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FUNCTIONAL COMPONENTS OF FLAXSEED AND THEIR ROLE IN ENHANCING THE HEALTH STATUS OF HUMANS

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Abstract

The growing interest in nutrition has increased the importance of functional foods for the prevention and treatment of diseases. Functional foods are those foods that contain functional elements which not only fulfil the body's nutrient requirements but provide additional health benefits to maintain health status. Nowadays, flaxseed is gaining popularity due to its unique nutritional profile. It represents a rich nutritional profile which includes protein, phenolic compounds, dietary fiber and a notable amount of omega-3-fatty acids. These nutrients make flaxseed an essential functional food to regulate body functions and to use for the prevention and treatment of various diseases. The presence of lignans makes it useful for treating diabetes, certain types of cancer, and cardiovascular diseases; similarly, alpha-linolenic acid and dietary fiber help in the regulation of blood lipid levels and glucose levels and help to control appetite. The anti-inflammatory and antioxidant properties of flaxseed are due to the presence of phytochemicals. Therefore, regular consumption of flaxseed helps to slow down the onset of many metabolic diseases, regulate the body's metabolic pathways, reduce inflammatory markers, and influence the early markers of cancer (colon and breast). There are many studies that indicate the beneficial effect of flaxseed on both human and animal health. This review explains the different functional components of flaxseed and the functional role of flaxseed in elevating health status.

Key words: *Disease prevention, Flaxseed, Functional components, Health benefits*

INTRODUCTION

From decades, plants are studied for their medicinal and functional components, to use for the wellness of human beings. The presence of bioactive elements and antioxidant properties enable the extended use of plants for both functional and nutraceuticals purpose (1). The interest in functional foods has gained popularity in recent years because they can be used as a substitute for medicine due to their health benefits (2). Due to growing interest in nutrition; functional foods are gaining importance in the prevention of diseases. The term functional or nutraceuticals is used for those foods who not only provide basic nutrition but also enhance the health status (3). Currently, flaxseed is gaining importance as a functional or nutraceuticals food due to its disease preventive attributes (4).

Flaxseed is an oldest crop and cultivated on a large scale since ages. The Latin name of flaxseed *is Linum usitatissimum,* which denotes it as very useful and it is a member of Linaceae family. Flax is an annual plant and grown on a large scale worldwide. The shape of flaxseed is oval with a plane surface and pointed tip. It is available in different colors; like dark brown, yellow, and golden (5-6). Flaxseed is an emerging functional food that helps in the prevention and treatment of various diseases; it is considered as an ironic source of valuable nutrients (7). Flaxseed is an oil seed crop due to large content of oil that constitute about 36-40% and its major component is ALA (57%) (8-9). It is also a rich source of protein and fiber which constitutes about 20% and 30%, respectively. Flaxseed is considered a good source of plant based lignans that makes it a valuable source to combat many health issues.

NUTRITIONAL PROFILE OF FLAXSEED

Current scenarios considering flaxseed as an emerging potential food source due to its unique nutritional composition. It exhibits an extremely high amount of α-linolenic acid (ALA), contains good quality protein, a large amount of dietary fiber, and phytoestrogens (10). It comprises of 55% of ALA, about 35% dietary fiber which includes both soluble and insoluble, and protein about 28-30%. Flaxseed gained attention due to the presences of biologically active components. The amount of omega-3 fatty acids is high that help in the maintenance of health (11). This unique nutritional profile of flaxseed makes it for the health. Along all this, it also contains a large number of minerals, vitamins, and a low amount of saturated fatty acids. Proteins present in flaxseeds contain a high amount of albumins and globulins, the ratio of globulin is higher than albumin.

FLAXSEED FATTY ACID CONTENT

Recent researches proved it as an imperative functional food due to the presence of valuable nutrients. Fatty acid structure of flaxseed and the presence of fat in a high amount making it unique from all other foods**).** Flaxseed is a rich source of essential fatty acids that cannot be produced by the body. The presence of essential ω-3 and ω-6 fatty acids and α-linolenic acid makes it useful to protect against diseases and maintaining a healthy status. Omega fats are of two types ω-3 and ω-6 fatty acids (12). Omega 3 fatty acids further divided into three types which include ALA, EPA, and DHA which play a vital role in nutrition. All these FAs play a part in the reduction of heart diseases and also lower blood lipid levels. The part of ALA and LA is 57% and 16% in flaxseed. That's why it shows a positive effect on blood lipid levels (13, 14). is shown in fig 1.

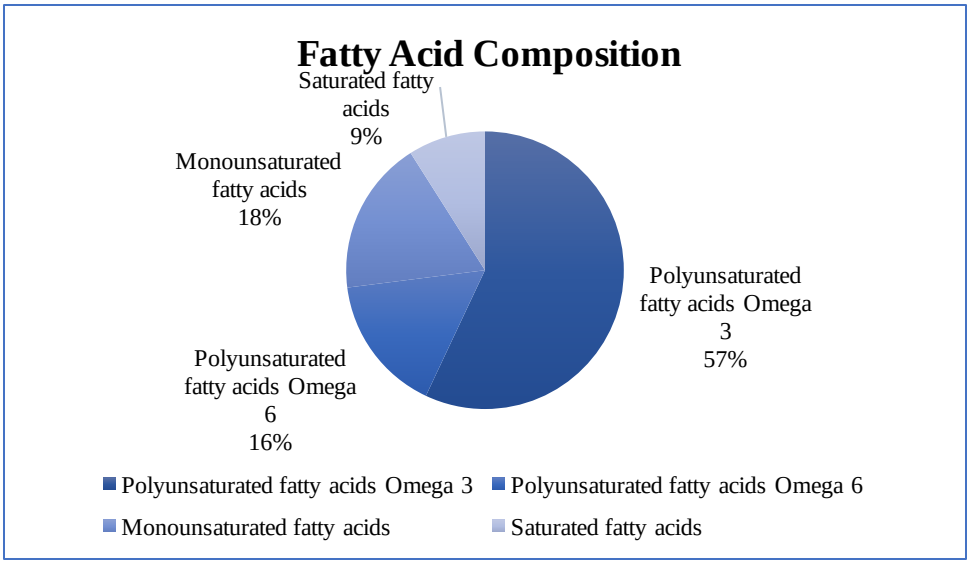

Fig. 1. Fatty acid composition of flaxseed

FLAXSEED DIETARY FIBER

Flaxseed contains a substantial amount of fiber which can be soluble and insoluble. The ratio of soluble and insoluble fiber in flaxseed is 20:80 and 40:60 (15). Lignin, cellulose and hemicellulose are main fractions of insoluble fiber (16). Flaxseed contains almost 26%-28% of dietary fiber. It is estimated that the consumption of a half-ounce of flaxseed in dry form meets 20%-25% of daily fiber requirements (17). Insoluble fiber reduces constipation by its laxation action. It also reduces bowel transmission time. The soluble dietary fiber assists in the maintenance of glucose level and lower cholesterol levels of blood (18). The total content of dietary fiber in flaxseed is shown in Table I (19).

