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Review Article

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Flaxseed Oil and Its Chemical Composition: A Comprehensive Review of Associated Health Benefits

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Abstract

Flaxseed (Linum usitatissimum L) is a time-honored perennial plant species known for its versatility, primarily due to its high content of omega-3 polyunsaturated fatty acids (PUFA), such as α-linolenic acid (ALA). Detailed biochemical studies of flaxseed have led to the discovery of its bioactive compounds, particularly lignans, which hold promise for enhancing human health. The oil, fibers, and lignans derived from flaxseed offer potential health advantages, including the mitigation of cardiovascular disease, atherosclerosis, diabetes, cancer, arthritis, osteoporosis, and various autoimmune and neurological disorders, thereby expanding the plant's range of applications. This review centers on flaxseed oil as the primary product highlighting the connection between its chemical makeup and its biological effects. This study provides a comprehensive overview of the effects of flaxseed oil, detailing the mechanisms of action associated with its phytochemical composition and comparing it to other oils. This study offers the most current and exhaustive review, summarizing the health benefits of flaxseed oil for treating various diseases.

1. Introduction

Flaxseed or linseed (*Linum usitatissimum*), is part of the Linum genus in the Linaceae family. It has been used for centuries in painting, varnishing, and treating medical conditions like respiratory issues, constipation, abdominal discomfort, urinary infections, and skin inflammation [1]. Flaxseed typically yields 35–45% oil, containing 9–10% saturated fatty acids (palmitic and stearic), about 20% monounsaturated fatty acids (mainly oleic acid), and over 70% α-linolenic acid. Its protein content ranges from 20 to 30% and dietary fiber can reach 28% [2]. Flaxseed oil's components vary by seed cultivar, location, environmental conditions, and analytical methods [3]. Known for health benefits, it is a rich plant-based source of polyunsaturated omega-3 fatty acids, particularly linoleic and α-linolenic acids [4]. Ingested linoleic acid (LA; 18:2n26) and α-linolenic acid (ALA; 18:3n-3) undergo desaturation and elongation to form 20-carbon fatty acids. Linoleic acid (n-6) becomes arachidonic acid, while α-linolenic acid (n-3) converts into eicosapentaenoic acid (EPA). Arachidonic acid is a precursor to PGH2, converted into PGE2 and TXA2 by cyclooxygenase, and to LTA4, converted into LTB4 using 5-lipoxygenase [5]. EPA, an n-3 homologue, can inhibit arachidonic acid metabolism through competitive inhibition and acts as a substrate for 5-lipoxygenase, forming LTB5, which has milder inflammatory activity than LTB4 [6]. α-Linolenic acid is used as an anti-inflammatory agent by reducing inflammatory cytokines, lipids, and lipoproteins [7]. Inhibiting proinflammatory cytokines affects bone resorption by promoting osteoclast proliferation and activation, and stimulating osteoblasts to release osteoclast differentiation factors [8]. Linolenic acid also has antimicrobial properties, inhibiting bacterial enoyl-acyl carrier protein reductase [9]. Flaxseed oil's health benefits include lowering cancer and cardiovascular disease risks and reducing cholesterol [10]. It also shows antioxidant activity, depending on chemical components like tocopherols, beta-carotene [11], phytosterols, polyphenols, and flavonoids [12]. Tocopherols, important lipid-soluble phytocompounds, mainly exist in four isomers: α, β, γ, and δ, possessing antioxidant and anticancer effects [13]. Tocopherols' antioxidant activity is due to donating phenolic hydrogens to lipid free radicals, with effectiveness α > β > γ > δ [14].

2. Aim of review

The primary aim of this review is to highlight the health advantages of flaxseed oil, comparing them to those derived from whole seeds, in relation to its chemical makeup by demonstrating cell-based studies, animal experiments, clinical trials, such as antioxidant, anti-inflammatory, antimicrobial, anticancer, antiulcer, anti-osteoporotic, cardioprotective, and neuroprotective.

