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REPORT

Soy & Cancer Prevention

By Edward R. Rosick, DO, MPH, MS

For the past decade, a controversy has raged over whether people can reduce their risk of cancer by increasing their consumption of soy foods and soy supplements. In response to the debate, a number of studies were initiated in the 1990s to ascertain soy's effects on human health.

Over the last year, the results of these studies began to be released. While ignored by the mainstream media, the startling findings indicate that prostate and breast cancer risk could be cut in half if people only consumed more soy.

Prevention Key to Halting the Epidemic

The incidence of cancers that are not predominately caused by smoking, such as lymphoma, multiple myeloma, and brain cancer, is increasing at alarming rates.

One of every two American men will develop cancer in his lifetime, as will one of every three American women. Despite billions of research dollars spent, the epidemic of cancer continues.

A small but growing number of leading cancer researchers—such as Dr. Samuel S. Epstein, head of the National Cancer Prevention Coalition—are calling for a major change in how the federal government fights cancer.

Epstein and other advocates of cancer prevention emphasize that cancer is a multistage disease that is amenable to prevention in its earliest stages of development. One of the most widely available means of cancer prevention—yet generally overlooked by major cancer organizations and mainstream medicine—is the use of natural chemopreventive agents.

More than 250 case-control and cohort studies have been conducted on natural chemopreventive agents such as those found in fruits and vegetables. The data from these studies are overwhelming and irrefutable: the greater the consumption of fruits and vegetables, the lower the incidence of cancer. A recent article on cancer chemoprevention summarized these data as follows:

“Numerous components found in fruits and vegetables might contribute to their ability to reduce the risk of cancer, including dietary fiber, micronutrients, and various phytochemicals . . . the biomedical community needs to recognize and advocate approaches to prevent cancer [such as the use of natural chemopreventive agents] with the same enthusiasm that it currently directs toward treating it.”¹

Soy: A Powerful Chemopreventive Agent

Isoflavones derived from soy have shown great promise in providing natural protection against multiple types of cancer. Isoflavones are phytochemical constituents of soy, with two of the best known being genistein and daidzein. Isoflavones are believed to exert a number of positive biological effects on the human body,² and many practitioners of integrative medicine (and even a small but growing number in mainstream medicine) now believe that consumption of soy and isoflavones can significantly reduce the risk of many chronic diseases, including cancer, heart disease, osteoporosis, and diabetes.





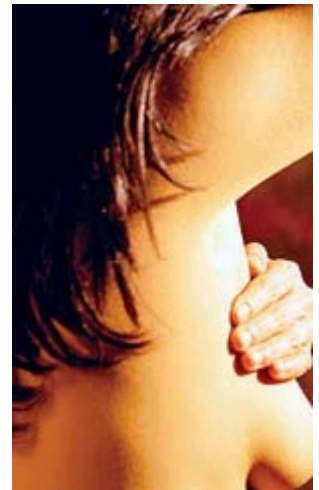
Significant interest in using soy and its isoflavone constituents as cancer chemoprotective agents began in the 1990s. Studies conducted in Asia found that Asian women, who consume many more isoflavones than American women, have significantly lower risks of developing breast cancer.³ Because animal studies have shown that a diet high in soy and genistein isolate can protect against mammary, colon, and skin tumors,⁴ it seemed reasonable to think that soy could also help prevent human cancers, and in particular, breast cancer. Yet many mainstream medical practitioners remain skeptical that something as “simple” as soy could have such a profound effect on human health.

Soy, Estrogen, and Breast Cancer

Some in the medical establishment believe that soy isoflavones have no role in preventing serious diseases such as cancer. Others feel that soy isoflavones should not be used as nutritional supplements because isoflavones act as natural estrogens and could cause many of the same problems—such as increased risk of stroke—that synthetic estrogens are now known to cause.

In fact, soy isoflavones do not simply act as “natural” estrogens. Soy isoflavones are correctly classified as selective estrogen receptor modulators. Due to their unique molecular structure, soy isoflavones can act as either estrogen receptor agonists or receptor blockers. With this ability, soy isoflavones are thought by many to confer the beneficial effects of estrogen without its potentially dangerous side effects, especially in hormonally sensitive tissues found in both the breast and endometrium.^{5,6}

Numerous studies show the potential benefits to women of incorporating soy in their diets to help prevent breast cancer. A landmark 1991 case-control study of women in Singapore, involving 200 case subjects and 420 control subjects, found that women with the highest consumption of soy-based products had a markedly decreased risk of developing breast cancer.⁷ An even larger Japanese case-control study in 1995, involving 1,186 subjects and 23,163 controls, also showed that women with increased tofu (soybean curd) intake had a significantly decreased risk of developing breast cancer compared to women who consumed small amounts of soy-based products such as tofu.⁸ Finally, a recent and very large population-based, prospective study of 21,852 Japanese women aged 40-59 found that women with the highest intake of soy isoflavones reduced their risk of breast cancer by up to 54% compared to women with the lowest intake of soy isoflavones.⁹



