

# The Functional Nutrients of Flaxseed and Their Effect on Human Health: A Review

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## Author's contributions

This work was carried out in collaboration between both authors. Author AA developed the analyses parameters, developed objectives and secured support. He also undertook analysis of the report, made detailed analysis and was involved in the write up and synthesis of the findings. Author TA has reviewed and standardized the study. Both authors read and approved the final manuscript.

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## ABSTRACT

**Introduction:** Humans have consumed flaxseed (*Linum usitatissimum*) since the earliest times. It has been used as ready-to-eat breakfast cereals, breakfast drinks, salad dressings, porridge, and as beverages. To date, flaxseed is recognized as a functional food in the world's food market because of its health benefits besides the basic nutrition.

**Objectives:** To review the functional nutrients of flaxseed with their respective health benefits.

**Methods:** Electronic search of Pub Med, Health Inter Network Access to Research Initiative (HINARI), and Google Scholar databases was conducted. Outcomes of interest were the functional nutrients of flaxseed and potential health benefits mainly; antioxidant, free radical scavenging, anti-carcinogenic, and anti-hypercholesterolemic.

**Findings:** Majority of the articles reviewed showed that flaxseed contains essential nutrients and non-nutrients such as alpha linolenic acid (ALA), lignans known as secoisolariciresinol diglucoside (SDG), and crude fiber that have important health benefits to humans.

**Conclusions:** Eating flaxseed meal in different forms may have beneficial effect in preventing or reducing various forms of cancer, cardiovascular disease, hypertension, diabetes, constipation, diverticular disease and others. Further studies about the Recommended Daily Intake (RDI) and more *in vivo* studies to ascertain the health benefits of flaxseed nutrients are recommended.

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**Keywords:** Flaxseed; functional food; Omega-3 fatty acids; lignans; crude fiber.

## 1. INTRODUCTION

Flaxseed (*Linum usitatissimum*) also known as linseed is an ancient crop with a long history of cultivation [1]. It was used for medical purposes in ancient Egypt and Greece, mainly to relieve abdominal pains. Currently, it is cultivated in more than 50 countries, the majority of them in the northern hemisphere. Canada is the main flaxseed producer, followed by China, United States, India and Ethiopia [2]. Its percentage of production by the aforementioned countries in 2004 was 26%, 24%, 14%, 11% and 4% respectively [3]. Ethiopia is the fifth largest producer worldwide and flaxseed is the second oil crop next to Niger seed (*Guizotia abyssinica*) [4].

Flaxseed has been used as food for centuries in Asia, Europe, and Africa. Some uses of flaxseed for human consumption include ready-to-eat breakfast cereals, breakfast drinks, salad dressings, biscuits, crackers, soups, and cakes. Flaxseed flour is used commercially to make bread in the United States [3]. In Ethiopia, flaxseed is used for food; the seeds are usually roasted, ground, mixed with spices and water, and served with Injera and breads. It is also consumed in the forms of porridge, and beverage called chillika. Limited amounts are also pressed locally for its edible oil [4].

To date, flaxseed is becoming popular as a functional food in the world's food market. Functional foods are inventive and potential products, which can provide health benefits in addition to the basic nutrition [5]. Flaxseed fits this depiction, because it is rich in ALA, phytochemical known as lignan, and crude fiber. Due to their anti-hypercholesterolemic, anticarcinogenic and glucose metabolism controlling effects, these nutrients may prevent or reduce the risk of various chronic diseases like cancer, diabetes, arteriosclerosis, hypertension and others [1,6,7].

The aforementioned chronic diseases have been increased from time to time and affect the majority of our people both in developing and developed countries. Incorporating flaxseed to our daily meal is very important in combating or reducing those chronic diseases. Hence, this review (or manuscript) is essential to provide a complete picture of flaxseed functional nutrients

with their health benefits and it is also used as basis for future research.

## 2. METHODS

Published results from experimental studies that describe the functional nutrients of flaxseed and having health benefit outcomes were all included to this literature based analysis. Electronic search of Pub Med, Health Inter Network Access to Research Initiative (HINARI), and Google Scholar data bases up to 2014 was conducted. Search was done in key words: "Flaxseed", "Functional food", "Omega-3 fatty acids", "Lignan", and "Crude fiber". Thirty seven full version articles written in English were used.

