

Soy and Your Health: Dispelling the Myths – Part Two

By Mark Messina, Ph.D.

Soy foods have been a part of Asian diets for centuries. Today, there is a growing interest in these foods among westerners because of their proposed health benefits and also because their versatility makes them valuable for replacing meat and dairy foods in the diet. Nevertheless, the role of soy foods in a healthy diet has become somewhat of a confusing issue in recent years because of concerns that these foods may exert adverse effects in some individuals. However, concerns about soy foods are based almost entirely on the results from studies involving rodents. Results from rodent studies often don't predict effects in humans. Furthermore, because rodents metabolize soy much differently than humans, they aren't particularly useful models for learning about the effects of soy foods.¹

Importantly, the human data are supportive of the safety and benefits of soy foods. With the exception of those allergic to soy protein, which is relatively rare, all healthy individuals can safely consume soy foods. Much of the concern about soy is based on the estrogen-like effects of isoflavones, a group of naturally occurring plant chemicals that are found in large amounts in soybeans.

Soy Isoflavones

Interest in the health benefits of soy foods—as well as some of the controversy surrounding these products—is, to a large extent, related to their isoflavone content. These compounds are essentially unique to soy foods; no other commonly consumed foods contain enough to impact health.² Although isoflavones are among a group of naturally occurring compounds known as phytoestrogens (plant estrogens), they're much different from the hormone estrogen. In fact, isoflavones are most accurately classified as SERMs (selective estrogen receptor modulators).³ Other examples of SERMs are the breast cancer drug tamoxifen and the breast cancer and osteoporosis drug raloxifene. The effects of SERMs vary depending upon a variety of circumstances. SERMs, like isoflavones, may have estrogen-like effects but, depending on a number of factors, they may also have effects opposite to those of estrogen or no effects at all in tissues that are affected by estrogen. Therefore, looking at the health effects of estrogen doesn't provide much information about how isoflavones act. The only way to learn about the effects of isoflavones is to look directly at their biological activity in studies.

Soy Foods and Breast Cancer

For more than 20 years, the U.S. National Cancer Institute and laboratories throughout the world have been rigorously investigating the role of soy in breast cancer prevention. However, in recent years, concerns have arisen that, because they contain isoflavones, soy foods may worsen the prognosis of women with a history of breast cancer and increase risk of breast cancer in women at high risk of developing this disease. These concerns are based on research in one particular type of mouse.⁴

In contrast to the animal research, human research is supportive not only of safety but also of potential benefit. For example, in clinical studies, when female subjects are given either soy foods or the isoflavones from soy foods, there is no effect on indicators of breast cancer risk, such as breast tissue density or breast cell proliferation.⁵⁻⁸ In contrast to isoflavones, hormone therapy, which increases breast cancer risk, increases breast tissue density and breast cell proliferation.

Furthermore, recently published studies from China⁹ and the United States¹⁰ show that soy consumption after a diagnosis of breast cancer reduces recurrence and improves survival. Women in these studies reported their soy consumption and were followed for several years so investigators could determine whether, during this time, soy consumers were more or less likely to have a recurrence or die from their disease. The benefits observed in these studies were associated with the consumption of one to two servings of soy foods per day. According to the investigators of the most recently published study, "...clinicians no longer need to advise against soy consumption for women diagnosed with breast cancer."¹⁰ Nevertheless, it is advisable for women with a history of breast cancer to first discuss adding soy to their diets with their health care providers.

Soy Foods and Male Reproduction

The estrogen-like effects of isoflavones have led to concerns that soy foods may exert feminizing effects in men, but a wealth of human data show these concerns to be without merit. Although two reports published in the scientific literature describe feminizing effects of soy in two individuals, these men consumed as many as 14 to 20 servings per day.^{11,12} Excessive intake of nearly any food can be expected to have negative effects on health.

