

Review

Nutritional and medicinal properties of flaxseed (*Linum usitatissimum*)

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ABSTRACT

Flax (*Linum usitatissimum*) is blue flowering annual herb that produces small flat seeds varying from golden yellow to reddish brown in color. It is cultivated in many parts of the world for fiber, oil as well as for medicinal purposes and also as nutritional product. Scientific evidences support consumption of flaxseed for the high content in omega-3, omega-6 rich oil, α-linolenic acid, lignans, high quality proteins and fibers and compounds which are biologically active in the prevention of some chronic diseases such as many types of cancer, diabetes, cardiovascular diseases, obesity and gastrointestinal disorders. Edible flaxseed products include the whole flaxseed, ground meal and extracted oil or mucilage. The present review focuses on the nutritional composition and evidences of its great potential as a medicinal food for a number of diseases inflicting human beings.

Keywords: Flaxseed; nutrient composition; medicinal food; chronic diseases

INTRODUCTION

Flax (*Linum usitatissimum*) belonging to the family Lineaceae is blue flowering annual herb that produces small flat seeds varying from golden yellow to reddish brown in color. Flaxseed possesses crispy texture and nutty taste (Morris 2007, Rubilar et al 2010). It has been cultivated for fiber as well as for medicinal purposes and as nutritional product (Tolkachev and Zhuchenko 2000). Currently it is cultivated in more than 50 countries predominantly in the northern hemisphere. Canada is the world's largest producer and exporter of

flaxseed (Oomah 2001). The important flaxseed growing countries include India, China, United States and Ethiopia (Oomah and Mazza 1998, Singh et al 2011). India ranks first among the leading flaxseed producing countries in terms of acreage accounting for 23.8 per cent of the total area and third in production contributing to 10.2 per cent of the world's production (Singh et al 2011). In India flaxseed is mainly cultivated in Madhya Pradesh, Maharashtra, Chattisgarh and Bihar. Flaxseed has been the focus of growing interest for the nutritionists and medical researchers due to its potential health

benefits associated with its biologically active components viz α -linolenic acid (ALA), lignan-secoisolariciresinol diglycoside (SDG) and dietary fiber (Toure and Xueming 2010). It has emerged as an attractive nutritional food because of its exceptionally high content of ALA, dietary fiber, high quality protein and phytoestrogens. Flaxseeds contain about 55 per cent ALA, 28-30 per cent protein and 35 per cent fiber (Carter 1993, Rubilar et al 2010, Rabetafika et al 2011).

Edible flaxseed products include the whole flaxseed, ground meal and extracted oil or mucilage. These products have been proposed as nutritional additives in the preparation of a number of dietary items such as baked cereal products, ready to eat cereals, fiber bars, salad toppings, meat extenders, bread, muffins and spaghetti (Singh et al 2011). Flaxseed is also added to animal feed to improve animal reproductive performance and health (Turner et al 2014). Minor components include cyanogenic glycosides, phytic acid, phenolics, trypsin inhibitor, linatine, lignans (phytoestrogens), minerals, vitamins, cadmium, selenium and cyclolinopeptides (CLs) (Bhatty 1995, Matsumoto et al 2001).

Flax protein helps in the prevention and treatment of heart disease and in supporting the immune system. Flaxseeds have nutritional characteristics and are rich source of ω -3 fatty acid (ALA), short chain

polyunsaturated fatty acids (PUFA), soluble and insoluble fibers, phytoestrogenic lignans (secoisolariciresinol diglycoside-SDG), proteins and an array of antioxidants (Ivanova et al 2011, Singh et al 2011, Oomah 2001, Alhassane and Xu 2010). Its growing popularity is due to its health imparting benefits in reducing cardiovascular diseases, decreased risk of cancer particularly of the mammary and prostate gland, anti-inflammatory activity, laxative effect, diabetes, neurological disorder, alleviation of menopausal symptoms, arthritis and osteoporosis. In spite of the multiple clinical evidences of flaxseeds people are still unaware about its nutritional as well as therapeutic benefits.

Nutritional properties

An analysis of brown Canadian flax averaged 41 per cent fat, 20 per cent protein, 28 per cent total dietary fibre, 7.7 per cent moisture and 3.4 per cent ash which is the mineral-rich residue left after samples are burned (Table 1) (Morris 2007). The protein content of flaxseed varies from 20 to 30 per cent constituting approximately 80 per cent globulins (linin and conlinin) and 20 per cent glutelin (Hall et al 2006). Flaxseed has an amino acid profile comparable to that of soybean and contains no gluten (Oomah 2001). The total nitrogen content in flaxseed is 3.25 g/100 g of seed (Gopalan et al 2007). Flaxseed protein is rich in arginine, aspartic acid and glutamic acid while lysine is limited (Singh et al 2011, Chung et al 2005).