## 3. RESULTS AND DISCUSSION

### 3.1 The Nutritional Profile of Flaxseed

Understanding the nutritional profile of flaxseed helps in recognizing its value in a healthy diet [8]. Flaxseed is a rich source of the ALA, phenolic compound known as lignans and crude fiber. Flaxseed also contains a high content of protein. However, the nutritional composition of flaxseed varies considerably between varieties and environmental conditions. It can also vary on seed processing and method of analysis [8].

### 3.2 Poly Unsaturated Fatty Acids

Flaxseed is rich in polyunsaturated fatty acids (PUFA's), particularly ALA, lower amounts of linoleic acid (LA), and oleic acid. Flaxseed oil has a very high ALA content, six times richer than most fish oils. Fifteen (15 g) of flaxseed oil provides 8 g of ALA, which is converted in the body to Eicosa Pentaenoic Acid (EPA) and then Docosa Hexaenoic Acid (DHA) at efficiency of 5–10% and 2–5%, respectively [9].

In flaxseed, 39 g/100 g of dry matter is oil. Cotyledons are the tissue in which oil is mainly stored, containing ALA, LA and oleic acids. Flaxseed oil is mainly found as triacylglycerol (98%) with lower contents of phospholipids (0.9%) and free fatty acids (0.1%) [10]. Oil extraction yield and fatty acid content vary slightly between authors, and both depend on oil extraction technology [11]. However, ALA is the major fatty acid found in flaxseed oil [12]. Table 1, shows the fatty acid profile for flaxseed oil.

**Table 1. Fatty acid profile for flaxseed oil**

Fatty acid	% methyl ester
C18:3, $\alpha$ -Linolenic acid	52
C18:2, Linoleic acid	16
C18:1, Oleic acid	21

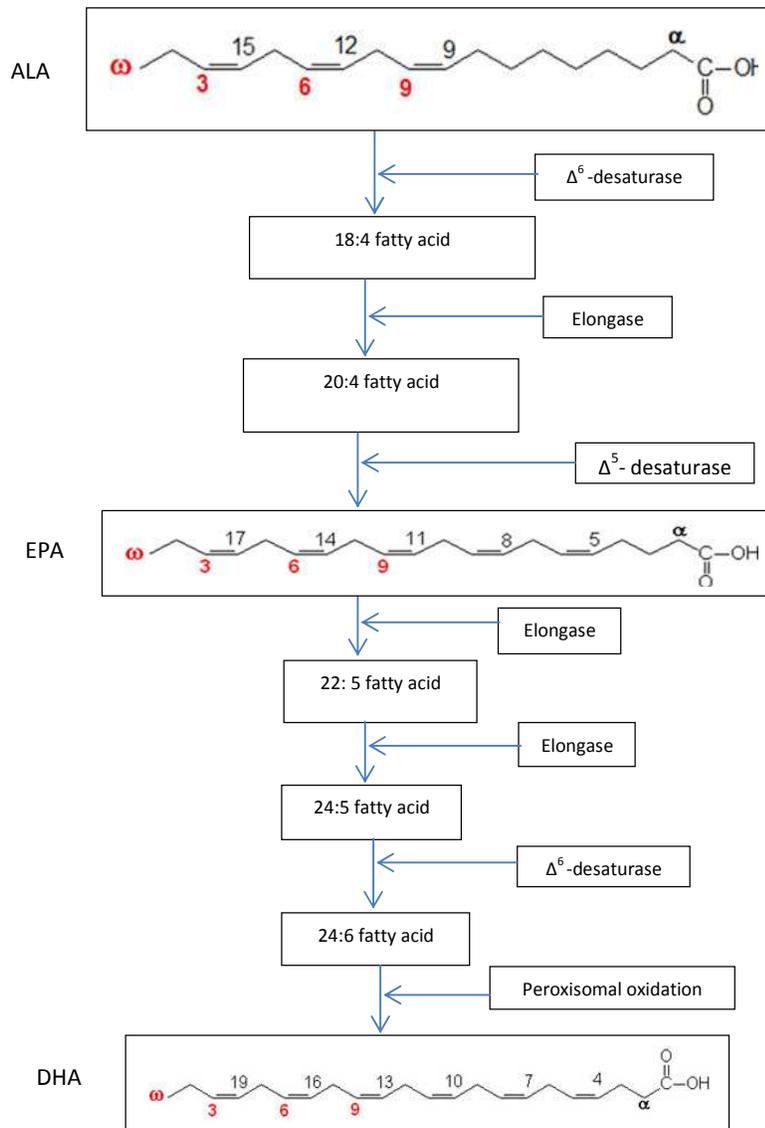
Source: Gutierrez et al. (2010)