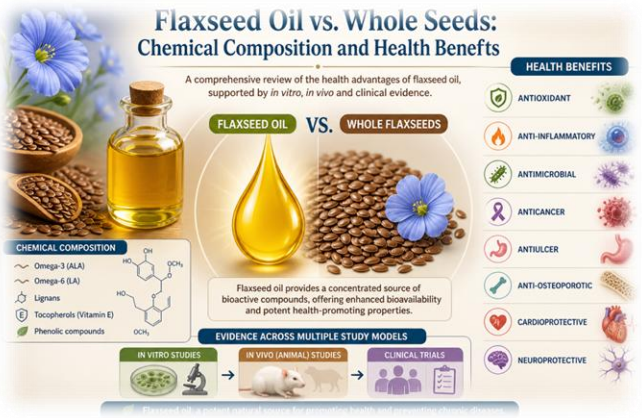

Fig1. Outline of the review

3. Methods

We reviewed the literature on flaxseed oil's health benefits and searched databases like Web of Science, PubMed, Scopus using terms such as flaxseed oil and specific biological effects: antioxidant, anti-inflammatory, antimicrobial, anticancer, antiulcer, anti-osteoporotic, cardio-protective, neuro-protective, and metabolic syndrome.

4. Flaxseed oil vigour assistance

4.1 Cardiac vulnerability

The beneficial impact of polyunsaturated omega-3 fatty acids on reducing heart disease risk is well-documented [15,16,17]. Research shows eicosahexaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3), the main components of cold fish oil, are linked to lower cardiovascular risks like arrhythmia [18, 19], sudden cardiac death [20], and atherosclerosis [21]. Flaxseed oil is rich in α-linolenic acid, a natural precursor to EPA and DHA. EPA and DHA levels in erythrocyte membranes rise with fish oil and flaxseed oil supplementation, proportional to dosage. Flaxseed oil led to a 133% EPA increase and a 120% DPA increase ($P < 0.05$ and $P < 0.01$) without changing DHA levels [22]. Flaxseed oil's cardiovascular benefits are mainly due to its lipid-lowering and antioxidant effects [23, 24].

4.2 Metabolic activity

The beneficial effects of omega-3 fatty acids in lowering the risk of cardiac arrhythmia and sudden death among coronary heart disease patients are well-documented additionally, to manage hyperlipidemia and hypertension [25]. The hypocholesterolemic properties of α-linolenic acid from flaxseed oil are also well recognized [26].

Study ON flaxseed oil's impact on blood lipids, atherosclerosis, serum malondialdehyde, aortic chemiluminescence, and ROS in rabbits on a high-cholesterol diet. Serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, serum malondialdehyde, and antioxidant markers increased similarly in both the 0.5% cholesterol diet group and the group with 0.5% cholesterol and 5% flaxseed oil, compared to the control and 0.5% flaxseed groups. The ROS activity of white blood cells rose in the 0.5% cholesterol group, but flaxseed oil prevented this increase [27]. Other studies confirmed plasma lipid profile and tissue lipid composition improvements [28, 29, 30].

In a clinical study compared effects of hempseed and flaxseed oils on serum lipids, plasma glucose, insulin, and hemostatic factors in 14 healthy individuals consumed oil (30 ml/day) for 4 weeks results showed hempseed oil increased linoleic and gamma-linolenic acids in serum cholesteryl esters (CE) and triglycerides (TG) more than flaxseed oil ($P < 0.001$), conversely flaxseed oil led to higher ALA in serum CE and TG ($P < 0.001$) [31].

A study on flaxseed oil aids obesity treatment, insulin resistance, and protects against diabetic retinopathy [32, 33, 34]. In mice, conjugated linoleic acid reduced liver lipids by 57% and 73% and increased the C-6: C-3 ratio by 58% compared to controls. Flaxseed oil increased C-6 and C-3 fatty acids by 33% and 342%, respectively, and decreased the C-6:C-3 ratio by 70% [35]. It also boosted plasma adiponectin, enhancing insulin sensitivity. Rats given flaxseed oil had 1.5 time's higher adiponectin than those given safflower oil [36], suggesting it's healthier.