Table 1. Chemical composition of nutrients and phytochemicals in flaxseed

Nutrients/bioactive compound	Quantity/100 g of seed	Nutrients/bioactive compound	Quantity/100 g seed compound
Carbohydrates	29.0 g	Biotin	6 mg
Protein	20.0 g	α -Tocopherolb	7 mg
Total fats	41.0 g	δ -Tocopherolb	10 mg
Linolenic acid	23.0 g	γ -Tocopherolb	552 mg
Dietary fiber	28.0 g	Calcium	236 mg
Lignans	10-2600 mg	Copper	1 mg
Ascorbic acid	0.50 mg	Magnesium	431 mg
Thiamin	0.53 mg	Manganese	3 mg
Riboflavin	0.23 mg	Phosphorus	622 mg
Niacin	3.21 mg	Potassium	831 mg
Pyridoxin	0.61 mg	Sodium	27 mg
Pantothenic acid	0.57 mg	Zinc	4 mg
Folic acid	112 mg		

Flaxseed contains substantial soluble and insoluble fiber. Cui (2001) reported the content of insoluble and soluble fiber to be 20 and 9 per cent whereas Hadley et al (1992) reported 30 and 10 per cent respectively. The major insoluble fiber fraction consists of cellulose and lignin and the soluble fiber fractions are the mucilage gums (Vaisey-Genser and Morris 2003, Mazza and Biliaderis 1989). Flaxseed is the richest source of phytoestrogens (lignans). The amount of secoisolariciresinol diglycoside (SDG) varies from 77 to 209 mg SDG/tbsp of whole flaxseed (Morris 2007, Toure and Xueming 2010). Lignan content in flaxseed is principally composed of secoisolariciresinol diglucoside (SDG) (294-700 mg/100 g), matairesinol (0.55 mg/100 g), lariciresinol (3.04 mg/100 g) and pinoresinol (3.32 mg/100 g) (Toure and Xueming 2010, Milder et al 2005).

Flaxseed contains very low level of carbohydrates (1 g/100 g) and thus contributing very little to total carbohydrates intake (Morris 2007). Basically flaxseeds have three different types of phenolic compounds viz phenolic acids, flavonoids and lignans. Major phenolic acids present in defatted flaxseed are ferulic acid (10.9 mg/g), chlorogenic acid (7.5 mg/g) and gallic acid (2.8 mg/g). Other phenolic acids include p-coumaric acid glucosides, hydroxycinnamic acid glucosides and 4-hydroxybenzoic acid that are present in low quantities (Beejmohun et al 2007, Mazza 2008). Flavone C and Flavone O-glycosides are the major flavonoids found (Mazza 2008). It serves as a good source of minerals especially phosphorus (650 mg/100 g), magnesium (350-431 mg/100 g), calcium (236-250 mg/100 g) and potassium (831 mg) and has very low amount of sodium (27 mg/100 g)

(Morris 2007). Its potassium content is high and comparable to those of recommended sources such as banana on a dry matter basis. Flaxseed contains small amounts of water-soluble and fat-soluble vitamins. Vitamin E is present as γ tocopherol amounting to 39.5 mg/100 g. Its oil is rich in polyunsaturated fatty acid (73% of total fatty acid), moderate in monounsaturated fat (18%) and low in saturated fat (9%) (Cunnane et al 1993, Dubois et al 2007). It serves as an exclusive source of omega-3 fatty acid in the vegetarian diets (Riediger et al 2008). Of all lipids in flaxseed (approximately 30%) 53 per cent are α -linolenic acid (ALA), 17 per cent linoleic acid (LA), 19 per cent oleic acid, 3 per cent stearic acid and 5 per cent palmitic acid which provide an excellent n-6:n-3 fatty acid ratio of approximately 0.3:1 (Simopoulos 2002).

Medicinal properties

A large number of clinical studies have recognized the tremendous potential of n-3 polyunsaturated fatty acids against inflammatory mediators like prostaglandins. Evidences showed that feeding with flaxseed (oil or enriched product) could help in prevent many diseases such as chronic, cardiovascular, obesity disorders and cancer.

