# Linum usitatissimum -A reliable Nutraceutical

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**ABSTRACT:** Nutraceuticals are the products, which could also used as medicine other than nutrition At present, nutraceuticals or Functional foods have acknowledged considerable interest among health conscious consumers due to potential nutritional, safety and therapeutic effects. A nutraceutical product may be defined as a substance, phytochemical or bioactive molecule of food, which has physiological benefit or provides resistance against chronic disease. Linum usitatissimum or flax seed is emerging as an important functional food ingredient because of its rich contents of α-linolenic acid, lignans and fiber. Flaxseed, its oil, fibers and lignans, have impending health benefits. Flax seed plays important role in reduction of cardiovascular disease, atherosclerosis, diabetes, cancer, arthritis, osteoporosis, autoimmune, neurological disorders and brain development and function, as well as hormonal status. Flaxseed is a good source of soluble fiber. Many experimental as well as human studies showed that the flax seed to possess antioxidant and anti-inflammatory functions. This review highlights the nutritional values and therapeutic and medicinal values of flax seed and its role as a potent neutraceutical.

**KEY WORDS:** Nutraceutical; Linum usitatissimum; α-linolenic acid; Lignans; Fiber

**INTRODUCTION:**

A nutraceutical may be definited as a substance, which has physiological benefit or provides protection against chronic diseases. Nutraceutic is a term derived from “nutrition” and “pharmaceutics.” It is applied to products that are isolated from herbal products, dietary supplements, specific diets, and processed foods such as cereals, soups, and beverages that other than nutrition are also used as medicine.[1] At present, nutraceuticals have received considerable interest due to potential nutritional, safety and therapeutic effects. A market research recently proposed that the worldwide nutraceuticals market is expanding and would reach US $250 billion by 2018.[2]

The European Commission’s Concerted Action on Functional Food Science in Europe, defined that a food product can only be considered functional if together with the basic nutritional impact it has beneficial effects on one or more functions of the human organism thus either improving the general and physical conditions and/or decreasing the risk of the evolution of diseases [3]. Functional characteristics of many traditional foods are being discovered, while new food products are being developed with beneficial components. Flaxseed continues to pace forward in its recognition as a functional food, being rich in the essential omega-3 fatty acid, alpha linolenic acid and many phytochemicals. Flaxseed also provides dietary fiber and protein as one of six

neutraceuticals [4]. The purpose of this review is to provide a broad summary of the studies that have supported the flaxseed as a product with significance in the fields of nutritional, health and medicine.

**PROXIMATE COMPOSITION OF FLAXSEED:**

Linum usitatissimum commonly known as Flaxseed or linseed is a member of the genus Linum in the family Linaceae. Flax is an older agronomic crop having more than 300 species and which are cultivated for food and fiber since ancient times. Flax seed is renowned either by variety or by color (brown and yellow) Fig. 1,2. Brown colored flaxseed is the most prevalent and high in alpha-linolenic acid, while there are two types of yellow colored flaxseed: Omega and Linola [5].

Fig. 1

Fig. 2

Brown and yellow (Omega) varieties of flaxseed are virtually identical in their nutrient content [6]. Flax is rich in protein, fat, and dietary fibre. An analysis of brown Canadian flaxseed averaged 41% fat, 20% protein, 28% total dietary fibre, 7.7% moisture and 3.4% ash [7,8]. Table 1

TABLE 1**:** Proximate composition of flax based on common measures[a].

| **Form of flax** | **Weight (g)** | **Common measure** | **Energy (kcal)** | **Total fat (g)** | **ALA[b] (g)** | **Protein (g)** | **Total CHO [c,d] (g)** | **Total dietary fibre (g)** |
|---|---|---|---|---|---|---|---|---|
| Proximate analysis | 100 | - | 450 | 41 | 23 | 20 | 29 | 28 |
| Whole seed | 180<br>11<br>4 | 1 cup<br>1 Tbsp<br>1 tsp | 810<br>50<br>18 | 74.0<br>4.5<br>1.6 | 41.0<br>2.5<br>0.9 | 36.0<br>2.2<br>0.8 | 52.0<br>3.0<br>1.2 | 50.0<br>3.0<br>1.1 |
| Milled seed | 50.0<br>3.0<br>1.1 | 1 cup<br>1 Tbsp<br>1 tsp | 585<br>36<br>12 | 53.0<br>3.3<br>1.1 | 30.0<br>1.8<br>0.6 | 26.0<br>1.6<br>0.5 | 38.0<br>2.3<br>0.8 | 36.0<br>2.2<br>0.8 |
| Flax oil | 100<br>14<br>5 | 1 cup<br>1 Tbsp<br>1 tsp | 884<br>124<br>44 | 884<br>124<br>44 | 57.0<br>8.0<br>2.8 | -<br>-<br>- | -<br>-<br>- | -<br>-<br>- |

[a]Based on a proximate analysis conducted by the Canadian Grain Commission (Anonymous. 2001). The fat content was determined by using the American Oil Chemists'
Society (AOCS) Official Method Am 2-93. The moisture content was 7.7%.
[b]ALA = Alpha-linolenic acid, an essential omega-3 fatty acid.
[c]CHO = Carbohydrate.
[d]Total Carbohydrate includes carbohydrates like sugars and starches (1g) and total dietary fibre (28g) per 100 g flax seeds.

