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Flaxseed: A Treasure Trove of Potential Bioactives for Disease Prevention and Health Promotion

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Abstract: Bioactives from natural sources are increasingly gaining importance due to their uses in human food and animal feeds. The plant world represents a largely untapped reserve of bioactive ingredients, and considerable potential exists for exploitation of these bioactives as functional food ingredients and nutraceuticals. Substances such as polyphenols, lignans, ω-3 fatty acids, carotenoids, vitamins, minerals and peptides provide a myriad of health benefits. Flaxseed (FS) is the richest sources of bioactives such as α-linolenic acid, dietary fibre, protein and secoisolariciresinol diglucoside (SDG), due to which it is recently gaining much attention, because they act multifariously as anti-diabetic, anticancer, anti-tumor antioxidant, antimicrobial, anti inflammatory agents; reduce the risk of cardiovascular diseases and other degenerative diseases. This review focuses on the therapeutic potential and applications of FS bioactives viz. α-linolenic acid, SDG, dietary fibre and some poyphenolics against a number of human diseases and it can be recommended for consumers.

Key words: Flaxseed, Bioactives, Omega fatty acids, Lignans, Nutraceuticals, Chronic diseases.

I. INTRODUCTION

Bioactives are the substances occur in small amounts as natural constituents in plants, animals and microbes having biological effects on living organisms. These effects can be either beneficial or adverse, depending on the nature of the compounds and the dose or the bioavailability in maintenance of humans, animals and also plants health. Consumer's interest is being shifted towards the healthy eating for potential health benefits which can be gained from the different natural food sources. Polysaccharides, fatty acids, polyphenols, carotenoids, and phytosterols are the major bioactives experiencing a growing interest in wide range of their applications in commercial sectors such as pharmacology, food and chemical industries, biotechnology, nanoscience, cosmetics etc. [1]. The result of evolution of scientific research in the last few decades led to the field of functional food and nutraceuticals, an emerging area, concerning the potential applications of various natural bioactive components.

Bioactives are synthesized by a number of microbial sources such as fungi, bacteria, microscopic algae, actinomycetes etc. The therapeutic drugs from these microbes are developed throughout the world. Animals are also one of the sources of bioactives such as, polyunsaturated fatty acids (PUFA), carotenoids and polysaccharides, which exhibit a variety of biological functions on human health [2]. Plants are the richest sources of bioactives, commonly found in a vast range of foods consumed as a part of human and animal diets. Nutrients in plants are not included generally in the term 'Plant bioactives'.

They may be consumed via., the leaves, stems, roots, barks, flowers, tubers, buds, fruits, seeds and whole grains or consumed as plant derived food and drinks such as chocolate, tea, coffee and fermented foods such as wine and bread [3]. Polysaccharides, fatty acids, vitamins, proteins, sterols, glucosinolates, sulphur containing compounds, flavonoids, carotenoids and many phenolic compounds have been recognized as a major plant derived bioactives in diet. They help reducing risk for developing many chronic diseases including cardiovascular disease (CVD), cancer, arthritis, obstructive pulmonary disease, diabetes and obesity disorders [4,5,6,7].

For the last few decades, the evolution of scientific studies in the area of bioactives present in the flax plant and its seeds and oil emerged it as a prime source of Functional or Designer food or a Nutraceutical. In this respect, flaxseed represents a largely untapped reserve of considerable potential bioactive ingredients, which can be exploited as functional food ingredients.

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II. FLAXSEED

Flaxseed (Linum usitatissimum) is belonging to family Linaceae, a blue flowering annual herb that produces small flat, oval seed with a pointed tip, comprising of an embryo with two cotyledon surrounded by thin endosperm (Fig.1). Flax seeds (Linseed) are little larger than a sesame seeds, measure about 4-6 mm (Fig.2) and having crisp, chewy texture possessing a pleasant nutty taste [8]. The seed coat (hull) color ranging from yellow to dark reddish brown, often shiny and it is economically important food and fiber crop, cultivated in cooler regions of the world [9,10]. Currently, flaxseeds (FS) are cultivated in more than 50 countries, predominantly in the northern hemisphere. Canada is the world's largest producer and exporter while India is the sixth largest producer of FS [11]. In 2014, world production of FS was 2.65 million ton, led by Canada with 33% of the global total FS production [12].