### 3.3 Health Benefits

PUFA's are important for all systems of the body to function properly. Fatty acids from flaxseed oil has been gaining popularity in the health food market because of its reported health benefits

and disease preventive properties on coronary heart disease, some kinds of cancer and neurological and hormonal disorders [13].

Certain population studies have shown that a diet rich in  $\omega$ -3 fatty acids, particularly EPA and DHA found in fish oil or metabolized product of ALA can help to prevent heart disease. In the body, ALA can be converted in to EPA and DHA at a rate of nearly 7 - 10 % with the help of elongase and desaturase enzymes (Fig. 1). EPA and DHA are highly unsaturated fatty acids that play vital roles in fetal development, cardiovascular function, and Alzheimer's disease [14].



**Fig. 1. Pathway for ALA conversion to EPA and DHA**

Omega-3 fatty acids (ALA, EPA and DHA) have been found to play a role in atherosclerosis and peripheral arterial disease. It is thought that both EPA and DHA improve plaque stability, decrease endothelial activation, and improve vascular permeability, thereby decreasing the chance of experiencing a cardiovascular event [15].

A study by Rodriguez-Leyva et al. reported that, flaxseed ALA has the most potent antihypertensive effects on hypertensive patients [16]. A review article by Caligiuri et al. also reported that, flaxseed is an alternative or complementary strategy for patients who cannot control their blood pressure with medication, or for those who cannot afford to medication, or for those who prefer a dietary approach [17].

Consumption of flaxseed oil has significant effect on slowing bleeding time thereby reducing the risk of myocardial infarction. A randomised controlled study by Oomah and Sitter reported that, consumption of flaxseed oil significantly increased the ALA, EPA and DHA content in red blood cells and in all tissues except brain [18].

Flaxseed has been reported to lower human serum total cholesterol and hepatic fat deposition in both lean and obese rats, and it has also been shown to suppress hypercholesterolemic atherosclerosis. Daleprane JB et al. reported that a diet supplemented with 25% flaxseed was able to improve the lipid profile, body mass, and vasodilator responses of healthy rats [19].

Lilian Thompson's research group at the University of Toronto studied the effects of flaxseed on cancer. In one study, they added the flaxseeds lignan fraction, or the oil to the diet of mice who had previously been administered a chemical carcinogen to induce cancer. All three treatments reduced the established tumor load [20]. More recently Thompson's research group studied mice that were injected with human breast cancer cells. After the injection the mice were fed a basal diet (lab mouse chow) for 8 weeks while the tumors grew. Then one group continued the basal diet and another was fed a 10% flaxseed diet. The flaxseed reduced the tumor growth rate and reduced metastasis by 45% [21].

Epidemiological studies by Sacco and Ward also reported that higher intakes of ALA from flaxseed may support bone health in aging men and women. However, further investigation is needed to determine whether and how flaxseed and its

components affect skeletal health during aging [22].

In line with the aforementioned health benefits of flaxseed oil, the EU registered the health benefits of flaxseed oil under the EU health claims Regulation 1924/2006 (<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:012:0003:0018:EN:PDF>). So the Regulation addresses the health benefits of the major components of flaxseed oil, ALA, in relation to brain and neurological development, molecule precursors regulating cell functions, maintenance of normal cardiac function, nutrient tasks and interactions, maintenance of normal blood pressure, and enhancement of mood. For flax, ALA, EU health related claims are depicted in Table 2. In contrast to the potential health benefits, all health claims in EU are not authorised because of non-compliance with the Regulation: on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.

