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REVIEWING FLAXSEED OIL: AN INSIGHT INTO EXTRACTION STRATEGIES, CHEMICAL COMPOSITION AND THERAPEUTIC IMPLICATIONS

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Abstract

Flaxseed has sparked a lot of attention as an edible and nutritional oil source due to its extraordinary protein level, high omega-3 fatty acid concentration, and potentially medicinal lignans content. One of the key components of flaxseeds is enriched oil content, which accounts more than 40% of their composition and is mainly responsible for dietary and nutritional significance. The bioavailability and health benefits of flaxseed constituents are greatly influenced by considerations such as the extraction process and the matrix in which they are contained. This article aims to review unique and advanced techniques used for extraction of flaxseed oil along with the comparison of maximum oil yield obtained from different procedures. This in-depth review, flaxseed oil is designed to highlight the correlations between the chemical composition of flaxseed oil and its potential physiological impacts with special reference towards heart, CNS, and bones. This study also represents summary of beneficial synergistic effects of flaxseed oil with other oils (olive oil & sesame oil) and medicines owing to its anti-inflammatory, antioxidant, antihypertensive and anticancer actions. This article offers the most recent and thorough investigation of lignan content of flaxseed oil and its potential health benefits for addressing a range of health problems. Additionally, efforts should be made to mitigate the presence of antinutritional factors in flaxseed oil and to develop innovative formulations and delivery systems that maximize their health benefits. Overall, flaxseed oil represents a favorable prospect for the expansion of functional foods and nutraceuticals aimed at improving human health and well-being.

Keywords: Flaxseed Oil, Lignans, Extraction Methods, Chemical Composition.

INTRODUCTION

Flaxseeds (Linum usitatissimumL.) belongs to the Linaceae family and is an annual herb. Flaxseed comprises two primary varieties: yellow or golden and brown (sometimes called

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golden linseeds, Figure 1), which are named after the Latin term for it, Linum usitatissimum L., which means "very useful" [1].

From 5000 BC, flaxseed, which obtained in Mesopotamia, has been grown and used, mostly for paper and cloth production, until the 1990s [2].

The entire structure of flaxseed is oval in shape, flat at the tips, and comprises a pair of embryos, an embryonic axis, a thin endosperm, and the seed coat, known as the hull [3].

A variety of components found within, including polyunsaturated fatty acids, proteins, lignan complex, cyclolinopeptides and polysaccharides [4, 5],

Constitute the main functional class of chemicals that impart therapeutic benefits. The components of flaxseed oil vary depending on the seed cultivar, region, climate, and analysis techniques [6].

Chemical composition

More than 40% of flaxseed, sometimes referred to as linseed, is oil. Its overall fatty acid content is about 57%, making it a valuable natural source of the ω-3 fatty acid which is β-linolenic acid (ALA). Its nutritional and health benefits are enhanced by this attribute [7]. Flaxseed oil mostly consists of linoleic and α-linolenic fatty acids [8]. Numerous antioxidants including tocopherols, phytosterols, polyphenols, beta-carotene and flavonoids are abundant in it [9].

The group of significant lipid-soluble phytocompounds known as tocopherols is primarily composed of four isomers: α, β, γ-, and δ. These chemicals have collection of biological functions, such as anticancer actions and antioxidant [10]. It has been found that the amount of protein of flaxseed varies between 20 and 35% [11].

Carbohydrates content (sugars and starches) is limited in flax; one gram (g) per 100 g is present. That is, the polysaccharide is comprised of two major portions: a neutral and an acidic arabinoxylan (75%) and rhamnogalacturonan (25%) respectively. D-galactose, D-galacturonic acid, L-rhamnose, and L-fucose acid make up the rhamnogalacturonan, while arabinose, xylose, and galactose make up the majority of the arabinoxylan [12].

The three main forms of flaxseed meal are crude, acid and neutral detergents, and total fibers (cellulose, lignine, and hemicellulose). It should be noted that the fiber content ranges from 22% to 26% [13].

Specifically, flaxseeds are the highest nutritional source of lignan precursors; the main lignan precursor present in flaxseed is secoisolariciresinol diglucoside [14]. Additionally, flaxseeds are comprised of minerals and vitamins, including phosphorus, calcium and magnesium(summarize in Table 1)[15].