Minor components are cyanogenic glycosides, phytic acid, phenolics, trypsin inhibitor, linatine, lignans or phytoestrogens, minerals, vitamins, cadmium, selenium and cyclolinopeptides [9,10]. The composition of flaxseed can vary with genetics, growing environment, seed processing and method of analysis [11]. The protein content of the seed diminishes as the oil content increases [12]. It is well known that flax seeds are a source of high content of polyunsaturated fatty acids [13].

Flaxseed is one of the affluent vegetarian source of α- linolenic acid, a omega 3 fatty acid and soluble mucilage. The level of the enviable monounsaturates in flax oil is modest. Flax contains a mixture of fatty acids, particularly two polyunsaturated fatty acids α- linolenic acid (ALA), and linoleic acid (LA) Figure 3, the essential omega-6 fatty acid are essential for humans. [6]. Table 2

TABLE 2. Fatty acids content of Flaxseed oil

| Parameter | Percentage (%) |
|---|---|
| Saturated fat | 9.0 |
| Monounsaturated fat | 18.0 |
| Linoleicacid (omega-6 fatty acid) | 16.0 |
| α-Linolenic acid (omega-3 fatty acid) | 57.0 |

(Source: Morris, D. H. 2003. Flax: A health and nutrition primer. p.11. Winnipeg: Flax Council of Canada)

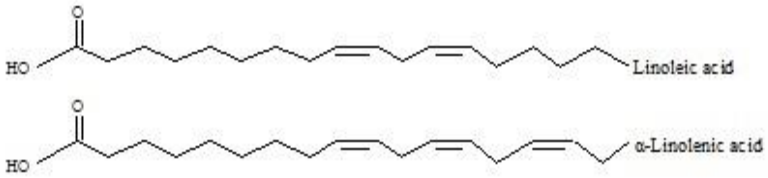



Fig. 3: Essential fatty acids in flaxseed

**PROTEIN:**

Flaxseed has two major storage proteins, a predominant salt soluble fraction with high molecular weight (11-12S; globulin; 18.6 % nitrogen) and a water soluble basic component with low molecular weight (1.6- 2S; albumin; 17.7 % nitrogen) [14]. The amino acid prototype of flax protein is similar to that of soybean protein, which is prominent as one of the most nutritious of the plant proteins. However appears to be little difference in the amino acid content of the protein from two flax varieties shown in Table 3. Flax is also a gluten free. The specific agent in gluten that causes a condition known as 'celiac disease' is gliadin, which is rich in the amino acids proline and glutamine [15]. The protein content of flaxseed has been reported to between 10.5% and 31% [16]. Khategaon cultivars grown in India had a protein content of 21.9% [17]. Differences in protein can be attributed to both genetics and environment.

**Table 3:** Amino acid composition of flax cultivar

| Amino Acid | Brown flax (Nor Lin) | Yellow Flax (Omega) |
|---|---|---|
| Alanine | 4.4 | 4.5 |
| Arginine | 9.2 | 9.4 |
| Aspartic acid | 9.3 | 9.7 |
| Cystine | 1.1 | 1.1 |
| Glutamic acid | 19.6 | 19.7 |
| Glycine | 5.8 | 5.8 |
| Histidine* | 2.2 | 2.3 |
| Isoleucine* | 4.0 | 4.0 |
| Leucine* | 5.8 | 5.9 |
| Lysine* | 4.0 | 3.9 |
| Methionine* | 1.5 | 1.4 |
| Phenylalanine* | 4.6 | 4.7 |
| Proline | 3.5 | 3.5 |
| Serine | 4.5 | 4.6 |
| Threonine* | 3.6 | 3.7 |
| Tryptophan*c | 1.8 | NR |
| Tyrosine | 2.3 | 2.3 |
| Valine* | 4.6 | 4.7 |

[a]Oomah and Mazza (2). bFriedman and Levin (84). cBhatty and Cherdkiatgumchai (mixture of NorLin, NorMan and McGregor cultivars) (85). dNR = Not reported.
*Essential amino acids for humans.

Total fibre is the summation of dietary fibre and functional fibre. Functional fibre consists of non digestible carbohydrates that have been extracted from plants, purified and added to foods and other products. Flaxseed is a rich source of dietary fiber (accounting 28% shown in Table 1), both soluble as well as insoluble fibers. Total dietary fiber content of flaxseed is given in Table 4 [11]. Dietary fibre and functional fibre are not digested and absorbed by the human small intestine and, therefore, pass relatively intact into the large intestine [18]. Diets rich in dietary fibre may help reduce the risk of heart disease, diabetes, colorectal cancer, obesity and inflammation [19-22].

