

The Line on Flax Lignans

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The phytoestrogen component of flax beneficial for breast, prostate cancers and heart disease



The flax plant has certainly been a friend of humankind. First used as a key structural component in linen and then in linoleum, it recently has been explored as a source of healing nutrients. During the 1990s, flax made headlines for being the highest source of the omega-3 fatty acid alpha-linolenic acid. Now flax is in the spotlight because it contains the highest-known concentration of another powerful plant compound: lignans.

Lignans, found in many plants, act as phytoestrogens. The primary lignans in flax are secoisolariciresinol diglucoside and Seco, which is SDG without attached sugar compounds. Other lignans found in lesser amounts are matairesinol and pinresinol. After being consumed, SDG and Seco are not absorbed directly into the body. Instead, they are acted on by colonic bacteria to produce another lignan, enterodiol, which in turn is transformed by more bacteria into the lignan enterolactone. Both enterodiol and enterolactone are directly absorbed into the body. While these mammalian lignans are created from plant sources that range from beans to pumpkin seeds, the concentration of precursor lignans in flax is greater than in all other sources.

Phytoestrogens such as lignans and the better-known isoflavones are plant compounds that appear to interact in some way with estrogen receptors in cell membranes. Because they can act either as estrogen-like compounds or block the effect of more powerful endogenous estrogens, lignans have been termed "selective estrogen receptor modulators," or SERMs. By acting at estrogen receptor sites, flax lignans appear to exert some control on the signaling of messages to the inside of cells that respond to estrogen. They also modify the levels of endogenous estrogens that are made by the body.¹

Oxidation protection is the other mechanism by which flax lignans affect the body. At the low concentrations found in the body, the mammalian lignans are highly powerful antioxidants in both aqueous and lipid, or fatty, environments.^{2,3} In one experiment, for example, the antioxidant activity of different substances was determined by the extent to which they reduced reactive oxygen species. The free radicals gave off a luminescence that could be measured. All lignans reduced the luminescence, therefore showing antioxidant capacity. Enterodiol reduced the luminescence by 94.2 percent, Seco by 91 percent, enterolactone by 82 percent and SDG by 23.8 percent. In contrast, vitamin E only reduced the luminescence by 19 percent.

Breast cancer protection

Most interest in flax lignans centers on their potential to reduce the risk of hormone-sensitive cancers, especially breast cancer.

In laboratory studies of breast cancer cells, enterodiol and enterolactone have been found to inhibit several steps involved in cancer metastasis: cancer cell migration, adhesion and invasion. Cell migration is the movement of cells from one part of the body to another. One of the steps that is essential to migration is adhesion; the use of special adhesive molecules that allow the cancer cell to attach itself to the extracellular matrix when it gets into the blood stream and is deposited elsewhere in the body. Once attached, the cell emits other chemicals that allow it to invade its new home and proliferate.

Both enterodiol and enterolactone—but not the drug tamoxifen—inhibit cell migration. As well, these mammalian lignans stop cell adhesion as effectively as tamoxifen, and their effect is synergistic with it.⁴

Animal studies have shown promise in this regard: Feeding flax or SDG to animals with breast cancer can slow tumor growth rates and prevent cancer from spreading. One study on animals with breast cancer found that flax supplementation reduced cells' metastasis to the lungs by 82 percent and the risk of metastasis to lymph nodes from 90 percent to 20 percent.⁵ Another study found an inverse relationship between cancer metastasis and the dose of SDG consumed.

How else do flax lignans protect against breast cancer? According to researchers, flax inhibits the compounds that cause metastasis—insulin-like growth factor and epidermal growth factor. By inhibiting vascular endothelial growth factor, flax lignans also halt the growth of blood vessels that nourish tumors.^{5,6,7}

While it is encouraging that flax may slow the spread of breast cancer in animals, women are wondering if it can reduce their risk of developing breast cancer in the first place. It is too early for prospective studies of flax supplementation, but there are numerous positive indications. Some of the body's own estrogens appear to have more or less estrogenic activity than others. Estrogens with more activity increase breast cancer risk. The ratio of 2-hydroxyestrone (a less-active estrogen) to 16-alpha hydroxyestrone (a more-active estrogen) is used as a measure of risk. Two studies of postmenopausal women have found that supplementation with 5, 10 or 25 grams of ground flaxseed per day for 16 weeks increases this ratio, altering the estrogen profile to reduce breast cancer risk.^{8,9}

