

Review Article

Chemical Composition and Health Benefits of Flaxseed

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Abstract

Flaxseed or linseed (*Linum usitatissimum* L.) comes from the flax plant, an annual herb. The main importance of flaxseed is in the human nutrition sector because it is emerging as an important functional food ingredient thanks to the content of active compounds, pointed to provide health benefits. There are several ways to eat flaxseed: milled, in the form of oil or added to bakery product.

Scientific evidences support consumption of flaxseed for the high content in omega-3, omega-6 rich oil, α -linolenic acid, lignans, high quality proteins and fibers, compounds which are biologically active in the prevention of some chronic diseases such as many types of cancer, diabetes, cardiovascular diseases and cerebrovascular stroke.

Furthermore, advantages in flaxseed consumptions are shown in animal nutrition sector and therefore result in healthier food from animal origin. In fact, the fatty acid profile of the meat and fat is directly affected by the source of fat in diet in swine and poultry, feeding omega-3 enriched diets by the addition of flaxseed would increase the omega-3 content in eggs and meat and thus enrich the products. The present review is focused on recent data on flaxseed chemical composition and its beneficial effects.

Keywords: Flaxseed; Chemical composition; Health benefits; Functional food; Human nutrition

Introduction

Consumer's interest in healthy eating, in the last decades, shifted towards the potential health benefits of specific foods and food ingredients. Foods, in fact, are not intended to only satisfy hunger and to provide basic nutritional requirements but also to prevent nutrition-related diseases and to improve physical and mental well-being of the consumers.

Consumer demand for foods with greater beneficial effects, led food industries in increasing the production of functional foods that now represents a significant share of new food products.

The result was a growing demand for marketing authorizations and the regulatory authorities had to face the problem of the evaluation of "claims" proposed by companies, in the absence of clear and global rules. Therefore, the need of a European Union law, which regulates the marketing of functional foods, has led to the definition of Regulation CE 1924/2006, with the aim of protecting consumers, promoting fair trade promotion and encourages product innovation in food industry [1].

In the relationship between diet, health and well-being, functional foods play an outstanding role. Many definitions exist worldwide for functional foods, but there is no official or commonly accepted definition [2]. The European Commission's Concerted Action on Functional Food Science in Europe (FuFoSE), 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 or/and decreasing the risk of the evolution of diseases [3].

In the last years, thanks to the evolution of scientific research, flaxseed is emerging as an important functional food ingredient.

Flaxseed is the seed from the flax plant, an annual herb, which is a member of the Linaceae family. It thrives in deep moist soils rich in sand, silt, and clay. The specie is native to the region extending from the eastern Mediterranean, through Western Asia and the Middle East, to India.

The Latin name of flaxseed (*Linum usitatissimum* L.) means "very useful", and it has two basic varieties: brown and yellow or golden (also known as golden linseeds) [4].

Flaxseed, of Mesopotamic origin, has been cultivated since 5000 BC, being used until the 1990s principally for the fabrication of cloths and papers. Today it is cultivated in over 2.6 million ha and the important linseed growing countries are India, China, United States, Ethiopia. Canada with 614,000 metric tonnes of flaxseed produced in the year 2013-2014, is the world's largest producer of flax and accounts for nearly 80% of the global trade in flaxseed [5,6].

The whole flaxseed is flat and oval with pointed tips and contains a seed coat or true hull (also called testa), a thin endosperm, two embryos and an embryo axis [7]. Every part of the linseed plant is utilized commercially, either directly or after processing. The shell yields good quality fiber having high mechanical properties and low density instead the seed provides oil rich in omega-3, digestible proteins and lignans; it is also use to manufacture paints, varnishes, linoleum, oilcloths, printing inks, soaps and numerous other products.

Thanks to its composition, flaxseed is emerging as an important

functional food ingredient because provides oil rich in omega-3, digestible proteins, and lignans. In addition to being one of the richest sources of α -linolenic acid oil and lignans, flaxseed is an essential source of high quality protein and soluble fiber and has considerable potential as a source of phenolic compounds [5,8].

For human consumption, flax meal is in the form of ground vacuum-packed grains or flaxseed enriched products.

For example, flaxseed that can be incorporated into traditional cereal-based matrices as bread and pasta, in egg products, in ready-to-eat snack foods known for their high consumer acceptability [9].

Flax seed sprouts are edible, with a slightly spicy flavour. Whole flax seeds are chemically stable, but ground flaxseed can go rancid at room temperature in as little as one week, although there is contrary evidence. Refrigeration and storage in sealed containers will keep ground flax from becoming rancid for a longer period. Milled flax is remarkably stable to oxidation when stored for nine months at room temperature if packed immediately without exposure to air and light and for 20 months at ambient temperatures under warehouse condition [10].

Flaxseed consumption is linked to several potential health benefits. Evidences showed that feeding with flaxseed (oil or enriched product) could help in prevent many diseases such as chronic, cardiovascular, obesity disorders and cancer. However, its chronic consumption may offer risks considering the effects of lignans in men and in pregnant women, as well as the existence of other phytochemicals and toxic factors with adverse health effects in the seed.

Nutrients Composition of Flaxseed and Health Benefits

Flaxseed is well-known for the content of chemical compounds with specific biological activity and functional properties: polyunsaturated fatty acids (PUFA) omega-3 family, soluble dietary fibers, lignans, proteins and carbohydrates. However, it is constituted by few levels of adverse health compounds such as Cadmium, protease inhibitors and cyanogenic compounds [11].

An analysis of brown Canadian flax averaged 41% fat, 20% protein, 28% total dietary fibre, 7.7% moisture and 3.4% ash, which is the mineral-rich residue left after samples are burned (Table 1) [7,12].

The composition of flax can vary with genetics, growing environment, seed processing and method of analysis.