### **3.4 Phenolic Compounds/ Lignans**

Flaxseed oil is rich in phenolic compound called lignans. Ferulic and vanillic acid [23], diphyltin, phenolic acids, simple phenols, vanillin, and p-hydroxybenzoic acid are phenolic compounds found in flaxseed oil [24].

A lignan is a phytoestrogen [25], and it is a diphenolic compound found in most fiber-rich plants, like grains (wheat, barley, and oats); legumes (beans, lentils, and soybeans); and vegetables (garlic, asparagus, broccoli, and carrots) [1].

Secoisolariciresinol diglycoside (SDG), matairesinol (Mat), pinoresinol (Pin), medioresinol (Med), lariciresinol (Lari), syringaresinol (Syr), sesamin (Ses), and 7'-hydroxymatairesinol are the types of lignans [26]. However, SDG is the major lignans found in plants. Flaxseed is the richest source of SDG, having 7 mg/g. This is 75 to 800 times more SDG than any other foods. Variety, location, and crop year are factors that affect the concentration of flaxseed lignans. Whole seed and ground flaxseed typically contain between 0.7% and 1.9% SDG respectively [1].

The biological activity of lignans is related to their bioactivation in to mammalian lignin (or enterolignan) called enterolactone (ENL) and enterodiol (END) [1,26]. The conversion of

lignans in to enterolignans (or its bioavailability) is depending on the presence of gastrointestinal microbiota. Deglucosylation, demethylenation, ring cleavage, demethylation, dehydroxylation and oxidation are the necessary chemical processes required to convert lignans to enterolignan [27].

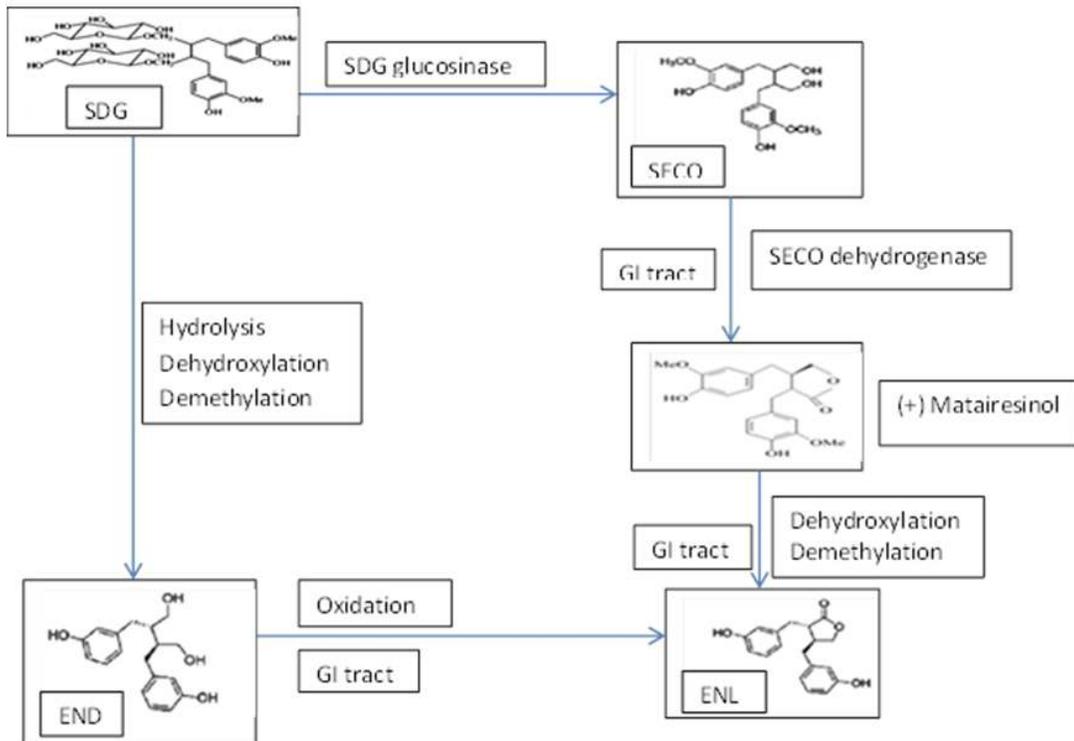
In the GI tract, the sugar moiety of SDG is hydrolysed with the help of bacteria and release SECO. This is followed by dehydroxylation and demethylation by the colonic microflora to give the mammalian lignan END (Fig. 2) [28]. By the GI microbial flora END is oxidized to give ENL. ENL may also be formed directly from matairesinol, although this is a minor metabolic route if other lignans are present in the diet. A human intestinal bacterium, Strain END-2 is responsible for demethylation as well as lactonization during plant lignan metabolism [29]. Besides, *Peptostreptococcus* and *Eubacterium* catalyze the demethylation and dehydroxylation of SDG. Recently, two *Peptostreptococcus productus* and *Eggerthella inta* were isolated that were able to demethylate and dehydroxylate SDG and

