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REVIEW ARTICLE

Linseed Essential Oil – Source of Lipids as Active Ingredients for Pharmaceuticals and Nutraceuticals

J.R. Campos[1], P. Severino[2,3], C.S. Ferreira[4], A. Zielinska[1], A. Santini[5], S.B. Souto[6] and E.B. Souto[1,7,*]

[1] Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Coimbra (FFUC), Polo das Ciências da Saúde, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal; [2]Biotechnology Industrial Program, Laboratory of Nanotechnology and Nanomedicine (LNMed), University of Tiradentes, Av. Murilo Dantas, 300, 49010-390 Aracaju, Sergipe, Brazil; [3]Institute of Technology and Research (ITP), Av. Murilo Dantas, 300, 49010-390 Aracaju, Sergipe, Brazil; [4]Institute of Environmental*, Chemical and Pharmaceutical Sciences, Federal University of São Paulo, Diadema, Brazil; [5]Department of Pharmacy, Università degli Studi di Napoli Federico II, Italy; [6]Department of Endocrinology, Braga Hospital, Sete Fontes, 4710-243 São Victor Braga, Portugal; [7]CEB - Centre of Biological Engineering, University of Minho, Campus de Gualtar 4710-057 Braga, Portugal*

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Abstract: Linseed - also known as flaxseed - is known for its beneficial effects on animal health attributed to its composition. Linseed comprises linoleic and α-linolenic fatty acids, various dietary fibers and lignans, which are beneficial to health because they reduce the risk of cardiovascular diseases, as well as cancer, decreasing the levels of cholesterol and relaxing the smooth muscle cells in arteries increasing the blood flow. Essential fatty acids from flax participate in several metabolic processes of the cell, not only as structuring components of the cell membrane but also as storage lipids. Flax, being considered a functional food, can be consumed in a variety of ways, including seeds, oil or flour, contributing to basic nutrition. Several formulations containing flax are available on the market in the form of *e.g.* capsules and microencapsulated powders having potential as nutraceuticals. This paper revises the different lipid classes found in flaxseeds and their genomics. It also discusses the beneficial effects of flax and flaxseed oil and their biological advantages as ingredients in pharmaceuticals and in nutraceuticals products.

Keywords: Linseed, flaxseed, nutraceuticals, pharmaceuticals, essential fatty acids, linseed essential oil.

1. INTRODUCTION

In the last few years, due to the increased consumer's interest in the relationship between diet and health, functional foods, dietary supplements and nutraceuticals have been receiving particular attention, and their market is increasing rapidly. One of the most promising bioactive molecules are the phytochemicals from plants [1]. A variety of functional foods and dietary supplements has been introduced to the market, and many have recognised the potential for beneficial effect on human health [2]. A diet where omega-3 fatty acids (FAs) are present in abundance brings many positive effects, which have contributed to the investment in research in this field [3]. Flax, a multi-purpose crop, has been applied in industrial and food uses [4]. Flaxseed can be used for medicinal purposes and as a nutritional product, and it can also be used for fiber and oil, being cultivated in various regions [1]. When linseed oil is drawn from seeds, it can be applied in varnishes, stains, manufacturing of paints as well as linoleum flooring, which are eco-friendly. In food products and also in nutraceuticals, flax seeds are very popular [4]. As a crucial functional food ingredient,

*Address correspondence to this author at the Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Coimbra (FFUC), Pólo das Ciências da Saúde, Azinhaga de Santa Comba, 3000-548 Coimbra, Portugal; Tel: +351 239 488 400; Fax: +351 239 488 503; E-mail: ebsouto@ff.uc.pt

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interest in flaxseed is growing, mainly due to the essential fatty acids (EFAs) that comprise omega-3 (C18:3; α-linolenic; ALA) and omega-6 (C18:2; linoleic) fatty acids, dietary fibres and lignans. Flax EFAs exhibit structural and storage functions. Condensing and desaturation enzymes that are located in plastids, while endoplasmic reticulum is responsible for catalysis of FA biosynthesis in oilseeds. Cutin and suberin production, storage lipid synthesis in developing seeds and also cuticular wax layer synthesis in distinct tissue types as well as developmental stages, are examples of various metabolic pathways where free FAs are implied. A thorough understanding of these multiple aspects of flax lipids is essential for the development of strategies to modify such essential metabolic components [4]. There are many health advantages of using linseed oil, flax fibers and lignans, among them, the reduction of autoimmune and neurological disorders, osteoporosis and atherosclerosis as well as arthritis, cancer, diabetes and also decreasing the risk of cardiovascular disease [5].

This manuscript revises the different lipid classes found in flaxseeds and their genomics, highlighting the benefits of the use of flax and flaxseed oil as components of pharmaceutical and nutraceutical formulations.

2. BIOCHEMISTRY

2.1. Lipids

In the constitution of lipids, FAs and their derivatives as well as substances that are related to them, either functionally or biosynthetically, are usually present. They are important forms of carbon storage in plant seeds and in cellular membranes [6]. Through an FA synthase complex, the FAs (natural compounds) are synthesized by condensation of malonyl CoA units. Commonly, they have even numbers of carbon atoms in straight chains, which can contain varied substituent groups and these chains are saturated or unsaturated. Generally, lipids can dissolve rapidly in organic solvents, including alcohols, chloroform, benzene, as well as ethers. In the plant, flax lipids are found in their different parts in form of free FAs, triacylglycerols (TAGs), oxylipins, waxes and many other lipophilic compounds [7]. Lipids have vital physiological functions, as in seed germination, desiccation [8-10], in the structural integrity of cell, tissues and organs [11]and in the protection against biotic and abiotic stresses [12].

2.1.1. Classes of Lipids

A growing number of lipids are expected to be described with the dawn of the lipidomics era. In 2005, a Lipids Metabolites and Pathways Strategy (LIPIDS MAPS) was developed, a new system that classifies them [13]. For classification purposes, lipids have been considered hydrophobic or amphipathic small molecules originating from carbanion-based condensations of thioesters and from carbocation-based condensations of isoprene units, being separated in simple lipids that produce up to two types of products on hydrolysis and also complex lipids that produce more than three products on hydrolysis [4, 13]. According to this system, lipids can be classified into eight categories, such as fatty acyls, glycerolipids, glycerophospholipids, sphingolipids, sterol lipids, prenol lipids, saccharolipids as well as polyketides [13, 14]. Seed storage lipids are more attractive targets for metabolic engineering, once they are less likely to disturb the physiology of the plant, also representing the major lipids used in food and non-food applications.

Fatty acyl and glycerolipid classes are the most prevalent lipid forms in flax seeds [4]. One of the most important categories of biological lipids is the fatty acyls that are also the main lipid building block of complex lipids [13]. In this category, there are FA subclasses, such as straight-chain saturated and unsaturated FAs, hydroperoxy FAs, hydroxy FAs and epoxy FAs, all representing biologically active lipid compounds either for food or for industrial purposes. Many of these FAs have been reported in different parts of flax plants where they play major roles in several plant developmental processes [4]. Seed storage lipids are found usually in the form of glycerolipids [9] and they are identified as mono-, di- and triacylglycerols in flax seed oil. The TAGs account for the highest proportion of neutral lipids, representing up to 30% of fresh seed weight while monoglycerols account for 0.34%, diacylglycerols for 0.64% and free FAs for 0.42% [15]. There are more than 20 TAGs identified from linseed oil samples that are composed of C18:3, C18:2, C18:1 (oleic acid) moieties and also of C18:0 (stearic acid) and C16:0 (palmitic acid) moieties. The FA composition of TAGs is strongly determined by genotypes and environment [4].