Omega-3 fatty acids in flaxseed and health benefits

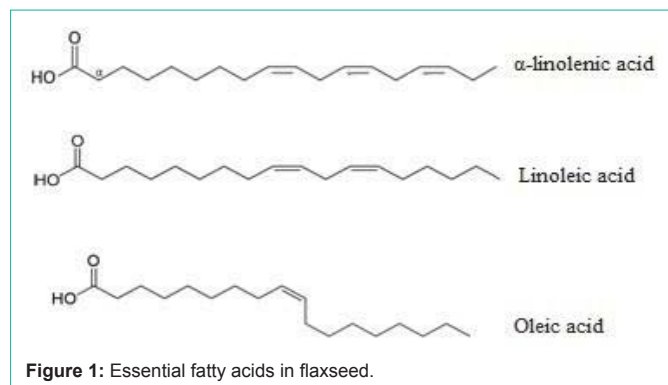
Of all lipids in flaxseed (approximately 30%), 53% are α -linolenic acid (ALA), 17% linoleic acid (LA), 19% oleic acid (Figure 1), 3% stearic acid, and 5% palmitic acid, which provides an excellent n-6: n-3 fatty acid ratio of approximately 0.3:1 [13]. Therefore, the seed may be an alternative for supplying this fatty acid to populations concentrated in regions of the world where there is not large access to marine foods, which are the best sources of n-3 fatty acids [14].

The tissue's fatty acid composition is not homogeneous. The linolenic acid contents in embryos, testa, and endosperm are all higher than that in the embryo axis. ALA is classified as an omega-3 fatty acid, a group that also includes long-chain metabolites of ALA [15].

Table 1: Chemical composition of flaxseed.

Fatty Acid [9]	g/100g of flaxseed	Minerals [9]	mg/100g of flaxseed
α -linolenic acid	22.8	Calcium	236
Linoleic acid	55.9	Magnesium	431
Oleic acid	7.3	Phosphorus	622
Stearic acid	1.3	Potassium	831
Palmitic acid	2.1	Sodium	27
Aminoacids [14]	g/100g of proteins	Zinc	4
Glutamic acid	19.6	Copper	1
Aspartic acid	9.3	Iron	5
Arginine	9.2	Manganese	3
Glycine	5.8	Vitamins [9] mg/100 of flaxseed	
Cysteine	1.1	γ -tocopherol	522
Histidine	2.2	α -tocopherol	7
Isoleucine	4	δ -tocopherol	10
Leucine	5.8	Ascorbic acid/vitamin C	0.5
Lysine	4	Thiamin/vitamin B1	0.5
Methionine	1.5	Riboflavin/vitamin B2	0.2
Proline	3.5	Niacin/nicotinic acid	3.2
Serine	4.5	Pyridoxine/vitamin B6	0.6
Threonine	3.6	Pantothenic acid	0.6
Tryptophan	1.8	Carbohydrates [14]	mg/100g of flaxseed
Tyrosine	2.3	Neutral arabinoxylan fraction	1.2
Valine	4.6	Acidic Rhamnogalacturonan Fraction	0.4
Dietary Fibres [9]	g/100g of flaxseed	Phenolic Compounds [14]	
Soluble Fibres	4.3-8.6	mg/g flaxseed powder	
Insoluble Fibres	12.8-17.1	Ferulic acid	10.9
Adverse Health Compounds [9]		Chlorogenic acid	7.5
Cadmium	0.52 μ g/kg of flaxseed	Gallic acid	2.8
Protease inhibitors	13.3 mg/g crude protein	mg/100g of flaxseed	
Cyanogenic Compounds:	mg/100g of flaxseed	Secoisolaricresinol	165
Limamarin	11	Laricinesol	1.7
Linustatin	150	Pinoresinol	0.8
Neolinustatin	140	Total Flavonoids	35-70

Researchers are investigating whether omega-3 fatty acids contained in flaxseed may help protect against certain infections and in treating conditions including ulcers, migraine headaches, attention deficit/hyperactivity disorder, eating disorders, preterm labor, emphysema, psoriasis, glaucoma, Lyme disease, lupus, and panic attacks [16]. Dugani et al. 2008 evaluated the anti-ulcer activity of the oil and mucilage obtained from flaxseed in a rat model of ethanol-induced gastric ulcer. Results indicated how the pre-treatment of rats with flaxseed oil and mucilage significantly



reduced the number and length of gastric ulcers induced by ethanol. Even if flaxseed oil was found to have a higher capacity in reducing the number of ulcers, both flaxseed oil and mucilage were pointed to provide a cytoprotective effect against ethanol-induced gastric ulcers in rats [17]. Same results about antiulcer and anti-secretory properties of flaxseed oil were obtained by Kaitwash et al. 2010. The oil also exhibited significant inhibitory effect on gastric secretion/total acidity and on aspirin-induced gastric ulceration in rats [18]. Clark WF et al 2001 studied the influence of flaxseed fatty acids on lupus nephritis disease. Plasma lipids and serum viscosity were unaltered by the flaxseed supplementation whereas serum creatinine in the compliant patients declined. Flaxseed appeared to be reno-protective in lupus nephritis, but authors suggested that their interpretation was affected by under powering due to poor adherence of patients [19].

Dupasquier et al.2007, investigated the anti-atherogenic capacity of flaxseed in an animal model that represents the human atherosclerotic condition. Supplementation of the cholesterol-enriched diet with ground flaxseed lowered plasma cholesterol and saturated fatty acids, increased plasma content of ALA and inhibited plaque formation in the aorta and aortic sinus compared with mice fed a diet supplemented with only dietary cholesterol. Authors demonstrated that dietary flaxseed can inhibit atherosclerosis through a reduction of circulating cholesterol levels and, at a cellular level, via anti-proliferative and anti-inflammatory actions [20].