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Table 1: Elemental and constitutional estimation of Flaxseeds

Chemical Components	Content of Constituents	Sub contents of constituents
Fatty Acids	Linoleic and α-linolenic acid	
Antioxidants	Tocopherols, Phytosterols, Polyphenols, Beta-Carotene Flavonoids	α, β, γ-, and δ
Protein		
Carbohydrates	Arabinoxylan Rhamnogalacturonan	D-galactose, D-galacturonic acid, L-rhamnose, L-fucose acid Arabinose, xylose, and galactose
Fibers	Cellulose, lignine, and hemicellulose	
Lignans	Secoisolariciresinol diglucoside lariciresinol, matairesinol and pinoresinol	
Added Contents	Minerals, Vitamins	Phosphorus, calcium and magnesium

Flaxseed: The Source of Lignan

Flax seeds are the leading source of lignans additionally to having significant concentrations of polyunsaturated fats and proteins [16]. In the seed coat of flaxseed, lignans are especially prevalent. [17] Higher concentrations of lignans are found in the hull alone than in the entire seed, indicating that this is where most of their production takes place [18]. SDG (secoisolariciresinol diglucoside) is the most predominant lignan of flaxseed, while more lignans (610 to 1300 mg per 100 g)— lariciresinol, matairesinol, and pinoresinol are present in smaller amounts—are unquestionably important [17, 19]. The coniferyl alcohol is the starting point for lignan production in plants. The occurence of dirigent proteins (DIR) causes the coupling of two units of this precursor to generate pinoresinol, which is then condensed to make lariciresinol and thereafter SECO (secoisolariciresinol). SECO is deprotonated to produce matairesinol, [20].

SECO constitutes higher proportion of the glycosylated lignans (95%) [21]. An oligomeric structure known as the lignan complex binds the SDG in flaxseed, in contrast to other lignans that are existing in freely form [18]. The 3-hydroxy-3-methylglugaric acid (HMGA) linkage holds SDG molecules together in a biopolymer that weighs around 4000 Da, with approximately 35% of its weight composed of SDG molecules. The biopolymer is composed of five SDG and four HMGA units [22]. The lignan complex has been found to contain the hydroxy-cinnamic acids, ferulic acid coumaric acid glucoside, herbacetin diglucoside and glucoside in addition to SDG and HMGA [23]. Because of this, there is significant variation in the amounts of SDG and SECO that are measured in flaxseed (and other matrices) depending on the cultivar, harvest year, and type of treatment the matrix received prior to analysis. In fact, the yield of lignans is significantly influenced by the extraction process. Treatments with alkali and acids in extreme circumstances can be harmful or result in other lignans [24]. In order to maximise lignan yields and simultaneously limit the extraction and concentration of harmful or antinutrient chemicals, makers of supplements or nutraceuticals must implement a lignans recovery method [25].

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Phytic acid, cyanogenic glycosides, and linatine are examples of antinutritional chemicals found in flax seeds in addition to their beneficial components [19]. There are no negative consequences linked to the direct ingestion of flax seeds reported in the scientific literature. However, if concentrated during the bioactive chemical extraction stages from flaxseed cake or flaxseeds following oil removal, these antinutrients may become hazardous at high concentrations [17]. The nutritional content of flaxseeds is also compromised by their presence in terms of bioavailability and bioaccessibility. Therefore, it is essential to use detoxification methods that can break down or eliminate these antinutrients [26]

Biological Properties of Lignan

Since lignans are phenolic compounds, they possess a potent antioxidant potential, which is directly linked to their positive benefits on human health [17]. Furthermore, secoisolariciresinol (SECO) and the other lignans (matairesinol, pinoresinol and lariciresinol) present in flaxseed are precursors of mammalian oestrogen that are transformed by the an-aerobic intestinal microbiota into enterolignans, enterolactone and enterodiol [27].

It is now known that lignans have cholesterol-lowering properties [4, 28, 29] , antiviral [30], anticancer [31, 32], antioxidant [33, 34], supplemental for improved muscular performance [35], anti-inflammatory [20] antidiabetic [36, 37], estrogenic and anti-estrogenic [38, 39], , anti-depressant [40, 41] , anti-bacterial and anti-fungal. Lignans are considered as a valuable defensive component against the progress of diseases caused by production of free radicals by oxidation of lipids in human body, carbohydrates, and proteins because of their phenolic features that enable them to play a crucial role as "hydroxyl radical scavengers". Free radicals cause harm to tissues, membrane lipids, proteins, and nucleic acids. They are also known to cause cancer, neurological disorders, lung illness, diabetes, and premature ageing [19].