Fig.1 Flax plant (A) Flaxseeds (B)

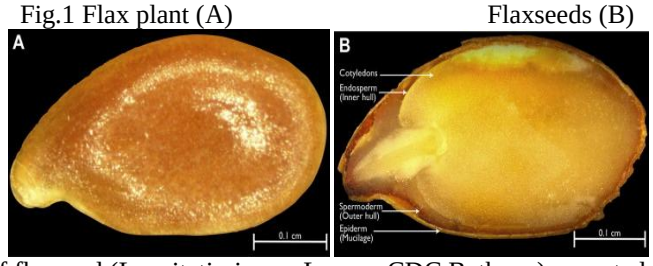

Fig.2 Hand-cut sections of flaxseed (L. usitatissimum L., var. CDC Bethune) mounted in distilled water showing anatomical structures. (A) The side of flaxseed. (B) Hand-cut section of flaxseed. Images were obtained (×1000 magnification) with a Canon Eos 300D digital camera mounted on a Zeiss Stemi SV 11 light microscope. The images were subsequently processed in Photoshop 7.
Courtesy: Shim et. al., 2014

Flaxseed is used in natural and industrial health products due to its various health beneficial promising components with multifarious effects. The bioactives of FS

Table 1: Proximate composition of flaxseeds[a]

Form of flaxseed	Weight (g)	Common measure	Energy in Kcal	Total fat (g)	ALA[b] (g)	Protein (g)	Total CHO[c,d] (g)	Total dietary fiber (g)
Proximate analysis	100	-	450	41.0	23.0	20.0	29.0	28.0
Whole flaxseed	180	1cup	810	74.0	41.0	36.0	52.0	50.0
	11	1tbsp	50	4.5	2.5	2.2	3.0	3.0
	4	1tsp	18	1.6	0.9	0.8	1.2	1.1
Milled flaxseed	130	1cup	585	53.0	30.0	26.0	38.0	36.0
	8	1tbsp	36	3.3	1.8	1.6	2.3	2.2
	2.7	1tsp	12	1.1	0.6	0.5	0.8	0.8
Flaxseed oil	100	-	884	100	57.0	-	-	-
	14	1tbsp	124	14.0	8.0	-	-	-
	5	1tsp	44	5.0	2.8	-	-	-

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

Courtesy: Morris, 2007

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include linolenic acid, linoleic acid, lignans, polysaccharides, cyclic peptides A and B, alkaloids, and cyanogenic glycosides. It is the richest source of α-linolenic acid and lignans, also an essential source of soluble mucilage, fiber and high quality protein and has considerable source of phenolic compounds [11]. Most studies on FS have mainly focused on extracts of FS containing ALA and lignans because other compounds have less attention. However, it is constituted by little levels of undesirable health compounds such as cyanogenic glycosides, phytic acid, phenolics, trypsin inhibitor, linatine, minerals, vitamins- tocopherol (α, β, γ forms), cadmium, selenium and cyclolinopeptides [14,15]. The proximate composition of FS is provided in Table 1. Owing to various beneficial effects, the FS is emerging as a potential source of functional food ingredients.

1. Health potential of flaxseed

Many studies have proved the beneficial effects of FS in believing the presence of three important components omega-3 fatty acids [α-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)], mainly ALA, lignans [mainly secoisolariciresinol diglucoside (SDG)] and fibers are nutritionally important.

Numerous studies have reported that there is evidence of protective effects on consumption of FS products such as whole flaxseed (WFS), ground FS, flaxseed oil (FO), fully and partially defatted meal (DFM), FS mucilage and flax hulls in the form of human food and animal feeds. These products are associated with specific health benefits attributed to the effects of the FS although each of them contained more than one bioactives. Many scientific evidences showed that human consumption of FS or FO could help preventing many diseases and disorders such as chronic, CVDs, cancer, obesity disorder, diabetes, arthritis and other health complications [4,6,7].

Flaxseed contains higher levels of lignans such as pinoresional, syringaresinol, lariciresional, secoisolariciresinol, matairesinol and hydromatarisinol among which SDG alone contributes highest proportion to the total content. Since, it is a functionally important principal lignan, specific attention has been focused on it due to its various potential biological activities.