Despite the evidence-based research showing soy isoflavones' preventive effects on breast cancer, along with epidemiological studies highlighting the much lower rates of breast cancer among Asian women who consume significant amounts of soy-based products, some doctors still caution women against using soy-based foods and supplements. They contend that because soy isoflavones have been labeled as estrogen “mimics,” they could potentially worsen or even cause breast cancer. With the current knowledge that soy isoflavones act as selective estrogen receptor modulators and are not simply estrogen “mimics,” these arguments simply do not hold up. As the authors of a recent study of soy isoflavones stated:



“Recommendations to avoid soy foods now being given by many health professionals to these patients [women with breast cancer] are not based on any clinical evidence to support this advice . . . the fact that an isoflavone like genistein acts more like a [selective estrogen receptor modulator] than an estrogen should be the basis for believing that soy foods [and supplements] are more likely to be beneficial for breast cancer treatment and prevention.”¹⁰

In addition to being a chemoprotective supplement for breast cancer, soy isoflavones also are thought to be effective in warding off other types of cancer that afflict women, including endometrial cancer. A recent case-control study reported the effects of soy isoflavones and other phytoestrogens on the risk of developing endometrial cancer.¹¹ The study compared 500 women aged 35-79 who developed endometrial cancer between 1996 and 1999 to 470 age- and ethnicity-matched controls. As in studies examining the effects of isoflavones on breast cancer, this study showed that women who had a higher intake of soy isoflavones had a significantly lower risk of developing endometrial cancer. Even more interesting was that the levels of isoflavones needed to provide protection against endometrial cancer were found to be much lower than the amount believed necessary to protect against breast cancer.

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Soy Counteracts Prostate Cancer in Men

Both animal and human studies have shown that soy isoflavones can help protect men from prostate cancer by slowing and even preventing the disease. Prostate cancer is the most common cancer in men and the second leading cause of death from cancer (after lung cancer) among men. As is the case concerning breast cancer in women, large epidemiological studies have shown that Asian men who consume large amounts of soy-based foods have a significantly lower incidence of prostate cancer compared to their Western counterparts.¹²

Most recently, in a study published in the journal *Cancer Science* in March 2004, researchers found that soybean products, as well as other Far Eastern dietary staples such as fish and tofu, were associated with a decreased risk of prostate cancer in Japanese men.¹³ Specifically, men who consumed the greatest amounts of soybeans and tofu were 47% and 53% less likely, respectively, to develop prostate cancer than those who consumed the smallest amounts. Furthermore, in men who consumed the greatest amount of the fermented soybean natto, the prostate cancer incidence was reduced a remarkable 75%.

Early animal studies found that this difference is most likely attributable to the cancer-inhibiting effects of soy isoflavones. In 1999, Harvard Medical School researchers studying mice with transplanted human prostate cancer cells found that those fed a diet high in soy isoflavones experienced tumor regression compared to mice fed a non-soy diet.¹⁴ The study authors noted that “our data suggest that dietary soy products may inhibit experimental prostate tumor growth through a combination of direct effects on tumor cells and indirect effects on tumor neovasculature.”

Newly published animal research lends strong support to this hypothesis. In a study published in January 2004, University of Colorado researchers fed inositol hexaphosphate (IP6), a dietary phytochemical found in cereals, soy, legumes, and other fiber-rich foods, to mice that had been injected with prostate cancer cells. Compared to controls, the mice fed IP6 exhibited suppressed hormone-refractory prostate cancer growth by as much as 66% when compared to littermates without the IP6-enriched diet.¹⁵

In another study published in March 2004, Japanese researchers evaluated the effects of Fuji-flavone, a commercial isoflavone supplement derived from soybean products, on rat prostate carcinogenesis. Rats fed a diet containing Fujiflavone showed a significantly lower incidence of prostate carcinomas than those fed a soy-free diet, leading the researchers to conclude that “intake of dietary isoflavones can be promising for prevention of human prostate cancer.”¹⁶

While animal-based studies are important in advancing scientific knowledge, not all results from animal studies are directly transferable to humans. Fortunately, human studies (in addition to the previously noted epidemiological reports) also support the theory that soy isoflavones can protect men against prostate cancer. One of the largest of these, a prospective study conducted between 1976 and 1992 on 12,395 men in Loma Linda, California, found that men who drank a glass of soy milk more than once a day reduced their risk of prostate cancer 70% compared to men who did not drink soy milk.¹⁷ Even after adjusting for various statistical confounders, the 70% reduction held firm, leading the authors to conclude that “our study suggests that men with high consumption of soy milk are at decreased risk of prostate cancer. This may also be the case for men who frequently consume other soy products with intact content of isoflavones . . .”