Gastro-intestinal disorders: Water-binding capacity of flaxseed insoluble fiber increases the intestinal bulk which is useful in the treatment of constipation, irritable bowel syndrome and diverticular disease.

Soluble fiber from flaxseed mucilage increases the viscosity of intestinal contents and delays gastric emptying and nutrient absorption. Constipation and abdominal symptoms were decreased significantly in patients with constipation pre-dominated irritable bowel syndrome after receiving 6-24 g (mean 17 g) of ground flaxseed for three months (Tarpila et al 2004). Mucilage gums are polysaccharides that become viscous when mixed with water or other fluids and have an important role in laxatives (Singh et al 2011). Insoluble fiber helps improve laxation and prevent constipation mainly by increasing fecal bulk and reducing bowel transit time (Greenwald et al 2001).

Diabetes mellitus: Diabetes mellitus is characterized by hyperglycemia and is associated with aberrations in the metabolism of carbohydrate, protein and lipid that result in development of secondary complications (Mani et al 2011). India has the largest diabetic population and one of the highest diabetes prevalence rates in the world (Bjork et al 2003, King et al 1998). Untreated diabetes can lead to cardiovascular diseases, kidney failure and blindness. Dietary fibers, lignans and ω -3 fatty acids present in flaxseed have a protective effect against diabetes risk (Prasad 2001, Adlercreutz 2007). Flaxseed lignan SDG has been shown to inhibit expression of the phosphoenolpyruvate carboxykinase gene which codes for a key enzyme responsible for glucose synthesis in the liver (Prasad 2002). Utilization of flaxseed for glycemic

control may also be associated to the decrease in risk of obesity and dyslipidemia since these are risk factors for the development of diabetes and resistance to insulin (Wu et al 2010, Morisset et al 2009). Kapoor et al (2011) studied the effect of supplementation of flaxseed powder on diabetic human females. Patients were provided 15 and 20 g/day of flaxseed powder for a period of 2 months. Postprandial blood glucose levels were found to be decreased by 7.9 and 19.1 per cent respectively. Similar results have also been reported by Nazni et al (2006). Studies in animal models of diabetes mellitus have shown that SDG from flaxseed can prevent the development of type 1 diabetes by approximately 71 per cent (Prasad 2000) and type 2 diabetes by 80 per cent (Prasad 2001). Pan et al (2007) reported more modest but statistically significant improvements in glycemic control in type 2 diabetic patients treated for 12 weeks with 360 mg/day of flaxseed-derived lignan supplement.

Cancer: Flaxseed lignans play an important role in preventing various types of cancer specially the hormone sensitive cancers such as those of the breast, endometrium and prostate by interfering with sex hormone metabolism. Experiments have shown that flaxseed inhibits the formation of colon, breast, skin and lung tumors and also reduces blood vessel cell formation in female rats all suggesting a protective effect against breast, colon and ovarian cancer (Truan et

al 2012). Flax lignans are reported to have antioxidant property which presumably is the main reason of the anticancer activity (Schweigerer et al 1992, Prasad 1997). Blood insulin has also been associated with increased risk of pancreatic and colorectal cancers (Pisani 2008). Various studies suggest that flaxseed added to the diet may lower circulating levels of insulin and IGF-1 (Woodside et al 2006, Chen et al 2011a). Flaxseed has a breast tumor-reducing effect possibly because of its high content of SDG lignan (Truan et al 2012, Chen et al 2011a, Chen et al 2009). Flax lignans have shown promising effects in reducing growth of cancerous tumors especially hormone-sensitive ones such as those of the breast, endometrium and prostate (Tham et al 1998). Flaxseed oil with its exceptionally high ALA content was also shown to reduce human estrogen receptor-positive breast tumors (MCF-7) growth by 33 per cent compared to control (Truan et al 2010). Chen et al (2007) studied that the groups of mice that received 5 and 10 per cent flaxseed in the diet for 8 weeks inhibited tumor growth by 26 and 38 per cent respectively. Flaxseed oil given at 14 g/d to human subjects over 4 weeks decreased the levels of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6) and cytokines. A lower dose did not have this effect (Caughey et al 1996, Thies et al 2001, Wallace et al 2003). Some encouraging results have been gained with pure enterolactone and enterodiol in prevention of human colon cancer cell growth (Qu et al 2005).