Lignans can aid in the treatment of malignancies associated with hormone metabolism because of their resemblance to mammalian oestrogens [22]. These substances have the ability to attach to oestrogen receptors and modify the actions of oestrogens, namely decreasing their bloodstream circulation and biological activity, which lowers the risk of cancer [22]. Given that they can affect intracellular enzymes and protein synthesis, as well as promote the liver's generation of sex hormone-binding globulin and lower the concentration of free hormones in plasma, their mode of action seems to be considerably more complex. Additionally, they can function as steroidal-metabolizing enzymes inhibitors and interact with sex binding proteins (steroids), possibly protecting against colon and breast cancers. Because zinc transporters are expressed at a higher level in breast tumor cells comparative to normal cells, secoisolariciresinol di glucoside (SDG) has been proposed to have a preventive effect in the particular case of breast cancer. Moreover, enterolactone, a metabolite of SDG, has the ability to inhibit the growth, migration, and metastasis of cancer cells [16].

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Lignans specifically block the action of aromatase in the fat cells of postmenopausal women. The outcome is clearly seen in the decline in blood levels of sex steroid hormones and circulating oestrogen, both of which are linked to the onset of breast cancer [16]. Because lignans, especially SDG, are powerful antioxidants, they can decrease oxidative stress linked to metabolic syndrome and lower the probability of lupus nephritis, lipid peroxidation oxidative and DNA damage [18]. One important function of flaxseed, especially its oil, which is high in lignans, ALA, and fibre, is to decrease cholesterol. As specific modulators of the oestrogen receptor, lignans can lower blood levels of triglycerides and LDL cholesterol (the "bad" cholesterol) while bringing HDL cholesterol back to normal [28]. Thus, the risk of cardiovascular disease is significantly decreased by flaxseed lignans. SDG in particular has the ability to stop or slow down the development of atherosclerosis, which in turn can stop coronary artery disease, peripheral vascular disease and stroke [16].

Additionally, lignans contain antiglycemic activity, which reduces the blood's glycemic response and prevents the onset of type 1 and type 2 diabetes [36]. In addition to flaxseed fibres' impact on insulin secretion and plasma glucose homeostasis, lignans also have antidiabetic effect. SDG may actually help lower the prevalence of type 1 diabetes and postpone the onset of type 2 diabetes by lowering the levels of C-reactive protein in humans, which is linked to insulin resistance in type 2 diabetes and glucosuria [18]. Furthermore, lignans actively contribute to a decrease in obesity by extending satiety [17].

Other known positive benefits on human health include great efficacy in preventing rheumatoid arthritis, immunomodulatory action, anti-leishmaniosis activity, and inhibition of 5-lipoxygenase. They have the ability to attach the cytoskeleton tubulins, which allows them to disrupt viral replication and provide a significant antiviral effect. They also effectively prevent RNA viruses from replicating because they inhibit reverse transcriptase [21]. Additionally, because pro-inflammatory cytokines like TNF- and IFN- are produced by the body at these times and lead to mood swings, lignans may help lessen the symptoms of stress and depression. Two polyunsaturated fatty acids that mitigate such mood swings, EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), appear to be produced more when lignans are consumed [16].

There are impacts of SDG on mental stress. Giving SDG to ovariectomized mice prevented behavioural abnormalities brought on by stress and undid the rise in cortisol and adrenocorticotropic hormone levels in the serum brought on by prolonged stress [40]. Furthermore, women (postmenopausal) with vascular disease who had signs and symptoms of stress because of having to complete cognitive tasks were examined to determine the effects of three flax cultivars with varying lignan contents. During the stressful time, the women's blood pressure was dramatically lowered by lignan intake; specifically, the cultivar with the highest lignan content decreased plasma cortisol levels more and elevated plasma fibrinogen levels far less than the other cultivars [16].