In contrast to these two reports, a comprehensive analysis of the human data, which involved more than 30 individual studies, found that neither soy foods nor isoflavones affect levels of the male sex hormone testosterone.¹³ In many of these studies, soy intake was far beyond what is typical for Asian men, so the lack of effect is very reassuring. In addition, a recent review of nine studies found that soy has no effect on estrogen levels in men.¹⁴ Men in these studies consumed as much as six servings of soy per day. The clinical studies also show there is no effect of soy on sperm or semen. In fact, there is one report describing a male with low sperm count whose sperm concentration normalized after taking isoflavones for 6 months.¹⁵ Thus, the evidence clearly shows that soy foods do not exert feminizing effects.

Thyroid Function

Although soy isoflavones can interfere with thyroid function in laboratory animals, they have no effect on thyroid activity in healthy people. More than 20 studies have examined thyroid function in response to the consumption of soy foods, soy protein, or isoflavones.¹⁶ One limitation of this research is that most of the studies were conducted for six months or less. However, recently, two three-year studies found no effects of large amounts of soy on thyroid function.¹⁷ As a result, the evidence overwhelmingly supports the safety of soy. In people who need to take synthetic thyroid hormone, soy foods are among many foods that can reduce absorption of this medication. However, these individuals can safely consume soy foods as long as they are consistent in the daily amounts of soy in their diet.¹⁸

Finally, approximately 5% to 10% of the population has subclinical hypothyroidism, which can progress to hypothyroidism (low thyroid function) over time. A small number of these people may be sensitive to soy foods and, therefore, they should be monitored by their physician if they begin consuming soy.¹⁹ However, even in these individuals, evidence indicates that consuming soy foods may markedly lower risk for chronic diseases such as diabetes and heart disease. In one study involving subclinical hypothyroid patients, soy protein dramatically reduced blood pressure and levels of inflammation, and increased the ability of the subjects to use the hormone insulin.

Cognitive Function

Nutrition epidemiologic studies record the dietary habits of subjects and then determine whether these habits are associated with higher or lower rates of a particular disease. In one epidemiologic study conducted in Hawaii, people who ate the most tofu had poorer cognitive function.²⁰ This study had some important limitations, however. For example, the main focus of the study was actually heart disease, not cognition. Also, the researchers only assessed the intake of 26 foods; in studies initiated today, it would be customary to assess the intake of more than 100 foods. In addition, the way in which tofu intake was assessed changed throughout the course of the study. Furthermore, in contrast to the Hawaiian study, in a study conducted in Hong Kong,²¹ tofu had no effect on cognition. And, in Indonesia, intake of the widely consumed soy food tempeh was linked to better cognitive health whereas tofu was unrelated.²² Even more important, the clinical studies, which are studies in which subjects are actually given the test product, suggest that soy may improve cognitive function.²³ These studies have involved primarily post-menopausal women. At this point, the totality of the evidence suggests soy may actually improve cognitive function, not impair it, but the data are far too limited for any claims about the impact of soy on cognition to be made.

Childhood Development

Asian women have been consuming soy foods for centuries without any apparent adverse effects in the offspring. In pregnant women who consume soy, isoflavones are transferred to the fetus. However, levels of the hormone estrogen are incredibly high compared with the small amounts of isoflavones in the womb or amniotic fluid. As a result, it's not likely that isoflavones would have any type of estrogenic effect on the growing fetus.

Very little soy research has involved children or young people, although several studies have found that adding soy foods to the diet allows for normal growth and development. Two studies, one in teenage boys²⁴ and another in children 5 to 12 years of age, found that isoflavones did not exert estrogen-like effects or produce any abnormalities.²⁵ Also, according to the American Academy of Pediatrics, soy infant formula leads to normal growth and development; furthermore, their position is that there is negligible (the safest possible rating) concern about the safety of soy infant formula. Finally, one advantage of consuming soy early in life may be protection against breast cancer. Epidemiologic studies show that consuming approximately one serving of soy per day during childhood and/or adolescence reduces breast cancer risk later in life by as much as 50%.^{26, 27}

Allergies

Allergy to soy is fairly rare. According to one U.S. study, around one out of every 2,500 adults has been diagnosed with an allergy to soy protein. For comparison, allergy to cow's milk protein is around 40 times higher.²⁸ Approximately 70% of children with soy allergy outgrow their intolerance by age 10.²⁹ And, in formula-fed infants who are allergic to cow's milk, research suggests that a switch to commercial soy infant formula can often alleviate symptoms.³⁰