2.1.2. Dietary Use of Lipids and Flaxseed

Due to dwindling fish resources and the high cost of extraction from marine microalga, there is increased search for nutritionally important omega-3 FAs namely, ALA (C18:39, 12, 15), eicosapentaenoic acid (C20:55,8,11,14,17; EPA) and docosahexaenoic acid (C22:64,7,10,13,16,19; DHA) [16]. C18 FAs (on their own and upon elongation to EPA and DHA) play a crucial role as membrane phospholipids, especially in the brain, the fetal neuronal system and in cardiovascular health. There is no possibility to synthesize C18 FAs, hence omega-3 FAs must be supplemented through diet [17]. One of the richest vegetal sources of omega-3 fatty acids is the flaxseed, therefore dietary intake of flax seed/oil represents an excellent source of ALA [18]. Linoleic and linolenic acids function as substrates for further elongation to produce arachidonic acid (C20:4,5,8,11,14;ARA; omega-6 FA), EPA and DHA. Flaxseed oil is composed of saturated fatty acids, monosaturated fatty acids and polyunsaturated fatty acids, in a percentage of 9 %, 18 % and 73 %, respectively [19]. The main fatty acid that is α-linolenic acid, varying over a range of 39-60 % followed by oleic, linoleic, palmitic and stearic acids [20]. Flaxseed oil is rich in anti-oxidants, including tocopherols and also betacarotene, but it is readily oxidized after being extracted and purified. The bioavailability of ALA is higher in oil, followed by the milled seed, and then the whole seed [5].

2.2. Linseed Oil and Protein Characteristics

Flaxseed makes meals richer in protein because of its fatty acid composition and oil content, which contributes to the high growth rate of oilseeds worldwide. However, for human use, flaxseed has not yet been investigated as a source of protein. It is well known that industry is looking for food protein ingredient based on plants as an alternative to animal-derived ingredients [21].

Flaxseed contains about 41% oil and its protein content ranges between 20-30 %, being nearly 80 % of globulins (linin and conlinin) and 20 % of glutelin but these can vary according to seeding and growing conditions. Oil, being a main component of flaxseed, contains various fatty acids, among which stearic acid (18:0) (3%), palmitic acid (16:0) (5%), linoleic acid (18:2n-6) (15%), oleic acid (18:1n-9) (17%) as well as ALA (18:3n-3) (59%), but between seeds when environmental factors are equivalent, these concentrations may also vary [22]. Flaxseed has limited amino acid lysine content, the reason why it is not a complete protein; in comparison to soybean, flaxseed has a similar amino acid profile and does not contain gluten. It is a rich source of glutamic acid/glutamine, arginine and branched-chain amino acids (valine and leucine) as well as aromatic amino acid (tyrosine and phenylalanine). Flaxseed has a nitrogen content of 3.25 g/100 g of seed. Oil is the primary product obtained from flaxseed but contains only about 21% protein while residual paste can be applied in the production of animal feed and has about 34% protein. In order to achieve a product with high protein content and advantageous functional characteristics, the flaxseed paste can be converted into protein concentrate and can be used in conventional foods [5]. Albumins and globulins are the main storage of proteins of flaxseed and can be classified according to their solubility in aqueous solvents. In the total content of protein flaxseed, globulins are about 58-66% and albumin is about 20% [23]. The protein secondary structure profile of globulin storage protein constitutes 3% α-helix, 17% β-sheet and 80% is aperiodic whereas the albumin constitutes26% α-helix, 32% β-sheet and also 42% aperiodic [24].Thus, taking into account these secondary structure profiles, it is obvious that the β-sheet is the predominant secondary structure in flaxseed protein. In the flaxseed, another crucial protein group - oleosins – can be found composing about 2-8% of total protein in oilseeds, and their function is oil storage. The activity of these oil storage proteins is due to an elongated and anti-parallel β-sheet which has a large number of hydrophobic residues, composing nearly 30 % protein *e.g.* peanuts. Oleosins are required to form the oil bodies. The amphipathic character of these proteins controls the oil/protein matrix of flaxseed that is important in protein and fat digestibility [25]. Flaxseed proteins are being studied also for their emulsifying properties [26, 27]. When compared to soybean protein, crude flaxseed protein that has flaxseed mucilage exhibits higher water absorption and oil absorption, as well as emulsifying activity [28, 29]. Karaca *et al*. showed that compared to whey protein isolates (WPI)-stabilized emulsions (90.8%), the creaming stability of emulsions (96.6%) stabilized by flaxseed proteins was similar [21]. At pH 6, flax protein concentrate has shown better oil absorption capacity (150.25%) as well as water absorption capacity (253.5%), high foam stability (83.33%), emulsifying activity (88.37%) and also emulsifying capacity (84.76 mL/g), which is crucial for the use of this protein concentrate in various products, including bread products, hamburgers and also salad dressings or mayonnaise [30,31].

2.3. Polyunsaturated Fatty Acids

The structures of the polyunsaturated fatty acids (PUFAs), omega-3 and omega-6 FAs are used to classify them. PUFAs are crucial because humans do not have desaturases and then they should get them by dietary supplementation [3]. Alpha-linoleic acid is enzymatically divided into eicosapentaenoic acid and docosahexaenoic acid, being precursors of many prostaglandins, thromboxanes as well as leukotrienes. Linoleic acid, as well as arachidonic acid, allows the production of eicosanoids, exhibiting proinflammatory and also prothrombic effects [32]. In the past, the consumption of omega-6 and omega-3 was in the ratio of 1 to 2:1, but nowadays, it increased up to the ratio of 20:1 with a ingestion of alpha-linoleic acid of less than 1 g/d in the western diet [33, 34]. This huge difference in the amount of omega-6 FAs in comparison to omega-3 FAs is mainly because of the modification of agriculture, as well as cooking practices [35]. Due to this proportion of FAs, in the last years, there has been an increase of health claims, the dietary proportion can control the consequence of inflammatory responses to depression and also stress in humans [3]. Several works have reported that omega-3 PUFAs avoid oxidative damage and allow the regulation of neurotrophic factor levels after traumatic brain lesion [36]. Other works have demonstrated that omega-3 PUFAs can decrease the risk of various disorders, including atherosclerosis, atrial fibrillation and sudden cardiac death, as well as coronary heart disease [37-39].

Table 1. Major fatty acids profile of flaxseed (Adapted from [1, 5]).

Fatty acids	Flaxseed (%)
Saturated	10
Monounsaturated	18.5
Polyunsaturated	71.8
Palmitic acid (C16:0)	4.90–8.00
Stearic acid (C18:0)	2.24–4.59
Oleic acid (C18:1)	13.44–19.39
Linoleic acid (omega-6, C18:2)	12.25 – 17.44
Alpha-linolenic acid (omega-3, C18:3)	39.90 – 60.42
Ratio omega-6/omega-3	0.3

3. FLAXSEED AND LINSEED ESSENTIAL OIL

Flax, a blue flowering annual herb, is characterized by golden yellow to reddish brown color flat seeds. It is a member of family Lineaceae of Latin name “Linum usitatissimum” (*i.e.* “very useful”) and each of its parties can be used commercially (after processing or even directly) [1, 40].

