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REPORT

Is Soy Safe?

Busting the Myths of a Nutritional Powerhouse

By Oscar Rodriguez

Rarely has a nutritional source gained such rapid acceptance and drawn the kind of hostile scrutiny focused on soy. No sooner did the FDA take the highly unusual step of allowing a health claim to be made for soy as a food in 1999,[1,2] than it came under attack by a vocal minority of "concerned citizens"—some of whom were found to represent a narrow segment of the food industry threatened by soy's profits.[3]

Thanks to their efforts, considerable misinformation now contaminates the discussion of soy's real impact on health. Instead of enjoying the broad range of benefits, many aging individuals are unnecessarily fearful of consuming soy products.

The good news is that the popularity *and* "controversy" surrounding soy have resulted in considerable clinical study and research, giving rise to a wealth of scientific literature that validates soy's health-promoting potential.

In this article, you will find out how soy became the subject of controversy—and why it shouldn't be. You will discover the latest findings on soy and its components, including ***isoflavones*** and ***soy protein.*** You will also learn how just **15-20 grams** of soy per day, (or **50-90 mg** of soy isoflavones) can operate at the cellular level to provide a formidable defense against cardiovascular disease, numerous forms of cancer, osteoporosis, and menopausal symptoms.[4]

SOY AND ESTROGEN: THE REAL STORY

At the center of the controversy surrounding soy is the "estrogen-like" molecular profile of some soy-based compounds—and whether they increase the risk of certain hormone-dependent cancers and other adverse effects associated with hormonal imbalance.

Soy contains antioxidant polyphenols (plant-based compounds) known as *isoflavones*. ***Isoflavones*** are considered "phytoestrogens" or "dietary estrogens" because of their molecular similarity to estrogen as *estradiol* (17-β-estradiol), the female sex hormone. The ability of isoflavones to "mimic" some of estrogen's effects has led many doctors and scientists to characterize isoflavones as "weak estrogens."

This is incorrect, according to Dr. Mark F. McCarty, an internationally recognized expert in soy isoflavones.[5] Advances in our understanding of how the body responds to estrogen (and estrogen-like compounds) explains why.

Estrogen exerts its influence upon cells directly through the presence of *estrogen receptors.* Until relatively recently, only one receptor was known to exist, now called the estrogen receptor alpha or **ER-alpha.** Overexpression of ER-alpha has been implicated in a variety of cancers in humans, including breast cancer, ovarian cancer, endometrial cancer, and colon cancer.[6-9]

In the late 1990s,[5,10] a second estrogen receptor was discovered, now known as **ER-beta.** Expression of this receptor appears to *counteract* many of the cancer-causing activities of ER-alpha.[10]

As Dr. McCarty points out, ***genistein***, one of the most abundant isoflavones in soy, is a highly potent activator of **ER-beta.** Critics of soy regard isoflavones' action on estrogen receptors as the source of concern, *without recognizing there is more than one type of estrogen receptor in the body, and that they exert very different effects.*

This highly *selective* mode of action explains why soy isoflavones promote beneficial estrogen-like effects in tissues where the ER-beta receptor predominates, but do not provoke the harmful effects of conventional estrogen replacement therapy in tissues where the ER-alpha receptor predominates.

For example, soy isoflavones have been shown to exert positive effects in tissues such as bone, vascular endothelium (blood vessel lining), and breast cells without the negative effects in those and other tissues such as liver and uterus, where side effects of estrogen therapy have been observed.[5] In fact, in breast tissue possessing both estrogen receptor types, ER-beta is now known to exert a restraining influence on cell proliferation stimulated by estrogen at ER-alpha sites, reducing the risk of breast cancer.[10] This balance helps to explain why soy isoflavones do not increase breast cancer risk despite their estrogen-like activity.[5]

Dozens of epidemiological (population-level) studies document the broad array of health benefits associated with a high-soy diet.[11-13] Diets rich in soy isoflavones are associated with lower rates of cardiovascular disease, osteoporosis, cancer, and obesity-related complications such as type 2 diabetes.[14-16]

Soy isoflavones have relaxing effects on blood vessels, mediated by their influence on nitric oxide synthase (NOS), as well as powerful antioxidant effects, which together explain their potential for treatment and prevention of hypertension and stroke.[11,17] Acting via yet another distinct mechanism, the isoflavones modulate signaling in pathways that control the interaction of oxidant stress with inflammation, leading to upregulation of detoxifying and antioxidant defense genes.[18]