Table I. Dietary fiber content in flaxseed

Dietary fiber	Quantity (g/100g)
Total Fiber	40
Soluble fiber	10
Insoluble fiber	30

FLAXSEED PROTEINS

Flaxseed contains high-quality protein which helps in the maintenance of a healthy status. The protein content of flaxseed may vary with both genetics and environmental factors. The range of protein in flaxseed is 20-30% from which 80% is comprised of globulins, and 20% glutelin is present (20). Flaxseed is considered as good source of protein because its amino acid pattern has a similarity to the protein of soybean which one of the popular plant-based protein sources. It also holds some limiting amino acids like cysteine, methionine, and lysine. The total content of amino acids in flaxseed is shown in Table II.

Table II. Amino acid content in flaxseed

Amino acids	g/100g of proteins
Glutamic acid	19.6
Aspartic acid	9.3
Arginine	9.2
Glycine	5.8
Cysteine	1.1
Histidine	2.2
Isoleucine	4
Leucine	5.8
Lysine	4
Methionine	1.5
Threonine	3.6
Tryptophan	1.8
Tyrosine	2.3
Valine	4.6

FLAXSEED LIGNANS

Flaxseed contains lignan in abundance than any other plant sources. In nature, lignans are secondary metabolites of phenolic compounds. In fiber-rich plants, lignans are present in abundance, in the form of phytoestrogens. The amount of lignans in flaxseed is 75 to 800 times higher as compared to cereals, seeds, fruits, pulses, and vegetable (21). Flaxseed provides plant-based lignans, these plant-based lignans transformed into enterodiol and enterolactone which are categorized as mammalian lignans. Flaxseed contains a large amount of SDG (secoisolariciresinol-di-glycoside). It is a plant lignan and by the action of gut microbiota, it is transformed into mammalian lignans such as EL and ED). The amount of SDG in both whole and ground flaxseed is 0.7% and 1.9%, respectively (22-23).

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VITAMIN AND MINERALS IN FLAXSEED

Flaxseed is an emerging functional food due to its exceptional and enriched nutritional profile. It contains both fat and water-soluble vitamins. Vitamin E is present in a plentiful amount in the form of gamma-tocopherol which acts as an antioxidant. It prevents fat oxidation and keeps the cell protein safe. It also enhances the excretion of sodium in urine which reduces blood pressure. Along with this, flaxseed also contains minerals including Ca, Fe, Mn, P, Mg, K, Cu, Na, and Zn. But the amount of sodium is low (24). Vitamins and minerals present in flaxseed are present in Table III.

Table III. Vitamins and minerals present in flaxseed

Vitamins	Mg per 100g of flaxseed	Minerals	Mg per 100g of flaxseed
δ-tocopherol	10	Potassium	831
α-tocopherol	7	Calcium	236
γ-tocopherol	522	Phosphorus	622
Thiamin/Vit. B1	0.53	Sodium	27
Riboflavin/Vit. B2	0.23	Magnesium	431
Pyridoxine/vitamin B6	0.61	Iron	5
Ascorbic acid / Vitamin C	0.50		
Niacin/nicotinic acid	3.21		(Mercier *et al.*, 2014)

ROLE OF FLAXSEED AS A FUNCTIONAL FOOD

Flaxseed serves as a functional food due to its enriched nutritional profile; that's why it helps in the prevention and inhibition of certain disease. It contains a significant amount of omega fatty acids, high-quality proteins, and lignans such as SDG, dietary fiber, and carbohydrates (25). Therefore, the functional content of flaxseed helps in the inhibition or treatment of various chronic disorders. The consumption of flaxseed helps hyperlipidemic patients in the maintenance of lipid profile which also decrease the risk of cardiovascular diseases. Presence of dietary fiber, fatty acids, and lignans in flaxseed makes it beneficial for patients suffering from diabetes (Fig. 2).

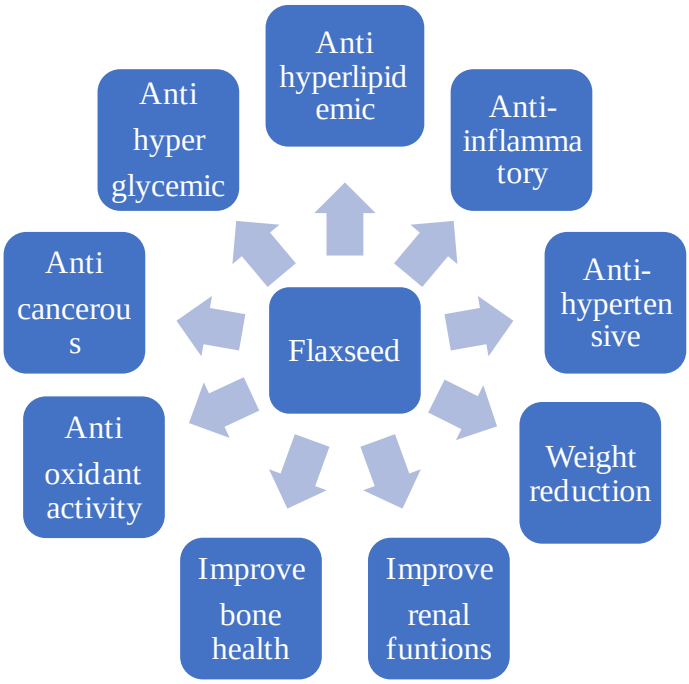

Fig. 2. Health benefits of Flaxseed (26, 27)

FLAXSEED IN HUMAN HEALTH

Due to rich nutritional profile, flaxseed is considered a good source of functional food to achieve health benefits. The nutrients present in flaxseed help to lower the risk of heart disease by controlling lipid level, lowering glucose levels, hypertension, cancer, and obesity (Fig. 3).