Mineral Absorption

Soybeans are high in compounds that can inhibit absorption of minerals such as calcium, iron, and zinc. However, recent research shows that the type of iron found in soybeans is absorbed at higher rates than previously believed. In fact, two studies in women found iron absorption from soy was excellent.^{31,32} Also, in a just-published study, replacing animal products in the diet with two to three servings of soy foods per day for 10 weeks did not affect iron status.³³

Calcium absorption from soy foods is also very good. In fact, calcium absorption from soybeans is much better than from other legumes,³⁴ and calcium absorption from a variety of calcium-fortified soy products is excellent, being similar to the absorption of calcium from cow's milk. This includes for example different types of calcium-fortified soymilks^{35,36} and calcium-set tofu.³⁷

Fermented Versus Unfermented Soy Foods

Fermented soy foods were the first forms of soy to be consumed, but historical records indicate that unfermented soy has been consumed for at least 1,000 years. Commonly consumed fermented soy foods include natto, miso, and tempeh; unfermented soy foods include edamame (green soybeans), tofu, soymilk, and isolated soy protein. In Japan, tofu, miso, natto, and fried tofu account for about 90% of total soy protein and isoflavone intake,^{38,39} whereas in Shanghai, soymilk, tofu, and processed soy products other than tofu accounted for about 80% of total soy protein intake.⁴⁰ Most soy consumed in Chinese cities such as Shanghai is in unfermented form, whereas in Japan roughly half comes from fermented foods. Interestingly, even in Indonesia, the birthplace of the fermented soy food tempeh, unfermented tofu accounts for about 40% of soy intake.

Fermented and unfermented soy foods have similar protein and isoflavone contents. Fermentation does reduce the amount of protease inhibitors in soybeans, compounds that can inhibit the digestion of protein. However, the protein digestibility of protein from unfermented soy foods is excellent, typically exceeding 90%. Epidemiologic studies from Asia generally show intake of both fermented and unfermented soy foods to be associated with benefits, although a few studies have found unfermented soy foods to be superior. Overall, however, the evidence indicates that both forms of soy can make important contributions to a healthy diet.

Safe Intake Levels

There is a considerable range of soy food intake among Asian countries. In Japan and some urban areas of China, average consumption is around 1.5 to two servings per day, but older people with more traditional diets may consume as many as three servings per day. Both fermented and unfermented soy foods are popular throughout Asia. Based on an understanding of the health of Asian people and traditional soy food consumption, as well as the clinical studies conducted in Asia and the West, those who enjoy soy foods can feel comfortable eating as much as three or four servings of these foods per

day. This amount provides around 25 grams of protein and about 100 milligrams of isoflavones. Exceeding these amounts is not harmful, but eating more than four servings of soy per day is inconsistent with the principles of variety and moderation, as no food should place too large a role in the diet, no matter how healthy it may be.

About the Author:

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References:

1. Gu L, House SE, Prior RL, Fang N, Ronis MJ, Clarkson TB, Wilson ME, Badger TM. Metabolic phenotype of isoflavones differs among female rats, pigs, monkeys, and women. *J. Nutr.* 2006, 136, 1215-21.
2. Franke AA, Custer LJ, Wang W, Shi CY. HPLC analysis of isoflavonoids and other phenolic agents from foods and from human fluids. *Proc. Soc. Exp. Biol. Med.* 1998, 217, 263-73.
3. Oseni T, Patel R, Pyle J, Jordan VC. Selective estrogen receptor modulators and phytoestrogens. *Planta Med.* 2008, 74, 1656-65.
4. Helferich WG, Andrade JE, Hoagland MS. Phytoestrogens and breast cancer: a complex story. *Inflammopharmacology.* 2008, 16, 219-26.
5. Greendale GA, Reboussin BA, Slone S, Wasilauskas C, Pike MC, Ursin G. Postmenopausal hormone therapy and change in mammographic density. *J. Natl. Cancer Inst.* 2003, 95, 30-7.
6. Hofseth LJ, Raafat AM, Osuch JR, Pathak DR, Slomski CA, Haslam SZ. Hormone replacement therapy with estrogen or estrogen plus medroxyprogesterone acetate is associated with increased epithelial proliferation in the normal postmenopausal breast. *J. Clin. Endocrinol. Metab.* 1999, 84, 4559-65.
7. Conner P, Skoog L, Soderqvist G. Breast epithelial proliferation in postmenopausal women evaluated through fine-needle-aspiration cytology. *Climacteric.* 2001, 4, 7-12.
8. Conner P, Soderqvist G, Skoog L, Graser T, Walter F, Tani E, Carlstrom K, von Schoultz B. Breast cell proliferation in postmenopausal women during HRT evaluated through fine needle aspiration cytology. *Breast Cancer Res. Treat.* 2003, 78, 159-65.
9. Shu XO, Zheng Y, Cai H, Gu K, Chen Z, Zheng W, Lu W. Soy food intake and breast cancer survival. *JAMA.* 2009, 302, 2437-43.
10. Caan BJ, Natarajan L, Parker BA, Gold EB, Thomson CA, Newman VA, Rock CL, Pu M, Al-Delaimy WK, et al. Soy Food Consumption and Breast Cancer Prognosis. *Cancer Epidemiol. Biomarkers Prev.* 2011.
11. Martinez J, Lewi JE. An unusual case of gynecomastia associated with soy product consumption. *Endocr Pract.* 2008, 14, 415-8.
12. Siepmann T, Roofeh J, Kiefer FW, Edelson DG. Hypogonadism and erectile dysfunction associated with soy product consumption. *Nutrition.* 2011.
13. Hamilton-Reeves JM, Vazquez G, Duval SJ, Phipps WR, Kurzer MS, Messina MJ. Clinical studies show no effects of soy protein or isoflavones on reproductive hormones in men: results of a meta-analysis. *Fertil. Steril.* 2010, 94, 997-1007.
14. Messina M. Soybean isoflavone exposure does not have feminizing effects on men: a critical examination of the clinical evidence. *Fertil. Steril.* 2010, 93, 2095-104.
15. Casini ML, Gerli S, Unfer V. An infertile couple suffering from oligospermia by partial sperm maturation arrest: can phytoestrogens play a therapeutic role? A case report study. *Gynecol. Endocrinol.* 2006, 22, 399-401.
16. Messina M, Redmond G. Effects of soy protein and soybean isoflavones on thyroid function in healthy adults and hypothyroid patients: a review of the relevant literature. *Thyroid.* 2006, 16, 249-58.
17. Bitto A, Polito F, Atteritano M, Altavilla D, Mazzaferro S, Marini H, Adamo EB, D'Anna R, Granese R, et al. Genistein aglycone does not affect thyroid function: results from a three-year, randomized, double-blind, placebo-controlled trial. *J. Clin. Endocrinol. Metab.* 2010, 95, 3067-72.

