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#### **Flaxseed in Cancer Reduction**

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Flaxseed contains three components that protect against cancer: lignans, alpha-linolenic acid, and dietary fibre.

Dietary lignan intake is associated with a decreased risk of developing postmenopausal breast cancer.

Alpha-linolenic acid possesses anti-inflammatory properties and may help to suppress the growth, size and proliferation of breast cancer cells.

High fibre intake is associated with decreased cancer mortality.

An estimated two out of five Canadians will be diagnosed with cancer during their lifetime and one out of four people are predicted to die from the disease.<sup>1</sup> In the United States, over 1.6 million new cancer cases were expected to be detected in 2014.<sup>2</sup>

A large number of cancers are preventable through dietary and lifestyle changes. An estimated one-third of cancers that occur in developed countries are related to overweight and obesity, sedentary lifestyle and/or poor nutrition.<sup>2</sup>

Figure 1. Effects of exposure to flaxseed, secoisolariciresinol diglucoside and flaxseed oil on carcinogenesis in a rodent model

Adapted from Mason and Thompson<sup>3</sup>



Table 1. Lignan content of some common foods as consumed (wet weight)<sup>6</sup>

Food item	<b>Matairesinol</b> (μg/100 g)	<b>Lariciresinol</b> (μg/100 g)	<b>Pinoresinol</b> (μg/100 g)	<b>SDG*</b> (μg/100 g)	<b>Total Lignans</b> (μg/100 g)
Flaxseed	153.3	2807.5	729.6	375321.9	379012.3
Sesame seed	123.1	1052.4	6814.5	7.3	7997.2
Garlic	4.8	54.4	481.9	42.0	583.2
Broccoli	0.1	82.0	6.1	5.8	93.9
Tofu	0.8	9.0	3.0	18.1	30.9
Lentils	0.2	16.3	9.0	1.2	26.6

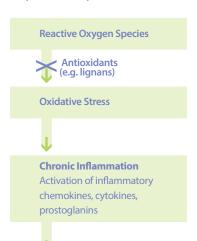
<sup>\*</sup>SDG, secoisolariciresinol diglucoside

#### Flaxseed is an ancient seed that fights modern disease

Flaxseed is a nutrient-dense food that contains three components that may help to lower cancer risk: the plant lignan secoisolariciresinol diglucoside (SDG), representing 1% of dry weight, the omega-3 polyunsaturated fatty acid alpha-linolenic acid (ALA), accounting for 20% of flaxseed dry weight, and soluble fibre representing 6% of dry weight. Flaxseed and its components have been shown to possess numerous anti-cancer properties (*Figure 1*).

## Figure 2. Molecular mechanisms involved in inflammation-related cancer

Adapted from Kamp et al.10



### Inflammation-related Cancer

Limitless replication, sustained angiogenesis, evasion of apoptosis, insensitivity to anti-growth signals, metastasis

#### Flaxseed lignans have anti-cancer effects

Lignans are phytoestrogens that are found in many plants, but flaxseed is the richest source (*Table 1*).<sup>4</sup> The predominant lignan in flaxseed is SDG, though small amounts of other lignans are also present, including pinoresinol, lariciresinol, and matairesinol. After ingestion, SDG is converted to mammalian lignans by bacteria in the colon. The first step in the conversion produces secoisolariciresinol (SECO), which is then converted to enterodiol and enterolactone.<sup>5</sup> These lignans are structurally similar to estradiol, the major form of estrogen in the body, which permits their binding to estrogen receptors.<sup>5</sup>

Prostate and breast cancers are the leading types of cancer diagnosed in men and women, respectively.<sup>2</sup> Sex hormones (estrogen and testosterone) play key roles in the development and progression of these cancers by increasing cell proliferation (production of new cells), metastasis (spread of cancer to other organs), and angiogenesis (growth of new blood vessels that support the spread of cancer).<sup>5</sup> Lignans compete with estrogen and testosterone for binding to their respective receptors.<sup>7</sup> When phytoestrogens bind to estrogen or testosterone receptors their estrogenic activity is weaker than that of endogenous hormones. Lignans also inhibit the enzyme aromatase which converts androgens into estrogen.<sup>7</sup>

SECO, enterodiol and enterolactone possess antioxidant activity.<sup>5</sup> Oxidative stress occurs when there is an imbalance between reactive oxygen species and antioxidants in the body which results in cellular damage. Oxidative stress and inflammation are closely linked, while inflammation and cancer are considered analogous to fuel and fire (*Figure 2*).<sup>8</sup> Plasma enterolactone concentration has been shown to be inversely correlated with plasma F2-isoprostane levels, a biomarker of oxidative stress.<sup>9</sup>

In animal models, flaxseed lignans have been shown to reduce tumour size, number, and degree of invasiveness of cancer cells as well as to induce physiological changes in the mammary gland and colon which are known to lower the risk of cancer development. Benefits of flaxseed lignans also include protecting healthy tissue while not hindering the effectiveness of the radiation in destroying tumours during cancer radiation therapy.