Fig. 3. Flaxseed and hyperlipidemia [*Adapted from Buckner et al., 2019* (28)]

Flaxseeds are considered cardio-protective because they contain significant amount of alpha linolenic acid, lignans, and dietary fiber. Alpha-linolenic acid (ALA) serves as a natural precursor for omega-3-fatty acids. According to (29-30), flaxseed consumption by humans showed a notable reduction in total cholesterol, low density lipoproteins, serum triglycerides and also increase omega-3 fatty acids concentrations and alpha linolenic acid levels in serum.

Due to the unique nutritional profile flaxseed has the ability to improve heart health and other related complications (31). According to Prasad, 2009, the rabbit model showed a reduction in the progression of hypercholesterolemic atherosclerosis by 46%, 73%, 34%, and 69% when treated with flaxseed with low ALA, flaxseed lignan complex (FLC), secoisolariciresinoldiglucoside (SDG) and flax oil respectively. This study also revealed that SDG and FLC does not showed any regression of atherosclerosis. Therefore, flax lignans helps in lowering serum low density lipoproteins and cholesterol and increase the level of good cholesterol in body. Supplementation of 8g flaxseed oil per day for a period of 12 weeks in men with dyslipidemia, showed a significant reduction in both systolic and diastolic blood pressure (Edel *et al.,* 2015 reported the antiatherogenic effect of dietary flaxseed on LDL receptor deficient mice model. He reported that the administration of 10% flaxseed for the period of 24 weeks showed a reduction in cholesterol levels and triglycerides that helps in the prevention of atherosclerosis.

Dietary flaxseed supports in the reduction of serum triglyceride level, total cholesterol, LDL levels and a rise in HDL levels by 36.3%, 17.2%, 3.9%, and 33.5% respectively. Therefore, experimental models showed that a mixture of flax and pumpkin seeds exhibit both hepatoprotective and antiatherogenic properties which is usually associated with fatty acid content of seeds. The lignans present in flax seeds converted to mammalian lignan enterolactone via intestinal microbiota. Enterolactone is associated to reduce the effects of atherosclerosis (32) described the hypolipidemic effect of raw flaxseed with normal diet on hypertensive rats. Consumption of 10g of flaxseed for the period of 8 weeks showed significant decline in serum total cholesterol and triglyceride levels.

Flaxseed supplementation associated with reduced serum lipid levels and systemic inflammation. A dose of 40g of flaxseed powder was provided to hyperlipidemic patients for 56 days and it showed 31% decline in triglyceride levels while 16% increase in serum HDL levels was observed (33). Flaxseed helps in the regulation of blood lipid levels. An animal trial was conducted by providing 25% flax powder for the duration of 4 weeks and result indicate a 12% reduction in serum triglyceride levels (34) demonstrated the therapeutic activity of flaxseed on hyperlipidemia. Supplementation of 30g of flaxseed powder on daily basis for 40 days showed a reduction in total cholesterol by 226.05→214.53 mg/dl. The intervention of flaxseed with changes in daily lifestyle performed to reduce the risk of metabolic diseases. A human study was performed for 12 weeks and patients were advised to consume 30g ground flaxseed per day. Results showed a decrease in serum TG levels by 64.34 mg/dl on average. Therefore, the lipid lowering capacity of flaxseed is associated with its fatty acid content, lignans and dietary fiber (35-36). Flaxseed contains large amount of dietary fiber, polyunsaturated fatty acids (PUFAs), and phytosterols which makes it enable to perform antiatherogenic and lipid lowering activities. A dose of 28g ground flaxseed per day was given to hyperlipidemic patients. After supplementation of 10 weeks, the total cholesterol reduced by 11.5% and triglycerides reduced by 14.9%. Thus, flaxseed has a potent effect on serum lipid levels and can be consumed as a functional food against hyperlipidemia (37). Different studies showing the effect of flaxseed against lipid profile in both animals and human presented in Table IV.

Table IV. Role of flaxseed and its functional components on lipid profile

Component	Subject	Dose	Duration	Results	Reference
Flaxseed	30 male rats	1% powdered flaxseed with normal diet daily per rat	28 days	The flaxseed supplementation showed 2.4, 3, and 1.5-fold reduction in TC, non-HDL cholesterol levels and TGs, respectively. It also showed reduced lipid peroxidation in RBCs, organs like heart, aorta and liver, and lipoproteins.	38
Whole flaxseed	48 male Wister rats	7.5 g/kg of	90 days	Administration of	39

powder		rat/day with normal diet 7.5 g/kg of rat/day along with HCD		flaxseed showed hypolipidemic effect by reducing the serum TGs, LDL, and TC levels ($p<0.05$) but no elevation was observed in HDL levels.	
Flaxseed Oil & sunflower seed oil	60 individuals of age range between 30-60 years with metabolic syndrome	Sunflower Oil (SO)= 25mL Flaxseed Oil (FO)= 25 mL	7 weeks	Group treated with FO showed significant reductions in parameters including weight, waist circumference, SBP and DBP when compared with baseline. Lipid profile (TC, TGs & LDL) was significantly reduced in both FO and SO groups.	40
Flaxseed oil	30 Sprague Dawely male rats	50%, 75% & 100% flaxseed oil	4 weeks	The supplementation of 100% flaxseed oil showed 16.93%, 45.65%, 65.14%, 45.65%, and 80.69% reduction in total lipids, TGs, TC, VLDL and LDL levels respectively. The levels of HDL increased by 49.74%.	41
Fat spreads containing flaxseed	Male albino rats	4 different fat spreads containing flaxseed were formulated (20%, 40%, 60% and 80%) and 1.8g of spread was provided per kg of body weight	8 weeks	The group fed with fat spread containing 80% of flaxseed showed 40.17% reduction in TC, 52.40–67.17% reduction in LDL, and 23.58% reduction in TGs levels respectively.	42
Seed Mixture	64 rats	Seed mixture containing Flax, Sesame pumpkin, Peanut, and purslane seeds in a dose of 2g per 100g of diet	30 days	The seed mixture in which there was an addition of flaxseed showed significant reduction in both lipid and hepatic parameters ($P< 0.05$) when compared with control. These groups also showed higher reduction rates when compared with other supplemented groups.	43