4.3 Musculoskeletal

In skeletal muscle, lipid transfer across the sarcolemmal membrane limits fatty acid oxidation. Flaxseed oil, rich in α-linolenic acid, alters plasma membrane lipids, boosting palmitate transport. Rats on a 10% α-linolenic acid diet showed a fivefold rise in omega-3 PUFAs in muscle and sarcolemmal membranes, a 20% increase in palmitate transport, a 50% rise in body fat oxidation, and doubled skeletal muscle triacylglycerol [37].

Flaxseed oil impacts femur bone mineral density, strength, and fatty acid composition; a study on male rats aged 6 to 15 weeks shows n-3 PUFA diets had stronger femurs than those on standard chow [38]. Research on flaxseed oil's effect on bone damage from high-fat diets in rats found it reduced trabecular bone damage, enhanced osteoblastic activity, and supported osteogenesis [39]. A study on rats fed flaxseed oil, rich in alpha-linolenic acid, had better bone microarchitecture than those on salmon oil; serum osteocalcin levels were higher ($P = 0.03$) in flaxseed-fed rats, linking osteocalcin to improved trabecular bone microarchitecture [40].

4.4 Anti-osteoporotic

Osteoporosis is a metabolic bone condition marked by reduced bone density and structural deformities, increasing fracture risk [41]. The World Health Organization estimates it affects 19.7% globally [42]. Bones undergo continuous resorption by osteoclasts and replenishment by osteoblasts to maintain strength. An imbalance, with resorption exceeding formation, leads to osteoporosis [43]. Hormones regulate bone formation; estrogen and testosterone prevent degradation [46]. Cytokines and prostaglandins reduce resorption [44].

To understand flaxseed oil's bone benefits, examine its components: oil and lignans such as α-linolenic acid (ALA), is a precursor to eicosapentaenoic (EPA) and docosahexaenoic acids (DHA), which regulate osteoblast and osteoclast formation, inflammation, eicosanoid synthesis, and calcium metabolism [45]. Flaxseed lignans act as phytoestrogens, affecting the estrogen receptor. While secoisolariciresinol diglucoside (SDG) is in flaxseed oil (4 mg/kg) [46],

research attributes flaxseed oil's effects to its polyunsaturated fatty acids (PUFAs), not SDG.

4.5 CNS depression

In a rat model of brain ischemia, flaxseed oil pre-treatment showed potential neuroprotective effects on the motor cortex after cerebral ischemic stroke, linked to increased neurotrophic factors, specifically brain-derived and glial cell-derived neurotrophic factors [47]. Another study with rats given flaxseed oil in microemulsion form showed synaptic membranes enriched with DHA, raising dopamine and serotonin levels in the brain [48]. Flaxseed oil as a dietary supplement has shown potential in alleviating depression research indicates that administering a 10% flaxseed oil diet to rats subjected to unpredictable chronic stress led to improvements in both behavioral despair and anhedonia [49].

Flaxseed oil from Egypt shows antidepressant-like effects in a rat postpartum depression model. Administered orally at 270 mg/kg/day for two weeks postpartum, it reduced anxiety and depressive symptoms. Improvement was seen in plus maze, forced swim, and open field tests [50].

4.6 Anticancer

Natural compounds serve as a valuable source of antioxidants [51] and anticancer agents, as documented from plant origins [52]. Numerous studies have highlighted the cytotoxic properties of flaxseed oil against different cancer cell types [53,54,55].

Flaxseed oil reduced B16-BL6 melanoma cell proliferation dose-dependently. A 0.3% (v/v) concentration decreased cell numbers by 50% in four days, while 0.9% (v/v) completely halted growth. Other cancer cell lines also showed growth suppression with 0.3% (v/v) flaxseed oil: 25% in HeLa, 75% in MCF-7, and 50% in MDA-MB-231 and MDA-MB-468 cells, with greater inhibition at 0.9%. The MTT assay showed 40–60% cancer cell growth reduction after four days, with non-cancerous cells unaffected, indicating safety over traditional chemotherapeutics. Flaxseed oil also impaired mitochondrial function in MCF-7 and B16-BL6 cells [56].

