A Review on Flax Seed: A Legume for Longevity

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Flax seed, tiny packs of nutrients supply a wealth of health benefits. Dietary flaxseed has an amazing use in different health conditions. Research evidences on the properties of dietary flaxseed have wide spread information. It has been found that the tiny, edible seeds of the flax plant, have gained superfood status because of its therapeutic values in preventing the diseases. From the past few years, there is growing evidences that the people have become more health conscious. Many trials have been conducted with the upgraded standards of control available in order to provide consistent information on its significance to the general community. The purpose of this review is to provide a comprehensive summary of the research that have reinforced the growth of flaxseed as a commodity with importance in the health and medicine fields. Flaxseed is emerging as a vital functional food element because of its rich contents of \(\omega-3\) fatty acid, lignans, and fiber. Flax lignans have potential health benefits such as in reduction of cardiovascular disease, cancer, atherosclerosis, diabetes, arthritis, osteoporosis, autoimmune and neurological disorders. The role of the Flax protein in the prevention and treatment of heart disease and in supporting the immune system has been proven. The present review focuses on the evidences of the potential health benefits of flaxseed through human and animals. Its role in enhancing the longevity by alleviating the common health challenges like hypertension, cancer and diabetes.

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ABBREVIATIONS

ALA: α-linolenic acid; B.C: before Christ; A.D: Anno Domini; pH: Power of hydronium; FS: Flax seed; PUFAs: Poly Unsaturated Fatty Acids; EPA: eicosapentenoic acid; DHA: docosahexaenoic acid; LA: linoleic acid; EL: enterolactone; ED: enterodiol; SECO: secoisolariciresinol; p-CA P-coumaric; FA: ferulic acid; SDG: secoisolariciresinol diglucoside; HTN: Hypertension; JNC-7: Joint National Committee 7; ACE: angiotensin-converting enzyme; CHD: Coronary Heart Disease; CAM: complementary and/or alternative medicine; LOBs: Linorbitides; p-AKT: protein kinase B; p-JNK: c-Jun N-terminal kinase; p ERK extracellular signal-regulated kinase; MAPK: mitogen-activated protein kinase; CRC: colorectal cancer; BMI: Body mass index; CFA: Complete Freund's adjuvant; PGE2: Prostaglandin E2; LTB4: leukotriene B4; WC: Waist circumference; TNF: Tumor necrosis factor; IL: Inter leukin; COPD: chronic obstructive pulmonary disease; SOD: superoxide dismutase; CAT: catalase; GSH: glutathione peroxidase; MDA: Malondialdehyde; NO: Nitrous oxide.

1. INTRODUCTION

In this modern period, one of the major obstacles that current living faces is excellent health, as individuals are suffering from a variety of degenerative lifestyle disorders. Foods that can act as medicine have sparked attention as people become more sensible of the importance of diet and their desire for wellness. With rapid changes in lifestyle and a growing awareness of the negative consequences of excessive consumption, the scientists and health professionals are exploring the plant products. The focus has switched from chemical-based therapy to natural-based therapy in the management of ailments. The focus is on extracting the functional dietary components of plants and seeds that were found in ancient nature [1]. In recent years, as empirical evidence on their safety and usefulness has become increasingly available, herbal (plant) treatments have aroused the curiosity of researchers. As a result, new terminology for herbal medicines is emerging in the scientific community, such as phyotherapy, phytotherapy, phytoneering, nutraceuticals. Flaxseed has been used in both nutrition and medicine. Flaxseeds have a wide range of nutritional properties that are encouraging health professionals and nutritionists to use them in the development of functional meals and the selection of a healthy diet [2].

Flax seed has been used from ancient civilizations and cultures. According to archaeological evidence, flax seeds have been used from the time of Nefertiti in Egypt. Flax, also known in India as "Tisi" or "Alsi," was utilised to supplement the food of the hardworking villagers. Flaxseed is an key oilseed crop for industrial, food, feed, and fibre production [3]. Almost every portion of the flaxseed plant is commercially useful, whether raw or processed. The stem produces high-quality fibre that is both strong and long-lasting. Linum usitatissimum Linn is the scientific name for flax. Katan (Linum usitatissimum Linn.) is an annual or biennial herb in the Linaceae family that grows to be approximately 2 feet tall. It likely was first grown in Egypt but has been cultivated all around the world. The flax plant can be woven into linen, its fibers are two to three times as strong as cotton! [4-7].

