

Pharmacological Activities of *Linum Usitatissimum* (Linseed/Flaxseed)

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ABSTRACT

Linseed, originating in Mesopotamia, has been cultivated since 5000 BC, and was used up to the 1990s primarily for the production of paper and cloth. It is mainly grown for its fiber content; however, its seeds are edible and can help prevent cancer, cardiovascular disease, diabetes, and stroke. Linseed oil is edible and considered one of the earliest marketable oils, also used for pharmaceutical purposes. The consumption of plant estrogens in the diet reduces total plasma cholesterol and low-density lipoprotein; moreover, it is proposed to decrease the risk of CVD. Plant estrogens found in flaxseed help control heavy periods by balancing estrogen levels in the body. Linseed exerts its protective effect by shortening the duration of the cardiac action potential and the QT interval. The constituents of flaxseed oil have bioactive properties that make it more effective than recognized commercial medicines in promoting wound healing. This review article focused on the medicinal use of Flaxseed, including its role in reproductive and cardiovascular health, diarrhea, burn healing, and utility for post-menopausal women.

Keywords: Linum usitatissimum, Linseed, Flaxseed, Pharmacology, Reproductive health, Diarrhoea, Burns, Cardiovascular health

Introduction

Linseed, belonging to the Linaceae family, is an annual herb with blue flowers and

produces small, smooth, even seeds that vary in color from yellowish to reddish brown. The seeds of flax have a nut-like taste and crispy texture(H. Morris, 2007)(Rubilar et al., 2010)The entire seed of flax is smooth, even, and oval with tapered tips, ranges in color from dark to yellow, and measures nearly $2.5 \times 5.0 \times 1.5$ millimeter. Linseed continues to grow in recognition as a functional food; it has numerous nutritional properties and is rich in the crucial ω -3 FAs, ALAs, and various plant chemicals. *Linum usitatissimum* also provides protein and dietary fiber(Oomah et al., 1995). Nearly all fragments of the flaxseed plant are used for numerous health reasons. The seed of flax consists of oil, which, after purifying, becomes consumable and can be taken as a functional food(Singh et al., 2011)(Singh et al., 2012).The plant's stem produces high-quality fiber with great strength and durability. It is one of the ancient fibrous crops and has been grown in India and China for 5,000 years, and was cultivated in Samaria and Egypt around 10,000 years ago(Akhtar et al., 2013)(Wiszniewska et al., 2016). The initial cultivation of flax in European regions was established in Scotland, Switzerland, and Poland. Flax is also grown as a decorative plant in gardens due to its beautiful flowers. It has been utilized for its fiber content, as flax fiber is used to produce linen in numerous textile industries due to its natural ability to straighten. The fiber of flax is strong and is also used to make embellished solid yarn, fabrics, and tires(Zhang et al., 2010)(Saleem, Fahad, et al., 2020).

People have been using *Linum usitatissimum* since prehistoric times. It has been fertilized for its fiber content, in addition to medicinal reasons, and as a nutritive product, mainly in the cooler regions of the world(Tolkachev & Zhuchenko, 2000).Linseed, which originated in Mesopotamia, has been cultivated since 5000 BC and was used up to the 1990s primarily for the production of paper and cloth. Nowadays, it is grown on more than 2.6 million hectares, and the major linseed-producing countries are China, India, Ethiopia, and the USA. Canada, with 6 lac 14 thousand metric kilograms of linseed generated in the year from 2013 to 2014, is the world's biggest producer of *Linum usitatissimum* and accounts for approximately eighty percent of the worldwide trade of linseed(Oomah, 2001)(Rajju Priya Soni et al., 2017)It is primarily grown for its fiber content; however, its seeds are edible and can prevent cancer, cardiovascular diseases, diabetes, and strokes(Imran et al.,

2019)(Saleem, Kamran, et al., 2020). Its oil, also known as 'linseed oil', is edible, considered one of the earliest marketable oils, and used for pharmaceutical purposes. (Saleem, Ali, et al., 2020)It is gaining a reputation as a functional food and is one of the abundant sources of plant EFAs.It is recognized to comprise 40-50% oil, 23-34% protein, mucilage or fiber 5%, ash 4%, and 9-30 milligrams per gram of lignin precursors, as well as other therapeutically active components(Palla et al., 2015).