18. Zeitler P, Solberg P. Food and levothyroxine administration in infants and children. *J. Pediatr.* 2010, 157, 13-14 e1.
19. Sathyapalan T, Manuchehri AM, Thatcher NJ, Rigby AS, Chapman T, Kilpatrick ES, Atkin SL. The effect of soy phytoestrogen supplementation on thyroid status and cardiovascular risk markers in patients with subclinical hypothyroidism: A randomized, double-blind, crossover study. *J. Clin. Endocrinol. Metab.* 2011.
20. White L, Petrovitch H, Ross GW, Masaki K. Association of mid-life consumption of tofu with late life cognitive impairment and dementia: the Honolulu-Asia aging study. *Neurobiol. Aging.* 1996, 17, S121.
21. Woo J, Lynn H, Lau WY, Leung J, Lau E, Wong SY, Kwok T. Nutrient intake and psychological health in an elderly Chinese population. *Int. J. Geriatr. Psychiatry.* 2006, 21, 1036-43.
22. Hogervorst E, Sadjimim T, Yesufu A, Kreager P, Rahardjo TB. High Tofu Intake Is Associated with Worse Memory in Elderly Indonesian Men and Women. *Dement. Geriatr. Cogn. Disord.* 2008, 26, 50-57.
23. Zhao L, Brinton RD. WHI and WHIMS follow-up and human studies of soy isoflavones on cognition. *Expert Rev Neurother.* 2007, 7, 1549-64.
24. Dwyer T, Hynes KL, Fryer JL, Blizzard CL, Dalais FS. The lack of effect of isoflavones on high-density lipoprotein cholesterol concentrations in adolescent boys: a 6-week randomised trial. *Public Health Nutr.* 2008, 11, 955-62.
25. Zung A, Shachar S, Zadik Z, Kerem Z. Soy-derived isoflavones treatment in children with hypercholesterolemia: a pilot study. *J. Pediatr. Endocrinol. Metab.* 2010, 23, 133- 41.
26. Messina M, Hilakivi-Clarke L. Early intake appears to be the key to the proposed protective effects of soy intake against breast cancer. *Nutr. Cancer.* 2009, 61, 792-798.
27. Messina M, Wu AH. Perspectives on the soy-breast cancer relation. *Am. J. Clin. Nutr.* 2009, 89, 1673S-1679S.
28. Vierk KA, Koehler KM, Fein SB, Street DA. Prevalence of self-reported food allergy in American adults and use of food labels. *J. Allergy Clin. Immunol.* 2007, 119, 1504-10.
29. Savage JH, Kaeding AJ, Matsui EC, Wood RA. The natural history of soy allergy. *J. Allergy Clin. Immunol.* 2010, 125, 683-686.
30. Sladkevicius E, Nagy E, Lack G, Guest JF. Resource implications and budget impact of managing cow milk allergy in the UK. *J Med Econ.* 2010, 13, 119-28.
31. Murray-Kolb LE, Welch R, Theil EC, Beard JL. Women with low iron stores absorb iron from soybeans. *Am. J. Clin. Nutr.* 2003, 77, 180-4.
32. Lonnerdal B, Bryant A, Liu X, Theil EC. Iron absorption from soybean ferritin in nonanemic women. *Am. J. Clin. Nutr.* 2006, 83, 103-7.
33. Zhou Y, Alekel DL, Dixon PM, Messina M, Reddy MB. The Effect of Soy Food Intake on Mineral Status in Premenopausal Women. *J Women's Health (Larchmt).* 2011.
34. Heaney RP, Weaver CM, Fitzsimmons ML. Soybean phytate content: effect on calcium absorption. *Am. J. Clin. Nutr.* 1991, 53, 745-7.
35. Zhao Y, Martin BR, Weaver CM. Calcium bioavailability of calcium carbonate fortified soymilk is equivalent to cow's milk in young women. *J. Nutr.* 2005, 135, 2379-82.
36. Tang AL, Walker KZ, Wilcox G, Strauss BJ, Ashton JF, Stojanovska L. Calcium absorption in Australian osteopenic post-menopausal women: an acute comparative study of fortified soymilk to cows' milk. *Asia Pac J Clin Nutr.* 2010, 19, 243-9.
37. Weaver CM, Heaney RP, Connor L, Martin BR, Smith DL, Nielsen E. Bioavailability of calcium from tofu vs. milk in premenopausal women. *J Food Sci.* 2002, 68, 3144-3147.
38. Wakai K, Egami I, Kato K, Kawamura T, Tamakoshi A, Lin Y, Nakayama T, Wada M, Ohno Y. Dietary intake and sources of isoflavones among Japanese. *Nutr. Cancer.* 1999, 33, 139-45.
39. Somekawa Y, Chiguchi M, Ishibashi T, Aso T. Soy intake related to menopausal symptoms, serum lipids, and bone mineral density in postmenopausal Japanese women. *Obstet. Gynecol.* 2001, 97, 109-115.
40. Zhang X, Shu XO, Gao YT, Yang G, Li Q, Li H, Jin F, Zheng W. Soy food consumption is associated with lower risk of coronary heart disease in Chinese women. *J. Nutr.* 2003, 133, 2874-8.