Flaxseed	Male rabbits (NZW)	Regular diet supplemented with 10% flaxseed	12 weeks	The supplementation of flaxseed significantly reduces the plaque formation about 40% (P 0.033). But this supplementation didn't showed significant variations in circulation cholesterol levels.	44
Flaxseed supplementation Flaxseed with exercise	40 rats	12.5 g oral administration of flaxseed daily	6 weeks	Flaxseed supplemented group showed a decrease in LDL levels by 63.4% while flaxseed with exercise showed a decrease in LDL levels by 59%. Flaxseed with exercise showed a significant increase in HDL levels (P <0.0001) while flaxseed supplemented group showed no such effect.	30
Flaxseed Lignan Concentrate (FLC)	18 male rats	125 mg of FLC/kg, 250 mg of FLC /kg and 500 mg of FLC/kg	10 days	The cardio toxicity induced with the help of isoprenaline was reduced effectively with FLC. These FLC concentrations were also effective against AST levels.	45
SDG extracted from flaxseed	30 men with high cholesterol levels	Capsules containing SDG (20 or 100 mg per day)	12 weeks	This intervention significantly reduced the ratio of LDL/HDL cholesterol ($P < .05$)	46
Purified flaxseed lignan-SDG	Hyperlipidemic rats	0, 3 or 6 mg SDG per kg of body weight	4 weeks	Both low and high amount of SDG reduced the rate of weight gain. The reduction in TC by the supplementation of 3 and 6 mg of SDG/kg reduce TC by 8 and 27%, LDL-C reduced by 11 and 39% respectively. It also decreased the buildups of hepatic fat by 8 and 24%.	46
Lignans extracted from flaxseed	55 Hyper-cholestrolemic patients	Flaxseed lignan-SDG was	8 weeks	The group treated with 600 mg of SDG	47

		provided in two different doses 300 mg or 600 mg per day		showed significant decrease in both TC and LDL levels by 22%-24.38% respectively. FBS was decreased by 24·96% after the consumption of 600 mg of SDG extracted from flaxseed.	
Flaxseed	Native American postmenopausal hypercholestrolemic women (n=55)	30g of flaxseed per day	3 months	Administration of flaxseed significantly reduce the levels of LDL and TC about 10% and 7%. However, no alterations were occurred in serum TGs and HDL levels.	48
Flaxseed	24 Syrian hamsters	Regular diet supplemented with 15% flaxseed	20 weeks	Flaxseed supplementation showed significant increase in serum HDL by +91% and decrease in serum TC by -24.9%, TC/HDL-C ratio by -60%. Reduction in hepatic cholesterol by -39.5% and TGs levels by -28.8% can be observed.	48
Flaxseed	40 individuals with hyperlipidemia	Low hypolipidemic diet with 20 g flaxseed powder/day	60 days	The supplementation of flaxseed significantly reduced TC (-17.2%), LDL (-3.9%), TC/HDL-C ratio (-33.5%) and TG (-36.3%).	49

FLAXSEED AND DIABETES

Antidiabetic activity of flaxseed is associated with its dietary fiber content and secoisolariciresinol diglucoside (SDG) which is a flaxseed lignan (Goyal *et al*., 2018). Prasad reported that the onset of diabetes can be slowed down to 80% by supplementation of 40 mg of SDG per kg daily in rat models. Flaxseed lignans also has the capacity to lower oxidative stress which not only reduce the occurrence of Type-1-Diabetes but it also holds up the progression of type 2 diabetes (50). Supplementation of 15g flaxseed per 100g diet for 20 weeks in diabetic hamsters showed delayed development of diabetic nephropathy, it also reduces oxidative stress by strengthening the antioxidant defense system.

Flaxseed plays a significant role in the regulation of blood glucose levels. A study was conducted on 60 diabetic patients for the period of 3 months. The patients were advised to consume chappatis made of wheat flour with the addition of flaxseed gum. The results indicated a significant decrease in fasting sugar levels6 from 154±8 mg/dl→136±7 mg/dl in the experimental group. Thus, it exhibits the effectiveness of flaxseed gum against blood glucose levels. Flaxseed is a potential functional food due to the rich amount of nutrients. A study was conducted on 29 patients having type 2 diabetes for 30 days to evaluate the effect of

10g supplementation of flaxseed powder in normal diet on blood glucose levels. The flaxseed intervention showed 19.7% reduction in the glucose levels during fasting state (51).

Flaxseed contains large amount of dietary fiber, antioxidants, and lignans. These nutrients play an important role in the prevention of many diseases. Flaxseed helps in lowering blood glucose level. To investigate the effect of flaxseed against glucose a study was conducted on Wistar rats. Rats were divided into 2 groups; one on casein-based diet and other was experimental group. Study was conducted for 2 months and rats were fed with 25% of flaxseed powder. At the end, results indicated 7% reduction in blood glucose levels (52).

Flaxseed is also effective against blood glucose levels due to the presence of dietary fiber. A study was conducted in randomized single control manner and 77 patients were selected. The patients were divided into three groups and provided cookies containing 10g of flaxseed and psyllium for the period of 12 weeks. The results indicated that the flaxseed supplementation was more beneficial when compared to the psyllium. Group treated with flaxseed showed a reduction in glucose levels from 164.8→137.0 mg/dl and psyllium group showed a reduction from 167.0→147.3 mg/dl. Therefore, flaxseed managed blood glucose better than psyllium (53).

The lipid and glucose lowering capacity of flaxseed can be linked with dietary fiber and lignans (54-55). Another study supported the fact that flaxseed helps in the regulation of blood glucose level. Diabetic rats were fed with 1.2 ml flaxseed oil/kg body weight daily for the period of 8 weeks. Result indicated a significant decrease in blood sugar from 243.87 ± 9.3→177.50 ± 5.1 mg/dl when treated with flaxseed oil (56). The supplementation of flaxseed for diabetic patients is due to its particular role in some of the pathophysiological processes (57). Presence of dietary fiber, fatty acids, and lignans in flaxseed makes it beneficial for patients suffering from diabetes Different studies showing the effect of flaxseed against elevated blood glucose/diabetes in both animals and human presented in Table V.

