

New FLAX FACTS

FLAX LIGNANS HAVE ANTICANCER EFFECTS IN BREAST TISSUE

by Dr. Diane H. Morris

Large-scale population studies show that diets rich in lignans are associated with a reduced risk of breast cancer. Flax and its lignans help protect against breast cancer by altering the metabolism of estrogen and by decreasing cell proliferation, according to findings from a small number of clinical studies. The animal data are strong – flax and its main lignans interfere with cancer processes and inhibit metastasis of mammary (breast) tumours to the lungs and other organs. One animal study found that the combination of flax and tamoxifen was better at decreasing tumour size in mice than tamoxifen alone. Eating flax regularly may reduce breast cancer risk and improve the clinical prognosis for women with breast cancer.

Whole flax seeds and milled flax are excellent sources of lignans. Indeed, flax is the richest known dietary source of lignans.¹ Lignans are phytoestrogens – plant compounds that can affect estrogen metabolism in animals and humans. The main flax lignan is secoisolariciresinol diglucoside (SDG). SDG is converted to the enterolignans or mammalian lignans – namely, enterodiols and enterolactone – by the action of bacteria in the colon.² Human and animal studies support a role for flax and its lignans in breast cancer prevention and control.

Information about flax lignans, their roles as phytoestrogens and antioxidants, and their anticancer effects can be found in Chapters 4 and 6 of the Council's book, *Flax—A Health and Nutrition Primer*, which is available on-line at www.flaxcouncil.ca

Flax Helps Protect Against Breast Cancer by Influencing Estrogen Metabolism

Breast cancer is hormone-sensitive, meaning that in the early stages, tumour growth is influenced by the sex hormones, particularly estrogen and its metabolites.³ The biologically active form of estrogen is estradiol, which is oxidized mainly in the liver to estrone. Estrone can be converted to two metabolites with different biologic effects – 2-hydroxyestrone has little biologic activity, while 16 α -hydroxyestrone enhances estrogen activity and promotes uncontrollable tumour cell growth or cell proliferation, as it is called.⁴ Women who produce more 16 α -hydroxyestrone may have an increased risk of breast cancer.⁵ Two clinical studies found that postmenopausal women who ate a diet supplemented with 10 g or 25 g of milled flax for 7 weeks⁶ or 16 weeks⁴ increased the excretion of 2-hydroxyestrone in their urine, without increasing the

excretion of 16 α -hydroxyestrone. In these studies, flax consumption shifted the balance toward production of the relatively inactive metabolite of estrogen, thus supporting a role for flax seed in breast cancer prevention.

Estrogen Receptors in Breast Tumours

Breast tumours that contain receptors for estrogen are estrogen receptor positive (ER+); tumours that lack estrogen receptors are called ER negative (ER-). Women with ER+ tumours are more likely to respond to hormone therapy than women whose tumours are ER-.³

Population Studies Suggest a Protective Effect of Dietary Lignans

According to two recent reviews of large-scale population studies published since 1997,^{7,8} plant and mammalian lignans appear to protect against breast cancer, at least in premenopausal women. The cancer protective effects of lignans in this population may be determined by the type of estrogen receptor in women's breast tissue.

One prospective cohort study among 58,049 postmenopausal French women found that those with the highest dietary lignan intake (>1395 μ g per day) had a significantly reduced risk of breast cancer.⁹ The beneficial effect of dietary lignans in this study was limited to ER+ and progesterone-positive breast cancers, suggesting a strong role for hormone receptors in controlling the biologic effects of lignans.

Flax Interferes with Cancer Processes in Animal Studies

Flax fed to carcinogen-treated rats and mice reduced tumour incidence, number, and size at the initiation, promotion and progression stages of mammary (breast) cancer.² Milled flax fed to rats decreased tumour incidence, number and size and resulted in lower levels of cell proliferation in mammary tissue.¹⁰⁻¹² Feeding milled flax slowed tumour growth rate in mice implanted with an ER- human breast cancer cell line¹³ and decreased tumour weight and volume in mice implanted with an ER+ human breast cancer cell line.¹⁴

Feeding pure SDG to rats appears to inhibit mammary tumour growth at the early promotion stage of cancer development.¹² Thus, pure SDG may affect new tumour development, whereas milled flax appears to exert its effects at later stages of tumour growth.¹⁵



Flax Enhances Tamoxifen's Anticancer Effects in Mice

Tamoxifen is widely used as adjuvant therapy for breast cancer, especially in women who have ER+ breast cancer. Despite its proven anticancer effects, tamoxifen has troubling side effects.^{16,17} A question often asked by women with breast cancer is this: Do flax lignans interfere with or enhance the anticancer actions of tamoxifen?

A mouse study was conducted at the University of Toronto to answer this question.¹⁴ The study assessed the effect of flax and tamoxifen, alone and in combination, on the growth of ER+ human breast cancer cells in mice.

Nude mice were injected with estrogen-dependent MCF-7 cells and then fed one of several diets. The diets contained 10% milled flax, a tamoxifen pellet (5 mg), or both. (A 10% flax diet is roughly equal to a human diet containing about 20-25 g or 2-3 tbsp of milled flax daily.) Tumour growth was monitored weekly.

In these mice, dietary flax inhibited the growth of human ER+ breast cancer cells. At low 17 β -estradiol levels, flax regressed tumour size by 74%; at high 17 β -estradiol levels, flax regressed tumour size by 22%. (17 β -estradiol is a key human estrogen.) Furthermore, flax enhanced the anticancer effect of tamoxifen – that is, flax + tamoxifen achieved a tumour regression >53% compared with tamoxifen alone.

Flax Lignans Block Metastasis in Mice

SDG inhibited metastasis in two studies of implanted ER– human breast cancer cells in nude mice. One study found that feeding SDG to mice decreased metastasis to lung, lymph nodes and other organs. Its effects were greater when it was combined with flax oil – the combination decreased total metastasis by ~43%.¹⁸

Another study assessed the therapeutic effect of flax and its main components – alpha-linolenic acid (ALA) and SDG – on the recurrence and metastasis after surgical resection of established primary mammary tumours in nude mice.¹⁹ The study was designed to mimic in mice the typical clinical situation in which there is a risk of tumour recurrence and metastasis in women who have had surgery to remove a breast tumour. The incidence of metastasis in nude mice was significantly lower in groups fed milled flax, pure SDG and SDG + flax oil. The study showed that dietary flax and its components (ALA and SDG) inhibited metastasis to lungs, lymph nodes and other organs, but had little effect on tumour recurrence in mammary tissue.

The researchers suggest that breast cancer patients who consume flax after surgery may experience reduced risk of metastasis and an improved clinical prognosis.¹⁹ Furthermore, consuming milled flax rather than pure SDG appears to be preferable – mice fed milled flax had the lowest incidence of metastasis among all diet groups.

Mechanisms of Lignans' Anticancer Effects

Mammalian lignans appear to exert anticancer effects through both hormone and non-hormone-related actions. The mammalian lignans enterodiol and enterolactone inhibit two key enzymes involved in estrogen synthesis; both enzymes are associated with increased breast cancer risk. Mammalian lignans may also have non-hormone-related actions, such as antioxidant activity, inhibiting angiogenesis and cell proliferation, and/or altering the expression of growth factors that stimulate tumour development.^{2,10,13,14}

More Clinical Studies of Flax and Cancer Are Needed

The findings of animal studies strongly suggest that flax and its lignans have anticancer effects. Although the clinical findings are promising, more clinical work is needed to confirm the anticancer effects of flax and the flax intake needed to achieve breast cancer protection.

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