2. Flaxseed lignan- SDG

Secoisolariciresinol diglucoside (Fig.3) is the main plant lignan found in FS at levels of 0.6% to 1.8% [18]. Secoisolariciresinol diglucoside found in FS as SDG oligomers, after ingestion by the action of intestinal colon bacteria, it is hydrolyzed to break the ester linkages for the release of SDG and the glycosidic bonds for the release of secoisolariciresinol (SECO) [19]. Secoisolariciresinol is metabolised to enterodiol and then to enterolactone. Matairesinol is also a FS lignan, metabolized to enterolactone. Other dietary enterolignan precursors include lariciresinol, pinoresinol, medioresinol, syringaresinol, arctigenin and sesamin. These FS lignans as well as the molecules enterodiol and enterolactone are metabolized by the body and excreted in the urine of mammals [20].

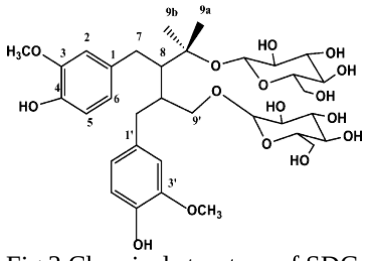

Fig.3 Chemical structure of SDG
Courtesy: Moree et. al.,2013

A. Extraction, Isolation and Purification of SDG

Current dietary guidelines on prevention of chornic diseases, including cancer and coronary heart diseases (CHD), recommend an increased intake of fruit, vegetables, seeds, oils, nuts, algae, microorganisms, marine products, and poly phenols, which are rich sources of bioactives with wide range of heath beneficial and disease preventive effects. Extraction, isolation and purification of SDG is conducted on WFS and DFM. Flaxseed lignan- SDG occur in ester-linkage form in the hulls enclosing the seeds, require special pretreatments including various steps and combinations of enzymatic, acidic and alkaline hydrolysis before extraction and analysis [22]. A variety of organic solvents such as methanol, ethanol, acetone, isopropanol, butanol and other chemical mixtures, and treatment with bases like sodium, calcium, ammonium and potassium hydroxides for liberation of SDG from FS polymer are used [23]. Further, structural elucidation of the extracted compound is confirmed by using infrared ray, mass and Nuclear Magnetic Resonance spectra [24,25]. The first report of laboratory extraction of SDG from DFM was given by Bake and Klosterman, using equal volume of 95% ethanol and 1,4-dioxane [26]. An effective method for purification of SDG from FS extract is by using aqueous ethanol with microwave irradiation [27]. Many studies on extraction of SDG from FS have used the methods involving time consuming, usage of organic solvents and high temperature which may cause damage to the products and finally resulting in lesser yield of the products or bioactives [28]. Now a days, high-

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throughput technologies like gas chromatography, high-performance liquid chromatography coupled with photodiode array detector and mass spectrometric procedures are being used to extract bioactives of FS, considering their potential in disease prevention and health promotion. Many studies have shown the benefits of consumption of SDG from any sources, contributes several health benefits such as prevention and treatment of diabeties [29], CVDs, cancer [30,31], atherosclerosis [32] and many other diseases and disorders.

B. Anti diabetic and antihypertensive activities of SDG

Secoisolariciresinol diglucoside is the main lignan, a phytoestrogen, present in FS known for its broad spectrum effects on human health. It shows antiviral, antibacterial, antifungal, anti diabetic, anti cancer and anti oxidant properties [30, 33, 34, 35, 36]. SDG having a great potential for reducing the incidence of type-1 diabetes and also retarding the development of diabetes, associated with increase in oxidative stress [37, 38]. Daily supplementation of flax lignan resulted in glycemic control in type-2 diabetic patients without affecting the fasting glucose, lipid profiles and insulin sensitivity [21,29]. Treatment with SDG proved its potential in neuropathic hyperalgesia and allodynia in mice with type-1 diabetes. Mechanistically, the analgesic actions of SDG in diabetic mice are associated with its antioxidant activity [39].