There is a linear relationship between the amount of flax consumed and serum enterolactone levels.¹⁰ An indirect way of determining flax's effect on breast cancer risk is to compare enterolactone levels and breast cancer rates. The results are mixed. In one study, serum enterolactone levels were measured in 383 women with breast cysts. Over the subsequent six years, 18 developed invasive breast cancer (about .05 percent), leading the researchers to conclude that "enterolactone concentration had a strong protective effect on breast cancer risk."¹¹ Several case control studies have confirmed this association. A study published in the September 2004 *International Journal of Cancer* on 1,122 women with breast cancer and 2,036 controls in New York state found that premenopausal women whose dietary lignan consumption ranked in the top 25 percent* cut their risk of breast cancer by 44 percent. There was no correlation in the postmenopausal women.¹²

A German case control study on women under 50 also found that high intake* of foods containing matairesinol, but not SDG, or foods that cause the body to produce enterodiol and enterolactone reduced breast cancer risk about 40 percent.¹³ A Swedish case control study found low serum enterolactone, levels associated with higher breast cancer rates; a Finnish study did not.^{14,15}

Some of the variances in these studies could be pinned to the use of different food sources, although it should be noted that none of these studies mentioned flax as a prominent dietary source in study participants. So there is still a need for studies that look at flax consumers.

Recent genetic research has shown that premenopausal women who carry the CYP17 genotype may be at a higher risk for cancer. Lignans may be especially protective for these women according to a New York study on 207 women with breast cancer and 188

controls. Premenopausal women with high lignan intake* cut their breast cancer risk by 55 percent; postmenopausal women by 40 percent—results quite different from the other New York study mentioned above. But the women with CYP17 genotype whose dietary lignan intake ranked in the top 20 percent* slashed their risk by 88 percent.¹⁶

While high enterolactone or lignan levels may simply be associated with a healthier diet overall rather than being the direct cause of reduced breast cancer risk, the combination of the human, animal and cell studies point to a possible protective effect of flax lignans. And unlike with isoflavones—where they may have a protective effect for breast cancer, but there is some concern that once there is a cancer they may have a different, promotional effect on the cancer itself—none of the literature indicated this as an issue for dietary lignans.

Menopausal symptoms

Surprisingly little research has been conducted on how flax lignans affect menopausal symptoms, considering how the complex orchestra of estrogenic hormones is modified by lignan intake. An Australian double-blind crossover study found that women who supplemented with flaxseed enjoyed a 41 percent reduction in hot flashes.¹⁷ A Canadian study on 25 menopausal women found flaxseed supplementation relieved mild menopausal symptoms as effectively as hormone replacement therapy.¹⁸

Prostate cancer risk

Sex hormones also influence prostate cancer risk. In the laboratory, enterolactone inhibited three types of human prostate cancer cells.¹⁹ As well, in an animal study, animals supplemented with 5 percent flax had smaller, less aggressive tumors resulting in reduced lung and lymph metastasis; lower rates of cell proliferation; and more programmed cancer cell destruction, called apoptosis.²⁰ One human pilot study on flax supplementation has been conducted. In this study, men with prostate cancer were supplemented with 30g/day of flaxseed for 34 days. Compared with historical controls, they had less cancer cell proliferation and more apoptosis.²¹ In contrast to these positive findings, several case control studies have found no correlation between serum or dietary enterolactone and prostate cancer or benign prostatic growth.^{22,23,24} It is possible there might be an effect at higher levels of dietary lignan intake but not at the lower levels seen in these studies.