pinoresinol. In addition, one bacterial strain (ED-Mt61/PYCT-s6) was also identified that are responsible to convert END to ENL [30].

### 3.5 Health Benefits

The SDG and its metabolites; END & ENL, have been reported to exert protective effects against diet-related chronic diseases through a variety of mechanisms including antioxidant and free radical scavenging activities [31].

Epidemiological evidence indicates that ENL and END may be protective against certain chronic diseases, although discrepancies are observed between “in vivo” and “in vitro” experiments. Thus “in vitro” results often do not match the findings of “in vivo” studies, this could be explained by the low bioavailability of lignans. Furthermore, END and ENL could display antioxidant, oestrogenic and/or anti-oestrogenic activities in addition to the aforementioned health benefits. However, to date, there is no report on recommended daily or minimum daily intake of lignans for disease prevention [27].



**Fig. 2. Biosynthesis pathway of flaxseed lignans SDG, SECO, and their corresponding mammalian lignans END and ENL**

(Source: Ford et al., 2001)

**Table 2. The flaxseed, ALA, EU health claims**

Claim type	Nutrient substance, food or food category	Claim	Conditions of use of the claim/Restrictions of use/Reasons for non-authorization	Health relationship	EFSA opinion reference / Journal reference	Commission regulation	Status	Entry ID
Art.13 (1)	Flax ( <i>Linum usitatissimum</i> )	Helps to support mood. Contributes to emotional wellbeing. Helps to support relaxation and mental wellbeing. Contributes to optimal relaxation.	Noncompliance with the regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Enhancement of mood	2011;9(4):20150	--	Non authorized	3182
Art.13 (1)	Flax ( <i>Linum usitatissimum</i> )	Helps to support mood. Contributes to emotional wellbeing. Helps to support relaxation and mental wellbeing. Contributes to optimal relaxation. Clarification provided thanks to its high essential fatty acids content, flax enhances mood. Flax increases relaxation.	Noncompliance with the regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Enhancement of mood	2011;9(4):20150	---	Non authorized	601
Art.13 (1)	Flaxseed oil	Stabilises moods	Noncompliance with the regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Enhancement of mood	2011;9(4):20150	---	Non authorized	578
Art.13 (1)	Flaxseed oil / alpha linoleic acid	Promotes heart health	Noncompliance with the regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	Maintenance of normal cardiac function	2011;9(4):20150	--	Non authorized	579
Art.13 (5)	A combination of flaxseed oil and Vitamin E	Contributes to maintain skin permeability barrier function	Noncompliance with the regulation because on the basis of the scientific evidence assessed, this claimed effect for this food has not been substantiated.	--	Q-2012-00337	Commission Regulation (EU) No1066/2013 of 30/10/2013	Non-authorized (expiry of transitional period 20/05/2004 (...))	Not applicable

Source: <http://ec.europa.eu/nuhclaims> (accessed 18 June 2015)

Researches also indicates that different types of cancer like breast, colon and prostate cancer can be reduced by eating dietary lignan and/or increasing the levels of ENL and/or END. However, more research is required to determine the cause and effect relationship and to evaluate the possible function of lignans and their metabolites in metabolomics [27].

Dupasquier CMC et al. reported that flaxseed lignan can improve endothelium-dependent vascular relaxation in the presence of a high-cholesterol diet. Another study by Fukumitsu S et al. determined the effects of daily intake of flaxseed lignan (SDG) capsules during 12 weeks on hypercholesterolemia and liver disease risk factors in moderately hypercholesterolemic men. They reported that intake of 100 mg of SDG for 12 weeks results in a significant decrease in the ratio of LDL/HDL cholesterol, which is a key predictor of the peril of cardiovascular disease [32].