Flaxseed or linseed are different terms that can be applied as synonymous, *i.e.* it is called flaxseed when it is for human usage, and linseed when it is for industrial applications [40-42]. Nowadays, it is planted in many countries, with an emphasis in the Northern hemisphere, being China, United States and Canada, as well as India and Ethiopia the higher producers. Among these, Canada is the largest producer and exporter worldwide, with about 80 % of world trade in flaxseed [5, 40, 43-45]. Flaxseed, an edible oilseed, possesses a crispy texture and nutty taste [41, 46]. Its interest is increasing as functional food, mainly due to the richest vegetable source of ALA and lignans (class of phytoestrogen), with a percentage of 50%–62% of flaxseed oil or 22% of whole flaxseed and a range of 0.2–13.3 mg/g flaxseed, respectively. About 28% of flaxseed is composed of dietary fibers, among which about one-third is soluble fiber [18, 40, 47, 48]. In its composition figure enterolignan precursors, primarily secoisolariciresinol diglucoside (SDG), fibers, ALA and also omega-3 FAs [49, 50].

Flaxseeds are available in brown and yellow or golden varieties with the same nutritional attributes and also amount FAs. However, there is a special case which is solin -also known as Linola-, a type of yellow flax with a distinct oil profile and low levels of omega-3 FAs [51]. Brown flax is known as one ingredient of cattle feed and fibers, as well as varnish or paints. It is also available in the food market in various edible forms of flax, such as flax oil and roasted flax or milled flax and whole flaxseeds [5]. Through the distinct percentage of compounds, the different varieties of flaxseed can be used for a set of health effects [52]. Epaminondas *et al*. demonstrated some differences in both varieties of flaxseed, *i.e.* in the golden flaxseed there is less quantity of fiber and higher quantity of soluble carbohydrates but no differences have been found in the quantity of lipids and proteins [53]. Sargi *et al*. demonstrated that golden flaxseed has a higher amount of omega-3 and omega-6 while brown flaxseed has higher antioxidant capacity [54]. Attributed to these properties, the interest of flaxseed in the food sector is being steadily increasing [5].

3.1. Form and Morphology of Flaxseed

Commercial flaxseed varieties are different in size and also in color. They have about 2.5 mm wide and 5 mm long, as well as 1.5 mm thick [55, 56]. The seed is composed of mucilage (epiderm), seed coat, as well as the layer of endosperm surrounding two cotyledons. It is known that the endosperm and also the cotyledons contain distinct oil compositions as well as soluble protein [55, 57, 58]. In the flaxseed aleurone cells are found disposed of by the endosperm and cotyledons, where the shape of its grains is different [55, 59]. The oil, on the other hand, is disposed of by the endosperm and cotyledons and are present as microscopic droplets [55, 56].

3.2. Functional Elements of Flaxseed

Due to its bioactive components, *i.e*. alpha-linolenic acid, lignans and dietary fibers as well as minerals, flaxseed can be considered as a functional food [1, 5]. Apart from these elements, flaxseed also contains vitamins (A, C, F and E), minerals (P, Mg, K, Na, Fe, Cu, Mn and Zn), soluble polysaccharides and phenolic compounds [5, 22, 60]. It also exhibits a high level of calcium, magnesium and also phosphorus, thus when a portion of 30 g is consumed it corresponds to 7-30 % of the recommended dietary allowances (RDAs) [61].

3.2.1. Alpha-Linolenic Acid

The essential element of flaxseed is alpha-linolenic acid, containing ca. 73% of polyunsaturated fatty acid,18% of monounsaturated fat, and 9% of saturated fat [62, 63]. Fatty acids - also known as essential acids - are necessary for the human body and are supplied by food since the body has no way of producing them [64].

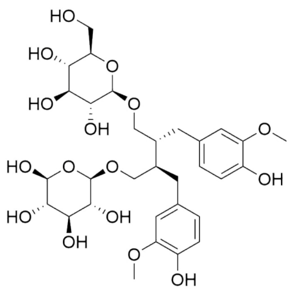
In the case of omega-3, the human body cannot add a double bond beyond the ninth carbon from carboxyl end of FA. The originator of the synthesis of polyunsaturated fatty acids (EPA and DHA) is ALA, but they can also be metabolized to eicosanoids, prostaglandins and also leukotrienes by the enzymes cyclooxygenase and lipoxygenase. During this transformation, many fatty acids are synthesized through the desaturation and elongation reactions with the help of specific desaturases and elongases. It was shown that the synthesis of linolenic acid also occurs with the same enzymatic reactions. However, the conversion of ALA into EPA and also DHA is not competent in humans and animals, leading to a competition between them for the same enzymes. Mammals do not have these enzymatic activities but lower order animals have such activities, although recent studies point out that mice have these enzymes and can transform omega-6 fatty acid to omega-3 fatty acid. In the human diet, a balanced intake of omega-3 and omega-6 essential fatty acids is therefore recommended [1, 65-67]. Both these essential fatty acids look for location within cell membranes. If there is an imbalance of one type of fatty acid, the predominant will be assimilated into the cell membrane, inducing adverse effects in the fluidity of membrane leading to changes of cellular functions. On the other hand, if there is a balance of these fatty acids, the omega-3 fatty acid is preferred over the other. It is known that the influence of these fatty acids on the physiological functions is opposite [1, 66, 68]. EPA and DHA are transformed into resolvins, neuroprotection and also protectins. Resolvins are efficient anti-inflammatory mediators, circumventing inflammation by inhibiting the work of prostanoids. To control the homeostasis, resolvins and protectins contribute to the elimination in gastrointestinal, kidney, oral, skin, lung, among other inflammations through the activation of special mechanisms. DHA, transformed into neuroprotectins, show neuroprotective effects. A balance between fatty acids is therefore essential in order to maintain good health [1, 69, 70].

The proportion of omega-6 to omega-3 fatty acid is currently being estimated as 38–50:1 in Indian diets and 20–30:1 in western diets, which confirms higher omega-6 fatty acids intake [1, 71, 72] and an imbalance of the pro-inflammatory and anti-inflammatory processes in the cellular functions (supporting more of pro-inflammatory). Food choices based on omega-3 fatty acids are therefore recommended to alleviate this imbalance. The suggested doses of omega-6 to omega-3 fatty acids are in a ratio of 4:1 to 10:1, accounting for 3 and 0.5% of total energy intake, respectively [1, 64, 73, 74].

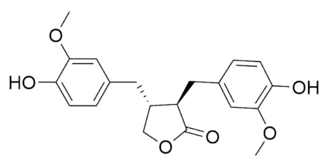
3.2.2. Lignans

Lignans are phenolic compounds composed of cinnamic acid present in cell wall of higher plants. Lignans are phytoestrogens and can also exhibit antioxidant properties [1, 75, 76]. Lignans are all over the vegetal kingdom, mainly in fiber-rich plants, vegetables (broccoli, garlic, asparagus and carrots), fruits, cereals (wheat, barley and oats), beans(lentils and soybean), as well as in berries, alcoholic beverages and also tea [1, 77]. In comparison to other plant foods, flax has 800 times more lignans [5]. The major lignan of flaxseed is secoisolariciresinol diglycoside, but it also has matairesinol, pinoresinol, lariciresinol and isolariciresinol [1, 78-80]. In the defatted flour, the concentration of SDG varies from 11.7-24.1 mg/g, while in whole flaxseed flour it varies from 6.1-13.3 mg/g [5, 81].