Cardiovascular disease and stress

Flax lignans might be expected to be protective against atherosclerosis, since other SERMs such as isoflavones protect against cardiovascular disease. In addition, lipid oxidation initiates atherosclerosis development and SDG is a strong lipid antioxidant. Indeed, men with low enterolactone levels have excessive lipid peroxidation, and a Finnish study on 1,899 men ages 42 to 60 found serum enterolactone levels inversely correlated with cardiovascular deaths.^{25,26}

Lignans may also help keep blood pressure under control. A Dutch study, described in the July 2004 issue of *Journal of Hypertension*, correlated the dietary lignan intake of postmenopausal women with their blood pressures. Women in the group with high lignan intake, an average daily consumption of 2.2 mg, had lower blood pressure than those in the group consuming only an average of 0.8 g/day. Their average systolic blood pressure was 11.2 mmHg lower; diastolic, 3.6 mmHg lower; and they were less apt to be hypertensive. The authors conclude: "The results suggest a protective effect of dietary lignan intake on blood pressure and hypertension, even at low levels."²⁷

A study that used several flax supplements with differing lignan concentrations is relevant in our high-stress world. Researchers at the Stroke Prevention and Atherosclerosis Research Center in Ontario, Canada, determined that people who respond

to stress with a blood pressure spike are apt to develop atherosclerosis. They conducted a random, double-blind, crossover study on 35 women ages 56 to 70 with cardiovascular disease and found that flax supplementation reduced hypertension resulting from mental stress. High-lignan flax provided the greatest protection. Flax also blunted a rise in the stress hormone cortisol. Those consuming the flax supplement highest in lignans had the lowest cortisol levels.²⁸ This has tremendous implications, because cortisol has been connected with a wide variety of problems from bone loss to memory loss.

Lignans and lupus

Animal studies have found that flax lignans can prevent renal damage including that caused by lupus.^{29,30} Adding SDG to the diet of animals with lupus can delay proteinuria (an indication of kidney malfunction) and protect the kidney's filtering apparatus in a dose-dependent manner.³¹ In a human crossover study on 23 lupus patients, half took flaxseed supplements for a year; the following year, the groups were switched. The participants who consumed the flaxseed supplements as ordered enjoyed lowered serum creatinine levels, while those who were noncompliant had an increase in serum creatinine, an indication of poor kidney function.³²

Flax and diabetes

Researchers are studying animal models of diabetes to see if flax can help. SDG supplements in animal studies lowered the rate of Type 1 diabetes by 71 percent and delayed the onset of Type 2 diabetes in an animal model. Researchers believe that SDG works by preventing the oxidative stress that is key to development of both types of diabetes.^{33,34}

Reproductive development

Exposure to sex hormones during early development may permanently affect the reproductive system. Research conducted in animals has used amounts of flax and SDG that are many times beyond the equivalent amount humans would consume. Most research has found little or no effect on reproductive organs or development.^{35,36,37,38} However, it may be circumspect to avoid large amounts of flaxseed supplementation during pregnancy and nursing.

** The amount of flax used in human studies ranges from approximately one-half teaspoon to 4 teaspoons per day of ground flax. A typical concentration of SDG in oil-free flaxseed is around 1.5 percent. According to Neil Westcott and Alistair Muir, two Saskatoon researchers in Saskatchewan, Canada, who have done considerable work on SDG, flax contains between 0.7 percent and 1.9 percent SDG, which is approximately 77 to 209 mg of SDG per tablespoon of whole seed, or 56 mg to 152 mg SDG per tablespoon of ground flax.*

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Availability of Flax Lignans

Flax lignans are available in many forms, ranging from high-lignan flax oil to flax meal-supplemented baked goods. Whole seeds must be chewed or crushed for the lignans to be absorbed. According to the Flax Council of Canada in Winnipeg, Manitoba, whole flax will keep stable for a year and ground flax is stable for four months at room temperature. Flaxseed oil in bottles does not require refrigeration until after it has been opened.³⁹

When flax oil was first brought onto the market, it had to be shipped refrigerated and stored refrigerated. To lower shipping costs, processors introduced a "nitrogen headspace" in the bottle that prevents oxygen from coming into contact with the unsaturated fats in the oil and thereby causing oxidation. This is also a common

method for bottling vegetable oils. Ground flax may be packaged in an aluminum-foil oxygen-barrier bag with the oxygen removed by flushing with three to 10 volumes of carbon dioxide or nitrogen.⁴⁰ This same approach can also be used with the oil and makes it stable for shipping to retailers.

—M.S.

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