This blue-flowered crop is greatly adaptable. The fact that different portions of the plant have unique economic purposes demonstrates the value of L. usitatissimum as a multipurpose crop. Brown flaxseeds and golden (or yellow) flaxseeds are the two most common types (Fig. 1). Both have a comparable nutritional profile and the same quantity of short-chain-3 fatty acids. Whole flaxseed, ground flaxseed, flaxseed oil, and partially defatted flaxseed meal are the four most frequent types of flaxseed for human consumption. Flax “milk” is a brand-new product on the market. Flax milk is a great alternative to dairy milk because it is cholesterol-free and lactose-free. It's suitable for anyone with soy, gluten or nut allergies, and it is better than almond milk in the health benefits features [5]. Oil is extracted from flaxseeds to produce flaxseed oil. To extract the liquid from flaxseed, it is ground and then pressed with an oil press. Even though flaxseed oil has a high concentration of ALA, some of the other nutrients contained in ground flaxseed may not make it into the oil version after processing. Small, nutty, and crunchy seeds have recently garnered superfood notoriety, they are one of the oldest
crops, having been farmed since the dawn of civilization.

3. PLANT MORPHOLOGY

The plant's root is made up of absorbent tissue that allows it to store all of the water obtained by the fine rootlets that protrude in all directions and at various depths. Flax fibres are discovered inside the plant as individually separated filaments of various lengths that vary depending on the leaf's height on the stem of the plant. The yellow maturity stage. Individual flax fibres are isolated in the plant, yet they are organised in bundles that are entirely and firmly enclosed by the holding tissue. Stem bends in all directions, the smooth glossy surfaces let them to effortlessly slide on one other [12,13,14].

4. BIO-CHEMICAL CONSTITUENT OF FLAX SEED

4.1 Fiber

Whole FS (flax seed) has a whole fibre content of roughly 28%. Insoluble fibres in FS include cellulose, hemicellulose, and lignans, while soluble fibres in the form of mucilage gums make up about a third of the fibre [5,15,16]. Because mucilage is found mostly in the epidermis of the seed coat, removing the seed coat removes a large portion of the soluble fibre in FS. Commercially available fibre supplements produced from FS currently include both soluble and insoluble fibres [17].

Flax is low in carbohydrates (sugars and starches), providing only 1 gram (g) per 100 g. Flaxseed polysaccharides composed of two major fractions: 3/4th of a neutral arabinoxylan and 1/4th of an acidic rhamnogalacturan. The arabinoxylan is composed primarily of xylose, arabinose, and galactose and the L-rhamnose, D-galactose, D-galacturonic and L-fructose acid are the part of rhamnogalacturan. Significant variations has been observed in monosaccharide composition, carbohydrate yield and quality among accessions from the different part of world collection of flaxseed [17].

4.2 Protein

Flaxseed grain and paste contain roughly 21% and 34% protein, respectively. Genetic and environmental variables can affect the protein level in flaxseed. Seeds grown in cool areas have a more oil and a low protein content. Flaxseed has two main storage proteins: a salt
soluble component with a high molecular weight (11-12S; globulin; 18.6% nitrogen) and a water soluble basic component with a low molecular weight (1.6-2S; albumin; 17.7% nitrogen). They contain all essential amino acids except lysine, making them a protein source that is incomplete [18].

4.3 Fatty Acid

The fatty acid profile of FS is PUFAs > monounsaturated fatty acids > few saturated fatty acids [5]. ALA is an n3 polyunsaturated fatty acid (PUFA) and is one of two essential fatty acids required in the human diet [19]. In human, the conversion rate of ALA to long chain PUFAs like EPA and DHA is low [19]. However, this conversion may be up controlled under certain conditions [20]. ALA has a higher affinity for Δ6-desaturase than the other essential fatty acid, linoleic acid (LA), but because the Westernized diets contain much higher levels of LA than ALA, ALA is often metabolized to longer chain n3 PUFAs at much lower rates than omega-6 (n6) PUFAs are converted [14]. This indicates that an improvement in n6 to n3 ratio in the diet could increase conversion rates of ALA to DHA and EPA. FS contains relatively high levels of both essential fatty acids, ALA and LA [5].

