



& HEALTH



**Emerging
Research Suggests
Diets Containing
Soy May Reduce
Prostate and
Colon Cancer Risk**

Soy and Prostate and Colon Cancers

Introduction

Cancer is the second leading cause of mortality in the United States, accounting for 23 percent of the death rate.¹ Very few American adults have not been touched by the difficulties and pain caused by this insidious disease. Cancer incidence and mortality rates vary widely throughout the world.² Diet and lifestyle are considered important factors contributing to the geographical variability in cancer.³

Prostate and colon cancer are strongly influenced by what we eat and how we live.⁵ Colon cancer occurs with nearly equal frequency in both women and men and is the third most frequent cancer in the United States; prostate cancer is the second most frequent cancer for males.¹ These cancers occur and are detected more frequently later in life, but most likely were initiated when people were in their thirties or forties, or even earlier. These cancers progress through several developmental stages and, if the cancer process could be slowed even a little during the 15 to 30 year period of growth before the tumor can be detected, much of the clinical severity of cancer would not occur during our lives. It is estimated that 75 percent of prostate and 70 percent of colon cancers in the United States could be avoided by dietary changes.⁴ There is evidence to suggest that eating soy is one thing we can do to slow the growth of cancers of the prostate and colon.

Epidemiology – Prostate Cancer

The early stages of prostate cancer occur at fairly similar rates throughout the world.⁵ However, the rates of more advanced, clinically important prostate cancer in the United States and other Western countries are much higher than in Asian countries. For example, latent prostate cancer in China is nearly the same as in the United States,⁶ yet prostate cancer mortality in the United States is 17 times greater.² In Japan, prostate cancer mortality is only 30 percent of that in the United States.²

Males of Chinese and Japanese descent who have lived in the United States for two or more generations have a lower rate of prostate cancer than African-Americans and whites,⁷ but their prostate cancer rate is still considerably greater than their counterparts who remain in China and Japan. These observations, and the fact that Asians eat much more soy than Americans do, led to the suggestion that soy consumption may in part protect against the development of clinically important prostate cancer.⁸

Studies that include populations with a wide range in prostate cancer rates and a wide variety of soy consumption patterns generally show that men who eat soy are less likely to develop prostate cancer. For example, consumption of soy products was much more protective than any other dietary factor in a study that examined nutritional and socioeconomic factors related to prostate cancer mortality in 42 countries.⁹ Likewise, consumption of

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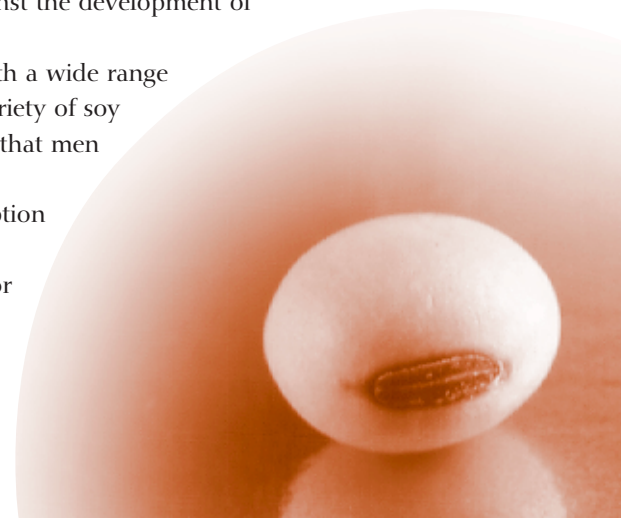
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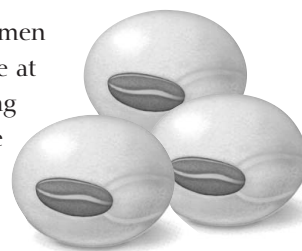
soymilk more than once per day was associated with a 70 percent reduction in prostate cancer risk.¹⁰ However, studies with populations that have small variations in prostate cancer rates and/or small variations in soy consumption tend to find that soy consumption reduces prostate cancer only slightly^{7,11,12} or not at all.¹³

Epidemiology – Colon Cancer

The epidemiological studies relating soy consumption and risk of colon cancer have been reviewed.¹⁴ Most epidemiological studies of dietary patterns and cancer incidence were not explicitly designed to determine if soy modifies colon cancer incidence or mortality; they were designed to answer general questions about diet and cancer. Most often there was just one item in the food intake questionnaire and that item included all pulses (nuts, seeds, lentils, peas and soybeans) and all types of dry beans. The studies often lacked statistical power to detect the existence of a relationship between soy consumption and colon cancer prevention. While some studies suggest that soy may reduce the risk of colon cancer, overall the epidemiologic studies to date do not suggest that eating soy protects against colon cancer. Prospective studies designed to determine if there is a relationship between soy intake and colon cancer are warranted.