Experimental evidence in animals has shown anticarcinogenic effects of flaxseed or pure lignans in many types of cancer; flaxseed oil can inhibit the growth and development of tumors in the breast of laboratory animals (Lamblin et al 2008). Ennis and Thompson (2014) researched the influence of flaxseed lignans and oil components in reducing breast cancer risk and tumour growth. Mechanisms included decreased cell proliferation and angiogenesis and increased apoptosis through modulation of estrogen metabolism and estrogen receptor and growth factor receptor signalling pathways.

Dyslipidemia and cardiovascular diseases (CVD): Serum lipid profile is directly related to the risk factors of cardiovascular diseases. It is the most intensely investigated effect studied in animals and humans after supplementation of flax in diet of rats, mice and rabbits that presented positive responses for biochemical parameters indicating the hypocholesterolemic activity of flaxseed generally related to the greater fecal content of lipids (Hassan et al 2012, Khalesi et al 2011, Mani et al 2011, Cardozo et al 2010, Barakat and Mehmoud 2011, Leyva et al 2011). SDG plays an important role in reduction of hypercholesterolemia, atherosclerosis, hypertension and diabetes (Prasad 2000, 2004). Daily administration of 100 mg SDG was found to be effective in reducing blood cholesterol and hepatic diseases risk in moderately

hypercholesterolemic men (Fukumitsu et al 2010). Gillingham et al (2011) reported reduced levels of HDL fraction in human serum after consuming flaxseed oil in diet for 28 days. When type 2 diabetic patients were fed defatted flaxseeds for 2 months patients showed significant reduction of plasma glucose, improvement in plasma lipid profile and significant reduction of lipid peroxidation (Mohamed et al 2012). Dietary flaxseed may also offer protection against ischemic heart disease by improving vascular relaxation responses and by inhibiting the incidence of ventricular fibrillation (Jennifer et al 2010). However Vedtofte et al (2011) reported that higher intake of ALA was not significantly associated with decreased risk of ischemic heart disease among women or men. Feeding Golden Syrian hamsters 20 g/d ALA for six weeks reduced serum cholesterol by 17-21 per cent (Yang et al 2005). Treatment of subjects with flaxseed lignin complex (40 mg/kg body weight, bw)/d for eight weeks suppressed the development of hypercholesterolemic atherosclerosis by 34 per cent in rabbits (Prasad 2005). The 300 mg dose of flaxseed lignin complex reduced total cholesterol and LDL cholesterol by 15 and 17 per cent respectively without any change in the ratio of total cholesterol/HDL cholesterol. A higher dose of 600 mg reduced the serum total cholesterol and LDL cholesterol by 24 and 22 per cent respectively with a decrease in the total cholesterol/HDL cholesterol ratio (Zhang et

al 2008). Supplementation of the cholesterol-enriched diet with ground flaxseed lowered plasma cholesterol and saturated fatty acids, increased plasma content of ALA and inhibited plaque formation in the aorta and aortic sinus compared with mice fed a diet supplemented with only dietary cholesterol (Dupasquier et al 2007). Marambe et al (2008) showed that flaxseed protein hydrolysate inhibited the enzyme responsible for conversion of the decapeptide angiotensin I to octapeptide angiotensin II, a vasoconstriction hormone causing an increase in blood pressure. After feeding rats with specific doses of flaxseed SDG decreased the systolic, diastolic and mean arterial pressure. Data suggested that SDG reduced the angiotensin I-induced rise in the arterial pressures and hence SDG was a potent ACE inhibitor. SDG can prevent the development of atherosclerosis and diabetes (Fukumitsu et al 2008, Prasad 2009) and additional benefits include modification of blood lipids and cholesterol levels (Fukumitsu et al 2010). It also contains peptides with bioactivities related to the decrease in risk factors of CVD (Udenigwe and Aluko 2010). Recently it was demonstrated that consumption of one whole flaxseed product in the form of a bagel, muffin, bar or bun that containing 30 g of flaxseed by a group of patients displaying pulmonary artery disease and elevated blood pressure significantly reduced both systolic and diastolic blood pressure (Rodriguez-Leyva et al 2013).

Atherosclerosis was significantly prevented by flaxseed supplementation in the hypercholesterolemic rabbit (Dupasquier et al 2006) and in the cholesterol-fed, low-density lipoprotein (LDL) receptor-deficient mouse (Dupasquier et al 2007). Flaxseed (0.4 g/day) effectively inhibited the expression of inflammatory markers such as interleukin (IL)-6, mac-3, vascular cell adhesion molecule (VCAM)-1 and the proliferative marker proliferating cell nuclear antigen in aortic atherosclerotic tissue from LDL receptor-deficient mice (Dupasquier et al 2007). Djousse et al (2005) found that dietary ALA (highest quartile 1.09 g/day) was associated with a lower prevalence of hypertension and lower systolic blood pressure in 4594 subjects. Others (Bemelmans et al 2000, Takeuchi et al 2007) have confirmed that dietary ALA is associated with lower blood pressure values. ALA may lower blood pressure by acting as a precursor for eicosanoids which can generate the production of prostaglandins and leukotrienes that may reduce vascular tone (Salonen et al 1988).