Medicinal Uses of Flaxseed

Linseeds as a functional food, as utilized and explained by Pliny the Elder and Dioscorides.(Hasler et al., 2000)Moreover, Ibn al-Baitar reported it as a substance that has good abortion inducing activities, and cited Dioscorides that consuming it mixed with honey and Piper nigrum arouses sexual need. (Noweir et al., 1975)The oil of *Linum usitatissimum* was prescribed in intestinal colic (caused by chronic lead poisoning) and other conditions of spasm in the bowel. In Persian medicine, seeds have been used to manage inflammatory bowel disease. (Rahimi et al., 2010)In total, and in the grounded form, the smaller seeds have a greater tendency to swell than the larger ones; however, the quantity of fatty oil is greater in the larger seeds compared to the smaller ones. In addition to being a rich source of ALA, they are also a valuable source of soluble mucilaginous fiber. Flax oil consists of unsaturated FAs, such as linoleic acid, oleic acid, and linolenic acid, as well as additional phenolic constituents, such as phenolic acids. Consumption of uncooked, powdered flax seeds for 4 weeks by healthy female volunteers reduced serum total Cholesterol by 9% and low-density lipoprotein by 18%, and significantly reduced post-meal blood glucose. In conventional medicine, flaxseed tea was consumed as a demulcent hot drink for coughs, not only alleviating inflammation and irritation but also soothing the mucous membranes of the pharynx and upper respiratory tract. It was similarly beneficial in discomfort or irritation of the intestines and urinary tracts. Greco-Arabic doctors consider flax seeds a laxative, anti-inflammatory, resolvent, mucolytic, concoctive, analgesic, wound-healing, and sexual stimulant; while the flowers are considered a heart tonic. A flax poultice is advised for rheumatic and gouty inflammations; with honey, it is recommended for colds and coughs. Moreover, oil is also applied to both internal and external inflammatory conditions, for instance, pneumonia, pleurisy, and arthritis—application of the oil with lime-water to burns is

handy—and taking oil internally aids in glomerulonephritis and atherosclerosis. *Linum usitatissimum* is now widely used in food, as a nutritional supplement for menopausal symptoms, and as a laxative (Flower et al., 2014), due to its high content of ω -3 FAs and ALA. α -linolenic acid has been reported to have a positive effect on cardiovascular disease (Rodriguez-Leyva et al., 2010). At moderate doses of 14 ng/day or greater, it decreases inflammatory markers (Prasad, 2009b). In addition to being one of the most abundant nutritional sources of α -linolenic acid, they are also a good source of mucilaginous soluble fiber (S. C. Cunnane et al., 1993; Rodriguez-Leyva et al., 2010). Linseeds are also one of the abundant sources of low molecular weight polyphenols or precursors of plant estrogen, i.e. lignans (Tham et al., 1998), that are metabolized after consumption by intestinal microbes into enterodiols, enterolignans, and enterolactone (Lamblin et al., 2008), and are not destroyed by heat, even subsequent of heating at 250 degree centigrade (Gerstenmeyer et al., 2013). Squashing and grinding seeds significantly improve the bioavailability of intestinal lignans (Kuijsten et al., 2005). The consumption of plant estrogens in diet (Xu et al., 2012) reduces total plasma cholesterol and low density lipoprotein, moreover proposed to decrease the risk of CVD (Bassett et al., 2009), (Peterson et al., 2010) by averting atherosclerosis (Prasad, 2009a), and hold back the advancement and development of chronic kidney disease (Velasquez & Bhatena, 2001). Lignans in linseed also exhibit anti-inflammatory and antioxidant activities (Alcorn et al., 2017). SDG (Secoisolariciresinol diglucoside), a lignan compound, is believed to have a protective effect on the heart due to its estrogen-like activities (Hallund et al., 2006) and may decrease the risk of breast cancer (Sturgeon et al., 2010). In Iranian patients, local application of *Linum usitatissimum* oil for up to 4 weeks significantly improves symptoms and function in ICTS (idiopathic carpal tunnel syndrome) (Hashempur et al., 2014; Setayesh et al., 2017). The oil also considerably improved symptoms of Attention Deficit Hyperactivity Disorder in Indian children (Joshi et al., 2006), and consumption of flax oil by German women for up to 12 weeks enhanced skin hydration and reduced TEWL (transepidermal water loss) (De Spirt et al., 2009).