The cumulative weight of the evidence for soy's health benefits led to the remarkable decision by the FDA to approve a food-labeling health claim for products containing 25 grams of soy proteins in the prevention of coronary heart disease in 1999.[14] This claim was based on a wealth of clinical trials as well as epidemiological data showing that high soy isoflavone intake could reduce LDL cholesterol, inhibit pro-inflammatory cytokines, reduce cell adhesion proteins, inhibit platelet aggregation, and improve blood vessel reactivity.[19] Many nations throughout the world have now similarly endorsed soy products based on these data.[10]

Dr. Mark Messina, a noted soy expert at the Department of Nutrition at the Loma Linda University School of Public Health, has summarized soy's remarkable benefits and provides specific recommendations on optimal soy intake. Messina suggests, based on the totality of available data and practical dietary standards, that aging individuals should ingest **15-20 grams** of soy per day, including **50-90 mg** of isoflavones—recommendations that have been echoed by other researchers worldwide.[20] He adds that an intake of **25 grams per day** of soy protein can be specifically used for cholesterol reduction.

PROTECTION FROM CARDIOVASCULAR DISEASE

Soy products, both soy protein isolates and soy isoflavones, induce *profoundly* beneficial effects on the human cardiovascular system. Early human studies showed that long-term intake of soy protein rich in isoflavones could improve blood lipid profiles, at least in part by increasing expression of receptor molecules that take up LDL cholesterol.[21] In fact, soy protein and isoflavones have *universally* been shown to lower LDL cholesterol and triglycerides, while some studies have also documented increases in beneficial HDL cholesterol as well.[22,23] Along with phytic acid, another soy component, soy isoflavones significantly lower homocysteine levels and positively influence other biomarkers of cardiovascular disease risk.[24-27]

These benefits are obtained through multiple mechanisms of action.[28,29] The various constituents of soy favorably regulate expression of numerous genes, including those involved in:

- Processing cholesterol and other lipids
- Synthesis and degradation of the cholesterol molecule
- Efficient utilization of adenosine triphosphate or ATP, the body's fundamental unit of energy "currency."[30]

These effects appear to be universal, benefiting young and the old, male and female, normal weight and obese.[31-34]

As the central role of inflammation in cardiovascular disease emerged, scientists became interested in how soy consumption might affect the inflammatory process.[28] They found that short-term soy consumption reduces some markers of inflammation while increasing plasma levels of vessel-relaxing nitric oxide in postmenopausal women with metabolic syndrome, and improves signs of the metabolic syndrome in general.[35,36] Soy protein also increases the activity of paraoxonase 1 **(PON1),** the natural antioxidant compound found in HDL cholesterol that prevents the inflammatory oxidation of cholesterol.[37] In a preclinical model, genistein inhibited the inflammatory control complex called **nuclear factor-kappaB** (NF-kB) and reduced expression of a molecule essential to production of atherosclerotic plaques.[38]

WHAT YOU NEED TO KNOW: SOY

- Soy proteins and isoflavones offer comprehensive health benefits through multimodal and complementary mechanisms.
- They act by diverse pathways to block oxidation, reduce inflammation, and favorably regulate gene expression.
- Soy isoflavones in particular function as estrogen-like compounds in myriad tissues, chiefly upregulating the recently-discovered estrogen beta receptors associated with healthy outcomes such as cancer inhibition and improved cardiovascular function.
- These effects provide multimodal protection against cardiovascular disease, cancer, obesity, diabetes, osteoporosis, and many other conditions associated with aging or poor dietary habits.
- A flurry of "anti-soy" publicity in the late 1990s drew increased scientific scrutiny that has since uncovered still greater health benefits from soy than originally thought.
- A diet with varied protein sources, including substantial amounts of soy and soy isoflavones, is both safe *and* preventive of degenerative disease.

Another factor that contributes to the risk of a cardiovascular event such as heart attack or stroke is the tendency of platelets to aggregate, or clump together, forming clots that can obstruct blood flow. Platelet aggregation is a complex, multi-step process involving a number of signaling molecules—and soy isoflavones act to *reduce* the density of vital receptors for one such molecule, **thromboxane A2,** in direct proportion to the isoflavone concentration in blood.[39] Thromboxane plays a central role in potentially lethal blood clot formation.