4.4 Lignans

Polyphenolic substances found in fiber-rich plant products called lignans. In comparison to other plants, FS contains 75–100 times more lignans [21]. In defatted FS flour and whole FS, SDG concentration can range from 11.7–24.1 mg/g and 6.1–13.3 mg/g, respectively [21,22]. The abdominal micro flora in the colon converts SDG into the mammalian lignans enterolactone (EL) and enterodiol (ED) after consuming FS. The consortium END-49, which includes Clostridium saccharogumia, Eggerthella lenta, Blautia producta, and Lactobacillus longoviformis, has been identified as the bacteria strains involved in the transformation of SDG to EL or ED [23,24]. In humans, the lignans are acted upon by the gastrointestinal micro flora to release EL and ED through secoisolariciresinol (SECO). P-coumaric (p-CA) and ferulic acid (FA) are the other reported phenolic compounds from FS.

Cellulose: It is a Plant cell walls' primary structural material.

Mucilage Gums: Flax mucilage is made up of three different types of arabinoxylan, each of which forms big aggregates in solution and contributes to the gel characteristics of the product [5].

4.5 Vitamins and Minerals

Flax has an abundance vitamin E, mostly in the form of gamma tocopherol. Flax tocopherol content is affected by the cultivar, seed maturity, growing region, growth conditions, and extraction process. Flax includes a modest quantity of vitamin K in the form of phylloquinone, which is an vital component of the blood clotting mechanism. In flax seed, P, Mg, K, Na, Fe, Cu, Mn, and Zn are reported [25].

4.6 Anti-nutritional Factors

In flax seed, there are trace levels of cyanogenic glycosides and linamarin. Vitamin B6 deficiency is caused by linatin [26]. Flaxseed depressed vitamin E levels in rats only when fed at very high levels [27]. Another anti-nutrient found in flaxseed is phytic acid, which varies from 23 to 33 g per kg of flaxseed meal. Calcium, zinc, magnesium, copper, and iron are all inhibited by phytic acid. It's a powerful chelator that forms protein and mineral-phytic acid complexes, lowering their bioavailability [28,29,30].

4.7 Storage

Due to high content of alpha linolenic acid (ALA), it is prone to oxidation. The oxidation and eventual rancidity will result in affect the flavours and a musty scent, both of which will be rejected in taste tests. So, proper storage condition is required.

Regardless of how you get your ground flaxseeds keep them in an airtight container in the refrigerator. If using glass, choose tinted glass to reduce the amount of light that the ground flaxseeds are exposed to. Flaxseeds are substantially more susceptible to oxidation and spoiling after processed. They may usually be stored safely for 6 to 16 weeks. If stored in an airtight container in a dark, cool, dry location, whole flaxseeds can last 6-12 months. Flaxseed oil is especially perishable and should always be purchased in opaque bottles that have been kept refrigerated [31].

5. THERAPEUTIC USES

5.1 Hypertension

One of the primary causes of global illness burden is hypertension. [32] Hypertension is the
leading cause of death worldwide. Hypertension (HTN) is well-defined as a blood pressure of 140/90 mmHg or higher, according to the Joint National Committee 7 (JNC-7) guidelines. A research for cost-effective medication for treatment of hypertension is going on [32,33]. Flaxseed and its components may prove to be an effective treatment for hypertension, either alone or in conjunction with other commercially available medications. The advantages of using flax seed and its components include their inexpensive cost and lack of adverse effects. Consumption of flaxseeds is a simple strategy to lower blood pressure. Previous clinical research suggests that patients who consumed flaxseeds on a daily basis for more than 12 weeks had their blood pressure under control. Potassium, which is found in seeds, is helpful in reducing blood pressure by reducing tension in blood vessel wall [33-35].