Flaxseed for Reproductive Health

Linseed consumption is one food option that helps regulate the menstrual cycle due

to its phytoestrogenic lignans. These plant estrogens exhibit weak anti-estrogenic and estrogenic activities, helping maintain the balance of the menstrual cycle (Phipps et al., 1993). Consumption of Linseed powder was consistently associated with prolonged luteal phase lengths in 3 successive cycles and progressively higher progesterone/estradiol ratios during this stage in females with regular menstrual cycles (Phipps et al., 1993). Meta-analyses of randomized controlled trials and various systematic reviews indicate that Linseed may have estrogen-like effects and help reduce the severity and frequency of hot flashes, but the evidence is inadequate (Dew & Williamson, 2013; Ghazanfarpour et al., 2016). The existence of ALAs makes Linseed beneficial in improving the symptoms of premenstrual syndrome.

Plant estrogens found in flaxseed help regulate heavy periods by balancing estrogen levels. The seeds also reduce breast pain, which is commonly associated with the menstrual cycle. However, not adequate scientific proof is there to back-up this statement (Jessica Bruso, 2013). It is also beneficial for reproductive health of males as in a small scale preliminary study and a multisite randomized controlled trials managed by M. D. Anderson Cancer Center, United states of America, the patients of prostate carcinoma continued on diet that is supplemented by flaxseed- in the entire duration before surgery and not fat-limited diet, had considerably reduce growth and spread of cancer cells. (W. Demark-Wahnefried et al., 2001) (Wendy Demark-Wahnefried et al., 2008).

Flaxseed in Diarrhea

Diarrhea is described as enhanced frequency of liquid stools frequently escorted with abdominal pain. Diarrhea and all its associated diseases influence around 3 to 5 billion individuals, ultimately leading to 5,000,000 deaths 5,000,000 demises every year. It can be a sign of an underlying chronic or infectious disease (WHO, 2013). Among the natural products, Linseed has been commonly used as a medication for the management of diarrhea (Duke & Duke, 2002; Fleming, 2000). Primarily, an introductory report on Linseed oil explained the mechanism of anti-inflammatory activity using Ricinus communis oil-prompted diarrhea as a signal of the prostaglandin mechanism (Kaithwas & Majumdar, 2010b). In one study, based on primary in vitro trials, a similar group reported that Linseed has the potential to reduce excessive secretions and heal ulcers due to anti-cholinergic or histamine-

reducing activities (Kaithwas & Majumdar, 2010a). The researchers found that linseed extract was effective in reducing the frequency and improving the consistency of loose stools. *Linum usitatissimum* oil was revealed to have anti-cholinergic activity in the ileum of *Cavia porcellus*, which has been demonstrated by means of a bar graph presenting a decline in cholinergic activity at growing doses of Linseed oil (Kaithwas & Majumdar, 2010a). The efficiency of *Linum usitatissimum* extract against Gram-positive and Gram-negative bacteria, as well as drug-resistant infectious agents, suggests the presence of components that could serve as a basis for novel and improved antibacterial compounds. Recent research suggests that the extract of *Linum usitatissimum* has anti-diarrheal activity, as evidenced by its effects on regularity and the incidence of loose faces, likely due to reduced gastrointestinal secretions and motility in mice. This, together with the antimicrobial effect against numerous intestinal and non-intestinal infectious agents, provides sufficient evidence to advise that Linseed extract could be consumed in both contagious and non-contagious diarrhea (Palla et al., 2015).