As lignans bind strongly to oestrogen, research has examined and determined that lignans may have a significant impact on the reproductive system. It is important to focus

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the use of flaxseed during pregnancy and lactation even though more research is required. While there were no negative impacts on mothers' or children's selective reproductive indices, the early results are encouraging in that lignan intake during nursing decreased susceptibility to mammary carcinogenesis later in life (Figure 2) [18]. Although the abundance of available data and the understanding of numerous lignan-related processes, additional research is still required to address open-ended issues (toxicity, bioavailability), as well as to gain a deeper comprehension of the function of lignans in maintaining health and preventing disease. This will enable the development of appropriate dietary recommendations and pharmaceutical or nutraceutical items that can aid in the anticipation of cancer and cardiovascular diseases. Consequently, in order to have significant amounts of pure lignans for in vitro and in vivo research as well as clinical studies, lignan extraction, purification, and analysis methods will need to be set up and optimized [16].

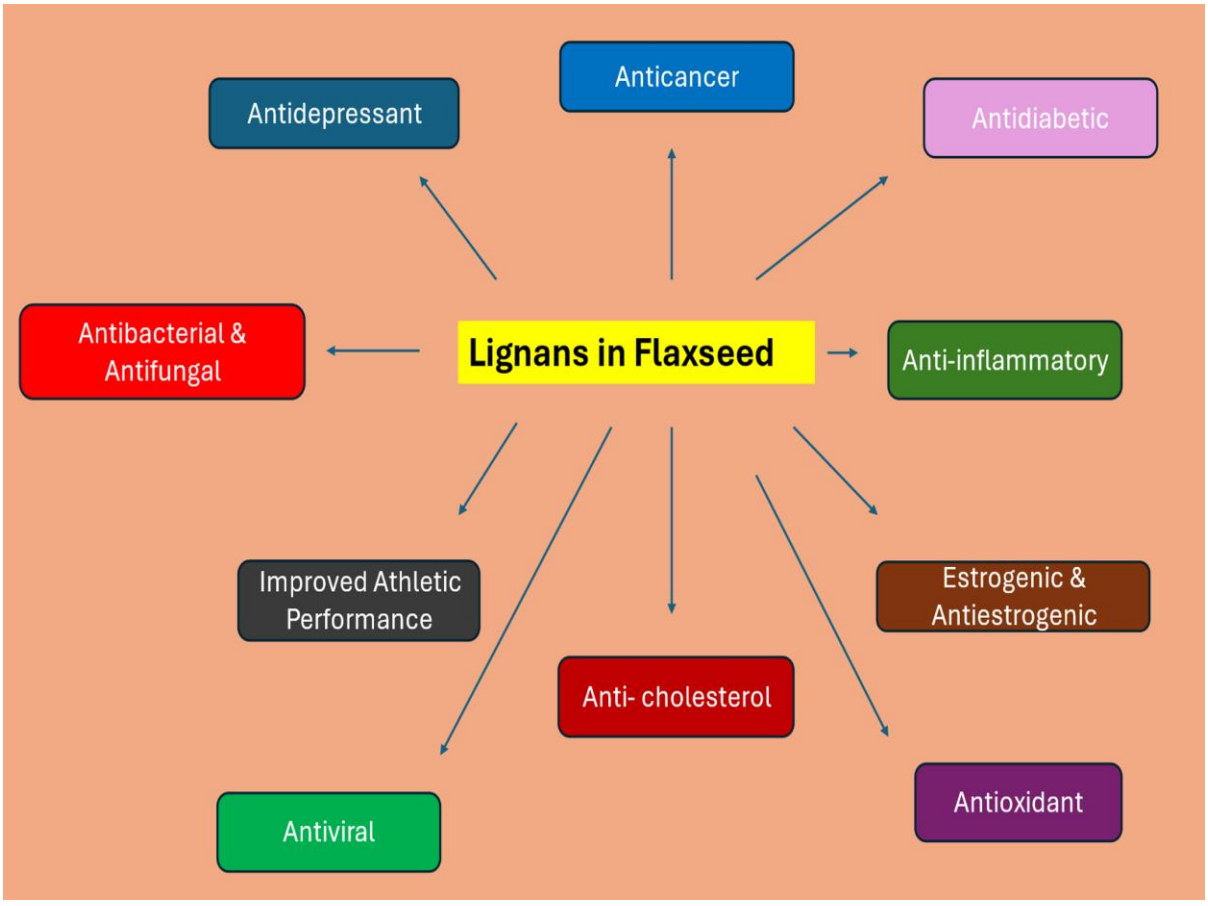

Figure 2: Biological properties of Lignans in flaxseed oil

Different Strategies Used for Extraction of Flaxseed Oil:

Different extraction techniques and solvent varieties (petroleum ether, diethyl ether, and n-hexane) can be used for extraction.