#### Flaxseed protects against breast cancer

A recent systematic review assessed the efficacy of flaxseed and its constituents (oil and lignans) on the risk of breast cancer development, recurrence, or mortality in humans. <sup>12</sup> Data from observational studies showed that ground flaxseed (32 g/day) may decrease the risk of breast cancer. <sup>12</sup> In patients with breast cancer, flaxseed intake of 25 g/day was associated with anti-tumour effects, including increased tumour apoptotic index (tumour cell death), decreased

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expression of HER2 (an oncogene associated with development and progression of breast cancer), and decreased tumour cell proliferation.<sup>12</sup>

In two meta-analyses, a higher intake of lignans from all dietary sources was associated with a modest reduction in postmenopausal breast cancer risk. <sup>13,14</sup> In five studies of patients with diagnosed breast cancer followed for 6.1 to 10 years, increased lignan exposure, measured by dietary records or serum lignan levels, was associated with a 40-53% reduction in all-cause mortality and a 33-70% reduction in breast cancer mortality.<sup>3</sup> Although not the focus of these assessments, flaxseed can contribute considerably to overall dietary lignan intake.

Flaxseed does not appear to interact with drug therapies for breast cancer and may in fact provide an additional protective effect when consumed concurrently with treatment. Flaxseed, flaxseed oil or SDG consumption in conjunction with tamoxifen, a standard breast cancer pharmaceutical has been shown in animal models to decrease tumour size to a greater extent than tamoxifen treatment alone.<sup>12</sup>

#### α-Linolenic acid: A cancer-fighting fatty acid

Flaxseed is the richest plant source of the essential omega-3 fatty acid ALA. Studies suggest that omega-3 fatty acids possess anti-cancer properties whereas omega-6 fatty acids promote the development of cancer. In the past, dietary intake of omega-6 and omega-3 fatty acids were approximately equal, but modern diets have significantly changed resulting in very high omega-6 to omega-3 ratios (16:1 or higher).<sup>15</sup>

ALA may protect against cancer via its anti-inflammatory properties and in particular its influence on eicosanoids - hormone-like substances with various metabolic functions. When omega-3 ALA intake is low and omega-6 intake is high, pro-inflammatory eicosanoid production from omega-6 is favoured. The opposite occurs when diets are higher in ALA. Similar to lignans, ALA has been found to suppress the growth, size and proliferation, and increase the death of, breast cancer cells in an animal model. Additional protective mechanisms of ALA include modulating the expression and function of numerous receptors, transcription factors and signaling molecules involved in reducing tumorigenesis.

#### Diets high in dietary fibre protect against cancer

Compelling evidence demonstrates that diets high in dietary fibre promote overall health and decrease mortality.<sup>17</sup> Flaxseed is a rich source of total dietary fibre providing 4 g of fibre per 2 tablespoon serving, or 16% of the recommended daily intake.

A recent meta-analysis investigated the association of fibre intake and all-cause and cause-specific mortality in large prospective cohorts. Mortality rate was reduced by 23 and 17 % for all-cause and cancer mortality, respectively, for individuals with the highest fibre consumption compared to those with lowest intake.

Obesity is a major risk factor for cancer and can impact survival rate for women with breast cancer.<sup>2</sup> Dietary fibre from flaxseed also may protect against cancer by preventing weight gain or assisting with weight loss by increasing satiety.

#### A little seed packed with big nutrition

Cancer is taking an enormous human toll around the world and is a growing threat to the health care system. The burden on individuals and families is profound. Flaxseed is a powerful food in the fight against cancer due to its content of three key components – lignans, ALA and fibre – all of which have been shown to help reduce the risk of several forms of cancer.

#### A Health Claim for Flaxseed



In 2014, Health Canada approved a health claim linking ground whole flaxseed to blood cholesterol lowering, a major risk factor for CVD. <sup>18</sup> The claim – only one of eleven approved in Canada - was based on seven clinical research trials of normal and hypercholesterolemic males and females aged 8 to 75 years who consumed 30 to 50 g/day of ground flaxseed. The primary endpoints in these studies were total cholesterol and low density lipoprotein (LDL) cholesterol, recognized risk factors for CVD. The pooled results from these studies found that compared to baseline, total cholesterol levels decreased by 0.21 mmol/L (- 0.56 to - 9.01 percent) and LDL decreased by 0.22 mmol/L (- 3.42 to -14.94 percent). <sup>18</sup> A reduction of 1 percent in total cholesterol levels is related to a 2 percent reduction in risk of CVD. Therefore, according to these studies, flaxseed intake may decrease the risk of CVD between 1 and 18 percent.

The "daily amount" referred to in the claim is 40 g (5 tablespoons) of ground whole flaxseed to be consumed over three eating occasions in the day.

An example of the permitted claim for ground flaxseed is: "16 g (2 tablespoons) of ground flaxseed supplies 40% of the daily amount shown to help lower cholesterol". In addition to this primary statement, the following additional statements may be used:

- Ground (whole) flaxseed helps reduce/lower cholesterol
- High cholesterol is a risk factor for heart disease
- Ground (whole) flaxseed helps reduce/lower cholesterol, (which is) a risk factor for heart disease

Flaxseed has been consumed for centuries due to its desirable flavor and nutritional properties. In recent years, as people have become more concerned about health, demand for flaxseed in food and beverages has risen dramatically. Scientific research and now regulatory approval supports the heart health benefits of flaxseed, particularly due to ALA, fibre and lignan contents.

HealthyFlax.org is the source of information on the health benefits and uses of whole flaxseed, ground flaxseed and flaxseed oil. Our website includes recipes, nutritional evidence, facts and news about flaxseed in all its forms. HealthyFlax.org is supported by Canada's flax growers, processors, food manufacturers and governments. For more information, email us at info@healthyflax.org





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