Flaxseed for Cardiovascular Health

There are many advantages of eating Linseed besides its anti-atherogenic potential. In conditions of atherosclerosis, the inner cellular linings of blood vessels are destroyed and impaired, leading to dysfunctional relaxation responses. A diet accompanied by 10% to 20% of Linseed guarded against the deprivation of endothelial-dependent relaxation of vessels, prompted by cholesterol feeding or conditions of high blood pressure after ten to twenty-four weeks of management (Talom et al., 1999), (Dupasquier et al., 2006). The total suppression of VF (Ventricular fibrillation) frequency has been established in patients who have been given a diet supplemented with 10 percent flaxseed for up to sixteen weeks, usually detected during ischemia, and has considerably decreased the occurrence of Ventricular fibrillation during cardiac reperfusion in cholesterol-fed rabbits. Linseed exerts its protective effect by shortening the duration of the action potential and the QT interval (Ander et al., 2004). Nearly 20 grams of squashed linseed/day for up to sixty days has been stated to have strong cholesterol-reducing (↓ seventeen percent) and triglyceride-reducing (↓ 36%) outcomes in slightly hypercholesterolemic adults

(Mandaşescu et al., 2005). ω -3 FAs employ an anti-inflammatory action (Sierra et al., 2006). Moreover, obese adults taking 30 g of linseed flour/day considerably reduced circulating levels of serum amyloid A, CRP, and fibronectin after only 2 weeks of nutritional management (Faintuch et al., 2007).

Flaxseed in Healing of Burns

Burns in humans are among the most common wounds resulting from contact with electricity, radiation, heat, chemical compounds (especially corrosive ones), friction, or extreme cold (Shan et al., 2010). Profound or extensive injuries from burns initiate a series of numerous physical abnormalities and the following psychological issues (De Sousa et al., 2013). Research has shown that the constituents of flaxseed oil have bioactive properties that make it effective in promoting wound healing compared with recognized commercial medicines. Furthermore, they do not cause any undesired or harmful effects, which makes this oil an encouraging option for managing skin ulcers or injuries (Beroual et al., 2017).

Flaxseed for Post-Menopausal Women

Women who are in their postmenopausal phase have an increased risk of developing atherosclerosis, ultimately leading to CVD. Menopause is linked with raised concentrations of free-flowing total cholesterol and LDL, which are identified risk factors for the growth and progression of atherosclerosis and, eventually, cardiovascular disease. (Fukami et al., 1995), (Bruschi et al., 1996), (Hong et al., 1992), (Walsh et al., 1991) Though HRT (hormone replacement therapy) has been revealed to make the lipid profile better and to alleviate symptoms related to menopause, its advantages on the cardiovascular system have been inquired recently. (Mendelsohn & Karas, 1999), (Clarkson, 2002), (Gupta & Aronow, 2002), (Hulley et al., 1998), (Herrington et al., 2000) Additionally, hormone replacement therapy may be associated with rising risks for carcinoma of the breast, (Judd et al., 1983) endometrial carcinoma, (Henderson et al., 1993) carcinoma of ovaries, (Rodriguez, 2001) SLE, (Mok et al., 2001) and thromboembolism. (Vehkavaara et al., 2001) The consumption of cholesterol-reducing pharmacological drugs has also been linked with numerous contraindications or adverse reactions. (*Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults*, 2001) Among the

functional foods studied for their anti-atherogenic activities, linseed has shown very encouraging potential to reduce atherosclerotic lesions. Flax seeds are an abundant source of soluble fiber (mucilage), ALA, and lignans (Stephen C. Cunnane & Thompson, 1995). Though the seed of flax is well-known to decrease serum cholesterol levels in both animal models (Lucas et al., 2004; Babu et al., 2000) and humans, experimental studies demonstrated that Linseed considerably reduced total cholesterol, lipoprotein(a), non-HDL, and concentrations of Apolipoprotein-B without changing high-density lipoprotein cholesterol in postmenopausal females (Arjmandi et al., 1998) (Lucas et al., 2002).

Conclusion

Flaxseed has significant medicinal value that cannot be ignored. Seeds of flax are a highly abundant source of soluble fiber mucilage, ALA, and lignans. Linseed considerably reduces total cholesterol, lipoprotein(a), non-HDL, and concentrations of Apolipoprotein-B without changing high-density lipoprotein cholesterol in postmenopausal females. Flaxseed oil has bioactive properties that make it more effective than recognized, commercial medicines in promoting wound healing.

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