SDG (precursors of enterolignan), fibres and oil are the important constituents in flaxseed. Prasad looked explored the effects of several intravenous dosages of SDG (3, 5, 10, 15, 20, 20 mg/kg) on the arterial pressures of anaesthetized Sprague Dawley rats. He found that 10 mg/kg resulted in a 32, 36, and 33 percent reduction in systolic, diastolic, and mean arterial pressures after 4 hours; 15 mg/kg resulted in a 15, 24, and 22 percent reduction; and 20 mg/kg resulted in a 20, 33, and 29 percent reduction. Hypotension is induced by SDG through angiotensin-converting enzyme suppression. Through ACE inhibition and guanylate cyclase activity, pure SDG, which is extracted from flaxseed, significantly lowers systolic, diastolic, and mean arterial pressures in a dose-dependent manner [36,37]. The drop in BP caused by flaxseed protein hydrolysate is mediated by a decrease in oxylipins caused by the suppression of soluble epoxide hydrolase activity by -linolenic acid. Some oxylipins have been shown to cause vasoconstriction [38,39]. As a result, lowering oxylipin levels lowers blood pressure. According to the findings, flaxseed and flax oil could be utilised as an additional therapy for hypertension [40]. Pure SDG may be useful as a treatment medication for hypertension due to its great and long-lasting pharmacological effect on blood pressure. The hypotensive effects of flaxseed are attributed to -linolenic acid’s suppression of soluble epoxide hydrolase activity, activation of guanylate cyclase and inhibition of ACE by SDG. High concentration of vitamin E also reported in flaxseed, which enhances sodium excretion in the urine, which may support in the reduction of blood pressure [41]. Ineffectiveness of flaxseed and its constituents may be accredited to a low dose, a long interval between doses and a short time of ingestion, as well as patient status [42].

6. LIPID LOWERING EFFECT

The human diet has shifted from unrefined whole grains and green vegetables to refined grains with low fibre content and more animal items since the industrial revolution. Whole flaxseed has been demonstrated in certain research to decrease serum cholesterol levels in animals and people both. Biochemical measures in rats, mice, and rabbits showed favourable reactions, demonstrating flaxseed’s hypocholesterolemic activity, which was connected to a higher lipid content in the faeces [43-50]. Many in vivo studies have observed that the different flax seed dosages modify the lipid profiles differently. Dawley rats were fed 10%, 20%, or 30% raw or heated flaxseed in the basal diet for 30 days. In the study conclusion, flaxseed was observed to considerably lower total cholesterol and boost high density lipoprotein cholesterol in blood [51]. The high levels of ALA, lignans, and fibre in flaxseed may contribute to improved lipid profile.

As a result, increasing the amount of flaxseed in one’s diet improves the blood lipid profile-improving effect of flaxseed. Both fibre and lignans bind to bile acids, amphipathic molecules generated from cholesterol in the liver, and transport them out of the body through the digestive tract. Flaxseed also includes phytoestrogens, which have a structure similar to cholesterol and hence inhibit cholesterol absorption in the intestines. Another mechanism of flax seed is that it interrupts cholesterol circulation in the enterohepatic system [52-54]. Increased bile acid synthesis is the main cholesterol-lowering mechanisms of flaxseed and another component, besides its oil, contributes to its hypocholesterolemic property [55,56]. Lignans are estrogen like components which also have antioxidant activity in reducing the oxidative damage in many diseases like heart disease, cancer and diabetes [57-59]. Flax seeds contain fiber, lignans and phytoestrogens, which decrease the levels of 7 alpha-hydroxylase and acyl-CoA cholesterol transferase. Incorporating 30 g of roasted flax seed in daily diet found the positive modification of lipid profile. In the Seven Countries Study, CHD (coronary heart disease) was reduced with increased consumption of ALA. At the end of 4 years’s Lyon diet clinical trial, data concluded the consumption of flax seed
condensed number of CHD patient and total deaths by 50%–70% [51].