In a study with athymic mice, researchers assessed the anticancer effects of combining low-dose trastuzumab (2.5 mg/kg) with 8% flaxseed oil against a higher dose (5 mg/kg) on HER2-positive breast cancer cells. Control tumors increased 187%, while the flaxseed oil and lower trastuzumab dose reduced tumors by 84% after four weeks. Flaxseed oil enhanced trastuzumab's effects, with the low-dose combination as effective as the high dose, suggesting potential for reducing chemotherapeutic doses [57].

The findings showed a 50:50 combination of Dox and phenolic extract from flaxseed oil decreased IC_{50} 15.7µg/ml for flaxseed oil extract and 0.3 µM for Dox in MCF-7 cells. A synergistic effect occurred with combination indices (CIs < 0.9) at equal potency doses. Combined treatment reduced Dox dose 20-fold and flaxseed oil extract 7.7-fold against MCF-7 cells, with a similar response in MDA-MB231 cells compared to individual treatments [58].

4.7 Anti-inflammatory

Natural sources often provide anti-inflammatory agents [59]. Inflammation is a protective response to eliminate invaders and repair tissues, marked by pain, redness, and swelling. Severe cases can cause loss of function. The response self-regulates to prevent host harm through negative feedback [60]. Inflammation involves increased blood flow, capillary permeability, leukocyte migration, and release of mediators like n-6 eicosanoids, PGE2, LTB4 [61], cytokines, IL-1b, TNF-a, reactive oxygen species, histamine, and enzymes [62]. EPA is a cyclooxygenase substrate for PGE3 synthesis, though inefficient, and a precursor for prostaglandins and leukotrienes, contributing to ALA's effects. DHA produces resolvins and protectins via cyclooxygenase and lipoxygenases these mediators, including resolvin E1, D1, and protectin D1, inhibit neutrophil migration and infiltration at inflammation sites. Resolvin D1 suppresses IL-1β, and protectin D1 inhibits TNF and IL-1β production [63].

5. Future outlook

Studies have explored flaxseed oil's health benefits, but more research is needed on how extraction techniques affect its chemical makeup and antioxidant properties.

Further investigations should examine chemical differences in flaxseed oil across varieties and their effects in animal models and human trials. More in vivo studies and clinical trials are crucial for evidence of lesser-known effects, like its neuroprotective potential for neurodegenerative diseases, especially Alzheimer's. Research should also explore flaxseed oil's combined effects with other PUFA-rich extracts. Flaxseed oil shows promise for pharmaceutical and nutraceutical industries, necessitating more information on its stability, formulations, and delivery systems.

6. Determination

Flaxseed oil, a prominent product derived from flaxseed, is renowned for its health benefits attributed to its chemical makeup. It is abundant in omega-3 and omega-6 fatty acids, particularly α-linolenic and linoleic acids. Research indicates that consuming large amounts of flaxseed oil can help in both treating and preventing various diseases. It lowers the risk of heart conditions, such as arrhythmia and sudden cardiac death, due to its high levels of EPA and DHA, which help reduce plasma cholesterol and blood pressure in patients with dyslipidemia. Elevated EPA levels also alleviate symptoms of CNS depression, such as behavioral despair. α-Linolenic fatty acids reduce inflammatory cytokines, providing anti-inflammatory benefits. The PUFAs in flaxseed oil offer anti-inflammatory, immunoregulatory, and antibacterial advantages. Including flaxseed oil in the diet improves osteoporotic conditions by enhancing bone mineral density, strength, and fatty acid composition, primarily due to its lipophilic PUFAs and, to a lesser extent, lignans.

Informed Consent

Not Applicable.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare no conflict of interest among themselves. The authors alone are responsible for the content and writing of this article.

Financial Interests

The authors declare they have no financial interests.

Human and Animal Rights

NA

Ethics approval and consent to participate

Not applicable.

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