

## Breast Cancer Prevention: A Top 10 List

### NUTRITION AND LIFESTYLE STEPS ALL WOMEN SHOULD KNOW

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In 1996, Dr. Walter Willett of Harvard University authored a report in the *Journal of The National Cancer Institute* stating that after reviewing the worldwide evidence, approximately 50 percent of breast cancer cases could be avoided if women in North America engaged in more prudent nutrition and lifestyle practices. It has been shown consistently that having a full-term pregnancy and breastfeeding before age 30 reduces a woman's lifetime risk of breast cancer by 25 percent to 30 percent, and that another 20 percent to 25 percent of breast cancer cases are linked to a strong family history (genetic risk factors). However, the remaining 50 percent of breast cancer cases are strongly linked to faulty nutrition patterns, excess body fat and insufficient exercise, according to numerous investigative studies on this subject.<sup>1,2</sup>

During the past 10 to 12 years, compelling evidence has emerged from research investigations, which identify the most important dietary and lifestyle strategies women should consider to reduce their risk of breast cancer. According to the available research, the following represents the 10 most important steps women should consider in this regard:

1. Don't eat high-fat animal foods (except fish) - Eating less red meat, pork, milk and yogurt products higher than 1 percent milk fat, cheeses above 3 percent milk fat, whole milk, butter, ice cream, cream, whipped cream and the like, is the first vital step in reducing breast cancer risk. These foods are not only high in saturated fat, which can overstimulate production of estrogen, but they also contain a polyunsaturated fat known as AA (arachidonic acid). Breast tissue converts AA into local mini-hormones (eicosanoids) that increase the cell replication rate of breast cells. When breast cells divide too quickly, they are inclined to make genetic errors that lead to breast cancer development. This is how hormone replacement therapy increases the risk of breast cancer (by speeding up the cell replication rate).

Follow-up studies on humans and numerous animal studies show that higher breast tissue concentrations of AA increase the risk of future onset of breast cancer. Overall, the goal is to slow down the rate of breast cell replication. When you do that, cancer is less likely to develop. Eating less high-fat animal foods is an important first step, as is remaining at your ideal weight and exercising, as we shall touch on next. Thus, if becoming a vegetarian is out of the question (vegetarians have low rates of breast cancer), it is best to derive your protein from chicken and turkey breast (skinless), Cornish hen, fish, soy products, peas and beans, egg whites, nonfat yogurt and milk (or 1 percent) and cheese that is less than 4 percent milk fat.<sup>3,4,5,6</sup>

2. Stay lean - It is a medical fact that women who are overweight after menopause have a three times greater incidence of breast cancer than women who are at their ideal weight. Studies, such as the New York University Women's Health Study, indicate that as women become fatter, they increase production of estrone hormone (a potent form of estrogen) in their fat tissues. The higher circulating levels of estrone in the body of an overweight woman overstimulate breast cells, leading to more rapid cell replication. As I said, faster cell replication rates increase the risk of breast cancer development. Not only that, but should breast cancer develop, breast cancer cells convert

estrone hormone into an even more potent estrogen, known as estradiol, which bolsters the ability of breast cancer cells to form masses and more readily metastasize to other areas of the body. The message is clear and simple - attain and maintain your ideal body weight. Very conveniently, giving up foods high in animal fat will help you get leaner, as will performing 30 minutes of endurance exercise, five times per week, which I will examine next.<sup>7,8,9</sup>

3. Perform a minimum of 30 minutes of endurance exercise, five times per week - Numerous studies indicate that women who are more active have a lower incidence of breast cancer. Endurance exercise is extremely useful because it burns fat, making fat cells smaller. When fat cells are smaller, they make less estrone hormone and thus, are less likely to overstimulate breast cells. This effect slows down the rate of replication of breast cells, which translates into a lower risk for breast cancer. As well, jogging, power walking, cycling and all other aerobic exercises speed up circulation of blood through the liver, enabling detoxification enzymes (which reside in the liver) to neutralize and remove excess estrogen from the circulation. In turn, this helps to keep female hormones in balance, which ultimately helps regulate the breast cell replication rate.<sup>10,11</sup>

4. Take a high-potency multiple vitamin containing vitamin E succinate and vitamin D - Investigative studies show that vitamin E succinate has important anti-cancer properties in regard to breast cancer. Vitamin E succinate has been shown to encourage certain types of human breast cancer cells to commit suicide by stimulating action of the cell's death receptors (*fas*-receptors). Vitamin E succinate also disrupts other signals within breast cancer cells, which inhibit cell replication and inhibit breast cancer cells from forming blood vessels to feed themselves. All of these effects are associated with decreased risk of breast cancer development. Overall, in all experimental and animal studies performed to date, only vitamin E in the form of vitamin E succinate has demonstrated these powerful inhibitory effects against breast cancer (and other cancers).