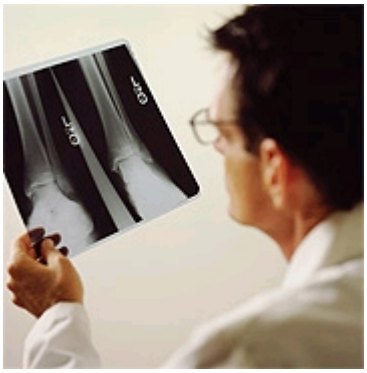
Short peptides (protein fragments) in soy proteins are among those recently shown to act against ***angiotensin-converting enzym***e (ACE), thereby helping to safely lower blood pressure.[40] Genistein inhibits the release of calcium within vascular smooth muscle cells, and helps to block constriction.[41] These effects directly mimic those of many prescription blood pressure medications and, along with their direct influence on nitric oxide synthesis and other endothelial health factors, account for the additional vascular benefits conferred by soy products.[42,43]

Several nutritional intervention studies in both animals and humans further indicate that consumption of soy protein reduces body weight and fat mass, in addition to the beneficial effects on lipid profiles.[44] The effect on blood lipid profile was recently shown to be dramatically enhanced by the addition of a prebiotic mixture to soy.[45] This study, conducted among a group of adults with high lipid levels, capitalized on the fact that intestinal bacteria can metabolize soy components to produce equol, a powerful lipid-lowering compound that many adults have trouble producing. The people on the prebiotic plus soy branch of the study experienced significant improvements in their lipid profiles not seen when either prebiotic or soy was taken alone.

COMBATING METABOLIC SYNDROME

The current epidemic of obesity and type 2 diabetes increases overall risk for cardiovascular disease and other metabolic complications. Soy components have direct benefits on several of the parameters that go awry in the development of metabolic syndrome. For example, soy proteins lower lipids, improve kidney function, and reduce urinary protein losses in type 2 diabetics with kidney disease.[46,47]

Soy protein combined with isoflavones improves blood sugar control, reduces insulin resistance, and lowers serum lipids in diabetic patients, and can also reduce serum CRP levels and restore lipid profiles towards normal.[48-51] These effects may account for the observation that including soy in the diet can improve features of the metabolic syndrome in adults.[36]



In a group of obese type 2 diabetics, replacement of animal-derived protein with soy protein helped improve hemoglobin A1c (a measure of long-term blood sugar control), reduced dependence on glucose-lowering drugs, lowered CRP levels, and triggered significant weight loss.[52] And soy isoflavones, particularly daidzein, can enhance gene expression of the vital metabolic regulatory protein PPARgamma, which helps cells absorb and use glucose.[53]

Replacing animal-derived proteins with soy-based meals can lower body weight and fat mass, while reducing LDL cholesterol even more than would be expected from weight loss alone, and can improve body composition, increasing the ratio of lean body mass to fat.[54,55] Even more exciting, soy product and isoflavone intakes were directly associated with a lower risk of developing type 2 diabetes in a group of overweight women![56]

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STRENGTH FOR AGING BONES

The intimate relationship between *osteoporosis,* which involves the loss of calcium from aging bones, and *atherosclerosis*, which involves the deposition of calcium into aging blood vessels, is growing rapidly clearer, and the connection involves the cellular signaling molecules known as *inflammatory mediators.*[57]

Since soy products have proven value in reducing markers of inflammation and preventing atherosclerosis, it follows that they should help prevent osteoporosis. For example, soy isoflavones have the ability to interfere with production of the "all-purpose" inflammatory cytokine interleukin-6 (IL-6).[58] IL-6 levels rise with advancing age, particularly after menopause and andropause, corresponding to a drop in sex hormone levels. This rise in IL-6 is associated with many of the chronic conditions of aging, including osteoporosis.[58]

Animal studies show that soy extracts and purified genistein act via different mechanisms to modulate gene expression in bone tissue.

By blocking IL-6 production, along with numerous other pathways, soy protects against age-related bone loss (resorption).[59] Animal studies show that soy extracts and purified genistein act via different mechanisms to modulate gene expression in bone tissue, resulting in beneficial three-dimensional changes in bone structure through reduced activity of multiple inflammatory pathways.[60,61]

In humans, the effects are no less dramatic. Soy isoflavone supplementation decreases bone resorption in postmenopausal women.[62,63] One year of supplementation with soy protein also increased bone formation.[64] The combination of enhanced new bone formation and reduced bone resorption may contribute to benefits in preserving bone mineral density, the chief marker of the progress of osteoporosis.[65] Notably, this effect is not limited to post-menopausal women: a 2008 study demonstrated a positive change in bone mineral density even in younger women, implying a powerful preventive effect.[66]