Clinical Studies – Prostate Cancer

Two studies have utilized changes in serum prostate specific antigen (PSA) levels to assess reduction, stabilization, or progression of prostatic cancer. The first study fed 38 grams of soy protein with 70 or 4 mg of total isoflavones for six-week periods in a crossover-study to 34 men with elevated PSA. Half of the subjects had pre-study biopsies and none of these had prostate cancer. The other half declined to have biopsies. Neither of the soy preparations altered blood PSA levels.¹⁵ A second study¹⁶ enrolled 41 patients with confirmed prostate cancer. All patients had progressive or recurrent cancer based on increasing concentrations of serum PSA or PSA concentrations greater than 10 micrograms per liter. The patients consumed pills containing 100 mg of soy isoflavones twice daily for a median time period of six months. Overall, soy isoflavone treatment slowed prostate cancer growth as assessed by a slowing of the rise in PSA levels. Four patients had not received treatment prior to the study. In three of these men, PSA levels were stabilized by consuming soy isoflavones, indicating a slowing of the prostate cancer growth. Eighteen patients had previously had surgery or radiation therapy, but serum PSA was increasing before the study. Consumption of soy isoflavones resulted in 15 of these patients having stabilized PSA levels. Nineteen men had previously received hormone therapy, but had recurrent or progressive disease at the beginning of the study. Six of these men's PSA levels stabilized after consuming soy isoflavones. Both studies indicate that soy isoflavones will not cause a decrease in serum PSA levels. However, the second study suggests that a significant number of men benefited by consuming soy isoflavones even after surgery, radiation, or hormonal therapy had not successfully stabilized the disease. Additional clinical studies are underway and are expected to help clarify the potential of soy and soy isoflavones to inhibit prostate cancer.



Clinical Studies – Colon Cancer

One clinical intervention study has been conducted to determine if eating soy would alter indicators of colon cancer risk and only preliminary data from this study have been published.¹⁷ The colon mucosa in people with increased risk of colon cancer have characteristic alterations in cell proliferation and maturation. Compared to young people with no known risk for colon cancer, people with increased risk have a delay in cell differentiation leading to an expanded and upward shift in the cell proliferation zone and an increase in the number of cells undergoing cell division. Therefore, cell proliferation and maturation were studied in subjects at moderate risk of developing colon cancer (i.e., the subjects had a history of colon polyps or cancer). The subjects were fed powdered supplements that were mixed with a beverage of choice. The supplements contained either 38 grams of soy protein with 70 mg of total isoflavones or 38 grams of casein protein. Biopsies of the colon mucosa were taken before the study started and after subjects consumed the protein supplements for a year.

There was a downward shift in the proliferation zone and an increase in cell differentiation in the colon mucosa of subjects fed soy protein with isoflavones, which indicates that they were at a significantly lower risk of developing colon cancer. For the subjects eating casein for a year, there was no change in cell proliferation patterns or cell differentiation, indicating colon cancer risk was unchanged.

Animal Studies – Prostate Cancer

Studies with laboratory animals and cultured cells provide evidence that soy can protect against prostate cancer. Feeding soy protein containing isoflavones to rats inhibited both spontaneous (naturally occurring) and carcinogen-stimulated prostate cancer.^{18,19} It was concluded that the isoflavones – genistein in particular – reduced prostate cancer by normalizing testosterone levels, which in turn slowed or prevented the progression of early precancerous lesions into tumors.

Typical variations in blood testosterone or its metabolite, dihydrotestosterone, are not highly correlated with prostate cancer rates in men.²⁰ However, agents such as genistein that bind to estrogen receptor beta reduce the number of androgen receptors in the prostate gland.²¹ The early stages of prostate cancer are testosterone-dependent and reducing the number of androgen receptors in the prostate effectively reduces the influence of testosterone. A reduction in androgen receptors in the prostate gland by genistein may explain why feeding a soybean extract containing genistein resulted in a 50 percent reduction in chemically-induced, testosterone-stimulated prostate cancer.²²

The potential for dietary soy to treat more advanced stages of prostate cancer has been studied by transplanting segments of prostate tumors or prostate cancer cells into rats and mice fed diets with or without soy and then measuring tumor growth. Feeding soy flour or protein that contained isoflavones resulted in a small inhibition of tumor growth.^{23,24,25} Greater reduction of prostate cancer was achieved by supplementing soy protein diets with an isoflavone-rich soy extract.²⁶ In a more aggressive cancer treatment model, prostate tumor growth and metastasis were decreased by injecting genistein twice a day.²⁷

There are at least three probable mechanisms for prostate cancer inhibition by soy and soy isoflavones. First, genistein can bind to estrogen receptor beta and reduce the number of androgen receptors in the prostate gland.²¹ Second, genistein can reduce blood levels of testosterone in laboratory animals^{18,19} and may reduce testosterone levels in men.²⁸ Third, genistein at physiological levels inhibits cancer cell growth^{29,30} at least in part by promoting gene activity to slow cell proliferation.³⁰

Animal Studies – Colon Cancer

With the exception of two studies,^{31,32} the majority of animal studies show that feeding soy protein with isoflavones,³³ full-fat soy flour,³⁴ or defatted soy flour^{35,36} significantly reduces chemically-induced colon cancer. The studies with full-fat or defatted soy flour have been repeated at least twice, include a large number of animals, and produce a consistent inhibition of colon cancer.

The type of soy consumed will impact the level of colon cancer inhibition. For example, extracting soy flour with alcohol to produce soy concentrate removes the cancer inhibiting properties.^{35,36} Feeding extracted soy isoflavones (a mixture of isoflavones) does not inhibit colon cancer³⁶ whereas colon cancer is actually increased by feeding purified genistein³⁷ or genistin³⁶ (the glucoside conjugate of genistein which is the form of genistein found in soy). It should be noted that genistein/genistin would only be available as a single isoflavone in pharmaceutical preparations and not in soyfoods or soy extracts. The adverse effects were observed only when the single isoflavone genistein/genistin was fed. The soy products that most consistently inhibited colon cancer are full-fat soy products and defatted soy flour.

Conclusions and Recommendations

While more research is needed, there is sufficient strength in the overall data to recommend eating soy as one dietary practice to help reduce prostate and colon cancer risk. When a variety of experimental approaches, methods, and endpoints are utilized in research, it is not unusual for some deviations in the results as noted above. Soyfoods fit into the recommendations made by experts^[3] for reducing cancer, heart disease and other chronic diseases.

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