7. CANCER

7.1 Breast Cancer

Breast cancer is a disease that affects the cells of the breasts. Breast cancer can affect both in men and women, however it is more common in women. Cancer awareness and research funding have aided in the advancement of breast cancer diagnosis and treatment. Clinical evidence suggests that flax seed has antitumor properties against several cancers [60,61–63], making it a CAM (complementary and/or alternative medicine) candidate for human cancer treatment. Linoorbitides (LOBs) are a class of cyclic cyclopeptide compounds found in flaxseed that have a cell-type specific and concentration dependent cytotoxic action on human breast cancer Sk-Br-3 and MCF7 cell lines, as well as melanoma A375 cells. LOBs’ anti-oxidative activity could be a key factor in their cytotoxic effects on cancer cells. After 24 hours of exposure at 400 ug/mL, cytotoxicity of LOB3, LOB2, [MetO]-LOB2, and [MetO]-LOB1 against Sk-Br-3 cells was 75 percent, 41 percent, 36 percent, and 28 percent, respectively.

Lignans have a unique phenolic structure and are found in small amounts in many foods, but in considerable quantities in flaxseed. Dietary ingestion of the flaxseed lignan, (secoisolariciresinol diglucoside (SDG)), consequences in glucosidic cleavage in the gastrointestinal tract to yield secoisolariiciresinol (SECO), which is further converted to the mammalian lignans, enterodiol (ED) and enterolactone (ENL), with the help of intestinal microflora [64-67].

According to the data, ENL is the most bioactive lignan. Non steroidal phytoestrogens that have a chemical structure similar to mammalian estrogens and induce estrogen-like actions in animals include flaxseed lignans. (Fig. 2) Enterolactone and enterodiol bind to oestrogen receptors, causing cell growth to alter. A link was discovered between a higher level of EL and a lower incidence of breast cancer in postmenopausal women. Lignans operate as weak estrogen in postmenopausal women, while oestrogen antagonists in women with normal oestrogen levels [68,69]. When Flax oil was combined with trastuzumab for epidermal growth factor receptor 2 positive breast cancer, the anti-tumour effects of trastuzumab were increased, and the trastuzumab concentrations required to eradicate tumours in athymic mice were suggested to be reduced [70]. Flaxseed and its bioactive components anti-tumour actions include a suppression of the phosphorylation of p-AKT, p-ERK and p-JNK kinases, resulting in a slowing of the MAPK pathway [71], inhibition of CDK4 down regulation of multiple miRNAs, decreased expression of mRNAs for Bcl2, cell cycle proteins, ER alpha and beta and epidermal and insulin-like growth factor receptors [71,72].
Clinical evidence suggests that combining metformin with flax seed lignans, ENL, improved metformin cytotoxicity in MDA-MB-231 cells in a concentration-dependent manner by inhibiting fatty acid synthase (FASN). Flax or lignan fraction were fed to mice groups for two weeks before and after the injection of melanoma cells. When compared to the control, the flax therapy (at 2.5, 5, or 10% of diet intake) reduced the number of tumours by 32, 54, and 63 percent, respectively. The SDG, provided in doses comparable to 2.5, 5, or 10% flax seed, also reduced tumour number, from 62 tumours per mouse in the control group to 38, 36, and 29 tumours per mouse in the SDG groups, respectively [70-74].

7.2 Colon Cancer

CRC (colorectal cancer) is a form of cancer that starts in the large intestine and spreads throughout the body (colon). The colon is a big intestinal section. In comparison to adults, older people are more likely to get colon cancer. Modifiable and non-modifiable risk variables are separated. Non changeable factors include ethnicity, age, and a family history of colorectal polyps, cancer, or inflammatory bowel disease. Modifiable factors include BMI (Body mass index), physical inactivity, alcohol consumption, and a diet high in red meats [75-77].

Increased dietary fibre intake, shortened transit time, and increased stool bulking have all been linked to CRC prevention. Increased ALA, as well as an improvement in the n6 to n3 ratio, improve gut health by lowering inflammatory and oxidative stress indicators, as well as inhibiting cell proliferation and promoting apoptosis. The bioactive components of FS (lignans, fibre, and ALA) have been linked to cell cycle disruption and a lower the risk of colon cancer. Various colon cancer cell lines were used to examine the cellular processes of FS lignans. Treatment of SW480 cells (human colon adenocarcinoma cells) with ED alone or in conjunction with EL resulted in a decrease in cell number, induction of S-phase cell cycle arrest, and elevated cyclin. A dose-dependent rise in the number of apoptotic cells (0–40 mg/L). In CaCo2 cells human colon adenocarcinoma cells, EL and ED at varied doses (50–150 M) were found to reduce cell growth and promote apoptosis [78,79].