Although direct studies on flaxseed and blood pressure are limited (and mostly confined to flaxseed oil versus ground flaxseed), 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 widely focusing attention of researchers. Rodriguez-Leyva et al. 2010 analysing epidemiological investigations and experimental studies suggested that ALA intake from flaxseed has been demonstrated to combat cardiovascular disease [21]. Caligiuri et al. 2014, focused on flaxseed consumption and blood pressure in patients with hypertension. The objective was to examine whether flaxseed consumption altered plasma oxylipins in a manner that influenced blood pressure. After the clinical trial, authors concluded that α -linolenic acid in flaxseed may have inhibited soluble epoxide hydrolase, which altered oxylipin concentrations that contributed to the antihypertensive effects in

patients with peripheral arterial disease [22]. Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA), derivatives of ALA, have cardioprotective 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 [16].

Proteins in flaxseed and health benefits

Like all vegetables, flaxseed proteins have techno-functional properties that affect their behaviour in a food system through interaction with other ingredients.

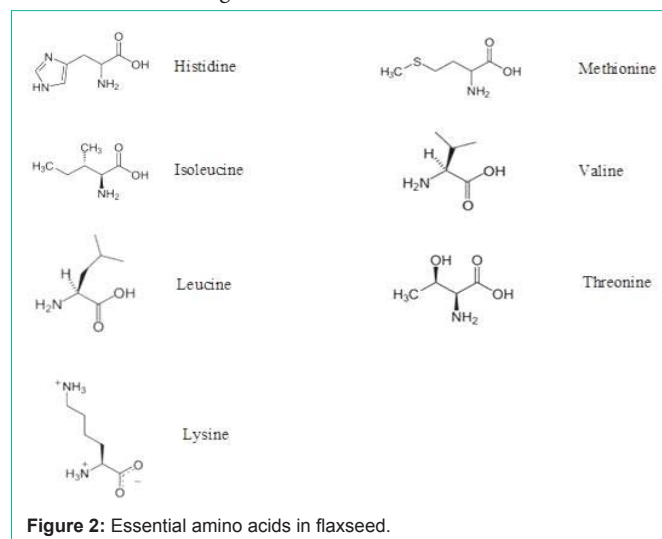
These properties are mainly dependent on their hydration mechanisms for solubility and water/oil retention capacity. The amino acid pattern of flax protein is similar to that of soybean protein, which is viewed as one of the most nutritious of the plant proteins [23]. Flaxseeds are not considered a source of complete proteins because the lack of some essential amino acids, necessarily introduced from the diet. Essential amino acids contained in flaxseed are shown in Figure 2.

Flaxseed grain and flaxseed paste contain about 21% and 34% protein respectively and may varies with the genetic and environmental factors [24]. Cool climates usually result in high oil and low protein content in the seeds.

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) [24].

Flaxseed has a favourable ratio of amino acids with Lysine, Threonine and Tyrosine as the limiting amino acids. Furthermore, it is a good source of sulfur amino acids (Methionine and Cysteine) and of branched chain amino acids (BCAA; Isoleucine, Leucine and Valine) [25].

Flaxseed is rich in essential amino acids of great importance in the synthesis of proteins that have the role of maintenance and repair of cells, tissues and organs.



Flaxseed protein biological effects were rarely studied; their physiological properties were mainly explained by both amino acid composition and interaction with other flaxseed components (polysaccharides, lignans and fatty acids). Omoni & Aluko 2006, observed that flaxseed protein hydrolysate were able to induce a change of secondary and tertiary structures of calmodulin, the cofactor involved in the production of nitric oxide responsible for several neurodegenerative diseases [26].

Marambe et al. 2008 showed that flaxseed protein hydrolysate inhibited the enzyme responsible for conversion of the decapeptide angiotensin I to octapeptide angiotensin II, a vasoconstriction hormone causing an increase in blood pressure [27]. About disease associated with obesity and diabetes, Bhatena et al. 2003 studying the beneficial effect of protein on hypertriglyceridemia and liver steatosis made a comparison between soy, flaxseed and casein. Only flaxseed and soy meals significantly decreased plasma triglyceride in both lean and obese rats compared to casein fed rats. Authors suggested that flaxseed meal supplementation may provide a new therapeutic strategy to reduce hypertriglyceridemia and fatty liver; further studies needed on human model [28]. Velasquez et al 2003, analyzed the impact of proteins on renal function and nephropathy in animal models of type II diabetes mellitus. Varying the source of dietary protein intake authors concluded that flaxseed meal was more effective than soy protein in reducing proteinuria and renal histologic abnormalities in this model [29].

Bioactive peptides, present in flaxseed, such as cyclolinopeptide A, have strong immunosuppressive and antimalarial activities, inhibiting the human malaria parasite *Plasmodium falciparum* in culture [30].

According to Oomah (2001) flaxseed contained a peptide mixture with high levels of branched-chain amino acids (BCAAs) and low levels of Aromatic Amino Acids (AAAs). This mixture has shown antioxidant properties by scavenging 2, 2-diphenyl-1-picrylhydrazyl radical (DPPH) and antihypertensive properties by inhibiting the angiotensin I-converting enzyme [31].

Dietary fibers in flaxseed and health benefits

Flaxseed meal is rich in crude, acid detergent, neutral detergent and total fibers (cellulose, lignine and hemicellulose). Fibers content varies between 22% to 26%, twice the percentage of high fiber beans. A half ounce of dry whole flax seed provides between 20% and 25% of your daily fiber needs. Flaxseed contains soluble and insoluble dietary fibers in a proportion that varies between 20:80 and 40:60. The major insoluble fiber fraction consists of cellulose and lignin and the soluble fiber fractions are the mucilage gums [32,33].

Dietary fibers from flaxseed were found to have a direct relation to health in particular in body weight regulation through both hunger suppression and diminished nutrient absorption [34] generally, soluble fiber forms a gel when mixed with water. This gel slows down the emptying of the stomach, potentially lowering blood glucose levels. Cholesterol is also lowered as it is surrounded by the gel, which inhibits its absorption and leads to more cholesterol being excreted. Ibburger et al 2012, conducted a crossover acute study about the influence of flax drink and flax tablet on hunger suppression. Sensation of satiety and fullness were similar for Flax tablets and Flax drink as they did not differ by more than 1-4% [35].