TABLE 4. Dietary Fibre content of flaxseed

| Dietary Fiber component | Gram per 100 gram of flaxseed |
|---|---|
| Total Dietary | 40 |
| Soluble fiber | 10 |
| Insoluble fiber | 30 |

(Source: Carter, J.F.1993. Potential of Flaxseed and Flaxseedoil in baked goods and other products in human nutrition. Cereal Foods World 38 (10): 753-759)

**VITAMINS AND MINERALS:**

Flaxseed contains several water and fat-soluble vitamins [23]. As listed out in Table 5. Vitamin E is present abundantly in flax primarily as gamma tocopherol [24]. Gamma-tocopherol is an antioxidant that protects cell proteins and fats from oxidation; promotes sodium excretion in the urine, which may help lower blood pressure; and helps lower the risk of heart disease, some types of cancer and Alzheimer disease [25,26].

TABLE 5: Vitamin Content in Flax.

| Water soluble | mg/100g[(a)] |
|---|---|
| Ascorbic acid / Vitamin C | 0.5 |
| Thiamin/vitamin B1 | 0.53 |
| Riboflavin/vitamin B2 | 0.23 |
| Niacin/nicotinic acid | 3.21 |
| Pyridoxine/viatamin B6 | 0.61 |
| Pantothenic acid | 0.57 |
| | mcg/100g |
| Folic acid | 112 |
| Biotin | 6 |
| **Fat soluble** | |
| Carotenes | not detected |
| Vitamin Eb | |
| Alpha-tocopherol | 7 |
| Delta-tocopherol | 10 |
| Gamma-tocopherol | 552 |

Source: http://www.ars.usda.gov/nutrientdata)
aComposite sample of whole flax (11).
bTocopherol values represent the average of four varieties (42). The following forms of vitamin E were not detected: beta-tocopherol and alpha-, delta- and gamma-tocotrienol.
cAs phylloquinone (Nutrient Data Laboratory, Beltsville Human Nutrition Research Center, Agricultural Research Service. USDA's National Nutrient Database for Standard Reference.

**MINERALS:**

The mineral content of flaxseed [23, 27] is shown in Table 5. Flax is low in sodium. Flaxseed have two compounds phytic acid and oxalate – that bind calcium, copper, iron, magnesium and zinc to form insoluble complexes in the intestine [28].

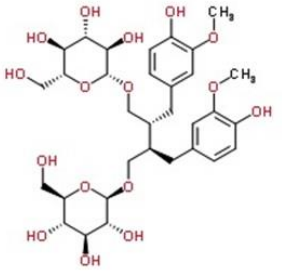
TABLE 6: Mineral Content in Flax.

| | mg/100gm |
|---|---|
| Calcium | 236 |
| Copper | 1 |
| Iron | 5 |
| Magnesium | 431 |
| Manganese | 3 |
| Phosphorus | 622 |
| Potassium | 831 |
| Sodium | 27 |
| zinc | 4 |

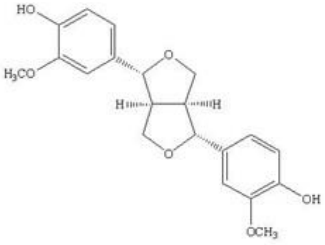
**PHENOLICS:**

Flaxseed is the richest source of plant lignans [29]. Secoisolariciresinol diglucoside (SDG) is the predominant lignan in flaxseed with minor amount of pinoresinol and matairesinol (MAT) [29,30] Figure 2. SDG was found 2653 mg/100 g of non defatted flaxseed extract [31]. The lignans of flaxseed are phytoestrogens and serves as precursors in the production of mammalian lignans.

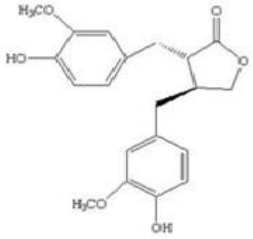
Lignans have antioxidant activity and thus may contribute to the anticancer activity of flaxseed [32-34]. A study suggesting that the lignan metabolites might be the reason for the health benefits of plant lignans. [35], the lignan may act to prevent oxygen radical production, thus effectively reducing atherosclerosis.



Secoisolariciresinol diglucoside



Pinoresinol



Matairesinol

Fig. 4 Chemical structures of flaxseed lignans

Flaxseed has been identified as a functional food due to its nutritional composition, which has positive effects on disease prevention providing health-beneficial components [36]. Flaxseed has long history of use in India and flaxseed preparations are particularly considered for its nutrients and therapeutic property [37]. The overall nutritional profile of flax seed depicted in Fig. 5.