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Some of the extraction techniques are discussed below:

1. Three Phase Partitioning Technique:

While other biomolecules like proteins and pigments are the byproducts that are simultaneously obtained utilizing TPP, oil seeds are the primary target for oil extraction [42].Protein-containing aqueous solution is treated with a salt (such as ammonium sulphate) and a water-miscible aliphatic alcohol (such as t-butanol) in a straightforward innovative bio separation and purification process called three phase partitioning (TPP) [43]. Ammonium sulphate causes complex ionic interactions that are osmotrophic, osmotic and colloidal in nature. As a result, t-butanol, which is normally soluble in the aqueous phase, becomes unsolvable, forming three layers above which proteins float due to their increased buoyancy [44]. This procedure has also been used for extracting oil from Oleaginous materials, including turmeric oleoresin [45], oleoresin from ginger [46], soyabean [47], rice bran oil from protein [48], jatropa [49].It is also been used to isolate and purify numerous enzymes such as zingibain from Zingiber officinale [50], peroxidase from Citrus sinenses [51], serratio-peptidase from Serratia marcescens [52].

The procedure that must be used to extract oil is explained in [53] .To maximize the extraction yield, the temperature, salt concentration, and t-butanol concentration were all adjusted. A maximum extraction yield (71.68%) was achieved under ideal conditions, which included a concentration of t-butanol (49.29%), a concentration of ammonium sulfate (30.43%), and an extraction temperature of 35 °C [54]. Since the flaxseed can be hydrolyzed using an enzyme solution (protease), this technique is also sometimes referred to as "enzyme-assisted three phase partitioning" (EATPP). This is because the slurry sample's influencing parameters, such as temperature, pH, and enzyme type and concentration, were optimized during the enzymolysis process [54].

2. High Performance Liquid Chromatography (HPLC):

The extraction and identification of various lignans and phenolic compounds are the main applications of the HPLC technology. Flaxseed contains a variety of phenolic compounds, including tannins, phenolic acids, flavonoids, and phenylpropanoid glucoside [55]. The objective to develop and test a novel technique that entailed quantifying the outcome using a reverse-phase HPLC system along with UV detection after removing herbacetin Di glucoside (HDG) from flaxseed cakes using microwave-assisted extraction (MAE) is carried out in [56].A Varian liquid chromatographic machine was used to quantify the chemicals [57]. In milled, defatted flaxseed flour, [58] Investigated the secoisolariciresinol Di glucoside (SDG) and hydroxycinnamic acid glucosides using HPLC. Both direct alkaline hydrolysis and the use of dioxane-ethanol followed by hydrolysis were used to achieve the extraction. As can be seen from the results, straight alkaline hydrolysis produced a higher yield. The findings indicated that the levels of SDG and phenolic glycosides in Swedish flaxseed samples varied greatly [59]. Additionally, also analyzed secoisolariciresinol diglucoside using high performance liquid chromatography. Using the HPLC method, cyclodipeptides were also extracted from samples of flaxseed oil [60, 61].

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3. Pressurized Low Polarity Water Extraction:

Pressurized low polarity water extraction(PLPW), or subcritical water extraction, is a technique that improves the extraction ability of water by raising its temperature to 374 °C and maintaining a high pressure to keep the water in its fluid state [62]. The whole flaxseed was subjected to PLPW extraction in order to extract lignans and beneficial components. In order to extract the chosen polyphenols, the effects of various process parameters, such as the ideal flow rate, temperature, and total volume, were investigated [55].

4. Ionic - Liquid Based Ultrasonic Assisted Extraction:

Extensive research has shown that ionic liquid-based ultrasonic-assisted extraction (IL-UAE) is an effective process for extracting active compounds from natural plants [63] such as liquiritin, glycyrrhizic acid and isoliquiritigenin from licorice [64], alkaloids from Phellodendron amurense Rupr [65], and forskolin from Coleus forskohlii roots [66].For the extraction of SDG and bioactive plant components, the ideal parameters include pH(11), temperature(22 °C), IL(45.86%), and Na_2SO_4(8.27%), in which the extraction efficiency was determined to be 93.35% [55].

