.[6,7,8,9,10] These include inhibition of tyrosine protein kinase, MAP kinase and DNA topoisomerase. For these reasons, findings first published in 1990 showing that the addition of soy protein to a typical research lab diet significantly decreased chemically induced breast cancer in mice,[11] and the low breast cancer mortality rates in Asian countries[12] were key issues that set the stage for research on the anticancer effects of soy.

Since then, animal data, studies on diets in women in different parts of the world (epidemiologic data), and actual clinical studies on women, have produced confusing and some mixed results. The animal data has been sometimes inconsistent but in general, they show that the substitution of soy protein for animal protein, and the addition of isoflavone supplementation to a standard laboratory diet substantially reduces the number of chemically induced breast tumors by 25% to 50%, although the percentage of animals with tumors is affected less often.[13,14,15,16,17,18] On the other hand, despite the low rates of breast cancer death rates in Asia, there is little evidence supporting that adult soy intake reduces postmenopausal risk of breast cancer. There does exist some evidence for a protective effect against breast cancer in premenopausal women.[19]

Clinical studies in humans, mostly look at markers associated with lower rates of breast cancer risk such as lengthening the menstrual cycle, and improved metabolism of estrogens with increased protective urinary estrogen metabolites.[20] Two studies have suggested that soy may have estrogen-like effects on breast tissue, although this does not mean it increases the risk of breast cancer. One showing association of 80 mg of isoflavones with an increase in breast nipple aspirate fluid and breast cell hyperplasia in premenopausal women.[21] In the second, biopsies in premenopausal women who had

consumed 60 gm of testured soy protein with 45 mg of isoflavones for 2 weeks, found that the expression of one protein pS2 was up-regulated and another apolipoprotein D was down –regulated, similar to the effects of estrogen. However, reassuringly, there was no effect of soy on hormone receptor status, cell division or cell proliferation. Even more comforting is that two recent laboratory studies showed that in contrast to estrogen/progestin hormone replacement therapy, soy isoflavones do not increase breast tissue density.[22]

The clearest data shows that in animal studies and in women, a diet higher in soy in earlier in life can clearly reduce the risk of breast cancer later in life. One study showed that Chinese women who consumed an average of 11 gm of soy protein per day during their teenage years were 50% less likely to develop breast cancer.[23] In the other study of Asian Americans, soy intake reduced breast cancer risk by 35% in women who consumed soy throughout their lifetime but was not protective in women only consuming soy during their adult years.[24] The most reassuring part of all is that no studies show that eating soy can increase the risk of breast cancer.

Soy in Breast Cancer Survivors

What is confusing is what to do if you are a breast cancer survivor. Most the evidence points to the safety of soy, even for those women who have had breast cancer, however one can find some conflicting reports in some of the animal and laboratory research. Some of the contradictory reports have to due with maybe an estrogen-like effect at lower concentrations of genistein when exposed to estrogen receptor positive cells (but not estrogen receptor negative cells), but an anti-estrogenic effect on breast cancer cells at higher doses.[25],[26],[27]

There are many important mechanisms by which soy foods would appear to lower the risk of breast cancer. Women who are given high soy diets have lower blood levels of estrogen. Soy foods also contain antioxidants and enzyme inhibitors that can inhibit malignant cell formation and division. The genistein in soy also is anti-angiogenic which means that it can limit the blood supply to a tumor. However, for those women on Tamoxifen, soy should be avoided. The reason is that there has been conflicting research: some show that soy interferes with the anti-estrogenic effect of estrogen and others show that soy augments the anti-estrogenic effect of Tamoxifen in women with ER + breast cancers. I would add that women who are on aromatase inhibitors should also avoid soy until we have further information. The most respected expert researchers on soy, advise breast cancer patients (who are not on Tamoxifen), that a moderate amount of soy in the diet that is consistent with the Asian diet is probably safe.

I know that there is much information out there on the pros and cons of soy and not all of it is either accurate or helpful, let alone conflicting. I encourage women to look for reliable sources of information with scientific citations and resources. The best review of the scientific literature I have seen on the subject can be found in the Journal of Nutrition 2008; 7:17. Authors Mark Messina and Charles Wood.