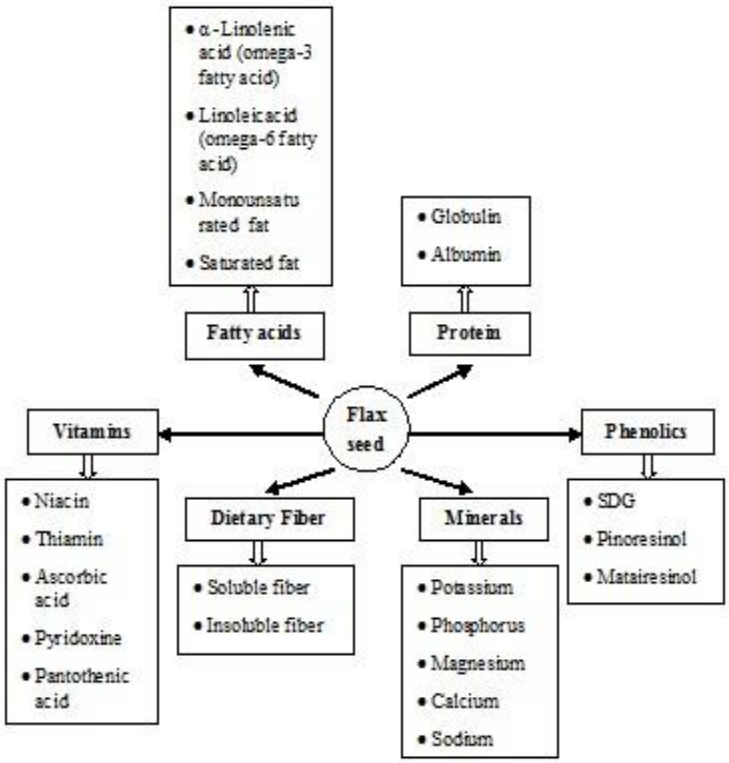



Fig. 5 Flaxseed Nutritional profile

**ANTI NUTRIENTS:**

Recently, a concern was raised about the presence of components in flaxseed that may have undesirable effects that could affect the bioavailability and bioaccessibility of essential nutrients [38]. Flax seeds also contain anti-nutrients which may pose adverse health effects and may influence the well-being of human population. compounds such as cyanogenic glycosides and linatine have been identifide as potential toxic compounds with in flaxseed. Major antinutrients in whole flaxseed are cyanogenic glycosides (250–550 mg/100 g) [39]

In the intestine, cyanogenic glycosides release hydrogen cyanide, a potent respiratory inhibitor, by intestinal β-glycosidase that produces thiocyanates. Hydrogen cyanide could cause acute cyanide poisoning, which may place this e respiratory and nervous system at risk [40]. However the release of hydrogen cyanide is approximately 5–10 mg from 1–2 tablespoons (recommended daily intake of flaxseed). This value is much lower than the acute toxic dose which is estimated to be 50–60 mg. Also, human beings can detoxify cyanide levels below 30–100 mg/day[41]. Also the human studies with 50 g/day flaxseed did not increase urinary thiocyanate levels [40].

Generally roasting is carried out to eliminate cyanogenic glycosides[42].

Another potentially toxic compound is linatine (antipyridoxin factor), which has been identified as a vitamin B6 antagonist in chicks [43]. However, flaxseed has never been shown to induce vitamin B6 deficiency in clinical studies [43]. Other compounds such as phytic acid and trypsin inhibitor have also been suggested to induce negative effects on the nutritional status after flaxseed ingestion. However, once again, no studies have reported any alterations in zinc status due to phytic acid, or any difference in trypsin inhibitor activity in flaxseed compared with canola or soybean seeds [43,44].

Trypsin inhibitor activity (TIA) in flaxseed was low when compared to those in soybean and canola seeds. Bhatty (1993) reported laboratory-prepared flaxseed meals containing 42 to 51 units of TIA [45]. Knowing that these compounds present instability when subjected to thermal and mechanical processes, including cooking in microwaves, autoclaving, and boiling its consumption is recommended in the form of flour (after thermal treatment) because the concentrations of compounds with adverse effects are eliminated or reduced; furthermore the trituration of the seed increases bioavailability of the bioactive compounds [46]. In conclusion, there are no deleterious effects reported of these components in human studies. it is important to recognize that no definitive scientific data have been produced to support the concept of toxicity from dietary flaxseed because of any of these compounds.