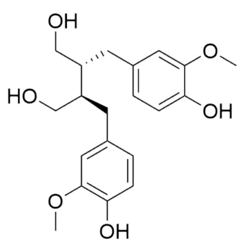
Acid hydrolysis of secoisolariciresinol diglycoside produces secoisolariciresinol (SECO). In the outer layers of the seed,secoisolariciresinol diglycoside forms a complex with HMGA (3-hydroxy-3 methylglutaric acid) residues [1, 82-84]. SDG, metabolized by bacteria in the colon of humans, allows the synthesis of enterodiol (END) and also enterolactone (ENL) [85]. In human body, through the gastrointestinal microflora, ligands release SECO, a non-sugar moiety of SDG. Besides, through the hydroxylation and demethylation, microflora can also produce mammalian lignan-END, oxidizing to give ENL [41, 75, 86]. It was shown that Bacteroides and Clostridia release glucosyl moieties from SDG to produce SECO [87, 88]. Eubacterium lentum is responsible for dehydroxylation reaction and Bacteroides methylotrophicum, Eubacterium callanderi, Eubacterium limosum and also Peptostreptococcus productus control the demethylation reactions [87, 89]. Clostridia and Ruminococcus sp are responsible for the dehydrogenation of END into ENL, being eliminated in faeces or assimilated by the human colon and go into the circulation [87, 90].



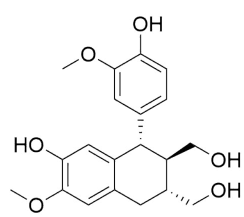
Secoisolariciresinol diglycoside (SDG)



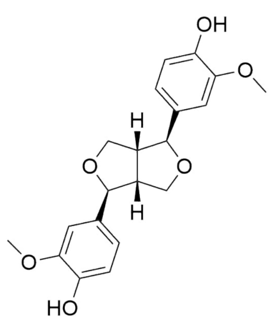
Matairesinol



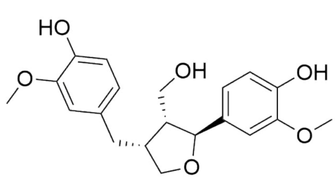
Secoisolariciresinol



Isolariciresinol



Pinoresinol



Lariciresinol

Fig. (1). Chemical structure of lignans existent in flaxseed.

3.2.3. Dietary Fibers

Worldwide, flax fibers are one of the oldest fiber crops. Total flax plant accounts for 25 % seed and 75 % stem and leaves, being its fiber obtained from the skin of the stem of the plant [91]. The non-seed parts corresponding to 20 % fiber, can be removed either chemically or mechanically. A flax fiber, biodegradable and natural composite, has low density and advantageous mechanical properties. It looks like blonde hair, thereby called "flaxen", as well as it is flexible, lustrous and soft. It is less elastic compared to cotton fiber, but it is also stronger [40].

Flaxseed is one of the best oilseeds, mainly because of the existence of mucilage located in outer layers of the seed, being an excellent source of soluble and insoluble dietary fibers [40, 43]. Flaxseed mucilage has excellent functional properties as well as health benefits [1]. It has a percentage of fiber of 35–45, among which one third is soluble (mucilage of seed coat) and two-third is insoluble fiber (cellulose, hemicellulose or lignin) [41, 92, 93]. Soluble fiber is composed of water-soluble polysaccharides and its purity and recovery is depending on the extraction conditions. The presence of polysaccharides in the seed coat allows the high water binding capacity of flaxseed mucilage (1600-3000g of water/100g of solids) [5, 94, 95]. Mucilage of flaxseed contains acidic polysaccharides (L-rhamnose, L-fucose, L-galactose and also D-galactouronic acid) as well as neutral polysaccharides (L-arabinose, Dxylose, D-galactose and also arabinoxylan), which functionally has identical properties to guar gum [95, 77]. It is known that the mucilage can be removed through the water and exhibits advantageous foam-stability properties [96].

The dietary fiber of flaxseed is fermented by colonic microflora when reaches the large intestine, originating short-chain fatty acids (SCFA), methane, hydrogen and carbon dioxide, biomass, as well as laxative effects. Due to the bulking effect of soluble and insoluble fibers, there is an increase dry and wet weight of the colon contents and faeces. Through the binding capacity of macromolecules either enhancing the mass of microbial cells, the soluble fiber increases water binding. Some works showed that the contribution of soluble fiber to faecal weight was the same [1, 97]. On the other hand, there is an enhancement of the viscosity of intestinal contents and a delay of gastric emptying and nutrient uptake with the water-binding capacity of flaxseed insoluble fiber occurring at pH 6–8 (pH environment in human intestines) [1, 77]. Thus, in order to increase daily fiber intake of soluble and insoluble fiber (1 and 3 g respectively), it is necessary to consume 10 g of flaxseed daily [98].

3.3. Nutritional Composition of Flaxseed

Some factors, such as genetics, growing environment and also processing conditions, modify the chemical composition of flaxseed [41]. Lipid content

Table 2. Functional properties of flaxseed constituents (Adapted from [1]).

Functional ingredient	Applications
Mucilage	Emulsifier and stabilizer in sauces, sausages, meat emulsions and salad dressings Anti-staling agent in baked products Improves cooking quality of noodles Functional food ingredient
Protein	Stabilizer and emulsifier in ice cream, sauces and meat emulsions Antifungal property Viscoelastic texture to extruded pastes for breakfast cereals and snacks Enhances nutrition in gluten free meal Egg and gelatine substitute in baked goods and ice cream Functional food ingredient

varies from 37-45g/100g of the seed [1, 41, 99, 100].The main seed oil storage tissues that contain 75% of the oil are cotyledons [1, 40, 43, 46].Flaxseed oil contains about 98 % phospholipids, triacylglycerols and only 0.1 % of free fatty acids. Protein content accounts21%, which it is concentrated in the cotyledons [1, 101, 102]. Globulin (26–58%) and albumin (20–42%) are their main protein fractions, also containingarginine, aspartic acid and glutamic acid in large quantities, but lysine is present in reduced quantities [1, 40, 43, 103]. It has a large amount of cysteine and methionine, which offers antioxidant activity [1, 44]. It is known that the protein content is affected by processing conditions, dehusking as well as defatting, having these latter higher protein content [1, 45, 104]. Flaxseed contributes very little to total carbohydrates intake, as it is rich in phytoestrogens and has decreased levels of carbohydrates (1g/100g) [1, 41]. It also has many phenolic compounds (phenolic acids, flavonoids and lignans), mainly ferulic acid (10.9 mg/g), chlorogenic acid (7.5 mg/g) and also gallic acid (2.8 mg/g), offering anti-oxidant and anticancer properties. Although in low quantities, it also possesses p-coumaric acid glucosides, hydroxycinnamic acid glucosides and 4-hydroxybenzoic acid [1, 105, 106]. The main flavonoids present in flaxseeds are flavone C- and O-glycosides, which are a good source of minerals, such as phosphorous (650mg/100g), magnesium (350–431mg/100g), calcium (236–250mg/100g), sodium (27mg/100g) and potassium (5600–9200mg/kg) [1, 41, 100, 106]. Besides, it also has low quantities of water-soluble and fat-soluble vitamins, *e.g.* γ-tocopherol (39.5 mg/100 g) [1, 41, 107].