Flaxseed protein demonstrated the reduction of the fat absorption by fecal excretion in animal and human. Mette et al. 2012 found that addition of a flax dietary fiber extract rich in viscous dietary fibers significantly increased fat excretion and lowered total and LDL-cholesterol, with no effect on appetite [34].

Carbohydrates in flaxseed and health benefits

Flax is low in carbohydrates (sugars and starches), providing only 1 gram (g) per 100 g. For this reason, flax contributes little to total carbohydrate intake; it's recommended for people with specific diseases. Flaxseed polysaccharide is composed of two major fractions: a neutral arabinoxylan (75%) and an acidic rhamnogalacturonan (25%). The arabinoxylan is composed mainly of xylose, arabinose, and galactose and the rhamnogalacturonan consists of L-rhamnose, D-galactose, D-galacturonic and L-fucose acid. Considerable and significant variations exist in monosaccharide composition, carbohydrate yield and quality among accessions from the world collection of flaxseed [36].

Micronutrients in flaxseed and health benefits

Flaxseeds are a source of many vitamins and minerals as calcium, magnesium and phosphorus. It is of great importance, being that a 30g portion of the seed constitutes 7% to 30% of the Recommended Dietary Allowances (RDAs) for these minerals [12].

The most abundant vitamins constituting flaxseed are tocopherols (α -, β -, and γ - forms) and niacin.

The tocopherols occur in α (alpha), β (beta), γ (gamma) and δ (delta) forms determined by the number and position of methyl groups on the chromanol ring.

Alpha-tocopherol is the form of vitamin E that is preferentially absorbed and accumulated in humans instead the mono-methylated form gamma-tocopherol is the most prevalent form of vitamin E in oils (Figure 3).

Vitamin E, a fat-soluble vitamin, is present in flaxseed, predominantly, in the isomer γ -tocopherol. Antioxidant nutrients like vitamin E protect cell constituents from the damaging effects of free radicals that, if unchecked, might contribute to cancer development. Vitamin E might also block the formation of carcinogenic nitrosamines formed in the stomach from nitrites in foods and protect against cancer by enhancing immune function [37]. Furthermore, vitamin E 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. Although α -tocopherol is preferentially absorbed in relation to the γ isomer; it has been considered the most effective against oxidation of low-density lipoprotein (LDL) [38]. No direct correlation between

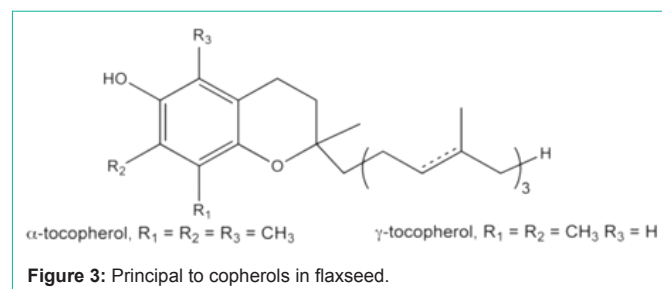


Figure 3: Principal tocopherols in flaxseed.

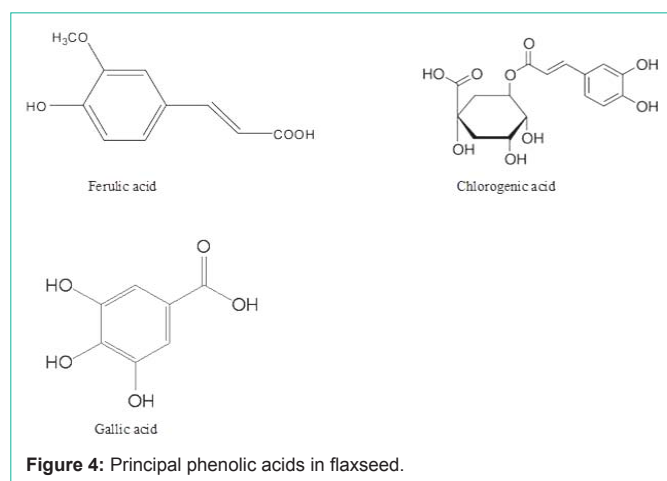


Figure 4: Principal phenolic acids in flaxseed.

flaxseed content of vitamin and benefits as been described so far. Further clinically studies are needed.

Lignans in flaxseed and health benefits

Other bioactive compounds of flaxseed are from the class of phenolic compounds, including lignans, flavonoids and phenolic acids [39,40].

In particular, flaxseeds are the richest dietary source of lignan precursors. When ingested, lignan precursors are converted to the enterolignans, enterodiols and enterolactone, by bacteria that normally colonize the human intestine. The principal lignan precursor found in flaxseed is *secoisolariciresinol diglucoside* [41].

Four phenolic acids identified in defatted flaxseed powder are ferulic acid (10.9 mg/g), chlorogenic acid (7.5 mg/g), gallic acid (2.8 mg/g), and traces of 4-hydroxybenzoic acid (Figure 4). The major flavonoids in flax are flavone C- and O- glycosides [42].

Lignan-rich foods are part of a healthful dietary pattern; the role of lignans is important in the prevention of hormone-associated cancers, osteoporosis, and cardiovascular diseases.

The flaxseed lignan *secoisolariciresinol* (SECO) and its diglucoside *secoisolariciresinol diglucoside* (SDG) are reported to have a number of health benefits associated with their consumption that have in part been attributed to their antioxidant properties. After ingestion, SDG is converted to enterolignans (enterodiols and enterolactone) by the intestinal microflora; then these metabolites (phytoestrogens) are absorbed and can provide health benefits. Prasad 2013 investigated if SDG from flaxseed could be an alternative to Angiotensin-Converting Enzyme (ACE) in the treatment of hypertension. In particular the study focused on SDG-induced hypotension through inhibition of ACE. After feeding rats with specific doses of flaxseed, SDG decreased the systolic, diastolic and mean arterial pressure. Data suggested that SDG reduced the angiotensin I-induced rise in the arterial pressures and hence SDG was a potent ACE inhibitor [43]. Adolphe et al. 2010, summarized results from scientific paper about health effects of the flax lignan *secoisolariciresinol diglucoside*. Animal studies using rat, mice and rabbit models suggested that SDG supplementation protects against the development of chronic diseases, cancer and diabetes. Several of the human studies that have included SDG were performed, but, more randomised controlled trials are needed before

to elucidate whether SDG supplementation protects against disease in human [44].