Table V. Role of flaxseed and its functional components on type II diabetes and blood glucose levels

Component	Subject	Dose	Duration	Results	Reference
Aqueous flaxseed extract	20 diabetic rats	1ml of AFE was injected Intraperitoneally	5 weeks	The administration of Aqueous Flaxseed Extract improved insulin tolerance, oral glucose tolerance, serum glucose levels, hyperphagia, and weight in diabetic rats. it was also effective against lipid peroxidation and antioxidant activity of body.	58
Flaxseed supplemented yogurt	57 diabetic individuals	200 g yogurt with 2.5% fat with addition of 30g flaxseed	8 weeks	Group treated with flaxseed showed significant reduction in HbA1c ($p = 0.007$), triglycerides ($p = 0.04$), total cholesterol ($p = 0.01$), SBP and DBP by ($p = 0.02$ and $p = 0.002$), respectively.	59
Flaxseed based omega-3 fatty acids	60 individuals with type 2 diabetes and diabetic foot ulcer	Supplementation of 1000 mg of omega-3-fatty acids from flaxseed oil	12 weeks	Significant reduction in ulcer length, depth and width was seen in intervention group (-2.0±2.3 vs. -1.0±1.1 cm, P=0.03), (-0.8±0.6 vs. -0.5±0.5 cm, P=0.01), (-1.8±1.7 vs. -	60

				1.0±1.0 cm, P=0.02), respectively. Moreover, insulin level reduced from 4.4±5.5 to 1.4±8.3 μIU/mL, P=0.002).	
Flaxseed	28 diabetic rats	Rats were treated with 0.714g of flaxseed per kg body weight daily	12 weeks	The administration of flaxseed improved reduced body weight ($p < .05$). It also showed significant reduction in blood glucose ($p < .001$), ALT ($p < .001$), AST ($p < .001$) and triglyceride levels ($p < .001$). Small decrease was observed in the levels of GR ($p < .01$) and 6PGD ($p < .05$) while G6PD remain unchanged.	61
Ground Flaxseed	25 postmenopausal women and overweight men	Different doses of flaxseed powder such 13 and 26 g	12 weeks	This study found that low dose of flaxseed showed significant results. Lose dose supplementation showed a decrease in glucose and insulin by −2.10 ± 1.66 mg/dL and −2.12 ± 1.00 mU/L, respectively when compared with control group.	62
Defatted flaxseed powder in bread	8 healthy individuals + 8 individuals with type 2 diabetes	Replaced simple bread with bread containing 200g of defatted flaxseed powder	2 months	After administration of flaxseed bread, it showed significant reduction in fasting and postprandial glucose levels by -15% and -14%, respectively. It also showed significant reduction in plasma TC, TGs and LDL levels of diabetic patients.	Mohamed *et al.* (2012)
Flaxseed (Dietary fiber)	17 male and female with T2D	Flaxseed based fiber rich drink and bread was provided-3 times a day	1 week	The reduction in both TC and LDL levels was 12 and 15% respectively after consuming flax drink while flax bread cause 7 and 9% reduction in TC and LDL. The mean reduction in glucose levels by using flax drink was from 5.4 ± 0.3→5.3 ± 0.4 and flax bread didn't provide significant reduction.	Kristensen *et al.* (2012)

Defatted flaxseed	30 diabetic rats	Addition of 15% powder of defatted flaxseeds in normal rat diet	6 weeks	The supplementation of defatted flaxseed powder showed significant reduction; -66% in serum insulin, -66.8% in VEGF levels, -68% in Glucose levels, -63% in uric acid, and -37.5% in nitric oxide when compared with control group.	63
Flaxseed powder	9 individuals with hyperglycemia	Flaxseed powder 40 g Wheat bran 40 g	12 weeks	The administration of flaxseed was effective against HOMA-IR ($p = 0.0382$) and TBARS ($p = 0.0215$)	64
Flaxseed lignans	73 diabetic and hypercholestrolemic patients	Three Capsules containing 0.6g of lignan per capsule were provided	12 weeks	HOMA-IR significantly decreased by 3.3% after Supplementation of flax lignans. Reduction in fasting glucose, HbA1c, and insulin levels was also observed.	64

FLAXSEED AND ANTI-OXIDANT FUNCTIONS

Flaxseed is the rich source of plant based lignan- secoisolariciresinol diglycoside (SDG) which converted into mammalian lignans enterodiol (ED) and enterolactone (EL) with the help of intestinal microbiota (65-66).The ability to reduce platelet aggregation, diabetes, and cholesterol level shows the antioxidant activity of flaxseeds Imran *et al.* (2015) reported that flaxseed lignans such as EL and ED are effective against lipid peroxidation and also prevent DNA damage. The antioxidant capacity of flax lignans can be associated with specific substituent of SDG and SECO which is called 3-methoxy-4-hydroxyl.The anti-cancer effect of SDG is linked with the suppression of enzymes that promote the carcinogenesis. The growth of abnormal crypts and crypts foci play a major role for the early detection of colon cancer. To identify the antioxidant activity of flaxseed SDG (67) did an animal trial. A dose of 5% defatted flaxseed, 5% whole flaxseed and 1.5 mg of flaxseed SDG was provided to rats with colon cancer daily. The results of all experimental groups showed a reduction in the multiplication of anomalous crypt. As all groups showed similar results so it can be concluded that lignan play a role in the prevention of colon cancer. SDG of flaxseed also has the role in controlling hyperglycemic conditions. It is reported that there is a possibility of suppressing the expression of enzyme phosphoenol pyruvate carboxy kinase. This enzyme limits the process of glyconeogenesis. A comparative study was conducted to observe the efficiency of both SDG and SECO. An animal trial was conducted, rats having oxidative stress were provided flaxseed oil and vitamin E orally. The results showed that the activity of enzymes taking part in antioxidant functions increased significantly in rat's hepatic tissues such as catalase, superoxide dismutase, and glutathione peroxide (68). It was also reported that a combination of flaxseed and vitamin E helps in the reduction of oxidative stress and it also possess high antioxidant activity (69).