**HEALTH BENEFITS:**

**ANTI-OXIDANT FUNCTION:**

Flaxseed lignans convert to mammalian lignans enterolactone and enterodiol by intenstinal flora [47,48]. The lignan of flaxseed Secoisolariciresinol Diglucoside and mammalian lignans- enterodiol (ED) and enterolactone (EL) were shown to be effective antioxidants against DNA damage and lipid peroxidation. Activated cell chemiluminescence inhibition by supraphysiological concentrations of secoisolariciresinol (SECO), ED and EL were also evaluated. The lignan antioxidant activity was attributed to the 3-methoxy-4-hydroxyl substituents of SDG and SECO [49]. The hypoglycemic effect of SDG in type-2 diabetes has been suggested to be due to its antioxidant activity. It may be possible that the hypoglycemic effect of SDG in type-2 diabetes is due to suppression of expression of the Phosphoenol pyruvate carboxy kinase enzyme, a rate limiting enzyme in glyconeogenetic pathway [50]. The health benefits of flaxseed lignans are thought to be due to antioxidant activity, primarily as hydroxyl radical scavengers [34,48 ] and also as estrogenic and antiestrogenic compounds due, in part, to the structural similarity to 17-b-estradiol [51,52].

**ROLE OF FLAXSEED IN CANCER PREVENTION:**

Lignans could be a significant part of a treatment regime for cancer based on the large number of small scale studies. The presence of flaxseed lignans in MCF-7 tumors and the observed lignan binding to ER suggests that the lignan function may be ER-mediated [51,52]. Flaxseed was among the best food sources in the prevention of *in vivo* spontaneous chromosomal damage in mice [53]. In a small clinical study, prostate cancer cell proliferation decreased and apoptosis increased in men fed 30 g of flaxseed per day [54]. A significant factor which may have influenced their study was that the subjects were on a low-fat diet. Another subsequent study by those authors further supported the role of flaxseed in combination with a low-fat diet as a means to control prostate growth. In this study, prostate-specific antigen level and cell proliferation both decreased from baseline after only 6 months on the dietary regime [55].

Though not extensively studied, flaxseed has been shown to inhibit colon and skin cancers in cell. cultures and in animal studies [56,57]. In general, flaxseed may be a valuable tool in the fight against various cancers [58]. Although there are some studies with either no conclusive or negative effect many studies on the activity of lignans on breast, colon, prostate and thyroid cancer have shown beneficial effects. Flaxseed has been shown to reduce the early risk markers for and incidence of mammary and colonic carcinogenesis in animal models [59-62].

Lignans from flaxseed have been shown to reduce mammary tumour size by >50% and tumour number by 37% in carcinogen-treated rats [63]. Effect of flaxseed feeding on risk markers of cancer in humans demonstrated that the ingestion of 10 g of flaxseed per day elicited several hormonal changes associated with reduced breast cancer risk [64]. Both phytoestrogen and dietary fibre have shown to have cancer protective properties. Flaxseeds significantly increased urinary excretion of lignans without changing the serum hormone concentration of premenopausal women suggesting that the chemo protective effects reported for flaxseed may have resulted from mechanism other than a hormonal effect [65].

**ANTI-DIABETIC FUNCTION:**

A study of type 2 diabetic patients with daily lignan supplementation resulted in modest, however statistically considerable development in glycemic control without apparently affecting fasting glucose, lipid profiles and insulin sensitivity [66]. It has been found that SDG isolated from flaxseed is effective in retarding development of diabetes in Zucker diabetic fatty/Gmi-fa/fa female rats [67]. Lignin of flaxseed, decreased high fat diet induced visceral liver fat accumulation and improved hyperlipidaemia, hypercholesterolemia, hyperinsulinaemia and hyperleptinaemia. These effects may prevent obesity and may reduce cardiovascular risk associated with lifestyle diseases, such as diabetes, atherosclerosis and hypertension. Flaxseeds, which also contain PUFA and dietary fiber,

are therefore a promising food to help decrease the risk of lifestyle related diseases [68]. Solublefiber and other components of flaxseed fractions might potentially influence insulin secretion and its mechanisms of action in maintaining plasma glucose homeostasis also flaxseed was shown to reduce the postprandial blood glucose response in humans [69,70]. Consumption of 50 g/d ground flaxseed by young females over a 4-wk period caused a reduction in blood glucose levels [69]. Comparable findings were observed in postmenopausal women fed a 40 g/d flaxseed fortification diet. Prasad et al (2000) reported that rats fed 22 mg SDG/kg and treated with the diabetes-promoting chemical streptozotocin had 75% lower incidence of type-1 diabetes than the streptozotocin-treated control group [71]. However, the serum glucose of the SDG plus streptozotocin-treated rats had significantly higher serum glucose levels than the streptozotocin-treated control group.