Peterson et. al., demonstrated that the flax lignan supplements showed beneficial effects with C-reactive protein and also suggested that the lignans have a possible lipid and blood pressure lowering associations [40]. Flax lignan concentrate exhibited antihypertensive effect via, modulation of endogenous enzymes in deoxycorticosterone acetate salt induced renal hypertension in rats [41].

C. Anti cancer/anti tumor properties of SDG

Several animal and human studies have demonstrated the protective effects of flaxseed against many cancers, including colon cancer, which is due to the presence of SDG [42]. Cell culture in animal studies have reported the inhibitory effects of FS on colon and skin cancers [43,44]. Flaxseed SDG and/or FO combined with tamoxifen helped in reducing MCF-7 tumor growth through estrogen receptor and growth factor-signaling pathways [45,46]. Dietary flax lignans and ALA in combination, especially SDG helps in decreasing cell proliferation and increasing in apoptosis resulted in the effective chemoprevention for intestinal and colon tumor development and reduced risk of certain types of cancer and CVDs [30, 47]. Flaxseed lignans exhibited reduction in the level of breast cancer risk [31,48]. Flax lignan complex supplementation potentially protects the normal lung parenchyma against radiation injury and also protects the cortical neurons by inhibiting the expression of glutamate [NMDA] receptor subunit epsilon-2 (GluN2B) and regulating the B cell lymphoma-2 family [49,50]. Boucher et. al., proved that the FS lignan, SECO helps to prevent breast cancer in woman [51]. It is effective in reducing the growth of human breast tumors (MCF-7) at high levels of circulating estrogen in athymic mice [52]. It is reported that SDG reduces acute asbestos induced peritoneal inflammation, oxidative, and nitrosative stress and also it acts as a promising agent in malignant mesothelioma chemoprevention [53].

D. Antioxidant activity of flaxseed lignan SDG

An In-vitro study showed that the SDG and its metabolites secoisolariciresinol, enterolactone and enterodiol possess antioxidant activity and SDG was effective in preventing lipid peroxidation of liver homogenate in a concentration dependent manner [54]. Protective effects of flax lignans in alleviating lead toxicity and lowering the incidence of coronary heart disease due to their antioxidant nature that combines free radical scavenging and metal chelating properties have been reported [55,56,57]. In our previous study, feeding of WFS and flax hull containing SDG showed antioxidant activity in carbon tetrachloride (CCl_4) treated albino rats and hepatoprotective effects on male wistar rats, respectively [33,34]. Secoisolariciresinol diglucoside and SECO both exhibited the strong antioxidant and protective effects in quenching the 2,2-diphenyl-1-picrylhydrazyl (DPPH) stable free radical and inhibiting 2, 2'-Azobis (2-amidinopropane) dihydrochloride (AAPH) peroxyl radical mediated damage of plasmid DNA and phosphatidylcholine liposomes [58,59]. Flaxseed lignan diet showed its protective effects against pulmonary fibrosis, inflammation and oxidative lung damage in murine model [60]. Additionally, effectively it slowed down the progression of atherosclerosis by 31%, which is associated with a reduction in oxidative stress [35].

SDG content in the dairy beverages and its products significantly improve the resistance to heat and light induced oxidation [61]. An In-vivo study has confirmed the antioxidant and free radical scavenging potential of naturally occurring (S, S)-SDG-1 (major isomer) and (R,R)- SDG-2 (minor isomer) [62]. Gaafar et al., reported that lignan extracts from different cultivars of FS exhibit high antioxidant potential for chelating with Fe^{2+} [63]. Ethanolic extract of FS lignan, SECO and its hydrolysate showed antioxidant activity in frozen storage of meat products by protecting them against lipid oxidation, deterioration of their nutritional quality, mayonnaise and dressing [64,65]. Genetically modified (GM) and non-GM flaxseed cake enriched with SDG, ferulic and kaempferol, p-coumaric acids, quercetin and their glycosyl derivatives significantly improved the total antioxidant status of mice serum and reduced the level of pro-inflammatory tumor necrosis factor (TNF-α) [66].