FLAXSEED AND ANTI-INFLAMMATORY ACTIVITY

Flaxseed demonstrated anti-inflammatory, antiproliferative and analgesic activities due to the presence of lignans and other functional components. The presence of ALA helps in the inhibition of atherosclerosis by reducing the amount of serum total cholesterol and LDL levels (70) reported that metabolic diseases such as obesity, CVDs, diabetes, cancer and neurodegenerative declines can be directly

linked with oxidative stress and chronic inflammation. The presence of omega-3 fatty acids helps in the reduction of inflammation by suppressing tumor necrosis factor-α, interleukin-1-b, and interleukin-6 Saini *et al.* (2010) conducted a study for two different duration 4 and 9 weeks to examine the effect of flaxseed oil supplementation on mice. Animals that were treated for 9 weeks showed reduction in the levels of pro-inflammatory cytokines including TNF- α and IL-1 while it also exerts strong impression on the makers of oxidative stress (Fig 4).

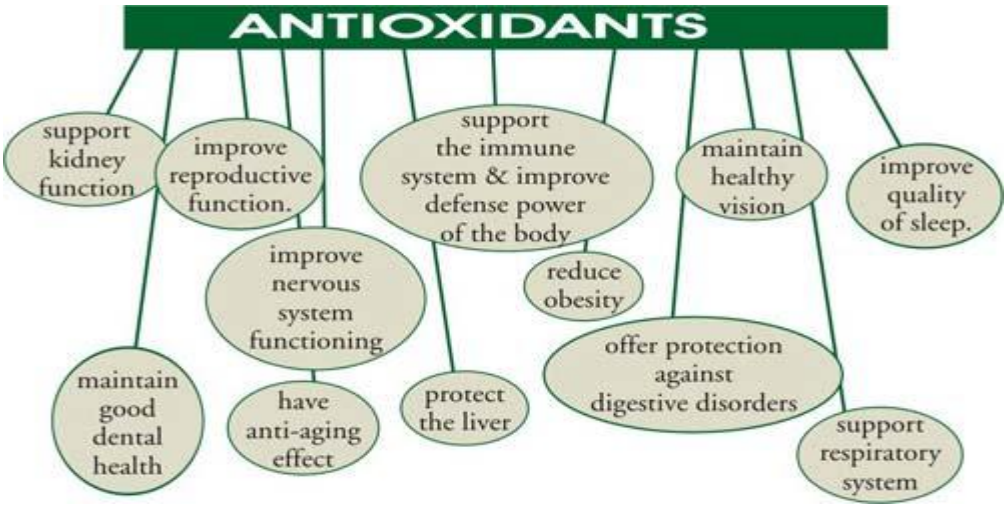

Fig. 4. Flaxseed and anti-oxidant functions [*Adapted from Stepień et al., 2025* (70)]

Flaxseed lignan contribute to its anti-inflammatory response. A study was conducted on diabetic patients with minor symptoms of hypercholesterolemia. Patients were advised to take lignan capsules approximately 360 mg per day for the period of 12 weeks. The results indicate that flax lignans significantly reduce the levels of C-reactive protein. There are not sufficient evidences that exactly explain the bioavailability of enterolignans but when whole and ground flaxseed were compared, the mean relative bio-availability of enterolignans was about 28% while the comparison between crushed and milled flaxseeds showed 43% bioavailability. Therefore, bio- availability of flaxseed enterolignans can be increased significantly by crushing and grinding (Fig. 5).

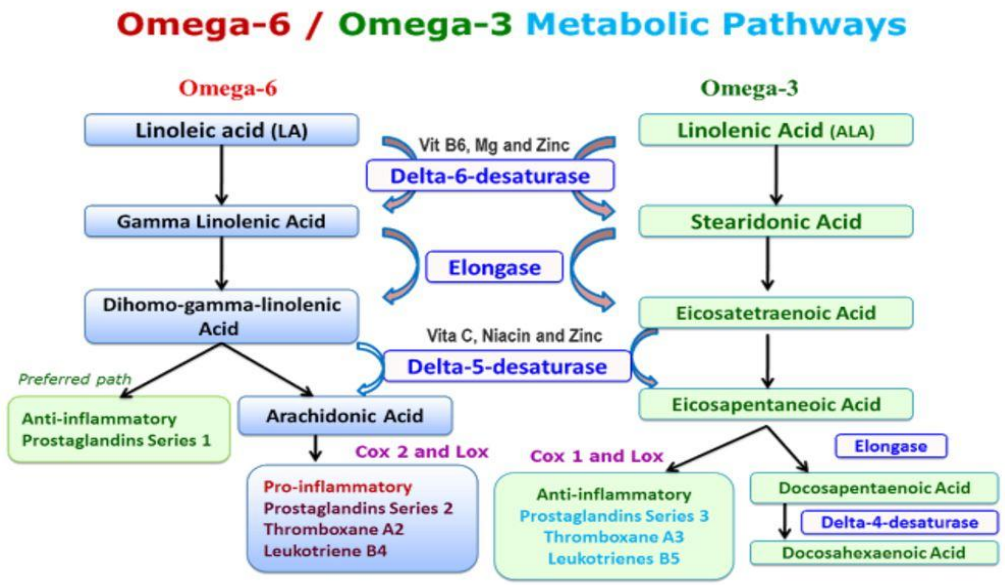

Fig. 5. Flaxseed and anti-inflammatory activity [*Adapted from Chera et al., 2022* (71)]

FLAXSEED AND OBESITY

The increasing interest in flaxseed to prevent noncommunicable diseases is due to the presences of significant amount of polyunsaturated fatty acids and dietary fiber (72). After hydration dietary fibers formed a viscous solution that helps in lowering the caloric density of food, reduce fat absorption in body, suppresses hunger, reabsorption of important nutrients from intestine, and delayed gastric emptying (73).