Many of these effects can be traced to the isoflavones' estrogen-like qualities and are borne out in multiple large epidemiological studies as well as in smaller clinical trials and laboratory research.[16] Contrary to fears expressed by some early researchers and vocal critics (See SIDEBAR), soy isoflavones do not produce breast tissue changes or modify breast density on mammography. In fact, they may actually help *reduce* fibrocystic disease of the breast.[67,68]

THE SOY "CONTROVERSY": SEPARATING MYTH FROM FACT

A relatively small group of outspoken critics have fueled the debate over the safety of soy products, many of whom have links to industries threatened by soy's widespread acceptance.[3] Here in a nutshell are their specious claims—and why they don't hold up:

"Soybeans contain 'anti-nutrients.'[3] In raw, unprocessed form, this is true of soybeans. In fact *all* raw, unprocessed beans contain a variety of enzymes and other biomolecules that can interfere with digestion and absorption of other nutrients. Soybeans are no different. Growers and processors are acutely aware of this as they develop the most nutritional cultivars of this universal food source.[104-108] The way around the "problem" of anti-nutrients is simple: don't eat raw soybeans, and be sure to eat a diet with varied sources of protein (good common sense). In fact, soy protein has been used successfully in treating mild and moderate protein-energy malnutrition in some of the world's sickest children.[109]

"Soybeans cause thyroid dysfunction." Based on a 1960 article describing the occurrence of goiter (thyroid swelling) in a single infant on a pure soy diet, soy opponents extrapolated—and *exaggerated*—this risk to the entire population.[3,110]

Isoflavone molecules in soy do inhibit an enzyme involved in thyroid hormone synthesis,[111-114] but that has not translated into poor thyroid function in otherwise healthy individuals (those without pre-existing thyroid disease and who have adequate iodine intake).[114-117] Again, the bottom line here is not to get all your nutrition from soybeans (or any other single source), and if you have a known or suspected thyroid disorder, get frequent thyroid function tests.

"Isoflavones disrupt sex hormones." Phytoestrogens by their very nature influence sex hormones, but those in soy chiefly affect ER-beta estrogen receptors, which have been shown to *inhibit* the detrimental effects associated with hormonal imbalance.[5] Frightening tales of accelerated puberty in children caused by soy are largely based on a single, small 1986 study showing a weak correlation between exposure to soy infant formula and premature breast development in girls.[118] That study's own authors questioned the validity of the relationship, and the medical establishment's own American Academy of Pediatrics has determined there is *"no conclusive evidence from animal, adult human, or infant populations that dietary soy isoflavones may adversely affect human development, reproduction, or endocrine function."*[119]

"Soy causes cancer." Again, the effects of isoflavones on hormonal function are clear. It made scientific sense early on to raise the question of whether they might adversely affect hormone-dependent cancers. A handful of studies from the mid-1990s showed cellular changes of the kind that can precede cancer—though none showed an actual increase or production of new cancers.[120,121] Since then, the discovery of ER-beta estrogen receptors, their cancer-inhibiting effects, and the preferential influence of isoflavones on these receptors—in addition to *extensive* human epidemiological and clinical studies—provide an extremely favorable profile for soy isoflavones with regard to cancer.[5,75]

SOY PROTEIN AND ISOFLAVONES: POTENT CANCER PREVENTION

Despite the early and isolated concerns regarding a possible link between soy products and cancer, there is now strong evidence that soy provides powerful cancer prevention. Isoflavones' powerful multitargeted modes of action operate across numerous pathways to fight cancer on multiple fronts simultaneously.[69] This allows reduction in cancer risk at every phase of its progression. Favorable modulation of gene expression is especially important in achieving this comprehensive effect.[58,70] Exciting recent work shows that *equol*, the intestinal metabolite of soy isoflavones, has potent anti-cancer effects as well.[71]

Breast Cancer

Early studies from Japan showed that frequent consumption of soy-based miso soup and isoflavones was associated with a reduced risk of breast cancer.[72] A recent prospective study in 5,042 female breast cancer survivors in China, who were followed for a median of 3.9 years, found that consumption of isoflavone-rich soy foods was significantly associated with a 29% lower risk of death and a 32% lower risk of cancer recurrence.[73] Additional evidence from epidemiological, animal, cell culture, and human studies has accumulated showing that isoflavones are promising agents for breast cancer chemoprevention.[74,75] Daidzein, a soy isoflavone, adds protective effect to the chemotherapy agent tamoxifen in animal studies of mammary cancer.[76] Some of this effect may be explained by soy protein's ability to alter signaling pathways involving the hormone receptors, and some by its ability to inhibit cell growth.[77,78] Genistein is unique among flavonoids of interest in cancer prevention in that it has both potent estrogen-like *and* growth inhibitory effects on breast cancer cells.[79]