8. RHEUMATOID ARTHRITIS

Rheumatoid arthritis is an autoimmune illness that causes chronic inflammation [80]. Effective novel anti-arthritic drugs are currently being researched. CFA (Complete Freund's adjuvant)-induced arthritis was significantly protected by L. usitatissimum fixed oil in a dose-dependent manner. CFA also causes a delayed hypersensitivity reaction, which is significantly reduced by flax seed. Alpha linolenic acid (ALA), a component of L. usitatissimum fixed oil, has a dual inhibitory effect on arachidonic metabolism, resulting in reduced PGE2 and LTB4 synthesis via inhibition of the cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism, as well as lower vascular permeability. Fixed oil revealed a dose-dependent protection compared to the swelling observed in the synovial cavity after turpentine oil administration. Between days 2 and 10 following formaldehyde administration, L. usitatissimum fixed oil (3 ml/kg) significantly reduced the arthritic score compared to control. On day 10, the anti-arthritic activity of L usitatissimum fixed oil (3 ml/kg) was superior to that of the standard drug aspirin (i.e. 70% inhibition). On the 14th day, L. usitatissimum fixed oil significantly reduced paw diameter in a dose-dependent manner, with percentage protection of 21.5, 75.3, and 91.7 percent, respectively, at dose levels of 1, 2, and 3 ml/kg. Reduced vascular permeability generated by the oil could potentially help with anti-arthritic properties. The fixed oil of L. usitatissimum, which contains 57.38 percent ALA, has been proven to be beneficial in inflammatory joint treatment [81,82].

9. OBESITY

Obesity is a common and preventable disease of public health, importance in all age groups and in both developed and developing countries. The increasing prevalence of obesity places a huge burden on health care use and cost. Weight loss is linked to numerous health and financial advantages. Dietary therapy, physical activity, and lifestyle changes are all effective weight loss strategies [82].

The main findings show that following the intervention, those who consumed flaxseed products had lower body weight, BMI and WC (Waist circumference) than controls. However, subgroup analyses revealed that body composition indices were reduced with whole flaxseed consumption only, in trials lasting ≥12 weeks, and among participants with BMI ≥ 27 kg per m² [83]. SDG may also help to regulate adiponectin levels and may help to prevent or reduce obesity by increasing fat oxidation in the
skeletal muscle. Dietary fibre, particularly soluble fibre, has been demonstrated to have anti-obesity properties and to help people lose weight [84]. Dietary fibre may help to promote weight loss by delaying stomach emptying, producing feelings of fullness by absorbing significant amounts of water [85], and/or increasing the concentration of short chain fatty acids, which induce satiety through a variety of pathways [86] (Fig. 2). When flax seed is mixed with water, it also acts as a gel. This gel delays stomach emptying, which may help to reduce blood glucose levels. Furthermore, dietary fibre can increase viscosity and inhibit bile acid re-uptake, lowering micelle production and lipid uptake [87-89].

10. DIABETES

Diabetes is an ailment in which blood glucose, also recognized as blood sugar, is abnormally high. Blood glucose is the main energy source, which arises from the food you consume. Pancreas secretes the hormone, Insulin which aids glucose absorption into cells for use as energy currency. Flaxseed has recently gained a lot of attention for its potential health benefits in a variety of metabolic illnesses, such as diabetes. Insulin resistance and the pathophysiology of many metabolic disorders associated with type 2 diabetes are influenced by fat accumulation, particularly abdominal obesity and visceral fat [90,91]. According to a clinical investigation data, flaxseed enriched yoghurt can help type 2 diabetic people better manage their diabetes. The flaxseed component secoisolariciresinol diglucoside (SDG), which is the major flaxseed lignin, has been shown to help glycemic management. In Zucker diabetic rats, pure SDG is likewise beneficial at delaying the onset of diabetes [92]. The hypoglycemic impact of SDG in type-2 diabetes is attributed to reduction of the Phosphoenol pyruvate carboxylase enzyme, which is a major enzyme involved in glucose production in the liver and also a rate limiting enzyme in the glyconeogenic pathway [93,94].