5. Microwave-Assisted Extraction:

By means of molecular interaction with the electromagnetic field, the microwave technology may supply energy directly to materials, save energy, and shorten processing times. Therefore, oil has been extracted from various agri-food sources using MW-assisted and MW pre-treatment as an example [67] citrus peels [68], sesame [69] and hazelnuts [70]. The impact of MW pre-treatments on flaxseed was examined in [67]. The findings demonstrated that, in comparison to untreated flaxseed, the yield of flaxseed oil extraction rose dramatically with MW pre-treatments. In order to extract SDS, p-coumaric acid, and ferulic acid, applied the microwave assisted approach [71].

6. Soxhlet Extraction

In this method oil was obtained using a Soxhlet equipment. The extraction process made use of both polar and non-polar solvents. Commercial solvents were procured for the extraction process. To extract oil, six distinct polar and non-polar solvents were utilized. Hexane was the non-polar solvent utilized for extraction, whereas methanol, n-Butanol, acetone, isopropanol and ethanol were the polar solvents used. Using the AOAC standard procedure, the oil was extracted [72].

A thimble containing five grams of ground flaxseed was put in the Soxhlet apparatus along with a water condenser and a round bottle flask. Using polar (methanol, acetone, n-butanol, isopropanol, and ethanol) and non-polar (hexane) solvents, the oil seed extraction was carried out for four hours at a temperature of 70°C. Following the extraction, the solvent-containing extractor was put inside a rotating evaporator to vanish the solvent. The oil was obtained and refrigerated for additional examination [73].

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The most significant benefit of the Soxhlet procedure, which is a solid-liquid extraction technique, is that the sample and solvent are in constant contact, which helps redirect the transfer balance of constituents in the solvent's favor. When compared to other methods, the Soxhlet extraction has fewer drawbacks, such as the prolonged extraction time and the need for considerable quantities of solvent. Furthermore, samples are heated to the solvent's boiling point for extended periods of time, which creates the potential for some oil constituents to thermally decompose [74].

7. Accelerated Solvent Extraction (Ase)

A contemporary method of extracting oil that uses organic and/or aqueous solvents at high temperatures and pressures is called accelerated solvent extraction (ASE), sometimes known as pressurized solvent extraction (PSE). High pressure allows solvent to boil at temperatures higher than its normal boiling point, as higher temperature speedsup the extraction process. Comparing this method to other solvent extraction procedures, time and solvent consumption are greatly decreased. Wheat germ [75] and flaxseed hulls [76] are two materials that have been extracted using ASE.[77].

8. Ultrasound Methods

Ultrasound therapy, which employs high-frequency sound waves between 20 and 40 kHz, helps plant materials undergoing extraction procedure liberate their oil from the walls of its cells. Usually, ultrasonic waves of higher frequency that are inaudible to the human. The resultant vibrations cause the material to expand and compress. This oscillating motion creates hollow spaces or bubbles in the liquid where the wavy movement raises the temperature and breaks the surface tension.

The mass transmission of solid constituents into the solvent that is exposed to ultrasound is therefore a key component of this extraction method, which employs convection in the solid component's pores and diffusion across the cell wall as modes of transport. As a result of the ultrasounds' continual vibration and propulsion of solid and liquid particles, the solute from the solid phase shifts quickly into the solvent [74].

9. Mechanical Oil Extraction:

Commercially, oils from vegetables and plant parts are extracted out through mechanical processes such as screw pressing; however, because of the current equipment and advanced techniques, the oil extraction efficiency is rather low (<70%) and is therefore deemed unsatisfactory [78].

The results of a study investigating the impact of applying single, double, and triple presses on the quality of linseed oil extracted mechanically show a progressive increase in oil yield from 19.2 ± 1.5% to 31.9 ± 0.2% when presses are applied in the following order: single, double, and triple pressed linseed oil [79].

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10. Oil- Assisted Extraction:

A research investigation conducted to examine the impact of moisture concentration on oil yield using mechanical screw pressers, organic solvent-based extraction, microwave assisted and organic solvent-based methods, ultrasonic-assisted and organic solvent-based techniques, and a hybrid of organic solvent with ultrasonic and microwave-assisted procedure showed maximal oil outputs of 22.6%, 36.3%, 10.0%, 42.0%, and 27.8% w/w, respectively [80].