Table 3. Chemical and nutritional composition of flaxseed (Adapted from [1, 5]).

Nutrients	Amount per 100g of flaxseed
Moisture	6.5 g
Protein	20 g
Total Fats	41 g
Minerals	2.4 g
Crude fiber	4.8 g
Total dietary fiber	28 g
Carbohydrates	29 g
Energy	530 kcal
Potassium	750 mg
Calcium	170 mg
Phosphorous	370 mg
Iron	2.7 mg
Vitamin A	30 µg
Vitamin E	0.6 mg
Thiamine (B1)	0.53 mg
Riboflavin (B2)	0.23 mg
Niacin	3.21 mg
Pyridoxin	0.61 mg
Pantothenic acid	0.57 mg
Biotin	0.6 µg
Folic acid	112 mg
Linolenic acid	23 g
Ligans	10-2.6 mg
Ascorbic acid	0.5 mg

3.4. Anti-Nutrients from Flaxseed

Despite its functional elements, flax also has anti-nutritional elements that may have adverse effects on human health [1, 5]. The main anti-nutrients present in flax are cyanogenic glycosides (CGs) (250–550 mg/100g), which are fractionated into linustatin (213–352mg/100g), neolinustatin (91–203mg/100g), and linamarin (acetone–cyanohydrinbeta–glucoside C10H17O6N) in small amounts (32mg/100g), its content depends on the farming conditions and place [1, 108, 109]. In comparison to seed type, the fiber type linseed has a high percentage of glycosides, being the ripe seed the one that contains less glycoside [1, 40, 43]. Cyanogenic glycosides release hydrogen cyanide by intestinal β-glycosidase that produces thiocyanates, interfering with iodine uptake by the thyroid gland and negatively influencing iodine-deficiency disorders, goiter as well as cretinism. They are heat labile and can be demolished through the processing methods (pelleting, microwave roasting or autoclaving), as well as through some detoxifying enzymes (β-glycosidases) that liberate hydrogen cyanide, can be evaporated through the use of steam [1, 63, 110, 111]. Park *et al*. related 207/100g seed of linustatin and 174mg/100g seed of neolinustatin in flaxseed. β-glucosidases are activated and allow the release of poisonous hydrogen cyanide (HCN) after seed damage [112]. Phytic acid, another anti-nutrient of the flaxseed, ranges from 23-33g/kg of the flaxseed meal [1, 113, 114]. This acid compromises the uptake of some nutrients (magnesium, iron, zinc, calcium as well as copper), which make it a powerful chelator, allowing the formation of protein and mineral-phytic acid complexes. It also decreases the bioavailability of micronutrients, however, some recent works have shown that this acid has hypocholesterolemic and hypolipidemic, as well as antioxidant and anticancer effects [1, 106, 115]. Flaxseed meal also contains 10mg/100g linatine (gamma-glutamyl- 1-amino-D-proline), inducing vitamin B6 deficiency [106]. Ratnayake *et al*. did not report any effect on the Zn status when rats were flaxseed fed [116]. Ratnayake *et al*. and Dieken showed that in flaxseed, a vitamin B6 antagonist (linatine) do not affect vitamin B6 contents or metabolism with a meal until 50 g of ground flaxseed per day [116, 117]. Ganorkar and Jain reported that in comparison to soybean and canola, flaxseed anti-nutrients have less negative effects on human health [118]. Bhatty reported the presence of trypsin inhibitors in flaxseed, however, in comparison to soybean and canola seeds, their activity has no significance[119].

3.5. Uses of Flaxseed - Diet with Linseed Oil and Its Effects

Flaxseed reappeared as a stronger functional ingredient with many medical benefits and it is utilized in many classes of food products. Flaxseeds have many versatile uses, mainly due to the fact that all parts of linseed plant can be used and their supplemented food products are enhancing popularity [1]. The oil of the seed is refined and then used in food, as whole flaxseed, ground meal as well as extracted oil or mucilage. It can be incorporated as nutritional additives in ready to eat cereals and baked cereal products, fiber bars, bread and muffins, salad toppings, meat extenders as well as spaghetti [40, 43]. The fibers that are produced by the stem exhibit durability and strength. Since ancient times flaxseeds are being consumed; seeds can be roasted and milled and their oil can be applied in many food formulations (micro- and nano-encapsulated powder, neat oils and also stable emulsions). It has also been cultivated for fiber, medicinal purposes and nutritional products [5, 73]. The fatty acids that are absorbed by the small intestine differ from those available in the diet, due to the extensive biohydrogenation that can be prevented by chemical treatments (by heating or by feeding whole oilseeds and also with formaldehyde) [55, 120].

The high benefits of linolenic acid at the health pushed forward scientific research in many fields. Many researchers, nutritionists and food technologists, as well as plant breeders, are applying molecular and conventional approaches in order to modify the fatty acid profile of flaxseed [1].

3.5.1. As an Ingredient

The ability to incorporate flax-based fatty acids into milk and meat gives a chance to make a value-added product with good benefits to health. It is accepted that contemporary human nutrition lacks in omega-3 fatty acids but it is abundant in omega-6 fatty acids and saturated fats. A diet abundant in omega-6 and poor in omega-3 fatty acids increases the mortality rate, as it favours clotting, vasospasm, as well as vasoconstriction [33, 55]. For example, around 15 g of milled flaxseed with about 45 mL of water can replace an egg, besides taking advantage of the absence of cholesterol in flaxseeds [121]. In the case of salad dressings, flaxseed gum can be used in order to stabilize the emulsion [1, 122]. Due to the ALA content, flaxseed provides omega-3 fatty acids that can modify milk and meat fat profiles. Scollan *et al*. showed that through the feed, whole bruised flaxseed can enhance the omega-6:omega-3 ratio in meat and adipose lipid profiles without altering the muscle fatty acid content [123]. Flaxseed products are stable at ambient temperature, which has been by some studies that show that store the milled flaxseed did not change the quality [40, 43]. Petit *et al*. fed cows with whole flaxseed and also showed a change in the ratio for milk fat [124]. In order to increase the nutritional quality of the meat and eggs rich in omega-3 and pork products, the flaxseed was included in the feed for animals [125]. In the bakery sector, with the purpose to satisfy customer demands, flaxseed was mixed with grain bread and the flaxseed oil was also introduced into milk and dairy products, pasta products and macaroni, dry and beef patties, juices, muffins and also baked foods, making them ideal foods for the daily consumption [5, 126]. With

Table 4. Traditional and medicinal uses of various food products enriched with whole flaxseed, flax flour and flax oil (Adapted from [1, 5]).