**FLAXSEED IN CARDIOVASCULAR HEALTH:**

Flaxseed has become significant resource currently in the area of cardiovascular disease mainly because of both Alpha-linolenic acid (ALA) and the phytoestrogen, lignans, as well as being a good source of soluble fiber.. Alpha-linolenic acid is the natural precursor of the cardioprotective long-chain n-3 fatty acids. A 12-week dietary supplementation with flaxseed oil, rich in ALA (8 g/day), on blood pressure in middle-aged dyslipidaemic men resulted in significantly lower systolic and diastolic blood pressure levels , also the human studies have revealed that flaxseed could moderately decreased serum total and low-density lipoprotein (LDL), cholesterol concentrations, reduce postprandial glucose absorption, reduce some markers of inflammation and raise serum levels of the ALA, omega-3 fatty acids and eicosapentaenoic acid [72,73]. Partially defatted flaxseed reduced total cholesterol (4.6 ± 1.2%; $P = 0.001$), LDL cholesterol (7.6 ± *1.8%;* $P < 0.001$), apolipoprotein B (5.4 ± 1.4%; $P = 0.001$) and

apolipoprotein A-I (5.8 ± *1.9%; P* = 0.005), but had no effect on serum lipoprotein ratios. There was no significant effect on serum HDL cholesterol, serum protein carbonyl content, or ex vivo androgen or progestin activity. Unexpectedly, serum protein thiol groups were significantly lower (10.8 ± 3.6%; *P* = 0.007) suggesting increased oxidation [74].

Dietary flaxseed has been shown to have effective anti atherogenic property in rabbits. When LDL receptor deficient mice (LDLrKO) were administered a 10% flaxseed-supplemented diet for 24w, a reduction of circulating cholesterol levels was observed indicating the anti-atherogenic effect of flax seeds [75]. Flaxseed supplementation was allied with significant reductions in serum total cholesterol (TC) , LDL- cholesterol, triglycerides (TG) and TC/HDL- cholesterol in the ratio of -17.2%, -3.9%, -36.3% and -33.5% respectively. Dietary flaxseed considerably improves lipid profile in hyperlipidemic patients and may positively modify cardiovascular risk factors. Studies on experimental animals showed that flax and pumpkin seed mixture had antiatherogenic and hepatoprotective effect probably mediated by unsaturated fatty acids in the mixture [76]. Flaxseed lignans are converted to enterolactone by intestinal microflora. Enterolactone has been suggested to be the prime active compound mediating atherosclerosis protective effects [77]. Flaxseed treatment reduced serum levels of both LDL and HDL cholesterol by 4.7% and triglyceride by 12.8%. Serum apolipoprotein A-1 and apolipoprotein B concentrations were significantly reduced by 6 and 7.5%, respectively, by the flaxseed administration in postmenopausal women. Markers of bone formation and bone resorption were not affected by either of the treatments. The flaxseed supplementation thus improves lipid profiles but has no effect on biomarkers of bone metabolism in postmenopausal women [78,79]. A study showed that Flaxseed supplementation along with HCD showed significant anti hypercholesterolemic effect and ameliorated the changes of initiated atherosclerosis in the aorta. [80] Studies on the Cardiovascular of effect of Flaxseed and its components concluded that flaxseed with very low ALA, Flaxseed lignan complex (FLC) secoisolariciresinol diglucoside (SDG) suppress the development of atherosclerosis, FLC and SDG slows the progression of atherosclerosis but do not regress atherosclerosis. [81]

Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA), derivatives of ALA, have cardio protective properties. Harper et al. (2005) studied the effect of daily supplementation of ALA from flaxseed on the plasma concentration of n-3 fatty acids in African-American population with chronic illness. Results demonstrate that plasma DHA levels did not change in either group; the efficacy of the conversion of ALA to EPA and DPA was found in a minority population with chronic disease [82].

Although direct studies on flaxseed and blood pressure are limited, numerous studies have shown the ability of increased omega-3 fatty acid intake to help regulate and reduce blood pressure in persons who have been diagnosed with hypertension. Furthermore, a diet low in saturated fats and rich in monounsaturated and polyunsaturated fats, including omega-3 fatty acids from flaxseed, can reduce heart disease. Preventing the occurrence of cardiovascular disease with nutritional interventions is a strategy that is extensively focusing attention of researchers. Epidemiological investigations and experimental studies suggested that ALA intake from flaxseed has been demonstrated to combat cardiovascular disease [83].

**ANTI-INFLAMMATORY FUNCTION:**

Administration of lignan capsules (360mg/d) for 12 weeks to diabetic subjects with mild hypercholesterolemia resulted in significant reduction in C-reactive protein levels [84]. Information on bioavailabity of enterolignans is inadequate and the mean relative bioavailability of enterolignans from whole compared with ground flaxseed was 28% (p<or =0.01), where as that of crushed compared with ground flaxseed was 43% (p<or =0.01). Crushing and milling of flaxseed substantially improve the bioavailabity of the enterolignans [85]. There was a significant increase in serum alpha linolenic acid, eicosapentaenoic acid and docosapentaenoic acid and serum enterolactove concentration was doubled during flaxseed supplementation [86].