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E. Antimicrobial activity of SDG

Secoisolariciresinol diglucoside is the main lignan component of flax seed, exerts multifarious effects including antiviral, antibacterial and antifungal on human health. Genetically modified FS cake is an effective source of antibacterial compounds and the promising alternative to antibiotic therapy [36]. Ethanolic and hydrolysate extracts of FS exhibited antimicrobial activity against gram-positive (Bacillus subtilis and Staphylococcus aureus) and gram-negative (Escherichia coli and Pseudomonas aeruginosa) bacteria, which owe to the use of FS as a natural sanitizer [63,67,68]. Genetically modified FS cakes show antibacterial action with a broad spectrum and partial selectivity with highest activity against Pseudomonas aeruginosa and higher concentrations, inhibited the growth of even staphylococci and enterococci [69].

3. Flaxseed Omega -3 fatty acid- ALA

Fatty acid is a carboxylic acid with a long aliphatic chain, which is either saturated or unsaturated. Essential fatty acids (EFA) are essential for survival of humans and they are not synthesized in the body. Hence, they must be obtained through the diet [70]. Alpha linolenic acid, an ω-3 FA and cis-linoleic acid (LA), an ω -6 fatty acid are the major types of EFA. Marine organisms and phytoplankton are the primary sources of ω-3FA. Flaxseed, walnuts, algal oils, hemp oil and edible seeds are the major sources of ALA. Fish, FO, squid oil, krill oil and some other marine organisms are the major sources of EPA and DHA fatty acids [71]. Both ω-3 and ω-6 FA are required for the structure of cell membranes and various other biological processes. Arachidonic acid (AA) is a precursor for 2 series of prostaglandins, thromboxanes and the 4 series of leukotrienes. Alpha linolenic acid is converted to EPA by Δ-6-desaturase and Δ-5-desaturase. Eicosapentaenoic acid acts as a precursor for the 3 series of prostaglandins, thromboxanes and the 5 series of leukotrienes. Linoleic acid (LA), Gamma linolenic acid (GLA), di-homo-gamma linolenic acid (DGLA), AA, ALA, EPA and DHA are all PUFAs, but only LA and ALA are EFAs. Arachidonic acid and EPA are also converted to their respective leukotrienes. Prostaglandins, thromboxanes, and leukotrienes are biologically active and involved in diseases such as atherosclerosis, bronchial asthma, inflammatory bowel disease, and several other inflammatory conditions [70].

A. Extraction, Isolation and Purification of ALA

Several solvent methods [72], supercritical fluid extraction [73] and cold pressing are used for extraction of oils from the samples. Later, it was purified by using urea complexation [74,75], fractional distillation [76], Low temperature crystallization [75] for the separation of PUFA, free fatty acids and omega fatty acids, respectively. The obtained fatty acids are usually confirmed by using Gas chromatography–mass spectrometry (GC/MS) and NMR. Numerous scientific findings have proven the benefits on consumption of ω-3FA from any sources, help in the prevention and treatment of CVDs [77], hypertension [78], atherosclerosis [79], obesity [80], inflammatory diseases [81], diabetes mellitus [82] and other diseases and disorders.

B. Anti diabetic activity of flaxseed ALA

Dietary supplementation of mixture of ω-3FA from flax and ω-6 FA from sesame seed to pregnant diabetic rats helped in preventing diabetic complications in adult dams and their off springs [83]. Jangale et. al., proved the beneficial role and protective effects of ω-FA diet in potential complications in injured liver tissue of streptozotocin-nicotinamide-induced diabetic rats [84]. Daily consumption of FS and FO decreases the glucose concentration, and improves insulin sensitivity and lipid abnormalities in overweight individuals with pre-diabetes and type-2 diabetes [85]. Reduction in the damage caused by maternal hyperglycemia, promoting normal pancreas histomorphometry and β-cell mass in female offspring by FO is highly useful in the treatment of brain dysfunction in diabetes [86,87]. Co-supplementation of ω-3FA (FO) and vitamin-E in gestational diabetes women proved beneficial effects on glucose homeostasis parameters, serum triglycerides, very low density lipoproteins (VLDL)-cholesterol and high density lipoproteins (HDL) and HDL-cholesterol levels [88]. In another study, supplementation of ω-3FA (FO) to diabetic nephropathy patients resulted in decreasing the end products of the glycation in serum [89]. Flaxseed oil with trientine exerted its beneficial effects in controlling serum oxidative stress, lipid abnormalities, restoring heart structure, reducing serum copper (II) oxide (Cu^{2+}) helps in slowing down the progression of diabetic nephropathy associated with oxidative stress, glycation, and inflammation in the kidney of diabetic rats [90,91]. Diabetic patients with foot ulcer exhibited positive effects in the ulcer size, markers of insulin metabolism and wound healing when they were subjected to ω-3FA for 12weeks [92]. Vicente et. al., demonstrated that FO helps to reduce damage caused by maternal hyperglycemia by promoting normal blood pressure and elasticity of the aorta in female offspring rats [93].