As for vitamin D, human observation studies indicate that women with vitamin D blood levels above 85 nmol/L have a lower risk of developing breast cancer. We know that breast cells extract vitamin D from the bloodstream, which in turn, slows down the rate of breast cell replication. Vitamin D also encourages breast cells to fully mature as they divide from one generation to the next. Fully mature cells are less prone to becoming cancer cells than are less mature-looking cells. As such, vitamin D is now regarded as a very important anti-cancer vitamin, in addition to its role in preventing osteoporosis. Most women do not achieve the vitamin D intake levels required each day to protect themselves from breast cancer and osteoporosis. Therefore, it is very prudent to take a high-potency multiple vitamin and mineral supplement each day that provides 400 IU of vitamin D along with 400 IU of vitamin E succinate.<sup>12-20</sup>

5. Drink less alcohol and get a B-50 complex as part of your high-potency multiple vitamin/mineral supplement -The Nurses' Health Study, along with other compelling evidence, indicates that women who consume more than one alcoholic drink each day, on average, double their risk of breast cancer (and colon cancer). Alcohol is known to generate free radicals that can lead to genetic mutations, which trigger cancer development. The body appears to have a capacity to handle only one alcoholic drink in any 24-hour period before risk begins for cancer and other problems. As such, the National Cancer Institute states that alcohol consumption is the second most important environmental cause of cancer in our society after cigarette smoking. Alcohol also depletes the body of folic acid, which is a B vitamin required for our DNA to replace itself when cells are undergoing replication.

In a state of suboptimal folic acid status, our DNA tends to be fragile and cancer cells form more easily when cells replace themselves from one generation to the next. Even the Nurses' Health

Study showed that higher intakes of folic acid could reduce, to some degree, the cancer-causing effects of alcohol, in women who took a B vitamin supplement each day. As many of the B vitamins work together in the body, it is wise to take a B-50 complex as part of your daily multiple vitamin and mineral supplement. This advice, along with consuming no more than one alcoholic drink a day, is also important as a preventive measure against breast cancer.<sup>21-24</sup>

6. Take a supplement containing fish oil, flaxseed oil and borage seed oil and eat fish twice a week - Fish and fish oil supplements contain an omega-3 fat that breast cells convert into a mini-hormone that slows down the rate of cell replication. Women with higher levels of this omega-3 fat in their breast cells (as well as the omega-3 fat that is richly supplied by flaxseed oil - alpha-linolenic acid) have been shown to have a significantly lower risk for future development of breast cancer, compared to women with lower breast levels of these omega-3 fats. Studies also show that the higher your ingestion of omega-3 fats, the higher your breast tissue levels of these fats, as well as the health-promoting mini-hormones your breast cells make from these fats. Borage seed oil contains a unique omega-6 fat that helps the body block the formation of mini-hormones made from AA (as discussed above). Thus, higher breast-cell levels of fish oil, flaxseed oil and borage oil help to counter the adverse effects of the AA derived from high-fat animal foods. The ultimate strategy is eating less high-fat animal foods while consuming two to three servings of fish each week and taking a supplement each day that contains 400 mg each of fish oil, flaxseed oil and borage seed oil (two to three capsules per day for optimal effects).<sup>5,25,26,27</sup>

7. Consume cruciferous vegetables and indole-3-carbinols daily - Studies demonstrate that women who consume cruciferous vegetables (broccoli, brussels sprouts, cabbage, cauliflower, bok choy) on a regular basis have a lower incidence of breast cancer. Cruciferous vegetables contain a unique molecule called the indole-3-carbinol, which enhances the ability of the body to detoxify cancer-causing agents. Indole-3-carbinol also stimulates enzymes that convert estrogen into a safer form of estrogen (more 2-hydroxy estrone and less 16-hydroxy estrone), which is associated with a lower risk of breast cancer. As such, it is prudent to consume at least one serving per day of a cruciferous vegetable. Some women prefer to consume a supplement each day of indole-3-carbinol, along with milk thistle. Milk thistle also enhances detoxification enzyme activity and supports liver function and immune-boosting agents (reishi mushroom extract and astragalus).<sup>28-32</sup>