Lignans have shown to have positive effects in lowering the risk factors for heart disease. Usage of flax seed or SDG has been revealed to have positive effects in both lupus and polycystic kidney disease models. Flax seed has also been shown to be hepatoprotective. There are many possible mechanistic explanations for the observed bioactivities including involvement in hormonal metabolism or availability, angiogenesis, antioxidation and gene suppression [87]. Both the flaxseeds and flaxseed oil possess anti inflammatory activity [88,89]. Flaxseed oil is a potent anti-inflammatory agent and diminishes signs of inflammation such as swelling, puffiness, sensitivity, eruption and infection [90,91]. Omega-3 fatty acid in flaxseed oil has proved to be beneficial in minimizing inflammatory disorders like arteriosclerotic vascular disease. Lignans and ALA in the seeds help to cease inflammation that affects the functioning of the immune system. A study conducted in middle aged men with inflammatory disorders, dietary augmentation with ALA resulted in a significant decrease in the inflammation within 24 hours. [92]

**FLAXSEED IN NEPHROLOGY:**

Flaxseed derivatives, as well as both oil and flax lignans, alter progression of renal injury in animal models, including Han: SP RDcy Polycystic Kidney Disease (PKD) [93]. A study concluded that replacement of dietary protein with flaxseed meal decreases proteinuria, glomerular and tubulointerstitial lesions in obese SHR/N-cp rats. Flaxseed meal is more effective than the soy protein in reducing proteinuria and renal histologic abnormalities in this model. The reduction in proteinuria and renal injury was independent of the amount of protein intake and glycemic control [94]. The dietary phytoestrogens have a beneficial role in chronic renal disease. Flaxseed has been shown to limit or reduced proteinuria and renal pathological lesion associated with progressive renal failure [95].

The anti-inflammatory properties of ω-3 fatty acids, has shown protective effects on kidneys from damage in adults. PUFA (polyunsaturated fatty acids) supplementation was observed as reducing renal inflammation and fibrosis in animal models. A study also shows that increased dietary intake of long-chain ω-3 PUFA was inversely associated with the incidence of CKD [96,97].

**FLAXSEED IN BONE HEALTH:**

Alpha linolenic acid in flaxseed promotes bone health by preventing excessive bone turnover-when consumption of foods rich in these omega-3 fat results in a lower ratio of omega-6 to omega-3 fats in the diet [98]. A systematic review controlled flax interventions on menopausal symptoms and bone health in premenopausal and postmenopausal women. The majority of studies considered, suggested that flax consumption alters circulating sex hormones and increased the urinary 2α-hydroxyestrone/16α-hydroxyestrone ratio associated with a lower risk of breast cancer. However, few studies considered bone mineral density or markers of bone turnover [99].

Flaxseed, in particular lignans could influence bone development. Ward et al. (2001) found that rats exposed to 88 or 177.3 mg SDG/kg of body weight/day had higher bone strength than the basal diet at 50 days post natal. However, by post natal day 132, no differences in bone strength, bone mineral density were observed. Exposure to SDG did not have negative effect on bone strength [100]. In an animal model Flaxseed supplementation when combined with estrogen therapy resulted an additional benefit . Flax oil rich in ALA showed a positive effect on bone health, particularly in pathological conditions such as obesity and kidney disease. ALA may be more responsible for this improvement in osteoporotic bone conditions than the estrogenic lignan content of flaxseed, [101].

**ANTI BACTERIAL ACTIVITY:**

The petroleum ether, ethanol, aqueous and chloroform extracts of flaxseeds subjected to screen anti bacterial activity against four types of Gram-positive and negative bacteria: *Staphylococcus aureus, Bacillus cereus, Klebsiella pneumonia, and Pseudomonas aeruginosa* using agar-well diffusion method and comparing their antibacterial activities with the antibiotics Ampicillin, Cefalexin, Chloramphenicol and Tetracycline. The petroleum ether extract demonstrated significant inhibitory effects against all tested bacteria using all extract concentration compared with used antibiotics except chloramphenicol, the clearest activity was seen against K. pneumonia using the extract concentration 50 mg/cm3. Ethanol extract possessed considerable antibacterial activities against the pathogenic bacteria, the highest inhibitory effect was observed against *B. cereus* using the extract concentration of 200 mg/cm3, followed by aqueous extract which revealed good inhibitory action against *P. aeruginosa* using the same concentration. The chloroform extract was the weakest, which was only active against *S. aureus* [102].