Prevention: The Key to Good Health

Despite decades of effort and the expenditure of billions of dollars on research, the war on cancer in America has produced little more than an increasingly lethal stalemate. While the medical establishment remains fixated on cancer diagnosis and treatment, a growing legion of researchers is calling for new approaches, with an emphasis on preventing cancer through the use of natural

Finally, in a case-control study published in January 2004, Japanese researchers sought to ascertain whether a high serum concentration of phytoestrogens reduces the risk of prostate cancer. The researchers collected lifestyle information and serum samples from more than 14,000 Japanese men in 1988-90, who were tracked until 1999. Phytoestrogens and sex hormones stored in serum were measured in 2002, and 52 case subjects and 151 controls were identified. This study clearly established that elevated serum levels of all three phytoestrogens assessed—genistein, daidzein, and equol—imparted a strong protective effect against prostate cancer.¹⁸ Men with the highest circulating levels of genistein, daidzein, and equol reduced their risk of prostate cancer by 62%, 57%, and 66%, respectively.



chemopreventive agents such as those found in fruits and vegetables.

Among the most powerful of these natural chemopreventive agents is soy. Soy and soy-based supplements can aid in the prevention of a variety of significant diseases, including breast, prostate, and endometrial cancers, as well as heart disease. New studies suggest that soy may even provide protection against premature skin aging and help lower harmful low-density lipoprotein (LDL) cholesterol. In fact, each passing month seems to produce new research heralding soy's remarkable disease-fighting and health-promoting effects.

Positive Effects on Skin Aging, Cholesterol

Very recent studies suggest that the soy isoflavone genistein may provide protection against skin aging caused by sun exposure, and may even inhibit skin cancer. In a report published last year in the *Journal of Nutrition*, researchers at the Mount Sinai School of Medicine examined the effects of both oral and topical genistein on ultraviolet radiation-induced skin cancer in mice.¹⁹ A significant reduction in cancer formation was found in animals that either drank water fortified with genistein or had the soy isoflavone directly applied to their skin. Moreover, the researchers also showed that genistein applied directly to human skin substantially decreases the amount of photodamage by ultraviolet radiation. The study authors stated that "the soybean isoflavone genistein has potent antiphotocarcinogenic and antiphototoaging effects and will have promising applications in the field of dermatology."

Multiple studies now show that soy isoflavones also reduce harmful levels of cholesterol and the resulting atherosclerosis. Asian men, who consume much more soy than Americans, have a sixfold lower mortality rate for coronary heart disease compared to American men. The difference also is seen in Asian women, who have an eightfold lower mortality rate from heart disease compared to their US counterparts.

Animal studies have confirmed that soy isoflavones have significant effects in lowering harmful LDL cholesterol,²⁰ as have studies in humans. In two recent studies at the University of Minnesota, women aged 18-70 who were given soy isoflavone supplements saw a marked decrease in their LDL cholesterol.^{21,22} An even more recent Canadian study examined the effects of soy isoflavones on cholesterol and homocysteine levels, as well as on blood pressure, in 41 men and women.²³ In this randomized crossover study, patients were fed a low-fat dairy-based diet, a diet low in soy isoflavones, or a diet high in soy isoflavones. After three months, the men and women who ate either the low- or high-isoflavone diet had significantly lower LDL cholesterol and homocysteine levels, as well as a reduction in blood pressure, compared to those who ate the low-fat dairy-based diet. This led the study authors to conclude that "soy protein foods, regardless of their isoflavone content, may improve many lipid and nonlipid risk factors for [coronary artery disease] and thus justify the use of soy foods as part of a dietary strategy to reduce [coronary artery disease] risk."

A Simple Food with Multiple Benefits

Despite the reticence of mainstream medicine to admit that natural supplements have any use in maintaining optimal human health, the studies of soy isoflavones conducted to date should make even the most ardent skeptic acknowledge a place in modern medicine for safe, natural food-based supplements.

With strong scientific evidence showing that soy isoflavones can help prevent breast, endometrial, and prostate cancer, as well as protect both men and women against heart disease, physicians should not hesitate to educate their patients on the need to incorporate soy in their diets. Soy isoflavones not only protect against the two most common and deadly killers in America today, but clinical research suggests that they also may protect against diabetes and obesity.^{24,25}



A small, nondescript legume, soy nevertheless continues to provide us with a bountiful harvest of health benefits.

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