Data from the Research supported the pharmacological effect of insoluble fiber, slows down the release of sugar into the blood and reduces blood sugar level. Supplementation of 10 g of flaxseed powder with diet for type 2 diabetics patients for duration of 30 days, at the end of study, data concluded the reduced fasting blood glucose and glycated haemoglobin by 19.7 % and 15.6 % respectively [95]. It could be because flaxseed has a lower glycemic carbohydrate level and a higher dietary fibre content. According to findings from a diabetic female clinical trial, supplementation of flaxseed powder in 15 and 20 g/day over a period of two months reduced postprandial blood glucose levels by 7.9% and 19.1%, respectively [96].

Another study on 25 diabetic participants supplemented flaxseed powder in bread form for 90 days and observed a substantial drop in blood glucose levels supported the favourable effect of flax seed in diabetes. In humans and animals, ALA from flaxseed oil has been related to enhanced insulin sensitivity. In instance, an 8-week research in 16 obese persons found an increase in insulin sensitivity after they received a daily oral dose of ALA in supplement form [92].

![Fig. 3. Effect of flax seed in gastrointestinal tract [4]](image-url)
11. RESPIRATORY DISEASES

Flaxseed appears to have a positive effect in mice, according to an in vivo study. When mice were given flaxseed for a long time, they were protected from bacterial colonisation of the lungs by Streptococcus pneumonia and had less histopathological involvement of lung tissue. The levels of pro-inflammatory (TNF- and IL-1) and anti-inflammatory (IL-10) cytokines are also altered by flaxseed [97]. Flex seed fatty acids and lignans have been demonstrated to have anti-inflammatory and antioxidant properties in Acute Lung Injury [98]. In vivo and in vitro studies strongly supported flaxseed’s beneficial role in asthma and allergic disease prevention.

In vivo and in vitro studies firmly confirmed flaxseed’s beneficial effect in asthma and allergy disease prevention. The discovery of fatty acid bioactive metabolites produced by lipoxygenase and cyclo-oxygenase has revealed some molecular processes [99,100] Rv and PD are two newly found lipid mediators produced by the oxidation of n-3 fatty acids (EPA and DHA), and they’ve been linked to inflammatory treatment. Reduced inflammation reduces asthma symptoms and has a bronchodilator effect [101]. A randomised controlled clinical trial was conducted on 60 COPD patients. In the test group, a Pharmacopeial Unani formulation called “Lauq Katan” (Lincus of Linum usitatissimum mucilage) was given three times a day in a dose of 10 gm, and in the control group, Theophylline 200 mg was given three times a day for six weeks. The test medicine Lauq Katan was found to have a substantial effect in the management of COPD based on spirometer measures FEV1 and FEV1/FVC [102].

12. ANTI OXIDANT

Oxidative stress is caused by an imbalance between the synthesis of oxidant chemicals and the antioxidant defence mechanism. Antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) are important regulators of the oxidant/antioxidant equilibrium. Flaxseed is abundant in -linolenic, and oleic acids, all of which play important roles in maintaining cell membrane integrity [103-105]. Clostridia sp., which is found in the colon, converts secoisolariciresinol diglucoside, which contains plant lignin, into enterodiol and enterolactone. Other minor lignins found in flaxseed include matairesinol, isolariciresinol, and pinoresinol. Acids have antioxidant capabilities due to their free radical scavenging activities [106]. During lipid peroxidation, certain compounds are formed. The detection of these products in biological systems may provide useful information about the severity of free radical-induced cell damage. Malondialdehyde (MDA) and nitric oxide are the most often used indicators for this purpose (NO). Changes in antioxidant enzyme activity in biological systems can also be used to estimate the level of oxidative stress [107-109].

Cadmium is used to induce oxidative stress in rats. Cadmium was administered to rats for 30 days, and the effects on a range of organs and erythrocytes were assessed using oxidative stress markers. As a result, specific conclusions on the therapeutic and protective uses of this chemical in cadmium overdose have been reached. This is corroborated by the fact that levels of MDA and NO, both of which are oxidative stress markers, have decreased, while antioxidant enzyme activity have near to the control group levels. As a result, it existed that, flaxseed oil might be utilised as a supportive treatment in conjunction with cadmium intoxication [107].