C. Anti cancer/anti tumor properties of ω-3FA (ALA):

A study on FS proved that high dosage of ALA from FO is beneficial in delaying the growth of mammary tumors [94, 95]. Flaxseed oil helps in the reduction of cell growth across breast cancer cell lines with varying estrogen, and progesterone receptor, human epidermal growth factor receptor-2 (HER2) and also it enhances the effectiveness of trastuzumab (monoclonal antibody) in reducing HER2 in human breast tumors [9697,98]. Dietary combination of flax seed meal and FO are effective in inhibiting the formation of aberrant crypt foci in azoxymethane induced colon cancer

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in fisher male rats [99,100,101]. Flaxseed combined with tamoxifen exhibited its agonistic property by enhancing anti-estrogenic effect in premenopausal breast cancer patients and also reduced MCF-7 tumor growth through estrogen receptor and growth factor-signaling pathways [47, 46,102]. Bommareddy et. al., reported that the ALA and lignans from FS help in decreasing the cell proliferation level and increasing in apoptosis, which result in the effective chemoprevention of colon and intestinal tumor development [47]. In a case study, supplementation of 10% FS to laying hens for a period of one year resulted in a significant reduction in the severity of ovarian cancer [103]. Efficacy of prebiotics improved by FO showed potential against colon cancer and treatment [104]. Flaxseed helps in reducing PGE2 concentrations by blocking its expression which is a suitable target to reduce ovarian cancer [105].

Chamberland et. al demonstrated that ALA inhibits cell proliferation, adhesion and invasion in both human and mouse colon cancer cell lines [106]. Protective effect of FO against lung cancer metastasis and also detoxification of the enzymes in the dimethylbenzanthracene-croton oil induced skin carcinogenesis in mice model are reported [107,108].

D. Anti oxidant properties of flaxseed ω-3FA (ALA)

In a study on rabbit meat indicated that the dietary inclusion of linseed from 3 to 6% shows the improved product quality concerning lipid oxidation and sensory properties [109]. Combination of FS supplement and regular muscular exercises showed cytoprotective effect against oxidative stress and inflammation caused by acute myocardial ischemia [110]. Regular supplementation of combined vitamin E and phytosterols in FO exerted synergetic effects on improving plasma oxidative stress and ameliorate the lipid profile in high-fat fed rats [111]. Haliga et. al., reported that high dose of ground FS shows better cardioprotective effect by reducing total cholesterol, non-high density lipoprotein cholesterol (HDL-C) levels and increasing HDL-C levels in diabetic hamsters [112]. In a recent study, ability of the FO to counteract arsenic trioxide (As_2O_3) induced cardio toxicity and its maintenance in the proper balance between pro-oxidant and antioxidant defense systems in the cells are demonstrated [113].

E. Anti microbial properties of flaxseed ω-3FA (ALA):

Nand et al., suggested that ALA solvent extract from FS helps to suppress the acne causing bacteria and also antimicrobial screening indicated that the light petroleum extract was more active against Staphylococcus aureus and Propioni bacterium acnes [114]. In-vitro evaluation of antimicrobial effects of fixed FO against Staphylococcus aureus, Streptococcus agalactiae and Escherichia coli suppressed the activity while in-vivo study exhibited significant reduction in California mastitis test (CMT) score and somatic cell count (SCC) in milk samples from the udders infected with bovine mastitis [115].