Utilization of flaxseed for glycemic control may also be associated to the decrease in risk of obesity and dyslipidemia, since these are risk factors for the development of diabetes and resistance to insulin. Sonali and Charu 2013, evaluated the therapeutic potential of flaxseeds in dyslipidemia. In the experimental group flaxseed supplementation resulted in an improvement in anthropometric measurements, blood pressure, and lipid profile. Body weight and Body Mass Index (BMI) of the experimental group were significantly reduced as well as systolic and diastolic blood pressure. At the same time, a highly significant reduction in total cholesterol, triglycerides, low density lipoprotein-cholesterol (LDL-C) and low density lipoprotein-cholesterol (VLDL-C) levels were observed [45]. Lignans may protect against certain cancers, particularly hormone-sensitive cancers such as those of the breast, endometrium and prostate, by interfering with sex hormone metabolism. Most of the research regarding flaxseed and breast cancer focuses on the lignin content in flaxseeds, and their potential for weak estrogenic or anti-estrogenic effects in a woman's body. Experimental evidence in animals has shown anticarcinogenic effects of flaxseed or pure lignans in many types of cancer: flaxseed oil can inhibit the growth and development of tumors in the breast of laboratory animals [46]. Mason et al 2014, researched the influence of flaxseed lignans and oil components in reducing breast cancer risk and tumour growth. In vitro, animal, observational, and clinical studies on FS and its lignan and oil components were reviewed. Results showed that flaxseed intake reduces tumour growth in breast cancer patients. Mechanisms included decreased cell proliferation and angiogenesis and increased apoptosis through modulation of estrogen metabolism and estrogen receptor and growth factor receptor signalling pathways. More clinical trials are needed to indicate that flaxseed components are effective in the risk reduction and treatment of breast cancer [47]. The systematic review by Flower et al. 2013 considered lignans and other flaxseed compounds (ALA and fiber content) to check the efficacy in improving menopausal symptoms in women living with breast cancer and for potential impact on risk of breast cancer incidence or recurrence. Making a comparison among all studies examined, authors concluded that flax may be associated with decreased risk of breast cancer. Furthermore, flax demonstrated anti-proliferative effects in breast tissue of women at risk of breast cancer. Mortality risk may also be reduced among those living with breast cancer [48]. Despite acting as an inhibitor to the development of cancer, recent evidence has shown that lignan and flaxseed oil reduced the growth of tamoxifen treated tumors by mechanisms involving signaling pathways, suggesting their potential use to aid in chemotherapy of some cancer types. Saggari et al. 2010, analyzed the effect of dietary flaxseed lignan or oil combined with tamoxifen (TAM) treatment on tumor growth. All treatments reduced the growth of TAM-treated tumors by reducing cell proliferation, expression of genes, and proteins involved in the growth factor-mediated signaling pathways with flaxseed oil having the greatest effect in increasing apoptosis compared with TAM treatment alone. SDG and flaxseed oil reduced the growth of TAM-treated tumors [49]. Sturgeon et al 2008, studied the effects of flaxseed lignans on serum sex hormones implicated in the development of breast cancer. Result suggested that dietary flaxseed may modestly lower serum levels of

Table 2: Health benefits from flaxseed compounds.

Compound	Health Benefit	Reference
Omega 3-fatty acids	anti-ulcer activity	Dugani et al. [17]
	anti-secretory effect	Kaitwah et al. [18]
	reno-protection in lupus nephritis	Clark et al. [19]
	anti-atherogenic effect	Dupasquier et al. [20]
	CVD prevention	Rodriguez-Leyva et al. [21]
	Decrease blood pressure	Harper et al. [16] Caligiuri et al. [22]
Proteins	Neurodegenerative disease prevention	Omoni and Aluko [26]
	Control blood pressure	Maramba et al. [27]
	Influence on hypertriglyceridemia	Bhatena et al. [28]
	Influence on diabetes mellitus	Velasquez et al. [29]
	Anti-hypertensive properties	Oomah et al. [5]
Dietary fibres	Hunger suppression	Ibbrugger et al. [35]
	Decrease total cholesterol in blood	Mette et al. [34]
Micronutrients (vitamin E and minerals)	Antioxidant properties Decrease blood pressure Promotion of sodium excretion	No direct correlation between flaxseed content of vitamin and benefits
Lignans	Control on hypertension	Prasad [43]
	Protection against cancer and diabetes	Adolphe et al. [44]
	Control on dyslipidemia	Sonali and Charu [45]
	Reduce breast cancer growth	Flower et al. [48] Saggar et al. [49]
		Strugeon et al. [50]
	Effects on postmenopausal women symptoms	Simbalista et al. [53] Nowak et al. [54] Dew et al. [55]

sex steroid hormones, especially in overweight/obese women [50]. Lignans have been shown, for example, to suppress the differentiation and growth of cultured human leukemic cells, possibly by interfering with DNA, RNA and/or protein synthesis [51]. Moreover, lignan cytotoxicity on normal immune cells appears to be low. Lignans may also exert fungistatic, cytotoxic, antiviral activities and a hormonal modulation, causing a decrease in hot flashes which are characteristic of menopause [52]. Simbalista et al. 2010 tested the effects of daily intake of bread produced with defatted ground flaxseed on the climacteric symptoms and endometrial thickness of postmenopausal women. Authors concluded that flaxseed consumption at certain levels (46 mg lignans/day) was effective as well as placebo for reducing hot flashes [53]. Lignans may reduce 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. Nowak et al. 2007, described the clinical case study based on the impact of flaxseed supplementation (30 g/day) on hormonal levels in a 31-year old woman with polycystic ovary syndrome. The clinically and significant decrease in androgen levels and the concomitant reduction in hirsutism viewed in patients demonstrated a need for further research of flaxseed supplementation on hormonal levels and clinical symptoms of polycystic ovary syndrome [54].