Obesity: Flaxseed fibers form highly viscous solution upon hydration which is similar to those observed for other gums (Goh et al 2006). Particularly viscous fibers appear effective in suppression of hunger (Wanders et al 2011, Kristensen et al 2011). Dietary fibers from it were found to have a direct relation to health in particular in body weight regulation through both hunger suppression and diminished nutrient

absorption (Kristensen et al 2012) generally soluble fiber forms a gel when mixed with water. This gel slows down the emptying of the stomach potentially lowering blood glucose levels. Cholesterol is also lowered as it is surrounded by the gel which inhibits its absorption and leads to more cholesterol being excreted. Soluble non- starch dietary fibers of flaxseed mucilage are multi-branched hydrophilic substances forming viscous solutions that delay gastric emptying and nutrient absorption from the small bowel. Leptin protein levels were elevated in animals taking diet supplemented with 10 per cent flaxseed. Weight gain was also limited in rats fed soluble fiber and dietary linseed in contrast to controls (Kristensen et al 2013). Kristensen et al (2012) found that addition of a flax dietary fiber extract rich in viscous dietary fibers significantly increased fat excretion and lowered total and LDL-cholesterol with no effect on appetite.

Menstrual cycle: Consuming flaxseeds is one of the food choices that help to regulate menstrual cycle due to the presence of lignans (phytoestrogens). These phytoestrogens have weak estrogenic and anti-estrogenic properties which help balance the menstrual cycle (Garvin 2011). Supplementation of dietary flaxseed (40 g/day of crushed flaxseed) exerts effects similar to that produced by hormone replacement therapy for decreasing menopausal symptoms (Lemay et al 2002) as well as hot flashes in post-menopausal

women not taking estrogen therapy (Pruthi et al 2007). Lignans are phytoestrogens that have been shown to exert hormonal effects (Hutchins et al 2001, Rodriguez et al 2010). Phytoestrogens present in flaxseed help to reduce menopausal symptoms such as hot flashes (Edwards 2003).

Other medicinal uses: Flax lignans-isolated SDG preparations are also commercially available as a dietary supplement (Chen et al 2011b). Flaxseed oil is rich source of essential fatty acids (EFAs): linoleic acid (ω -6) and α -linolenic acid (ω -3) which regulate prostaglandins synthesis and hence induce wound healing process. Flax preparations were widely used in medicine as an enveloping and wound-healing agent in the treatment of gastrointestinal disorders (Ivanova et al 2011). It was also used for the treatment of freckles (in a mixture with soda and figs) and nail disorders (with garden cress and honey) (Tolkachev and Zhuchenko 2000). Flaxseed also acts as anti-arrhythmic (Ander et al 2004), anti-atherogenic (Dupasquier et al 2006, 2007), and anti-inflammatory (Dupasquier et al 2007) agent in addition to helping in improving vascular function (Dupasquier et al 2006).

CONCLUSION

Flaxseed is the richest source of α -linolenic acid and lignans. It is also a considerable potential source of soluble fiber and antioxidants. Flaxseed coat

materials are a rich source of lignans and the polysaccharide mucilage. The latter has profound effects on digestive health. Healthy properties are related to anti-inflammatory, anti-oxidant, anti-carcinogenic activities and to the lowering of cholesterol, the decrease of cardiovascular disease and the prevention of diabetes. A large number of nutritional attributes present in it are attracting the health professionals and nutritionist to consider the flaxseed in the formulation of functional foods and in the choice of a healthy diet. It is a rich source of alpha linolenic acid (ALA), fiber and lignans, gums which make it a potentially attractive functional food for modulating several risk factors responsible for causing diseases. Flaxseed constituents provide disease preventive and therapeutic benefits. The role of flaxseed lignans and ω -3 fatty acid in reducing the risks associated with cardiac and coronary disease, cancer (breast, colon, ovary and prostate) and other human health risk factors is well known. Therefore the use of flaxseed in whole seed or ground form can be recommended as a dietary supplement.

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