<table>
<tr><th>Flax form consumed</th><th>Traditional/medicinal health benefits</th><th>Flax enriched food product</th></tr>
<tr><td>Flaxseed tea</td><td>Useful against dyspnoea, asthma, dysphonia, bad cough and bronchitis</td><td rowspan="3">Bread
Yeast bread
Unleavened flat bread
Brown bread
Muffins and snack bar
Cheese
Shortening and biscuits
Corn snacks
Bagels
Ice cream
Muffins
Cookies</td></tr>
<tr><td>Flaxseed drink</td><td>Helps out constipation</td></tr>
<tr><td>Flaxseed flour</td><td>Used against pulmonary tuberculosis, haemoptysis, splenomegaly and stomach ulcer
Cures inflammations of intestines and abdominal pains
Disinfects gastrointestinal tract
Strengthens the nervous system
Strengthens the memory
Good in treating the impairment of concentration
Good in the management of age-associated distractibility
Ensures rapid healing of wounds through external use
Protects the skin against getting dry
Used in eczema and psoriasis diseases
Exercises a positive impact on respiratory tract diseases
Good in curing mental disorders
Cures bad cough
Used as mouthwash in oral cavity, throat and gingival disorders</td></tr>
</table>

various studies evidencing the advantages of food products rich with flax, few studies shown neutral health impacts and less sensory acceptability. Ramcharitar *et al*. showed that muffins with milled flaxseed were less acceptable than the control [127]. It was also related that Pretzel type yeast bread containing flax was also less acceptable in comparison to the control [128]. The most interesting benefit of milled flaxseed to be applied in bakery products is the fractions of carbohydrate and protein. It has been shown that flaxseed increases viscosity, improves absorption and characteristics of bread, stabilizes foam and protein-based emulsions, changes shear rate as gum arabic does, and can also be used as a “food thickener” and “enhancing agent” in baked goods [100, 129]. Hall *et al*. used flaxseed particles in bread in order to obtain the good quality of the products [130]. Mentes *et al*. reported that the use of ground flaxseed can enhance loaf volume and Dallman degree, as well as retarded bread staling [131]. Hao and Beta have shown an enrich phytochemical profile of the bread and improve antioxidant activity through the incorporation of flaxseed hull into Chinese steamed bread (CSB) [132]. Lipilina and Ganji developed bread with flaxseed flour and also observed that such flour can enhance linolenic acid and dietary fiber [133]. Minker *et al*. reported the promising industrial use by showing that linseed mucilage has emulsifying properties, Arabic gum, and tragacanth gum [134]. Due to the high mucilage content, flaxseed exhibits a high capacity for water absorption, lubricity and also moisture-binding capacity, allowing the production of throughput and puffing during extrusion processing or being an alternative to trans-fat free shortening in foods where the water absorption affects the mixing time and dough-handling attributes [135]. It was shown that the bread made with the flaxseed oil cake has lower peroxide levels than the threshold limits of storage [136]. An important characteristic is that flaxseed no contains gluten, being beneficial to gluten-intolerant humans. Thus, part of the flour can be replaced by whole or ground flaxseed in muffin and pancake, as well as bread and cookies [137]. Therefore, the involvement of flaxseed in food, once models the fatty acid profile of the human's diet is evident [55].

3.5.2. As An Edible Oil

As said before, flaxseed oil is abundant in alpha-linolenic acid. In the old days, flaxseed was useful in the fabrication of paints or printing inks, coating as well as drying oil. Recently, it is used for edible purposes due to its nutraceuticals values [1]. When it is meant for edible purposes, due to its characteristics, fresh flaxseed is extracted through cold pressing [138, 139]. Its high amount of alpha-linolenic acid has also disadvantages, flaxseed oil is easily oxidized, being susceptible to rancidity and has also poor sensory quality [140, 141]. These can cause chronic diseases. Some studies showed that high temperature changes its nutritional composition, deteriorating the alpha-linolenic acid [138, 139]. Flaxseed oil is commonly used in cooking purposes and some investigations prove that stir-frying of flaxseed oil can reach up to 177°C without changing its qualities [142, 143]. In flaxseed oil, various components act as natural antioxidants, such as phenolic acids, flavonoids and lignans, among others [138, 139, 144]. It is also being made attempts in terms of encapsulation of the oil to contribute for protection of oxidative products that are created on processing or storage [145]. Aguiar *et al*. proved that replacing soy oil by flaxseed oil in bread formulations lead to enhanced ALA content and also decreased ratio of omega-6:omega-3 without affecting the quality of the product [146]. Ivanova *et al*. proved that flaxseed additive can obtain a better butter at the level of flavor, odor, color as well as spreadability and plasticity [147]. Giroux and Matumoto-Pintroa *et al*. developed dairy beverages that were rich with linseed oil, improving oxidative stability [148, 149]. Cloughley *et al*. showed that when laying hens were fed with a special flax diet, eggs were rich in omega-3. Other products are also rich in omega-3 when the flax is included in animal feed, such as pork [150].

3.6. Diseases and Health Benefits of Linseed Protein and Oil

Besides the nutritional benefits, flaxseed has also other health benefits because of its components that act as anti-oxidants and as phytoestrogens. Some studies showed various techno-functional properties and benefits of flaxseed proteins [5]. Benefits of flaxseed protein in coronary heart and disease, as well as in cancer have been described [151-153]. Flax protein is abundant in glutamine and also arginine, which allows the prevention, as well as treatment of heart disease and also helps in supporting the immune system [154, 155]. Flaxseed is composed of bioactive peptides that have strong immunosuppressive and antimalarial activities [156]. Some studies showed that flaxseed proteins are very useful for therapeutic uses [157, 158]. Other studies demonstrated that a peptide mixture from flaxseed with increased branched-chain amino acids and also decreased levels of aromatic amino acids has antioxidants and antihypertensive properties [159]. Omega-3 fatty acids' health benefits have been shown useful for many disorders, such as cancer, diabetes, also exhibiting anti-arrhythmic and anti-atherogenic, as well as anti-inflammatory, improving vascular function [5].

3.6.1. In Treatment of Diabetes Mellitus

Cardiovascular diseases can be caused by an enhanced blood sugar. Diabetes is identified by hyperglycemia being also related to changes in the metabolism of carbohydrates, proteins and also lipids, leading to adverse effects [160, 161].The quantity of patients with diabetes has been increased exponentially in the latest years. If not treated, diabetes can develop into cardiovascular diseases, kidney failure as well as blindness [162]. Diabetes develops together with other risk factors, such as obesity, hypertension and low HDL cholesterol, as well as high triglyceride levels. The components of flaxseed exhibit a protective effect on diabetes risk [5]. Prasad reported that flaxseed lignan SDG can inhibit expression of the gene that is responsible for glucose synthesis in the liver [163]. It was shown that in patients with T2D, the supplementation of diet with flaxseed decreased fasting blood glucose and also glycated hemoglobin [160]. This can be explained by the less content of glycemic carbohydrates and also by the abundance of dietary fibers of flaxseed. Some studies have shown a decrease in postprandial blood glucose levels in women that consume flaxseed [63, 164]. Kelley *et al*. used rats predisposed to obesity and diabetic tumors and observed a reduction in glycaemia when conjugating linoleic acid and flax oil in their diet [165]. Kapoor *et al*., while studying the effect of supplementation with flaxseed powder on diabetic human females, have shown the decreased postprandial blood glucose levels [166]. Nazni *et al*. reported similar results, diabetic subjects have showed decreased blood glucose levels when the supplementation was made with flaxseed powder [167]. Dodin and Barre *et al*. did not report any change of glucose and insulin levels after ingestion of flaxseed [168, 169]. Other studies also showed that the use of flaxseed for glycemic control can also reduce the risk of obesity and dyslipidemia [170, 171].