Competition of lignans with estrogen for receptor sites causes dual effects. Considering that lignan possesses a weak hormonal action, during phases of life when there is a large production of estrogen, the chronic ingestion of flaxseed may exert an antiestrogenic action because it competes with estrogen for the same receptors. By means of this mechanism, flaxseed may protect women with risk of cancer by decreasing hormonal signaling involved in the beginning of tumor development. Consuming lignans may lower the risk of endometrial cancer in post-menopausal women, and it might also help reduce the severity of osteoporosis. Dew et al. 2013 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 2 α -hydroxysterone/16 α -hydroxysterone ratio associated with a lower risk of breast cancer. However, few studies considered bone mineral density or markers of bone turnover; more investigation needed to confirm influence of flax lignan intake on postmenopausal bone mineral density [55].

Anti-nutritive compounds in flaxseed and adverse health properties

The presence in flaxseed of the inhibitors trypsin, myo-

inositol phosphate, cadmium, and cyanogenic glycosides [56,57], phytoestrogens with adverse health effects and toxic compounds has to be underlined.

Infact, in addition to bioactive compounds, flaxseed contains 264–354 mg of cyanogenic compounds per 100 g of seed, being 10–11.8 mg of linamarin/100 g, 136–162 mg of linustatin/100 g, and 105–183 mg of neolinustatin/100 g of flaxseed. These compounds are toxic to the human organism and it is estimated that ingestion of 100 mg may be lethal to adult individuals.

Cyanogenic glucosides are nitrogenous secondary plant metabolites derived from amino acids. Their causes chronic effects, manifested in the nervous system and are observed in populations that ingest high quantities of cyanate in foods [58]. However, these compounds present instability when subjected to thermal and mechanical processes, including cooking in microwaves, autoclaving, and boiling [58,59].

Cadmium is potentially toxic to the human organism. When accumulated in the kidney, this metal can cause renal dysfunction, as well as pulmonary emphysema, aminoaciduria, glycosuria, phosphaturia and even compromise mineral reabsorption, making organisms susceptible to osteomalacia.

Trypsin inhibitors present in the diet have been known for decades to diminish growth in animals, since they decrease the digestion and consequent absorption of proteins by the inhibition of proteases [60].

Trypsin inhibitor activity (TIA) in flaxseed was low when compared to those in soybean and canola seeds. Bhatti (1993) reported laboratory-prepared flaxseed meals containing 42 to 51 units of TIA [61].

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 [62].

Conclusion

Flaxseed has nutritional and functional properties. In fact the content of compounds such as polyunsaturated fatty acids, essential amino acids, vitamin E, lignans and dietary fibers makes flaxseed a source to satisfy basic needs in the human diet and health maintenance.

Healthy properties are related to anti-inflammatory, anti-oxidant, anti-carcinogenic activities and to the lowering of cholesterol, the decrease of cardiovascular disease and the prevention of diabetes.

However, in state of functional properties, flaxseed contains low quantities of adverse healthy compounds such as cadmium, cyanogenic glycosides, inhibitors of trypsin that are commonly removed through thermal and mechanical processes, including cooking in microwaves, autoclaving and boiling (Table 2).

References

- van Kleef E, van Trijp HC, Luning P. Functional foods: health claim-food product compatibility and the impact of health claim framing on consumer

evaluation. See comment in PubMed Commons below *Appetite*. 2005; 44: 299-308.

- Kalra EK. Nutraceutical--definition and introduction. See comment in PubMed Commons below *AAPS PharmSci*. 2003; 5: E25.
- Doyon M, Labrecque J. Functional foods: a conceptual definition. *British Food Journal*. 2008; 110: 1133- 1149.
- Daun JK, Barthelet VJ, Chornick TL, Duguid S. Structure, composition, and variety development of flaxseed. *Flaxseed in human nutrition* Thompson LU, Cunnane SC. 2003; 1-40.
- Oomah DB. Flaxseed as a functional food source. *J Sci Food Agr*. 2001; 81: 889-894.
- Bhatti RS. Nutritional composition of whole flaxseed and flaxseed meal. *Flaxseed in Human Nutrition*. Cunnane SC, Thompson LH, editors. AOCS Press, Champaign IL. 1995; 22-45.
- Morris DH. *Flax Primer, A Health and Nutrition Primer*. Flax Council of Canada. 2007; 9-19.
- Pengilly NL. Traditional food and medicinal uses of, axseed. *Flax: the genus Linum*. Springer-Verlag. Berlin. 2003; 252-267.
- Mercier S, Villeneuve S, Moresoli C, Mondor M, Marcos B, Power KA. Flaxseed-enriched cereal-based products: A review of the impact of processing conditions. *Compr Rev Food Sci F*. 2014; 13: 400-412.
- Malcolmson LJ, Przybylski R, Daun JK. Storage stability of milled flaxseed. *JAOCS*. 2000; 77: 235-238.
- 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.
- Singh KK, Mridula D, Rehal J, Barnwal P. Flaxseed: a potential source of food, feed and fiber. See comment in PubMed Commons below *Crit Rev Food Sci Nutr*. 2011; 51: 210-222.
- Simopoulos AP. The importance of the ratio of omega-6/omega-3 essential fatty acids. See comment in PubMed Commons below *Biomed Pharmacother*. 2002; 56: 365-379.
- El-Beltagi HS, Salama ZA, El-Hariri DM. Evaluation of fatty acids profile and the content of some secondary metabolites in seeds of different flax cultivars (*Linum Usitatissimum* L.). *General Applied Plant Physiology*. 2007; 33: 187-202.
- Kris-Etherton PM, Taylor DS, Yu-Poth S, Huth P, Moriarty K, Fishell V, et al. Polyunsaturated fatty acids in the food chain in the United States. See comment in PubMed Commons below *Am J Clin Nutr*. 2000; 71: 179S-88S.
- Harper CR, Edwards MJ, DeFilippis AP, Jacobson TA. Flaxseed oil increases the plasma concentrations of cardioprotective (n-3) fatty acids in humans. See comment in PubMed Commons below *J Nutr*. 2006; 136: 83-87.
- Dugani A, Auzzi A, Naas F, Megwez S. Effects of the oil and mucilage from flaxseed (*linum usitatissimum*) on gastric lesions induced by ethanol in rats. See comment in PubMed Commons below *Libyan J Med*. 2008; 3: 166-169.
- Kaithwas G, Majumdar DK. Evaluation of antiulcer and antisecretory potential of *Linum usitatissimum* fixed oil and possible mechanism of action. See comment in PubMed Commons below *Inflammopharmacology*. 2010; 18: 137-145.
- Clark WF, Kortas C, Heidenheim AP, Garland J, Spanner E, Parbtani A. Flaxseed in lupus nephritis: a two-year nonplacebo-controlled crossover study. See comment in PubMed Commons below *J Am Coll Nutr*. 2001; 20: 143-148.
- Dupasquier CM, Dibrov E, Kneesh AL, Cheung PK, Lee KG, Alexander HK, et al. Dietary flaxseed inhibits atherosclerosis in the LDL receptor-deficient mouse in part through antiproliferative and anti-inflammatory actions. See comment in PubMed Commons below *Am J Physiol Heart Circ Physiol*. 2007; 293: H2394-2402.
- Rodriguez-Leyva D, Dupasquier CM, McCullough R, Pierce GN. The cardiovascular effects of flaxseed and its omega-3 fatty acid, alpha-linolenic acid. See comment in PubMed Commons below *Can J Cardiol*. 2010; 26: 489-496.