Flaxseed components has ability to modify the biological activities such as visceral adipose deposition, satiety, thermogenesis, and postprandial substrate trafficking to reduce the risk of obesity (74). The presence of amino acids such as arginine and glutamine help in the production of thermogenic effect to burn excessive calories .The dietary fiber present in flaxseed suppress hunger by stimulating the secretion of cholecystokinin which is a peptide hormone and released by the duodenum's enteroendocrine cells in response to stimulate the digestion of fatty and protein rich food (75).

Dietary fiber plays a role in the prevention of excessive fat buildups in abdominal region and also prevents weight gain in both men and women. Because the foods that are rich in fiber are low energy dense thus provide the feeling of fullness for longer period and slow down the process of digestion. To evaluate the effect of flaxseed against obesity, a study was conducted for 12 weeks. This indicated that consumption of 30g of flaxseed daily, showed a significant effect on the central obesity. A study was conducted to examine the effect of flaxseed polysaccharide on obesity. For establishing the obesity model, the rats were fed with high fat diet for the period of 8 weeks. These obese rats divided into 2 groups one fed on control diet and other received 10% flaxseed polysaccharide in normal diet for 54 days. The result indicated that the intervention of FP shows significant reduction in weight and abdominal fat. When FP group compared with HFD group it showed a reduction from 530 ± 16 g and 2.15% ± 0.30% to 478 ± 10 g & 1.38% ± 0.48%. Thus, it can be claimed that it occurs by the removal of leptin resistance and increasing satiety (76).

Flaxseed is considered a functional food due to the presence of active biological components such as ALA, dietary fiber and lignans (77). To examine the effectiveness of flaxseed against weight loss and other anthropometric measurements in obese women suffering from PCOS, the participants were divided into two groups; one consumed 15g flaxseed/day for 12 weeks and other was placebo. The measurements after intervention showed a decrease in body weight, waist circumference, visceral fat, BMI, and body fat percentage. The mean change in BMI was (P-value= 0.04) and the significance of body weight was minor (P-value= 0.05). However, other measurements were non-significant statistically when compared with control group (78).

The growing interest in flaxseed is due to its functional components that provide a range of health benefits. To investigate the effect of flaxseed gum against obesity and gut flora, 5 weeks rat trial was conducted. After establishing the obesity model, rats were randomly divided in 4 groups. Where one served as a control group fed with standard diet while other received flaxseed gum with normal diet in different concentrations such as high 30% FG (FGH), medium 20% FG (FGM), and low 10% FG (FGL). The control group showed significant body weight gain at week 2 ($P < 0.05$) which remained similar at week 5. The groups that were consuming flaxseed gum showed that the BWG is lowered than control group ($P < 0.05$) (79). A study was conducted to evaluate the effect of lignan enriched flaxseed powder (LEFP) on body weight. Rats were divided in 4 groups and each group fed for 12 weeks with specialized diet; normal control (NC), normal diet + 0.02% LEFP (NCL), high fat+ high fructose diet (HFD), and high fat + high fructose diet including 0.02% LEFP (HFDL). The result indicated a significant reduction in weight from 657 g - 606 g, when HFD and HFDL was compared (80). Studies showing the effect of flaxseed against obesity presented in Table VI.

Table VI. Role of flaxseed and its functional components against obesity

Component	Subject	Dose	Duration	Results	Reference
Flaxseed	50 obese individuals	Supplementation of 30g flaxseed powder daily	12 weeks	The mean differences in flaxseed and control group were; BMI [-3.34 vs. -1.2 kg/m²; P < 0.001], weight [-9.36 vs. -3.09 kg; P < 0.001] triglyceride [-62.88 vs. -9.85 mg/dL; P < 0.001] total cholesterol [-32.2 vs. -14.95; P = 0.04]	81
Whole flaxseed	Obese individuals	Supplementation of 30g of whole flaxseed	12 weeks	A significant reduction in weight, BMI and waist	82

		daily		circumference can be seen in flaxseed supplemented group (p = 0.004, p = 0.008, p = 0.008), respectively.	
Flaxseed oil	30 Sprague Dawely male rats	50%, 75% & 100% flaxseed oil	4 weeks	A significant reduction in body weight by 10.51%, 13.35%, and 19.95% in hypercholestrolemic rats using different replacements of flaxseed oil such 50, 75 and 100%, respectively.	83
Flaxseed lignan complex	16 individuals with T2D	600 mg of SDG daily	3 months	The administration of FLC decreased fasting blood plasma glucose by 0.6 mmol, interleukin-6 and CRP. Increased wait circumference was reduced partially.	84
Dietary flaxseed	16 rabbits	10% ground flaxseed in 125g of rabbit diet per day	8 weeks	Increased levels of ALA in plasma and adipose tissues after the consumption of flaxseed. Groups fed with flaxseed powder showed higher levels of mRNA and lepton protein. Any alterations in lepton levels can be associated with ALA levels in adipose tissues.	85
Flaxseed oil	32 male albino rats	1g per kg/ body weight was provided to obese rats	60 days	The administration of flaxseed significantly reduced the gain in both liver and body weight ($P < 0.05$) when compared with high fat diet group. A reduction in plasma TC and TGs was also observed.	85

FLAXSEED AND CANCER

Flax lignans exhibit multiple properties such as antioxidant, anti-estrogenic, anti-angiogenic, and antiproliferative which make it a good source to prevent certain types of cancers such as lung, breast and colon. Lignans also has the ability to inhibit some enzymes that can be involved in the progression of tumor (86) supplementation of flaxseed lignans in female rats showed 38.8-55.4% reduction in the production of epithelial cells and a reduction of 58.8-65.9% in nuclear aberration were observed. The use of flaxseed lignans can be related with the reduction of carcinogenesis in both colon and mammary glands. It can also be associated with early reduction of risk markers for certain types of cancers investigated the effect of dietary lignan-SDG on pulmonary metastatic tumor growth in rats after feeding with normal diet and SDG rich diet in different concentrations such as 2.5%, 5%, and 10% for two weeks before and after injecting the tumor cells intravenously. To determine the size and number of tumors formed in lungs necropsy was performed which showed 62 tumors in control group while the groups treated with SDG diet showed 38, 36, and 29 tumors respectively. Thus, the supplementation of SDG with normal diet showed a reduction in size, volume and cross-sectional area of tumor but it totally depends on the dose of the supplementation.