3.6.2. Tumor and Cancer Reducing Effects

It was suggested that flaxseed, because of the high level of phytoestrogen lignans and -linolenic acid-rich oil, has anticancer effects [172]. There is a relationship between flaxseed ingestion and risk of cancer. Some researches reported that flaxseed can inhibit the formation of colon and lung tumors and decrease blood vessel cell formation in female rats, showing a protective effect on breast, colon and also ovarian cancer [173]. It was shown that elevated levels of insulin and insulin-like growth factor 1 (IGF-1) also enhanced cancer risk [174].It has also been proven that insulin is related to the risk of pancreatic and colorectal tumors [175]. Other works report that adding flaxseed in fed can decrease the levels of insulin and IGF-1 [176, 177]. Sturgeon *et al*. showed, however, that incorporation of flaxseed in the diet of healthy postmenopausal women has a smaller effect on blood levels of IGF-1 [174].

Mainly due to its elevated content of SDG lignan, flaxseed has a reduction effect on a breast tumor [173, 177-181]. From flax lignans, enterodiol (ED) and enterolactone (EL) are produced in an animal body. As they are identical to human estrogen-17β-estradiol (E2), they can bind to estrogen receptors (ER) [182]. Flaxseed and its SDG component can influence tumorigenesis [178, 179]. The protective effect of flax lignans on breast cancer can be explained by decreased estrogenic activity as well as antioxidant properties. Flaxseed oil also proves to decrease the human estrogen receptor-positive breast tumors (MCF-7) growth [183]. Chen *et al*. related that the groups of mice that have been fed with flaxseed can avoid tumor growth [85]. Some researchers proved that flaxseed helps to limit early stages of cancer, as well as alter estrogen metabolism [109, 184]. *In vitro*, animal, observational and clinical studies were conducted on flaxseed and its components in order to evaluate the reduced cancer risk. Almost all studies in diverse rodent models and also clinical trials showed that the intake of flaxseed can decrease the tumour growth, mainly breast cancer [172].

3.6.3. Prevention of Kidney Diseases

Chronic kidney disease (CKD) commonly requires dialysis or transplantation for patients' survival and can eventually lead to dead [185, 186]. It has been reported that, because of their anti-inflammatory properties, omega-3 fatty acids can also preserve kidneys. The ingestion of PUFAs proved to decrease renal inflammation and also fibrosis in animal models [187]. When rats had a fed with a high-fat diet, ALA showed anti-inflammatory effects and decreased levels of plasma CRP [48]. Gopinath *et al*. observed that the ingestion of long-chain omega-3 PUFAs was opposite to the prevalence of CKD [188]. Cicero *et al*. also proved that the ingestion of omega-3 fatty acids was related to a decrease in systolic and diastolic blood pressure. This supplementation can be a good mechanism to protect the kidneys since a risk factor for CKD is hypertension [189]. Gopinath *et al*. showed a relationship between α-linolenic acid and CKD [188]. Wang *et al*. tried to explain the cardioprotective results, showing that they can be due to the limited conversion of α-linolenic acid in EPA and DHA [190]. It was also shown that flaxseed fibers consumption can decrease the lipid uptake, by limiting re-uptake of bile acids that enhance hepatic synthesis of bile acids and also limit the formation of micelles [191].

3.6.4. Reduction of Dyslipidemia and Cardiovascular Diseases (CVD)

Cardiovascular disease (CVD) is the leading cause of mortality worldwide. The risk factors of CVD are directly related to serum lipid profile. The supplementation of flax in diet was intensely investigated in animals and humans. Works made with flaxseed and its components have shown positive effects [192, 193]. CVD and its risk factors have a common characteristic which is inflammation [194]. The changes of inflammation can be measured by C-reactive protein (CRP) levels [48, 195, 196]. In studies performed in rats, mice and also in rabbits, the effects of flaxseed on risk factors for CVD were described, showing hypocholesterolemic activity of flaxseed due to its lipid content [160, 197-203]. Gillingham *et al*., on the other hand, reported that after the consuming of flaxseed oil, decreased levels of high-density lipoprotein (HDL) fraction in human serum was observed [204]. No changes in HDL fraction in animals were also reported in different studies[192, 205, 206]. Mohamed *et al*. reported that type 2 diabetic patients fed with flaxseeds, have a reduction of plasma glucose, enhancement in plasma lipid profile and also decrease lipid peroxidation [207]. Jennifer *et al*. showed that fed with flaxseed can protect ischemic heart disease, enhancing vascular relaxation responses and inhibiting the ventricular fibrillation [208]. Vedtofte *et al*. did not report any relation with intake of ALA and the risk of ischemic heart disease [209]. Dietary factors have been playing a cardiovascular protective role based on evidences from randomized controlled trials (RCTs). Reducing the inflammation can reduce the risk of CVD [48]. Flaxseed is capable of reducing the risk of cardiovascular disease through the decrease of lipid profile parameters, plasma trans fats as well as atherogenicity, glycemia or pro-inflammatory oxylipins. They have also been related to blood pressure (BP) reduction [50, 210]. These hypotensive effects can be due to the synergistic action of potent antioxidants or different ingredients. A decrease of systolic BP (SBP) and diastolic BP (DBP) was observed with flaxseed powder oil preparations, which observe differences between the flaxseed supplement and blood pressure (BP), attributed to the different qualities of flaxseed supplements [50].

3.6.5. Prevention and Treatment of Obesity

Plant materials, including flax, allow to treat and prevent obesity-related disease conditions [40, 211]. Flaxseed fibers after hydration are capable to create viscous solutions that allow the suppression of hunger and delay gastric emptying and nutrient absorption from the small bowel [197, 212, 213]. In obesity, leptin is present at high levels [214]. McCullough *et al*. observed an enhanced plasma and adipose levels of ALA with the intake of flaxseed. Modifications on the expression of leptin were related to adipose ALA levels and also with risk of atherosclerosis [215]. When ingested as flaxseed oil, a higher bioavailability of ALA was observed, decreasing with the ingestion of whole seed. [50].

3.6.6. Natural Treatment of Bowel Syndrome

Constipation can also be a serious health problem, which can be prevented/treated with dietary fibers [77]. Flaxseed fibers can act as dietary fiber, being the first line of treatment for constipation. Cunnane *et al*. related the influence of ingestion flaxseed on several indices of nutrition [164]. Dietary fiber slows down gastric emptying, control glucose levels, as well as cooperates in the prevention of constipation. Kristensen *et al*. showed the effect of flax fibers on the fat excretion, as well as on the energy balance. They showed that drinks rich with flax fiber can decrease cholesterol levels in comparison to bread also rich with flax fiber but the ingestion of bread enhanced fecal fat excretion and also maintained an appropriate energy balance [1, 216]. Some works have described the effects of flax fiber, including gastrointestinal (GI)-motility, constipation, glucose tolerance and hypocholesterolemic effect, as well as fermentation [5, 160, 197].