Impacts of Flaxseed Oil on Different Aspects of Human Body:

- **Effect on Bone and Skeletal Muscles:**

The rate-limiting phase in the oxidation of fatty acids in skeletal muscle is thought to be the passage of lipids over the sarcolemmal membrane. The lipid makeup of the plasma membrane and its ability to transport palmitate are impacted using flaxseed oil enrich in α-linolenic acid. The entire muscle and sarcolemmal membranes of rats given a meal supplemented with 10% α-linolenic acid exhibited a five-fold rise in polyunsaturated fatty acids (omega-3 PUFAs). Additionally, increases in the rates of sarcolemmal palmitate transfer (20%), total body oxidative fat (~50%), and triacylglycerol concentration (twofold) in skeletal muscle were noted [81].

Increased femur bone mineral density, fatty acid composition and bone strength, have all been reported to benefit from PUFA-rich diets, such as those that include flaxseed oil. Rats aged 6 to 15 weeks that were fed diets rich in omega-3 polyunsaturated fats had stronger femurs than the rats who were fed chow[82]. Conversely, rats were used to evaluate the impact of flaxseed oil on bone injury brought on by a high-fat diet. The results showed that the oil reduced trabecular bone damage, enhanced osteoblastic activity, and stimulated osteogenesis.

- **Effects of Flaxseed Oil on Heart:**

It is anticipated that the size of the hypotensive impact will significantly lower the overall risk of CVD in patients with dyslipidemia, and that it is clinically important [83]. Flaxseed oil has been shown to have positive health impacts, such as lowering cholesterol and minimizing cancer risk. It also possesses cardioprotective properties [84].

- **Effects on CNS:**

The growing astrocytes is closely associated with oils high in ALA, like flaxseed. Additionally, DHA affects healthy and visual cognitive development. The ALA included in flaxseed oil demonstrated both a neuroprotective and a neuroplastic impact [85].

- **Anticancer activity:**

Antioxidants are abdundant in natural compounds[86]. and anticancer compounds as well, which have been documented from plant sources[87]. Numerous investigations documented flaxseed oil's cytotoxic potential against various kinds of cancer cells.[88,

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89]. In vitro studies revealed that α-linolenic acid, and its metabolites, EPA and DHA, can suppress the proliferation of breast malignant cells. [90].