8. Consider supplementation with curcumin and other natural anti-inflammatory agents - In recent years, we have recognized that as much as 40 percent of breast cancer occurs in women who, for genetic reasons, express an abnormally high number of receptors on the surface of their breast cells known as epidermal growth-factor receptors. There are four types of receptors in the family of epidermal growth-factor receptors and women who are genetically prone to breast cancer tend to overexpress the type-2 epidermal growth-factor receptor, usually referred to as ErbB2. This receptor (ErbB2) sends continuous messages to the interior of the breast cell, instructing the cell to replicate on an on going basis, speeding up replication and increasing the risk of cancer.

As such, medical science has been looking for a drug or chemical agent that could inhibit the firing of the ErbB2 receptor and thus slow down the breast cell replication rate. In recent years, medical science has produced a drug (a monoclonal antibody) called Herceptin, which is now used in some cases of breast cancer treatment. However, the drug has unpleasant side effects and cannot be used on a preventive basis. Interestingly, the natural agent called curcumin (derived from the spice turmeric) has been shown to silence the ErbB2 receptor without causing side effects. A recent study with colon cancer patients showed that curcumin supplementation reduced the recurrence of colon cancer in this high-risk population. In this type of colon cancer, epidermal growth-factor receptors are also over expressed and contribute to constant signaling that leads to rapid cell

replication and cancer development. Experimental studies suggest that curcumin may help silence ErbB2 breast receptors as well. In addition, supplementation with the natural anti-inflammatories white willow-bark extract, boswellia and ginger helps the body block the conversion of AA into mini-hormones that cause rapid cell replication. This is how aspirin is related to lower risk of breast, colon and prostate cancers. However, aspirin causes intestinal-tract bleeding and ulcers and thus, cannot be recommended as a cancer- preventive strategy. Many holistic doctors recommend supplementation with a combination product containing curcumin, white willow extract, boswellia and ginger. These four natural agents work synergistically to help regulate epidermal growth-factor receptors and block the production of mini-hormones involved in rapid cell division at the tissue level.<sup>33-49</sup>

9. Take two heaping tablespoons of ground flaxseed each day - Ground flaxseed contains 800 times more of the raw material from which the body makes two important phytoestrogens (enterolactone and enterodiol) than any other food source. Enterolactone (ENL) and enterodiol (EDL) have been shown to slow down the rate of breast cell replication by competing with the body's potent estrogens for entry into breast cells, inhibiting enzymes that produce highly potent estrogens and inhibiting enzymes directly involved in cell replication. Human studies demonstrate that 50 gm of ground flaxseed per day can reverse fibrocystic breast disease and reduce firing of the ErbB2 receptor that is associated with breast cancer development and progression. All indicators suggest that two heaping tablespoons of ground flaxseed per day (e.g., sprinkled onto cereal, mixed into yogurt, or mixed into juice or a protein shake) is an exceptional way to help control regulatory mechanisms at the cellular level that are associated with reducing breast cancer risk.<sup>50-59</sup>

10. Eat at least one serving of a soy food each day - Although there is controversy about soy and breast cancer, the evidence is quite convincing that consuming soy foods provides significant protection against reproductive organ cancers in women and men. To start with, breast cancer rates are 75 percent lower in countries where soy foods are a main staple of the daily diet. Experimental evidence indicates that soy isoflavones (phytoestrogens) exhibit a number of anti-cancer properties, some of which include reducing the effects of more potent estrogens, inhibiting enzymes that are directly related to rapid cell division, and enhancing the conversion of potent estrogens to less potent estrogens, all of which slow down the rate of breast cell replication - a major factor in reducing breast cancer development. Most recently, a study involving breast cancer patients showed that providing them with 200 mg per day of soy isoflavones (as a supplement) helped to shrink the tumors (increased the apoptosis to mitosis ratio), while the patients were awaiting surgery. In my view, women should consume at least one generous serving per day of a soy food (soy milk, tofu, soy nuts, etc.) as a means to derive the health-promoting benefits of soy isoflavones and other constituents found exclusively in soy foods.<sup>60-67</sup>

My suggestion is that you speak to your health practitioner about the appropriateness of these strategies in your individual case and seek their guidance as to how to access supplements that meet the requirements outlined in this review.