13. OTHER PHARMACOLOGICAL EFFECTS

- Flaxseed lignans in the diet helped mice to recover after being exposed to radiation. A similar outcome was discovered in humans. While compared with control group, there were lower levels of inflammation, injury, oxidative damage, and fibrosis, as well as a higher survival rate [110].
- When platelets aggregate at the site of injury, the clotting mechanism begins. Flaxseed, like other omega-3 fatty acids, makes platelets less "sticky," preventing them from forming huge clots and interfering with the clotting process, as well as acting as a blood thinner [111].
- The astringent qualities of flaxseed raw oil in several fungicidal lotions are also suggested by data. Raw oil is said to provide moderate insect repelling effects [112].
- During pregnancy and early childhood, when flaxseed consumed, due to presence of high levels of long chain polyunsaturated fatty acids, it revealed as immunomodulatory agent [113,114].
Flaxseed constituents such as alpha linolenic acid, and the omega-3 fat found in it promotes bone health by helping to prevent excessive bone turnover [2,115].

As stated by Ayurveda, flaxseed has properties like Madhura (balances the skin pH), Picchaila (lubricous), Balya (improves elasticity of the skin), Grahi (as moisturizer), Tvagdoshahrit (removes skin blemishes), Vranahrit (wound healing) and useful in Vata (skin) disorders including dryness, undernourishment, lack of glow [2,116].

Serotonin (sleep hormone) levels in the blood is enhanced by flax seed due to its high content of omega-fatty acids and tryptophan. Magnesium works by relaxing the nervous system and muscles, as well as preventing night terrors, both of which are effective in the treatment of anxiety, stress, and depression. As a result, flax seed can be included in the daily diet of insomniacs [117].

When pregnant woman diet fed with flaxseed, benefits reported like decreased the depressive symptoms and neuroprotection during experimental neonatal hypoxic-ischemic encephalopathy by lessening brain mass loss together with improvements in motor hyperactivity and spatial memory [118,119]

Flaxseed is used to treat persistent cough and asthma, according to some scientific evidence. Ayurveda is a very old and still alive tradition that is widely practised in India, Sri Lanka, and other nations with a good philosophical and experimental foundation. In 650 B.C Scientist theophrastus recommended the use of flax mucilage as a cough remedy. The omega - 3 fatty acid which is seen in flaxseed may beneficial for avoiding and treating hardening of the arteries. So, it may help to fight against covid 19 as an immune booster [2,120].

14. POSSIBLE SIDE EFFECTS

- Raw flaxseed contains toxins, so one should limit consumption, though the toxins are killed when the seeds are roasted or cooked.
- Higher doses of flaxseeds may cause side effects like diarrhoea, nausea, stomach pain, flatulence, bloating.
- Most experts recommend you consume no more than 5 table spoon full of flaxseed a day. All that fiber is good for digestive system - but only if it should eat with plenty of water. Otherwise, it can backfire and make constipation worse.
- Flaxseed may interfere with hormonal level during pregnancy.
- Flaxseed oil may inhibit the clotting of your blood, so avoid taking it for a few weeks after the surgery [2].

15. CONCLUSION

In light of the information provided above, it is evident that flaxseeds are rich in linolenic acid and lignans. It is also an excellent source of soluble fiber, antioxidants and high-quality protein. Since its journey from being a medicine in ancient time to being superfood nowadays, it has become an increasingly popular source. Clinical trials have shown that flaxseed’s constituents offer disease prevention and therapeutic benefits, which has led to the development of new branded healthy and functional foods using flaxseeds and oil. Researcher concluded that flaxseed lignans and omega-3 fatty acids are effective in reducing the risks associated with heart disease, cancer (breast and colon,) and other human health diseases such diabetes, obesity and rheumatoid arthritis. So, flaxseed can be used a dietary supplement in whole or ground forms. As a result, flaxseeds and flaxseed oil may be preferred ingredients in functional foods and nutraceuticals in future.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.
COMPETING INTERESTS
Authors have declared that no competing interests exist.

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