### **3.6 Crude Fiber**

Flaxseed contains both soluble and insoluble fiber, which is about 28% of the dry weight of flaxseeds [8]. Two-thirds of flaxseed fiber is insoluble and one-third is soluble [30]. Cellulose and lignin are the main insoluble fiber fraction in flaxseed, while mucilage gums are the main soluble fiber fractions. Flaxseed fiber can be either dietary or functional. Dietary fiber consists of non-digestible plant carbohydrates. Non digestible carbohydrates that have been extracted, purified and added to foods and other products are recognized as functional fiber. Mucilage gums are a famed functional fiber extracted from flaxseeds. They are commonly added to laxatives and cough syrups [8].

Flaxseed mucilage (soluble flaxseed gum, SFG) was reported to have low viscosity; hence it has latent applications as a fiber fortifier [33]. SFG occurs mainly at the outermost layer of the hull. When the hull is soaked in water, it releases mucilaginous material. Qian KY et al. reported that 9.7% of the hull mass is SFG, although the composition and yield of SFG vary with extraction conditions, and genotypes [33].

SFG are two fractions; neutral fraction gum (NFG) and acidic fraction gum (AFG). NFG is about- 27% of SFG. Xylose (68.2%) and arabinose (20.2%) are the major components of NFG; hence it is identified as arabinoxylans. Its minor components included galactose (7.9%)

and glucose (3.7%). AFG mainly consisted of rhamnase (38.3%), galactose (35.2%) and fucose (14.7%). Due to the high content of rhamnase and galacturonic acid, AFG is referred to as rhamonogalacturonans [33].

### **3.7 Health Benefits**

Traditionally humans have been used flaxseed for the prevention of constipation. Recently, researches indicated that flaxseed fiber has an effect on blood glucose metabolism and hyperlipidemia. The insoluble flaxseed fiber, due to its water binding ability, increases the intestinal bulk which is helpful in the treatment of constipation, irritable bowel syndrome and diverticular disease. While, SFG delays gastric emptying, improves glycemic control, prevents constipation and reduces serum cholesterol [34].

#### **3.7.1 Constipation and crude fiber**

Flaxseed mucilage is multi-branched hydrophilic substances, forming viscous solutions that delay gastric emptying and nutrient absorption from the small intestine. That's why; it improves glycemic control in diabetes, and assuages constipation [34].

#### **3.7.2 Serum lipids and crude fiber**

Flaxseed mucilage binds bile acids in the intestine to increase the excretion of cholesterol in faeces; hence it decreases blood total cholesterol. Kristensen M et al. reported that consumption of dietary fibers (5 gm) from flaxseeds daily for one week considerably increased fecal excretion of fat and reduced total and LDL-cholesterol markedly [35].

Kristensen M et al. also reported that, giving 5 g of flaxseed gum per day for three months in type 2 diabetics reduced total and LDL cholesterol by 10 and 16% respectively [35]. The probable mechanism of action is through an intrusion with bile acid metabolism. Flaxseed mucilage can hinder micelle formation and thus diminish lipid uptake and inhibit re-uptake of bile acids. Flaxseed mucilage reduces serum cholesterol by causing hepatic synthesis of bile acids which diverts cholesterol away from lipoprotein synthesis in the liver [36].

#### **3.7.3 Cardiovascular diseases and crude fiber**

Crude fibers have the tendency to lower blood cholesterol, thus it may shield against coronary

heart disease, decreasing hypertension and normalizing blood glucose levels occurring after a meal [37].

### **3.7.4 Crude fiber and colorectal cancer**

A study by Bingham SH et al. showed that total dietary fiber consumption is inversely associated with colorectal cancer risk. Hence, they conclude that doubling of total fiber intake from foods could reduce the risk of colorectal cancer by 40 %. The possible explanation is that, different types of cell walls adsorb a range of carcinogens to different extents. Especially lignin, an important component in flaxseed cell walls, is good adsorbers [38].