[1] Arjmandi B, Smith B. Soy isoflavones' osteoprotective role in postmenopausal women: mechanism of action. J Nutr Biochem 2002; 13:130-137.
[2] Messina M, Gugger E, Alekel D. Soy protein, soybean isoflavones, and bone health: a review of the animal and human data, in Wildman R (ed): Handbook of Nutraceuticals and Functional Foods. Boca Raton, CRC Press LLC 2001;pp 77-98.
[3] Upmalis D, Lobo R, Bradley L, et al. Vasomotor symptom relief by soy isoflavone extract tablets in postmenopausal women: a multicenter, double-blind, randomized, placebo-controlled study. Menopause 2000;7:236-242.
[4] Duncan Am Underhill K, Xu X, et al. Modest hormonal effects of soy isoflavones in postmenopausal women. J Clin Endocrinol Metab 1999;4:3479-84.
[5] Anderson J, Johnstone B, Cook Newell M. Meta-analysis of the effects of soy protein intake on serum lipids. N Engl J Med 1995;333:276-282.
[6] Weber G, Shen F, Yang H, et al. Regulation of signal transduction activity in normal and cancer cells. Anti-cancer Res 1999;19:3703-3709.
[7] Ford D. Mechanistic explanations for the chemopreventive action of soyabean isoflavones: reducing the possibilities. Br J Nutr 2002;88:439-441.
[8] Upadhyay S, Neburi M, Chinni S, et al. Differential sensitivity of normal and malignant breast epithelial cells to genistein is partly mediated by p21 (WAD1). Clin Cancer Res 2001;7:1782-1789.
[9] Constantinou A, Kiguchi K, Huberman E. Induction of differentiation and DNA strand breakage in human HL-60 and K-562 leukemia cells by genistein. Cancer Res 1990;50:2618-2624.
[10] Kim H, Peterson T, Barnes s. Mechanisms of action of the soy isoflavone genistein: emerging role for its effects via transforming growth factor beta signaling pathways. Am J Clin Nutr 198;68:1418S-1425S.
[11] Barnes S, Grubbs C, Setchell K, et al. Soybeans inhibit mammary tumors in models of breast cancer. Prog Clin Biol Res 1990;347:239-253.
[12] Pisani P, Parkin D, Bray F, Ferlay J. Estimates of the worldwide mortality from 25 cancers in 1990. Int J Cancer 1999;83:18-29.
[13] Barnes S, Grubbs C, Setchell K, et al. Soybeans inhibit mammary tumors in models of breast cancer. Prog Clin Biol Res 1990;347:239-253.
[14] Hakkak R, Korourian S, Shelnutt S, et al. Diets containing whey proteins or soy protein isolate protect against 7,12-dimethylbenz(a)anthracene-induced mammary tumors in female ratrs. Cancer Epidemiol Biomarkers Prev 2000;9:113-7.
[15] Gotoh T, Yamada K, Yin H, et al. Chemoprevention of N-nitroso-N-methylurea-induced rat mammary carcinogenesis by soy foods or biochanin A. Jpn J Cancer Res 1998;89:137-42.
[16] Hawrylewicz E, Huang H, Blair W. Dietary soybean isolate and methionine supplementation affect mammary tumor progression in rats. J Nutr 1991;121:1693-8.
[17] Baggott J, Ha T, Vaughn W, et al. Effect of miso (Japanese soybean paste) and NaCl on DMBA-induced rat mammary tumors. Nutr Cancer 1990;14:103-9.
[18] Ohta T, Nakatsugi S, Watanabe K, et al. Inhibitory effects of Bifidobacterium-fermented soy milk on 2-amino-1-methyl-6-phenylimidazo (4,5-b) pyridine-induced rat mammary carcinogenesis, with a partial contribution of its component isoflavones. Carcinogenesis 2000;21:937-41.
[19] Peeters P, Keinan Boker L, van der Schouw Y, Grobbee D. Phytoestrogens and breast cancer risk: review of the epidemiological evidence. IARC Sci Publ 2002;156:331-6.
[20] Kurzer M. Hormonal effects of soy in premenopausal women and men. J Nutr 2002;132:570S-3S.
[21] Petrakis N, Barnes S, King E, et al. Stimulatory influence of soy protein isolate on breast secretion in pre and postmenopausal women. Cancer Epidemiol Biomarkers Prev 1996; 5:785-94.

[22] Laya M, Gallagher J, Schreiman J, et al. Effect of postmenopausal hormonal replacement therapy on mammographic density and parenchymal pattern. Radiology 1995;196:433-437.
[23] Shu X, Jin F, Dai Q, et al. Soyfood intake during adolescence and subsequent risk of breast cancer among Chinese women. Cancer Epidemiol Biomarkers Prev 2001;10:483-488.
[24] Wu A, Wan P, Hankin J, et al: Adolescent and adult soy intake and risk of breast cancer in Asian-Americans. Carcinogenesis 2002;23:1491-1496.
[25] Wang T, Sathyamoorthy N, Phang J. Molecular effects of genistein on estrogen receptor mediated pathways. Carcinogenesis 1996;17:271-275.
[26] Hsieh C, Santell R, Haslam S, Helferich W. Estrogenic effects of genistein on the growth of estrogen receptor-positive human breast cancer (MCF-7) cells in vitro and in vivo. Cancer Res 1998;58:3833-3838.
[27] Zava D, Duwe G. Estrogenic and antiproliferative properties of genistein and other flavonoids in human breast cancer cells in vitro. Nutr Cancer 1997;27:31-40.