3.6.7. Implication in Bone Health

Omega-3 PUFAs also benefit bone. Some works reported no improvements on osteoporotic bones in humans and animals with the intake of whole flaxseeds, but its combination with estrogen therapy had an extra benefit to the bone in animal models. The same results were reported with flaxseed oil, but this role was better on other pathologic conditions which in turn result in enhanced bone properties. The bone-protective effect is due to ALA content of flaxseeds and not the lignin fraction. As said before, PUFAs have an advantageous role in inflammatory diseases, which include bone disorders. The fed with flaxseeds or flaxseed oil in older adults has a marginal benefit to the bone, mainly through the inhibition of bone resorption. In animals, the supplementation with flaxseed/oil enhanced lipid profiles in plasma, bone and also in other tissues. This increased bone properties in mature animals are however not shown in growing animals. The positive role of flaxseed/oil enhanced bone strength in animals with secondary osteoporosis that can be used as a dietary supplement in those conditions. It is clear that the use of flaxseed oil can be beneficial for bone health, mainly to osteoporosis' patients and those with diseases that cause bone loss. Besides the reported benefits, there is still a need to understand if or how ALA regulates bone metabolism [217].

Table 5. Biological and functional properties of flaxseed proteins (Adapted from [5]).

Function of flax protein	Effects and Mechanism
Antifungal	Act against food spoilage fungi Penicillium-chrysogenum, Fusariumgraminearum and Aspergillusflavus
Antioxidant	Hydrolyzed flaxseed proteins exhibited anti-oxidant property by scavenging 2, 2-diphenyl-1- picrylhydrazyl radical, superoxide radical and hydroxyl radical
Antihypertensive	Inhibits angiotensin I-converting enzyme
Cholesterol lowering effect	Due to their bile acids binding activity
Anti-diabetic	Flax proteins can interact with fiber and mucilage By stimulating the secretion of insulin
Anti-thrombic	Flax proteins - hirudine and linusitin
Anti-tumor	Presence of low lysine/arginine ratio

4. FLAX: A NUTRACEUTICAL OR FUNCTIONAL FOOD?

Nutraceutical and functional foods are incorrectly referred to be the same because there is a difference between them. Compared to a conventional food, a functional food having the same appearance, is part of the diet and has physiological benefits or to decrease the risk of chronic disease. Functional foods above their nutritional value contribute to a specific health benefit to the consumer and many examples derive from vegetal origin food [1, 5]. On the other hand, a nutraceutical is extracted or purified from foods that are not associated with foods, being sold in medicinal forms. It can be a part of functional foods, but a functional food has to contribute to essential nutrients and also with qualities necessary for normal maintenance, growth as well as development [5]. Nutraceuticals are nowadays attracting growing interest for their potential use a toolbox to prevent and, in some cases, cure some pathological conditions, *e.g*. dyslipidemia. While pharmaceuticals have specific legislation on production, efficacy and safety, as well as use in therapy to be validated by clinical trials, before being put on the market, nutraceuticals are considered to belong to food supplements and these rules many times are not followed. There is a lack of regulation regarding nutraceuticals since they should have proven advantageous effect as a requirement before being authorized and marketed. To fill this gap, there was a redefinition of the concept of nutraceuticals in order to differentiate them of food supplements, functional foods as well as from pharmaceuticals. The clinical test should be performed to assess their safety of use, efficacy and ability to provide beneficial health effects in particular for patients not eligible for the conventional pharmacological therapy [218-220]. Flax, consumed in diverse forms, is considered a functional food attributed to its several health benefits [5, 221]. Various stable preparations of flax (oils, capsules and also microencapsulated powders) are available in the market in the form of nutraceuticals. As a dietary supplement, flax lignans-isolated SDG preparations are also in the market [222]. In ancient times, flaxseeds had already been used as a cough remedy and also to alleviate abdominal pain. Food science and technology researchers are designing a framework for food-based dietary recommendations to obtain optimal nutrition through the intake of healthy foods in diverse areas (*e.g.* food physics, methods of food storage and preservation, nutrient restoration, fortification of foods, as well as the development of health-focused designer foods and also functional foods). Flaxseed has drawn the attention of scientists, researchers and industry due to their contents, the fact that it is a rich source of ALA, dietary fibers, as well as high-quality proteins, antioxidants and lignans, offering synergistic health benefits. Flaxseed can be used due to its various nutraceuticals and therapeutic attributes, making it an advantageous value-added food ingredient. Flax almost has no digestible and glycemic carbohydrates. It contributes to a model for whole grains or seeds and highlights the recognition given to the nutritional value of "whole grains", "whole seeds" as well as "whole foods" [5]. A strengthening consumer demand for foods enhancing health and wellbeing is recent, making functional foods also a recent area of research [1].

CONCLUSION AND FUTURE PERSPECTIVES

In the last few years, the popularity of flax as a food ingredient has increased especially due to its high content of ALA. Important for brain function, essential fatty acids have shown to reduce "bad" cholesterol and to mitigate the risk of heart diseases amongst other health benefits. The high level of unsaturated fatty acids makes it also attractive for industrial applications in stains, paints and linoleum flooring. As demonstrated by clinical trials, flaxseed can contribute to prevent diseases, which enhances the design of new branded healthy and functional foods using both flaxseeds and the oil. However, more *in vivo* studies are still needed to understand the health benefits of the constituents of flaxseed and also to know the amount required to increase its therapeutic potential. Faster, reproducible and more sustainable techniques for the analysis of nutraceuticals are also needed. While its usage goes long back to ancient times, flaxseed is nowadays exploited as a health food source. It increases the availability of healthy food choices, enhancing the nutrient profile of foods by the reduction in the salt, sugar and also saturated fat content, as well as by increasing the content of bioactive compounds. Worldwide market healthy foods are growing and in future, flax and flaxseed oil will choose ingredients of functional foods and nutraceuticals. Omega-3 and high fiber enriched diets would be beneficial, thus flaxseed can be recommended as a dietary supplement in whole seed and ground form. Besides, flax/flaxseed oil can be used in the enrichment of diets of animals for production of omega-3 enriched animal origin products. In the flaxseed, the absorption of nutrients is influenced by the content of cyanogenic glycosides, linatine and phytic acid. Although it is undesirable the presence of these compounds, some studies indicate that no apparent illness has been reported at the intake of 50 g/day. Flaxseed usage is generally recognized as safe (GRAS). FDA previously authorized the addition of flaxseed to foods while many governmental and public health authorities recommend an optimal health, an increase of omega-3 fatty acids in diet.

LIST OF ABBREVIATIONS

ACE	=	Angiotensin I–Converting Enzyme
ALA	=	α-Linolenic Acid, Omega-3 Fatty Acid
ARA	=	Arachidonic Acid
BP	=	Blood Pressure
CGs	=	Cyanogenic Glycosides
CKD	=	Chronic Kidney Disease
CVD	=	Cardiovascular Diseases
DHA	=	Docosahexaenoic Acid
DPPH	=	2,2-Diphenyl-1-Picrylhydrazyl Radical
DSP	=	Diastolic BP
EFAs	=	Essential Fatty Acids
END	=	Enterodiol
ENL	=	Enterolactone

EPA	=	Eicosapentaenoic Acid
FAs	=	Fatty Acids
GRAS	=	Generally Recognized as Safe
HCN	=	Hydrogen Cyanide
HDL	=	High-Density Lipoprotein
HMGA	=	3-Hydroxy-3 Methylglutaric Acid
PUFAs	=	Polyunsaturated Fatty Acids
RCTs	=	Randomized Controlled Trials
RDAs	=	Recommended Dietary Allowances
SBP	=	Systolic BP
SDG	=	Secoisolariciresinol Diglucoside
SECO	=	Secoisolariciresinol
T2D	=	Type 2 Diabetes
TAGs	=	Triacylglycerols

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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