## References

1. Willet W. Estimates of cancer deaths avoidable by dietary change. *J Natl Cancer Inst*, 1996;86(14):948.
2. Simone B. *Cancer and Nutrition*. Avery Publishing Group, Inc., 1992:219-23.
3. Rose DP. Dietary fatty acids and cancer. *Am J Clin Utr*, 1997;66(suppl.):998S-1003S.
4. Carroll KK. Experimental evidence of dietary factors and hormone-dependent cancers. *Cancer Res*, 1975;35:3374-83.
5. Pala V, Valeria V, Muti P, et al. Erythrocyte membrane fatty acids and subsequent breast

- cancer: a prospective Italian study. *J Natl Cancer Inst*, July 18, 2001; 93:1088-95.
6. Dwyer JT. Health aspects of vegetarian diets. *Am J Clin Nutr*, 1988;48:712-38.
  7. Toniolo G, Levitz M, Zeleniuch-Jacquotte A, et al. A prospective study of endogenous estrogens and breast cancer in postmenopausal women. *J Natl Cancer Inst*, 1995;87(3):190-9.
  8. Lew EA, Garfinkel L. The American Cancer Society Study. Variations in mortality by weight among 750,000 men and women. *J Chronic Dis*, 1979;32:563-76.
  9. Tannenbaum A. The relationship of body weight to cancer incidence. *Arch Pathol*, 1940;30:509.
  10. Sprague BL, Trentham-Dietz A, Newcomb PA, et al. Lifetime recreational and occupational physical activity and risk of in situ and invasive breast cancer. *Cancer Epidemiol Biomarkers Prev*, 2007;16:236-43.
  11. Steege JF, Blumenthal JA. The effects of aerobic exercise on premenstrual symptoms in middle-aged women: a preliminary study. *J Psychosom Res*, 1993;37(2):127-33.
  12. Malafa MP, Neitzel LT. Vitamin E succinate promotes breast cancer dormancy. *J Surg Res*, 2000;93(1):163-70.
  13. Fang X, Birringer M, Dong L, et al. A peptide conjugate of vitamin E succinate targets breast cancer cells with high ErbB2 expression. *Cancer Research*, 2007;67:33373344.
  14. Yu W, Israel K, Liao Q, et al. Vitamin E succinate (VES) induces Fas sensitivity in human breast cancer cells. *Cancer Research*, 1999;59:953-61.
  15. Garland CF, Garland FC, Gorham ED. Can colon cancer incidence and death rates be reduced with calcium and vitamin D? *Am J Clin Nutr*, 1991;54(Suppl. 1):193S-201S.
  16. Garland CF, Garland FC, Gorham ED. Calcium and vitamin D. Their potential roles in colon and breast cancer prevention. *Ann NY Acad Sci*, 1999;889:107-19.
  17. Garland FC, Garland CF, Gorham ED, Young JF. Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation. *Prev Med*, 1970;19:614-22.
  18. Schmidt J, Wittenhagen P, Harder M. Molecular effects of vitamin D on cell cycle and oncogenesis. *Ugeskrift for laeger*, July 20, 1998;160(30):4411-4.
  19. Lappe JM, Travers-Gustafson D, Davies KM, et al. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. *Am J Clin Nutr*, 2007;85:1586-91.
  20. Longnecker M. Alcoholic beverage consumption in relation to risk of breast cancer: meta-analysis and review. *Cancer Causes Control*, 1994;5(1):73-82.
  21. Smith-Warner SA, Spiegelman D, Yaun SS, et al. Alcohol and breast cancer in women: a pooled analysis of cohort studies. *JAMA*, 1998;279(7):535-40.
  22. Giovannucci E, Stampfer MJ, Colditz GA, et al. Folate, methionine, and alcohol intake and risk of colorectal adenoma. *J Natl Cancer Inst*, 1993;85(11):875-83.
  23. Goelez SE, Vogelstein B, Hamilton SR, et al. Hypomethylation of DNA from benign and malignant human colon neoplasms. *Science*, 1985;228:187-90.
  24. Yee LD, Young DC, Rosol TJ, et al. Dietary (n-3) polyunsaturated fatty acids inhibit HER-2/neu-induced breast cancer in mice independently of the PPAR gamma ligand rosiglitazone. *J Nutr*, 2005;135:983-8.
  25. Bougnoux P, Koscielny S, Chajes V, et al. Alpha-linolenic acid content of adipose breast tissue: a host determinant of the risk of early metastasis in breast cancer. *Br J Cancer*, 1994;70:330-4.
  26. Fan, Yang-Yi, Chapkin RS. Importance of dietary gamma-linolenic acid in human health and nutrition. *J Nutr*, 1998;128(9):1411-4.
  27. Hecht SS. Chemoprevention of cancer by isothiocyanates, modifiers of carcinogen metabolism. *J Nutr*, 1999;129:7688-74S.
  28. Verhoeven DT, Goldbohm RA, van Poppel G, et al. A review of mechanisms underlying anticarcinogenicity by brassica vegetables. *Chem Biol Interact*, 1997;103:79-129[review].
  29. Beecher CW. Cancer preventive properties of varieties of Brassica oleracea: a review. *Am J Clin Nutr*, May 1994;59(5 suppl.):1166S-70S.