22. Caligiuri SP, Aukema HM, Ravandi A, Guzman R, Dibrov E, Pierce GN. Flaxseed consumption reduces blood pressure in patients with hypertension by altering circulating oxylipins via an α -linolenic acid-induced inhibition of soluble epoxide hydrolase. *Hypertension*. 2014; 64: 53-59.
23. Rabetafika HN, Van Remoortel V, Danthine S, Paquot M, Blecker C. Flaxseed proteins: food uses and health benefits. *Int. J. Food Sci. Technol*. 2011; 46: 221-228.
24. Chung MWY, Lei B, Li-Chan ECY. Isolation and structural characterization of the major protein fraction from NorMar flaxseed (*Linum usitatissimum* L.). *Food Chem*. 2005; 90: 271-279.
25. Oomah BD, Berekoff B, Li-Chan C, Mazza G, Kenaschuk E, Duguid S. Cadmium-binding protein components of flaxseed: Influence of cultivar and location. *Food Chem*. 2007; 100: 318-325.
26. Omoni AO, Aluko RE. Mechanism of the inhibition of calmodulin-dependent neuronal nitric oxide synthase by flaxseed protein hydrolysates. *Journal of American Oil Chemistry Society*. 2006; 83: 335-340.
27. Marambe P, Shand P, Wanasundara P. An in-vitro investigation of selected biological activities of hydrolysed flaxseed (*Linum usitatissimum* L.) proteins. *Journal of American Oil Chemists Society*. 2008; 85: 1155-1164.
28. Bhatena S, Ali A, Haudenschild C, Latham P, Ranich T, Mohamed A, et al. Dietary Flaxseed Meal is More Protective Than Soy Protein Concentrate Against Hypertriglyceridemia and Steatosis of the Liver in an Animal Model of Obesity. *Journal of the American College of Nutrition*. 2002; 22: 157-164.
29. Velasquez MT, Bhatena SJ, Ranich T, Schwartz AM, Kardon DE, Ali AA, et al. Dietary flaxseed meal reduces proteinuria and ameliorates nephropathy in an animal model of type II diabetes mellitus. See comment in PubMed Commons below *Kidney Int*. 2003; 64: 2100-2107.
30. Tolkachev ON, Zhuchenko AA. Biologically Active Substances of Flax: Medicinal and Nutritional Properties (A Review). *Pharmaceutical Chemistry Journal*. 2004; 34: 360-367.
31. Picur B, Cebrat M, Zabrocki J, Siemion IZ. Cyclopeptides of *Linum usitatissimum*. See comment in PubMed Commons below *J Pept Sci*. 2006; 12: 569-574.
32. Qian KY, Cui SW, Goff HD. Flaxseed gum from flaxseed hulls: Extraction, fractionation, and characterization. *Food Hydrocolloids*. 2012; 28: 275-283.
33. Cui W, Kenaschuk E, Mazza G. Influence of genotype on chemical composition and rheological properties of flaxseed gums. *Food Hydrocolloids*. 1996; 10: 221-227.
34. Kristensen M, Jensen MG, Aarestrup J, Petersen KE, Søndergaard L, Mikkelsen MS, et al. Flaxseed dietary fibers lower cholesterol and increase fecal fat excretion, but magnitude of effect depend on food type. See comment in PubMed Commons below *Nutr Metab (Lond)*. 2012; 9: 8.
35. Ibrügger S, Kristensen M, Mikkelsen MS, Astrup A. Flaxseed dietary fiber supplements for suppression of appetite and food intake. See comment in PubMed Commons below *Appetite*. 2012; 58: 490-495.
36. Ho C, Cacace J, Mazza G. Extraction of lignans, proteins and carbohydrates from flaxseed meal with pressurized low polarity water. *LWT-Food Sci Technol*. 2007; 40: 1637-1647.
37. Winter R. Vitamin E: Your Protection Against Exercise Fatigue, Weakened Immunity, Heart Disease, Cancer, Aging, Diabetic Damage, Environmental Toxins. Crown Publishing Group. 2013.
38. Meagher EA, Barry OP, Lawson JA, Rokach J, FitzGerald GA. Effects of vitamin E on lipid peroxidation in healthy persons. See comment in PubMed Commons below *JAMA*. 2001; 285: 1178-1182.
39. Basavaraj M. Potential Benefits of Flaxseed in Health and Disease - A Perspective. *Agriculturae Conspectus Scientificus (ACS)*. 2009; 67-72.
40. Lowcock EC, Cotterchio M, Boucher BA. Consumption of flaxseed, a rich source of lignans, is associated with reduced breast cancer risk. See comment in PubMed Commons below *Cancer Causes Control*. 2013; 24: 813-816.
41. Adlercreutz H. Lignans and human health. See comment in PubMed Commons below *Crit Rev Clin Lab Sci*. 2007; 44: 483-525.
42. Siger A, Nogala-Kalucka M, Lampart-Szczapa E. The content and antioxidant activity of phenolic compounds in cold-pressed plant oils. *J Food Lipids*. 2008; 15: 137-149.