Increased isoflavone intake also directly influences sex hormone concentrations and menstrual cycle length in women, effects with the potential for reducing breast cancer risk.[80,81] And recent exciting work demonstrates that genistein interacts directly with the notorious HER2 cancer-causing gene, inhibiting its activation by cellular machinery and preventing cancer promotion.[82]

Prostate Cancer

Prostate cancer, like breast and uterine cancer, may be stimulated or worsened by sex hormones. Soy isoflavones, with their partial stimulatory/partial inhibitory effects, act by multiple pathways to reduce prostate cancer risk.[83,84] Genistein from soy reduces signaling between early prostate cancer cells and helps prevent their progression.[85] Genistein sensitizes cancer cells to apoptosis induced by chemotherapy drugs, and blocks activation of NF-kappaB, which is responsible for the connection between inflammation and cancer development.[78,86] Related studies show that isoflavone supplementation may decrease prostate cancer risk both by reducing NF-kappaB activation and by decreasing levels of damaged DNA strands, an early step in cancer development.[87] Several soy protein components protect against chemically-induced prostate cancer in rats, and isoflavones specifically inhibit synthesis of inflammatory prostaglandins in human prostate cancer cells and in living patients.[88-90]

An entirely different mechanism of genistein in prostate cancer is the downregulation of sex hormone receptors in prostate tissue, making the cells less responsive to stimulation and cancerous growth.[91,92] Other cellular signaling systems are also disrupted by genistein, further reducing cancer risk.[93] And in men already diagnosed with prostate cancer, high-dose soy supplements produced an overall decrease in the tumor marker

prostate-specific antigen (PSA), which rose alarmingly in control patients.[94] Similarly, genistein alone is known to arrest the cell cycle and induce cell death by apoptosis, as well as preventing metastatic spread of already-established prostate cancers.[84]

Colon Cancer

Soy derivatives reduce aberrant crypt foci, the early abnormal changes in intestinal lining cells that may herald the onset of colon cancer.[95] And the combination of genistein with indole-3-carbinol, derived from cruciferous vegetables, dramatically enhanced cell death by apoptosis in human colon cancer cells.[96] A prospective study published in 2009 demonstrated that consumption of soy foods may reduce the risk of colorectal cancer in postmenopausal women.[97]

As with the other cancers, colon cancer prevention by soy is accomplished through multiple pathways. Genistein, for example, inhibits intercellular signaling by insulin-like growth factor-1 (IGF-1), with the end result of blocking cancer cell proliferation and inducing apoptosis.[98]

SLOWING MENOPAUSE WITH SOY

Menopause produces a host of changes in a woman's body as her natural estrogen levels subside—changes that may be, at least to some extent, more safely slowed by soy isoflavones than estrogen replacement therapy. The decline in cardiovascular function that has its onset at menopause is one such change. Soy protein and isoflavones exert favorable effects on endothelial function in postmenopausal women.[99] A low-glycemic index diet fortified with soy protein and phytosterols has been shown to reduce total and LDL cholesterol and triglycerides, and improve HDL ratios, while tending to normalize blood pressure, in a group of postmenopausal women.[27]

Body composition changes after menopause include increase in fat below the skin and in the abdomen, as the normal effects of estrogen fade. These changes were prevented by a daily soy protein supplement over a three-month period in a group of postmenopausal women.[100] A similar study showed that six months of supplementation with soy protein plus isoflavones produced modest favorable effects on body composition in postmenopausal women.[101] And many of the uncomfortable physical effects of menopause, such as hot flushes, respond well to daily doses of isoflavones, particularly genistein.[102]

SUMMARY

Soy derivatives, particularly ***soy proteins*** and the ***isoflavones,*** exert powerfully beneficial effects across multiple systems of the body. Despite popular misconception at the hands of a vocal group of detractors, soy protein's action on estrogen receptors gives them unique capabilities not found in drugs or other natural compounds. By preferentially acting upon estrogen receptors associated with cancer suppression, soy isoflavones can *reduce* cancer risk. Soy isoflavones demonstrate remarkable abilities to improve cardiovascular function through multiple pathways in cardiac tissue and in blood vessel linings. Soy proteins and isoflavones also act as powerful antioxidants[103] that modulate cellular function through control of gene expression and cell signaling pathways. These effects in turn allow them to help quench inflammatory stimuli that both contribute to and result from modern scourges such as obesity, type 2 diabetes, and metabolic syndrome.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

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