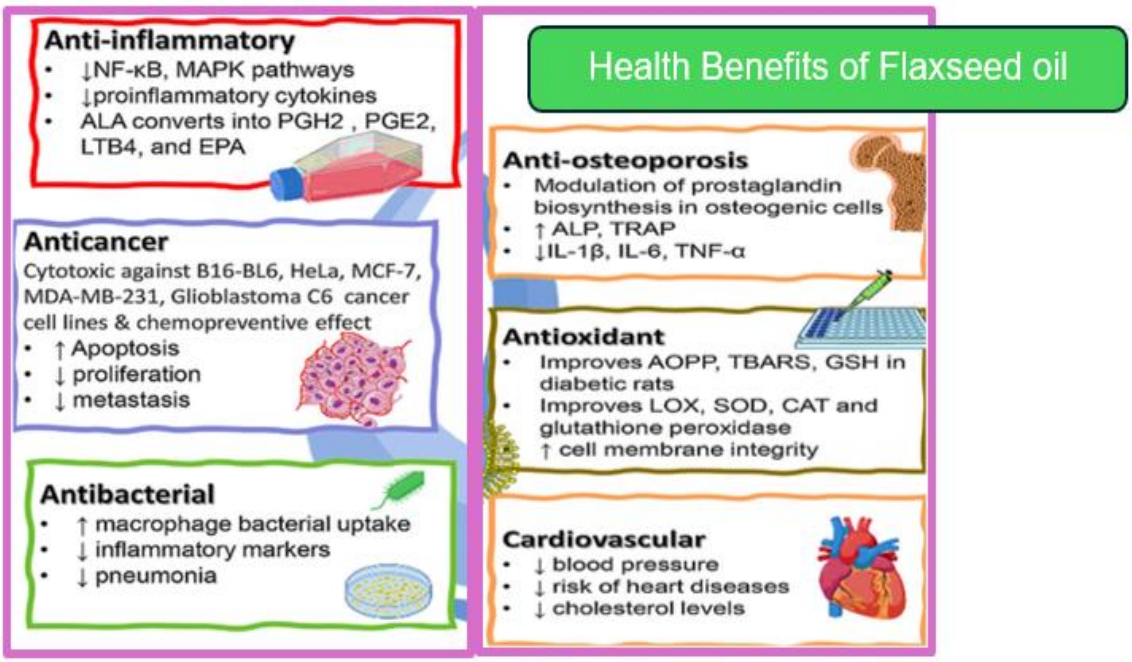

Figure 3: Beneficial effects of flaxseed oil in various parts of human system

Combined Effects of Flaxseed Oil with Other Oils Medicines:

- **Flaxseed oil with olive oil; a synergetic anti-inflammatory effect**

According to a study, olive oil and flaxseed oil affect wound healing and inflammatory indicators. During the three-week trial, 112 burn patients were split into four groups—the one on flaxseed oil, other took olive oil, the group that received both oils in combination, and the control group—and given 30 g of each oil. The outcomes demonstrated that the combination of olive and flaxseed oil (− 21.38 ± 44.41) (− 132.79 ± 165.36) had the greatest drop in serum high-sensitivity C-reactive protein levels, whereas the control group (− 36.36 ± 79.03) (141.08 ± 262.36) exhibited the least amount of reduction [91].

- **Flaxseed oil with sesame seed oil and coconut oil; a synergistic antioxidant effect**

It has been shown that flaxseed and sesame seed oils work synergistically to protect rats' livers from damage caused by carbon tetrachloride. Both oils' ω-3 and ω-6 FAs demonstrated noteworthy hepatoprotective and synergistic antioxidant effects. Increased in vivo antioxidant enzymatic action, including those of peroxidase, superoxide dismutase and catalase , were indicative of these outcomes [92]. When added as a supplement alongside coconut oil, flaxseed oil further demonstrated a synergistic antioxidant impact [93].

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- **Flaxseed oil with ACE inhibitor; a synergistic antihypertensive effect**

Rats with spontaneous hypertension who were 7 weeks old had their blood pressure lowered when ALA-rich oils and angiotensin-converting enzyme inhibitors were administered. When rats were administered ALA together with ACE-I, their systolic blood pressure was considerably lower than it was before to delivery [94].

- **Flaxseed oil with Doxorubicin; a synergistic anticancer activity**

Another synergistic effect was described in which doxorubicin plus a phenolic extract from flaxseed oil caused MCF-7 cells to become cytotoxic, undergo apoptosis, depolarize their mitochondria, and alter their cell cycle. This combination could indicate that cancer patients' doxorubicin dosages should be lowered in the future [95].

CONCLUSION

Flaxseeds, also known as linseeds, are renowned for their nutritional richness, offering a plethora of health-promoting compounds that make them a valuable addition to the diet. One of the key components of flaxseeds is their high oil content, which accounts for more than 40% of their composition. This oil is predominantly composed of polyunsaturated fatty acids, with a notable proportion being alpha-linolenic acid (ALA), an omega-3 fatty acid known for its various health benefits. In addition to ALA, flaxseeds are rich in lignans, which are phenolic antioxidant compounds. The bioavailability and health benefits of flaxseed lignans are influenced by reasons such as the extraction process and the matrix in which they are contained. Various extraction techniques, including three-phase partitioning, high-performance liquid chromatography, and microwave-assisted extraction, etc have been developed to isolate and purify lignans from flaxseeds. These techniques aim to maximize the yield of bioactive composites by minimizing the extraction of unsuitable components.

In addition to lignans, flaxseeds contain other functionalised compounds such as tocopherols, beta-carotene, phytosterols, polyphenols, and flavonoids, each contributing to their overall nutritional value and health-promoting effects. These compounds work synergistically to exert beneficial effects on human well-being, including reducing inflammation, lowering cholesterol levels, and improving glycemic control. Looking to the future, further research is necessary to explore the synergistic effects of flaxseed with other dietary components and medications, as well as to optimize extraction techniques to enhance the bioavailability and bioactivity of flaxseed bio actives.

Conflict of Interest

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