43. Prasad K, Mantha SV, Muir AD, Westcott ND. Reduction of hypercholesterolemic atherosclerosis by CDC-flaxseed with very low alpha-linolenic acid. See comment in PubMed Commons below *Atherosclerosis*. 1998; 136: 367-375.
44. Adolphe JL, Whiting SJ, Juurlink BH, Thorpe LU, Alcorn J. Health effects with consumption of the flax lignan secoisolariciresinol diglucoside. See comment in PubMed Commons below *Br J Nutr*. 2010; 103: 929-938.
45. Saxena S, Katare C. Evaluation of flaxseed formulation as a potential therapeutic agent in mitigation of dyslipidemia. See comment in PubMed Commons below *Biomed J*. 2014;.
46. Lamblin F, Hano C, Fliniaux O, Mesnard F, Fliniaux MA, Lainé E. Interest of lignans in prevention and treatment of cancers. See comment in PubMed Commons below *Med Sci (Paris)*. 2008; 24: 511-519.
47. Mason JK, Thompson LU. Flaxseed and its lignan and oil components: can they play a role in reducing the risk of and improving the treatment of breast cancer? See comment in PubMed Commons below *Appl Physiol Nutr Metab*. 2014; 39: 663-678.
48. Flower G, Fritz H, Balneaves LG, Verma S, Skidmore B, Fernandes R, et al. Flax and Breast Cancer: A Systematic Review. See comment in PubMed Commons below *Integr Cancer Ther*. 2013; 13: 181-192.
49. Saggari JK, Chen J, Corey P, Thompson LU. Dietary flaxseed lignan or oil combined with tamoxifen treatment affects MCF-7 tumor growth through estrogen receptor- and growth factor-signaling pathways. See comment in PubMed Commons below *Mol Nutr Food Res*. 2010; 54: 415-425.
50. Sturgeon SR, Heersink JL, Volpe SL, Bertone-Johnson ER, Puleo E, Stanczyk FZ, et al. Effect of dietary flaxseed on serum levels of estrogens and androgens in postmenopausal women. See comment in PubMed Commons below *Nutr Cancer*. 2008; 60: 612-618.
51. Cardoso Carraro JC, De Souza Dantas M, Rocha Espeschit AC, Duarte Martino H, Rocha Ribeiro SH. Flaxseed and Human Health: Reviewing Benefits and Adverse Effects. *Food Rev Int*. 2012; 28: 203-230.
52. Xu Y, Hall C 3rd, Wolf-Hall C, Manthey F. Fungistatic activity of flaxseed in potato dextrose agar and a fresh noodle system. See comment in PubMed Commons below *Int J Food Microbiol*. 2008; 121: 262-267.
53. Simbalista RL, Sauerbronn AV, Aldrighi JM, Arêas JA. Consumption of a flaxseed-rich food is not more effective than a placebo in alleviating the climacteric symptoms of postmenopausal women. See comment in PubMed Commons below *J Nutr*. 2010; 140: 293-297.
54. Nowak DA, Snyder DC, Brown AJ, Demark-Wahnefried W. The Effect of Flaxseed Supplementation on Hormonal Levels Associated with Polycystic Ovarian Syndrome: A Case Study. See comment in PubMed Commons below *Curr Top Nutraceutical Res*. 2007; 5: 177-181.
55. Dew TP, Williamson G. Controlled flax interventions for the improvement of menopausal symptoms and postmenopausal bone health: a systematic review. See comment in PubMed Commons below *Menopause*. 2013; 20: 1207-1215.
56. Lei B, Li-Chan EC, Oomah BD, Mazza G. Distribution of cadmium-binding components in flax (*Linum usitatissimum* L.) seed. See comment in PubMed Commons below *J Agric Food Chem*. 2003; 51: 814-821.
57. Haque MR, Bradbury JH. Total cyanide determination of plants and foods using the picrate and acid hydrolysis methods. *Food Chem*. 2002; 77: 107-114.
58. Tarpila A, Wennberg T, Tarpila S. Flaxseed as a functional food. *Curr Top Nutraceut R*. 2005; 3: 167-188.
59. Guerrero-Beltrán JA, Yokiushirdhilmara Estrada-Girónb, Swansonc BG, Barbosa-Cánovas GV. Pressure and temperature combination for inactivation of soymilk trypsin inhibitors. *Food Chem*. 2009; 16: 676-679.

60. Puvaca N, Stanacev V, Milic D, Kokic B, Cabarkapa I, Stanacev V. Limitation of flaxseed usage in animal nutrition. XV International Feed Technology Symposium. COST-"Feed for Health" joint Workshop, Proceedings. Novi Sad, Serbia, 3-5 October, 2012. 2012; 58-63.
61. Bhatti RS. Further compositional analyses of flax: mucilage, trypsin inhibitors and hydrocyanic acid. JAOCS. 1993; 70: 899-904.
62. Austria JA, Richard MN, Chahine MN, Edel AL, Malcolmson LJ, Dupasquier CM, et al. Bioavailability of alpha-linolenic acid in subjects after ingestion of three different forms of flaxseed. See comment in PubMed Commons below J Am Coll Nutr. 2008; 27: 214-221.