The effect of flax seed proteins are investigated on the several species of gram positive and gram negative bacteria, inhibitory effect of flax seed total protein extract on the growth of 10 bacterial species was determined. The effect is more prominent on *Salmonella typhimurium* :40%, *Enterococcus foecalis:*45%, *Escherium:*40% and 45% and *Klebsilla pneumonia:*38%. Also, some antibacterial activity appears on *Staphylococcus epidermidis:*19% and *Klebsiella pneumonia* :15%. The antimicrobial activity of hexane, methylene chloride, and butanol extract of flax were examined by disc diffusion assay method, using pathogenic microbial species. The activities of hexane, methylene chloride and butanol fraction were comparable to ampicillin. The activities against *E. coli* were correspondingly 29.2%, 37.5%, and 66.7%; against *S. aureus* were 45.4%, 36.4% and 63.6%; and against *C. albicans* were 26.9%, 46.1% and 73.1% [103]. Antibacterial and antifungal properties of different extract of *L. usitatissimum* and were screened against two type Gram-positive and negative bacteria: *S. aureus*, *K. pneumonia*, and *A. oryzae*, using agar well diffusion method and compared their antibacterial activities with the antibiotics gentamicine, cephalexin, and amphotericin B. Furthermore flax root extract demonstrated for significant inhibitory effect against all tested bacterial and fungal [104]. An in vitro antimicrobial assay of ethanol and chloroform extracts was carried out by disc diffusion method and showed that chloroform extract are more effective than ethanol extract of seeds against various test microorganism [105]. There is a positive antibacterial effects of flaxseed extract against selected oral pathogen Streptococcus mutans, Streptococcus Pyogenes, Pseudomona Aerigenosa and was comparable in efficacy to that of Streptomycin in-vitro. [106]. Bioactive peptides of (present in) flaxseed, such as cyclolinopeptide A, have stro0ng immunosuppressive and antimalarial activities, which shows the inhibition of the human malaria parasite Plasmodium falciparum in culture [107].

**ANTI-DIARRHEA ACTIVITY:**

The effects of Flaxseed in infectious and non infectious diarrhea were investigated. The result suggested that the *Linum usitatissimum* extract exhibit anti diarrheal and antispasmodic activities by virtue of its antimotility and antisecretory effects which are mediated possibly through inhibition of ca+ + channels, thus Flaxseed extract proved effective against both enteric and non enteric pathogens causing diarrhea [108].

**FLAXSEED AND THE BRAIN:**

Studies shows that dietary flaxseed may also improve facet of brain function during conditions of neural disease. Flaxseed reduced all parameters of chronic stress in mice exposed to chronic mild stress[109].

Supplementation to the diet with flaxseed lignans like SDG have shown anti-depressant-like effects in mice subjected to chronic stress [110] and verified protective effects in cortical neurons against NMDA-induced neurotoxicity [111]. Furthermore accessible data suggest that omega-3 fatty acid, ALA, which is enriched in flaxseed, may have similar functional significance like DHA for the

brain. When mothers of rats were fed flaxseed during pregnancy, the brains of newborn were heavier and contained significantly greater amounts of both ALA and DHA [112]. whereas In pups given milled flaxseed or flaxseed oil soon after birth, the pups showed higher brain mass, demonstrating the value of milled flaxseed particularly in contributing to early postnatal brain development [113]. However, though dietary flaxseed may improve brain development and spatial memory, study has cautioned that the diet may depress body growth due to an imbalance between omega-3 and omega-6 fatty acid levels [114].

**FLAXSEED ON HORMONAL STATUS:**

Flaxseed also showed a protective effect against menopausal symptoms [115]. Several studies were carried out to examine the effects of flaxseed or its bioactive ingredients on the quality of life and the frequency and severity of hot flashes in post-menopausal women. The estrogenic action of certain metabolites of flaxseed suggested a potentially positive effect on these post-menopausal symptoms. In a study of 140 postmenopausal women, menopausal symptoms decreased and the quality of life increased in women who ingested a flaxseed supplemented diet [116]. Another study reported similar inconclusive evidence of a positive effect of flaxseed on menopausal symptoms with up to 90 g of flaxseed per day [117]. Further randomized controlled trials and systematic reviews of clinical trials found no significant effect of flaxseed on quality of life or hot flashes during menopause [118-121].

Lignans may minimize the level of free circulating testosterone and when bonded together are excreted in the bile, potentially reducing the risk of polycystic ovary syndrome in susceptible women, since this syndrome is associated to high levels of androgens[122]. A case study demonstrated that clinically-significant decrease in androgen levels are associated with the reduction in hirsutism [123]. This therapeutic use of flaxseed has yet to be tested for further confirmation.

Lipids present in flaxseed may also influences on the spermatogenic process. Lipids are the primary components of sperm and changes in its composition may cause alterations in physiological events related to sperm production [124]. Studies shows decrease in the n-6:n-3 fatty acid ratio promoted by the ingestion of flaxseed results in a rearrangement in the spermatic composition, positively affecting fluidity, which is increased, as well as the integrity and viability of the spermatozoide membrane associated to its fusion with the oocytes [125] and greater velocity[124] showing the positive effect of n-3 fatty acid. A positive effect may also be attributed to the ingestion of antioxidants, including vitamin E and the phenolic compounds present in flaxseed, associated to greater sperm count and greater motor force of spermatozoa in men [126]

However caution has been advised for flaxseed consumption during pregnancy and lactation. Studies on humans are also necessary to increase understanding of the positive and negative effects of flaxseed on males related to the reproductive system and fertility.

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