## **4. CONCLUSION**

Due to the presence of functional nutrients; ALA, phytochemicals such as lignans (especially SDG), and crude fiber in flaxseed; flaxseed has additional health benefits beyond the basic nutrition. As a result, it is marked as functional food in different parts of the world. Due to their antioxidant, free radical scavenging, anti-hypercholesterolemic, and glucose metabolism controlling effects, the aforementioned nutrients may combat or reduce the risk of various important diseases such as cancer, diabetes, hypertension, cardiovascular disease, coronary heart disease, constipation, irritable bowel syndrome, diverticular disease and others. Although, further studies about the minimum recommended daily intake for all population groups and more in vivo studies are required to ascertain the health benefits of flaxseed nutrients.

## **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

## **REFERENCES**

1. Toure A, Xueming X: Flaxseed lignans: Source, biosynthesis, metabolism, antioxidant activity, bio-active components, and health benefits. *Comprehensive Reviews in Food Science and Food Safety*. 2010;9:261-269.
2. Jacobsz MJ, Van der Merwe WJC: Production guidelines for flax (*Linum usitatissimum* L.). Department of agriculture, forestry and fisheries directorate: Plant production 2012. South Africa.
3. Smith VH, Jimmerson J. Flaxseed. Briefing. Agricultural marketing policy center. Montana State University; 2005.
4. Negash W, Asfaw Z, Yibrah H. Linseed (*Linum usitatissimum* L.) ethnobotany and cultivation status in Ethiopia. *Int. J. Agric. Appl. Sci.* 2012;4:48-57.
5. Hao M, Beta T. Development of Chinese steamed bread enriched in bioactive compounds from barley hull and flaxseed hull extracts. *Food Chemistry*. 2012;133:1320–1325.
6. Fofana B, Cloutier S, Kirby CW, McCallum J, Duguid S. A well balanced omega-6/omega-3 ratio in developing flax bolls after heating and its implications for use as a fresh vegetable by humans. *Food Research International*. 2011;44:2459–2464.
7. Gutierrez C, et al. Flaxseed and flaxseed cake as a source of compounds for food industry. *J. Soil Sci. Plant Nutr.* 2010;10:454-463.
8. Flax Council of Canada (FCC). *Flax-a Health and Nutrition Primer*; 2007.
9. Asif M. Health effects of omega-3,6,9 fatty acids: *Perilla frutescens* is a good example of plant oils. *Orient Pharm Exp Med*. 2011; 11:51–59.
10. Mueller K, Eisner P, Yoshie-Stark Y, Nakada R, Kirchhoff E. Functional properties and chemical composition of fractionated brown and yellow linseed meal (*Linum usitatissimum*). *J. Food Eng.* 2010; 98:453-460.
11. Rubilar M, Gutierrez C, Verdugo M, Shene C, Sineiro J. Flaxseed as a source of functional ingredients. *J. Soil Sci. Plant Nutr.* 2010;10:373-377.
12. Yuksel F, Karaman S, Kayacier A. Enrichment of wheat chips with omega-3 fatty acid by flaxseed addition: Textural and some physicochemical properties. *Food Chemistry*. 2014;145:910-917.
13. Herchi W, et al. Characterisation of the glycerophospholipid fraction in flaxseed oil using liquid chromatography–mass spectrometry. *Food Chemistry*. 2011;129:437–442.
14. Swanson D, Block R, Mousa SA. Omega-3 fatty Acids EPA and DHA: Health benefits throughout life. *Adv. Nutr.* 2012;3:1-7.