30. Osborne MP, et al. Increase in the extent of estradiol 16 alpha-hydroxylation in human breast tissue: A potential biomarker of breast cancer risk. *J Natl Cancer Inst*, 1993;85:1917-20.
31. Michnovicz JJ. Increased estrogen 2-hydroxylation in obese women using oral indole-3-carbinol. *Int J Obes Relat Metab Disord*, 1998;22:227-9.
32. Reddy S, Rishi AK, Xu H, et al. Mechanisms of curcumin-and EGF-receptor related protein (ERRP) - dependent growth inhibition on colon cancer cells. *Am J Clin Nutr*, 2006;55(2):185-94.
33. Ciardiello F, Caputo R, Bianco R. Antitumor effect and potentiation of cytotoxic drugs activity in human cancer cells by ZD-1839 (Iressa), an epidermal growth factor receptor-selective tyrosine kinase inhibitor. *Clin Cancer Res*, May 2000;6:2053-63.
34. Ciardiello F, Tortora G. Interactions between the epidermal growth factor receptor and type I protein kinase A: biological significance and therapeutic implications. *Clin Cancer Res*, 1998;4(4):821-8.
35. Al-Achi A. Anti-inflammatory herbs. *U.S. Pharmacist*. 29:03 (Posted 03/15/2004).
36. Satoskar RR, Shah SJ, Shenoy SG.. Evaluation of anti-inflammatory property of curcumin in patients with post-operative inflammation. *Int J Clin Pharmacol Ther Toxicol*, 1986;24:651-4.
37. Murray MT. *The Healing Power of Herbs*. Rocklin, Calif.: Prima Publishing, 1995:327-35.
38. Arora RB, Kapoor V, Basu N, Jain AP. Anti-inflammatory studies on curcuma longa (turmeric). *Ind J MedRes*, 1971;50:1289-95.
39. Heck A, DeWitt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. *Am J Health-Syst Phar*, 2000;57(13):1221-7.
40. Schweizer S, von Brocke AF, Boden SE, et al. Workup-dependent formation of 5-lipoxygenase inhibitory boswellic acids analogues. *J Nat Prod*, Aug. 2000;63(8):1058-61.
41. Etzel R. Special extract of boswellia serrata (H15) in the treatment of rheumatoid arthritis. *Phytomed*, 1996;3:91-4.
42. Bradley PR, Ed. *British Herbal Compendium, Vol. 1*. Bournemouth, UK: British Herbal Med Assoc, 1992:224-6.
43. Mills SY, Jacoby RK, Chacksfield M, Willoughby M. Effects of a proprietary herbal medicine on the relief of chronic arthritic pain: a double-blind study. *Br J Rheum*, 1996;35:874-8.
44. Chrubasik S, Eisenberg E, Balan E, et al. Treatment of low back pain exacerbations with willow bark extract: a randomized double-blind study. *Am J Med*, 2000;109(1):9-14.
45. Srivastava KC, Mustafa T. Ginger in rheumatism and musculoskeletal disorders. *Med Hypotheses*, 1992;39:342-8.
46. Bliddal H, Rosetzky A, Schlichting P, et al. A randomized placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis, osteoarthritis cartilage. *Osteoarthritis Cartilage* Jan 2000;8(1):9-12.
47. García-Mediavilla V, Crespo I, Collado PS, et al. The anti-inflammatory flavones quercetin and kaempferol cause inhibition of inducible nitric oxide synthase, cyclooxygenase-2 and reactive C-protein, and down-regulation of the nuclear factor kappa-B pathway in Chang Liver cells. *Eur J Pharmacol*, 557;2-3:221-9.
48. Steele VE, Holmes CA, Hawk ET, et al. Lipoxygenase inhibitors as potential cancer chemopreventives. *Cancer Epidemiol Biomarkers Prev*, 1999;8:467-4893.
49. Jacobs EJ, Thun MJ, Bain EB, et al. A large cohort study of long-term daily use of adult-strength aspirin and cancer incidence. *J Natl Cancer Inst*, 2007;99(8):608-15.
50. Nesbitt PD, Lam Y, Thompson LU. Human metabolism of mammalian lignan precursors in raw and processed flaxseed. *Am J Clin Nutr*, 1995;69(3):549-55.
51. Huthcins AM, Martini MC, Olson BA, et al. Flaxseed influences urinary lignan excretion in a dose-dependent manner in postmenopausal women. *Cancer Epidemiol Biomarkers Prev*, 2000;9(10):1113-8.
52. Tham DM, Gardner CD, Haskell WL. Clinical Review 97: Potential health benefits of dietary phytoestrogens: A review of the clinical, epidemiological, and mechanistic evidence. *J Clin Endocrinol Metab*, 1998;83(7):2223-35.
53. Zeigler J. Just the flax, Ma'am: Researchers testing linseed. *J Natl Cancer Inst*,