Flaxseed contains the precursors of mammalian lignans in abundance which are considered to be beneficial against tumor growth. Patients were randomly divided and advised to consume either control muffins or muffins containing 25 g flaxseed daily for the period of 32 days. At the end of the experimental trial, a greater reduction in proliferation of tumor cells and in the expression of c-erbB2 can be observed in flaxseed group while cell apoptosis increased in both groups. The total decrease in proliferation of tumor cells was 34.2%, significant reduction of 71.0% in c-erbB2 expression and apoptotic index increased by 30.7%

in flaxseed group. The results indicate that the supplementation of flaxseed has ability to inhibit tumor development in patients suffering from breast cancer. A combination of flaxseed lignans [enterodiol (ED) and enterolactone (EL)] and tamoxifen clinically used drug for the treatment of breast cancer, results indicated suppressed growth of tumors in mice.

To investigate the effect of flaxseed against prostate cancer, transgenic adenocarcinoma mouse prostate (TRAMP) model was used. Total 135 TRAMP mice were randomly divided in control group and flaxseed supplemented group (normal diet with 5% flaxseed). The study was performed for two periods 20 and 30 weeks. The addition of flaxseed exhibited the delay of the prostate cancer at advanced stage. The rats treated for longer period showed significant results in terms of tumor growth (P 0.01) when compared with control and rats treated for shorted time period. The consumption of flaxseed is also linked with the treatment of prostate cancer. Patients with prostate cancer were randomly divided to evaluate the effect of flaxseed and low-fat diet on prostate biomarkers. The groups were advised to take 1) normal diet, 2) diet with the addition of 30g of ground flaxseed/day, 3) diet with low fat <20% of energy from fat, and 4) combination of both flaxseed powder (30g/day) + low-fat diet. This 30-day experimental design showed a significant reduction in proliferation rates ($P < 0.002$) in group treated with flaxseed. The average Ki-67-positive cells ratio was 1.66 in group treated with flaxseed, 1.50 in flaxseed + low fat diet group and while control and low fat showed 3.23 and 2.56 respectively.

To identify the mechanism that is involved in the anti-cancerous activity of ground flaxseed both human and animal trials were conducted. Studies showed that the rich amount of alpha linolenic acid and lignans present in flaxseed exhibit a beneficial effect on cancer and tumor growth (86). Clinical studies showed that the consumption of flaxseed lignans-SDG 25g daily or 50 mg lignans for 32 days reduces the growth of tumors in case of breast cancer and hence it also reduces the mortality rate by 33–70% (87) reported the anti-cancerous activity of flaxseed lignans. This study stated the beneficial impact of flaxseed on different types of cancers including colon, breast, and ovarian. Thus, it prevents the production of tumors that further leads to cancer.

FLAXSEED AND HYPERTENSION

Hypertension is considered as single most important risk factor that is associated with the development of cerebrovascular and cardiovascular diseases. A person having systolic blood pressure (SBP) higher than 140 mm Hg or a diastolic blood pressure (DBP) higher than 90 mm Hg is considered as hypertensive. Flaxseed is the richest source of polyunsaturated fatty acids, dietary fiber, lignans, and arginine that helps in the reduction of blood pressure (88).

A potential dietary intervention can help in lowering the risk factors associated with hypertension. Patients having hypertension along with peripheral artery disease (PAD), advised to consume 30g of ground flaxseed per day for the duration of 6 months, this intervention exhibited a dropout of 22.4% in blood pressure where -10-mmHg decline in systolic and 7 mm Hg decrease in diastolic blood pressure was observed. The patients also showed a significant increase in plasma levels of enterolignans and ALA.

The health promoting traits of flaxseed are due to the presence of ALA; which accounts for 20% of seed's total dry weight, lignans, and dietary fiber. Studies show that the supplementation of ALA rich flaxseed oil reduces both systolic and diastolic blood pressure in patients with dyslipidemia. The consumption of 20g flaxseed oil daily in obese individuals for the period of 4 weeks showed 13 mm Hg improvement in total arterial pressure. To evaluate the effect of flaxseed lignan-SDG in individuals with metabolic syndrome and high blood pressure which are risk factors for cardiovascular diseases. The ingestion of 543 mg of SDG daily reported significant reduction by 4mm Hg in diastolic blood pressure and 6.7 mm Hg reduction was observed in individuals with metabolic syndrome.

Antihypertensive effect of flaxseed is associated with diverse range of mechanism. SDG is considered as an important hypotensive agent because it helps in the reduction of angiotensin I that is responsible for the rise in blood pressure and act as a powerful ACE inhibitor (Prasad, explained that the bioactive components present in flaxseed inhibit soluble epoxide hydrolase to reduce the high blood pressure. The assay of SEH inhibitor showed that the high concentration of ALA reduces SEH activity. Thus,

the ALA and lignans present in flaxseed was found effective against high blood pressure used the ethanolic extract of flaxseed to reduce the levels of blood pressure. Similarly, (90), treated hypertensive rats with flax lignan extract and reported that SDG is responsible for lowering high blood pressure. It can be occurred by inhibiting renin-angiotensin-aldosterone system which is associated with tissue vasodilation. Different studies showed the effect of flaxseed against elevated blood pressure in both animals and human.

CONCLUSION

From the past few decades the concept of functional and nutraceutical foods is emerging and research showed that simple foods have the ability to act as functional foods. One of the emerging functional food is flaxseed because it is the rich source of dietary fiber, ALA, and plant based lignans. The use of such foods in product development sector is also growing and it needs more innovative strategies to make the use of functional foods in both health and product development sector. Previous studies showed that the rich nutritional profile of flaxseed is beneficial in combating various diseases. Thus, regular consumption of flaxseed in safe limits provide variety of health benefits that's why it should be incorporated in food products to increase their nutritional profile. Moreover, further clinical research is needed on its bioactive components mostly in terms of cancer and hormonal balance.

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Conflict of interest:

There is no conflict of interest among authors regarding this article.

Authors` contribution:

MF, NK, RS & AAK Conceptualized the study; MF, MA, SM & NK Manuscript writing, review, critical analysis and editing. All authors have reviewed and consented to the final version of the manuscript for publication.

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