15. Dawczynski C, Martin L, Wagner A, Jahreis G. n-3 LC-PUFA-enriched dairy products are able to reduce cardiovascular risk factors: A double-blind, cross-over study. *Clin Nutr.* 2010;29:592-599.
16. Rodriguez-Leyva D, et al. Potent antihypertensive action of dietary flaxseed in hypertensive patients. *Hypertension.* 2013;62:1081-1089.
17. Caligiuri SPB, Edel AL, Aliani M, Pierce GN. Flaxseed for hypertension: Implications for blood pressure regulation. *Curr Hypertens Rep.* 2014;16:1-13.
18. Oomah BD, Sitter L. Characteristics of flaxseed hull oil. *Food Chemistry.* 2009; 114:623-628.
19. Daleprane JB, et al. Dietary flaxseed supplementation improves endothelial function in the mesenteric arterial bed. *Food Research International.* 2010;43: 2052-2056.
20. Donaldson MS. Nutrition and cancer: A review of the evidence for an anti-cancer diet. *Nutrition Journal.* 2004;3:1-21.
21. Chen J, Stavro PM, Thompson LU. Dietary flaxseed inhibits human breast cancer growth and metastasis and down regulates expression of insulin-like growth factor and epidermal growth factor receptor. *Nutrition and Cancer.* 2002;43:187-192.
22. Sacco SM, Ward WE. Flaxseed to maintain bone health during aging: What do the human studies tell us? *Agro Food Industry Hi Tech.* 2014;25:40-43.
23. Siger A, Nogala-Kalucka M, Lampart-Szczapa E. The content and antioxidant activity of phenolic compounds in cold-pressed plant oils. *Journal of Food Lipids* 2008;15:137-149.
24. Herchi W, et al. Determination of phenolic and other polar compounds in flaxseed oil using liquid chromatography coupled with time-of-flight mass spectrometry. *Food Chemistry.* 2011;126:332-338.
25. Nemes SM, Orsat V. Modeling the recovery patterns from solid phase extraction purification of secoisolariciresinol diglucoside, p-coumaric acid glucoside, and ferulic acid glucoside from microwave-assisted flaxseed extracts. *Food and Bioproducts Processing.* 2012;90:453-465.
26. Umezawa T. Diversity in lignan biosynthesis. *Phytochemistry Reviews.* 2003;2:371-390.
27. Landete JM. Plant and mammalian lignans: A review of source, intake, metabolism, intestinal bacteria and health. *Food Research International.* 2012;46:410-424.
28. Ford JD, Huang KS, Wang HB, Davin LB, Lewis NG. Biosynthetic pathway to the cancer chemopreventive secoisolariciresinol diglucoside-hydroxymethylglutaryl ester-linked lignan oligomers in flax seeds (*Linum usitatissimum*). *J Natural Prod.* 2001;64: 1388-97.
29. Jin J, Hattori M. Human intestinal bacterium, strain END-2 is responsible for demethylation as well as lactonization during plant lignan metabolism. *Biol. Pharm. Bull.* 2010;33:1443-1447.
30. Patel D, Vaghasiya J, Pancholi SS, Paul A. Therapeutic potential of secoisolariciresinol diglucoside: A plant lignan. *International Journal of Pharmaceutical Sciences and Drugresearch.* 2012;4:15-18.
31. Dupasquier CMC, et al. Effects of dietary flaxseed on vascular contractile function and atherosclerosis during prolonged hypercholesterolemia in rabbits. *Am J Physiol Heart Circ Physiol.* 2006;291: H2987-H2996.
32. Fukumitsu S, Aida K, Shimizu H, Toyoda K. Flaxseed lignan lowers blood cholesterol and decreases liver disease risk factors in moderately hypercholesterolemic men. *Nutrition Research.* 2010;30:441-446.
33. Qian KY, Cui SW, Wub Y, Goff HD. Flaxseed gum from flaxseed hulls: Extraction, fractionation, and characterization. *Food Hydrocolloids.* 2012;28:275-283.
34. Tarpila A, Wennberg T, Tarpila S. Flaxseed as a functional food. *Current Topics in Nutraceutical Research.* 2005;3: 167-188.
35. Kristensen M, et al. Flaxseed dietary fibers lower cholesterol and increase fecal fat excretion, but magnitude of effect depend on food type. *Nutrition & Metabolism.* 2012;9:1-8.
36. Theuwissen E, Mensink RP. Water soluble dietary fibers and cardiovascular disease. *Physiol & Behavior.* 2008;94:285-292.
37. Penttinen-Damdimopoulou PE, Power KA, Hurmerinta TT, Nurmi T, van der Saag PT, Makela SI. Dietary sources of lignans and isoflavones modulate responses to

- estradiol in estrogen reporter mice. *Mol. Nutr. Food Res.* 2009;53:996-1006.
38. Bingham SH, et al. Dietary fibre in food and protection against colorectal cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC): an observational study. *Lancet.* 2003;361: 1496-1501.

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