1994;86(23):1746-8.

54. Brzzinski A, Debi A. Phytoestrogens: the natural selective estrogen receptor modulators? *Eur J Obstet Gynecol Reprod Biol*, 1999;85(1):47-51.
55. Tou JC, Thompson LU. Exposure to flaxseed or its lignan component during different developmental stages influences rat mammary gland structures. *Carcinogenesis*, 1999;20(9):1831-5.
56. Haggans CJ, Hutchins AM, Olson BA, et al. Effect of flaxseed consumption on urinary estrogen metabolites in postmenopausal women. *Nutr Cancer*, 1999;33(2):188-95.
57. Haggans CJ, Travelli EJ, Thomas W, et al. The effect of flaxseed and wheat bran consumption on urinary estrogen metabolism in premenopausal women. *Cancer Epidemiol Biomarkers Prev*, 2000;9(7):719-25.
58. Thompson LU, Seidl MM, Rickard SE, et al. Antitumorigenic effect of mammalian lignan precursor from flaxseed. *Nutr Cancer*, 1996;26:159-65.
59. Gross PE, et al. Effect of dietary flaxseed in women with cyclical mastalgia. Program and abstract of the 23rd Annual San Antonio Breast Cancer Symposium. Dec 6-9 2000; San Antonio Texas. Abstract 153. *Breast Cancer Res Treat*, 2000;64:49.
60. Muir C, Waterhouse J, Mack T, et al. *Cancer Incidence in Five Continents. Vol. 5*. Lyon, France: International Agency for Research on Cancer, 1987. (IARC Scientific publication no. 88).
61. Coward L, Barnes NC, Setchell KDR, Barnes S. The isoflavones genistein and daidzein in soy bean foods from American and Asian diets. *J Agric Food Chem*, 1993;41:1961-7.
62. Barnes S, Grubbs C, Setchell KDR, Carlson J. Soybeans inhibit mammary tumor growth in models of breast cancer. In: Pariza MW, ed. *Mutagens and Carcinogens in the Diet*. New York: Wiley-Liss, 1990:239-53.
63. Cassidy A, Bingham S, Setchell KD. Biological effects of a diet of soy protein rich in isoflavones on the menstrual cycle of premenopausal women. *Am J Clin Nutr*, 1994;60:333-40.
64. Molteni A, Brizio-Molteni L, Persky V. In vitro hormonal effects of soybean isoflavones. 1995. *J Nutr*, 1995;125(suppl.):751S-6S.
65. Chen X, Anderson JJ. Isoflavones inhibit proliferation of ovarian cancer cells in vitro via an estrogen receptor-dependent pathway. *Nutr Cancer*, 2001;41(1&2):165-71.
66. Constantinou AI, Lantvit D, Hawthorne M, et al. Chemopreventive effects of soy protein and purified isoflavones on DMBA-induced mammary tumors in female Sprague-Dawley rats. *Nutr Cancer*, 2001;41(1&2):75-81.
67. Sartippour MR, Rao JY, Apple S, et al. A pilot clinical study of short-term isoflavone supplements in breast cancer patients. *Nutr Cancer*, 2004;49(1):59-65.

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