4. Flaxseed dietary fibres

Dietary fibres are the type of carbohydrates found in FS and edible plant foods such as cereals, nuts, lentils, fruits, vegetables and legumes, which cannot be digested by our body enzymes. Total fibre content in the FS (functional and dietary fibres) accounts to 28% of its total weight. These fibers are grouped into soluble and insoluble [116]. Insoluble fibres do not dissolve in water and mainly found in foods like wheat bran, whole meal bread, nuts, vegetables etc. while, soluble fibres dissolve in water and mainly found in fruits, oats, beans and barley etc. Cellulose, hemicellulose and lignins are the insoluble fibres of FS help in adding bulk to stools by absorbing water, soften stools and shorten transit time through the intestinal tract, whereas, soluble fibres form a gel-like substance.

Consumption of dietary soluble fibers has been associated with health benefits such as lowering blood pressure and cholesterol levels, reducing risk of colon cancer, heart disease, diabetes, obesity and inflammation, losing weight, improving blood glucose control, treating various gastrointestinal disorders, controlling appetite and improving immune function [117,118,119,120,121,122,123,124].

A. Biological activities of dietary fibres

Flaxseed holds a unique place among all the oil seeds, due to its appreciable amount of dietary fibres present in the outer layers of the seed. It contains both soluble and insoluble dietary fibres (44). Flaxseed dietary fibers help to improve laxation, prevent constipation by increasing fecal bulk and reduce bowel transit time [125]. Water soluble fiber (mucilage gum) fraction of FS helps to maintain blood glucose level, improves liver functions and lowers blood cholesterol levels [126]. Dugani et. al., demonstrated that FS mucilage and FO reduce the number and length of gastric ulcers induced by ethanol in rats [127]. Incorporation of flax mucilage and ALA in the diet exerted cholesterol lowering effects, regulated blood sugar levels and helped to reduce diabetes [15]. Polysaccharides from FS reduced the risk in a variety of diseases such as lupus nephritis, hormone dependent types of cancer and arteriosclerosis [15,101,128]. A study on flax drink and flax bread rich in dietary fibers reported that they help in decreasing plasma total and LDL-cholesterol and increasing fat excretion [129]. Kristensen et. al., reported that dietary fibres extracted from FS help to reduce fat digestibility and apparent energy, resulted in restriction of body weight gain in growing rats [130]. Some studies have shown the effects of FS dietary fibre in suppression of the postprandial lipemia and appetite and

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unaffected subsequent energy intake [131,132]. Galvão et. al.,reported the beneficial effects of FS, oat bran and unripe banana flour to shakes help to reduce post-prandial glycemic response and FS alone helps in prevention of type-2 diabetes, which is attributed to its dietary fibre [133].

5. Phytochemicals of flaxseed and their biological activities

Flaxseed is reported to contain several phytochemicals such as phenolic acids, cinnamic acids, flavonoids and lignins. Total phenolic acids constitutes 8-10g/kg, out of which 5g/kg is esterified and 3-5g/kg is etherified phenolic acids. About 0.3-0.71g of flavonoids are also present in FS [134,135]. Many evidences have suggested that FS is a hub of natural antioxidants due to the presence of phenolic acids, which affect the cell growth and viability, and protect against many cancers and heart diseases [136].

III. CONCLUSION AND FUTURE ASPECTS

Considering the lengthening of life expectancy, our eating habits will be crucial in preventing diseases and promoting health in human. Flaxseed has nutritional and functional properties. The most important components of FS such as PUFA, lignans and dietary fibers, that have immense potential for use direct or in various food formulations have made FS as a complete functional food. Several research findings have shown that dietary supplementation of FS in livestock helped in increasing milk, meat and eggs qualities and also showed synergistic beneficial effects with oilseeds, cereals, microbial components, and some chemical drugs.

Many scientific findings are growing in support of FS consumption in the form of oil, whole seed, partially or fully defatted meal, hull, and mucilage help in prevention and/or treating many diseases and disorders related to diabetes, arthritis, CVDs, cancer, ulcer, obesity, and microbial infection. Thus, FS components with other bioactive molecules also show another platform to treat health complications in human and animals and proved it, a promising nutraceutical and functional food agent. Flaxseed bioactives could potentially develop as functional/designer food and nutraceutical agents, since their biological activities appear to influence the pathogenesis and clinical course of some chronic and cardiovascular diseases. Therefore, further research on FS bioactives is warranted in this direction in order to unravel their new preventive and potential therapeutic strategies against several chronic and degenerative diseases.

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