EXPLORING FLAXSEED IN PHARMACEUTICAL APPLICATION AND THERAPEUTIC POTENTIAL: A COMPREHENSIVE REVIEW

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Abstract

One crop used for fibre is flax seed (Linum usitatissimum). It is loaded with lignans, which are phytoestrogens. Flax seed has a variety of nutritional components, including omega-3 fatty acids, polyunsaturated fatty acids (PUFA), and alpha-linolenic acid (ALA), as well as several phenolic substances, including lignans, flavonoids, and phenolic acids. Since it works to balance the three Doshas—Pitta, Kappa, and Vata—flaxseed is called Tridoshas in the Ayurvedic medical system. It also helps to improve digestion and lessen constipation. Flaxseed is a great complement to a balanced diet because of its wide range of health benefits and rich profile of vital elements. Its rich lignan, fibre, and omega-3 fatty acid content promotes digestive and, cardiovascular health, and may even have anti-cancer effects. Numerous research has narrowed down the broad range of uses for flaxseed and whether you use whole seeds, powdered seeds, or flaxseed oil, adding flaxseed to your food can be easy and increase your intake of nutrients. But it's crucial to use it sparingly and speak with a doctor, particularly if you're experiencing underlying medical concerns or are taking medicine. All things considered; flaxseed sticks out as a nutrient-dense, adaptable diet that can improve general health.

Keywords: Lignans, omega-3 fatty acids, Tridoshas, anti-cancer, flaxseed oil.

Introduction

Flax seed's high lignan, linoleic acid, and fibre content make it a significant developing functional food (1). China and Canada use flax seed oil as a major oil source plant. There are two forms of flaxseed oil: oil and fiber. Oil flax is cultivated for its seeds, which are used to extract oil, while fiber flax is farmed for its stem. Its oil content ranges from 20 to 40 percent (2-4). Studies have demonstrated the several benefits of flax seed in preventing a wide range of illnesses, including hyperlipidemia (5), atherosclerosis (6,7), colon tumors (8), and breast cancer (9,10). Flaxseed oil supplements, particularly those in the form of gelatin capsules, are widely available on the global market (11). According to an analysis, Canadian-origin brown flaxseed contains 4.1% fat, 20% total dietary fiber, 7.7% moisture, and 3.4% ash (12-13). The oil content of a seed increases as the protein level decreases(14). Because flax seed has a high viscosity in aqueous solution, it is also highly active in the culinary, cosmetic, and pharmaceutical industries. The current study was developed to look at the impact of pH on the yield of fiber extracted (15). Additionally, flax seed's potential applications are used in treatments and nutraceuticals (16). As a treatment for iron deficiency anemia (IDA), nanocomposites based on soluble flax seed gums and iron salts have been developed. The in vitro release of iron kinetics for stimulated gastric fluid (SGF) is also assessed (17). The goal of the current study's experiment is to understand the relevance of iron oxide (IO) nanoparticles, which are utilized as priming agents (18). The ethanol extract from flax seeds exhibits anticancer, antioxidant, and anti-inflammatory properties. It also demonstrates a noteworthy antioxidant impact in vitro and demonstrates distinct inhibitory effects on various cell lines (19). Some researchers have discovered that the interaction between mammalian miRNA and the gut microbiota may help treat breast cancer. These bioactive activity plant compounds are thought to be rich and valuable for creating nanomaterials (20). While some research indicates that flaxseed has no discernible impact on adult sex hormones, other studies indicate that supplementing with flaxseed enhanced SHBG in subjects under 50 years old and in males with PCOS and TT (11).

Flax Seed as Pharmaceutical Excipient

Excipients are crucial in transforming a medication into a dosage form that provides the desired effect. Flaxseed is a rich source of naturally occurring polysaccharides, which have a high swelling index at different physiological pHs. So, it shows that flax seed's biocompatibility, biodegradability, and accessibility

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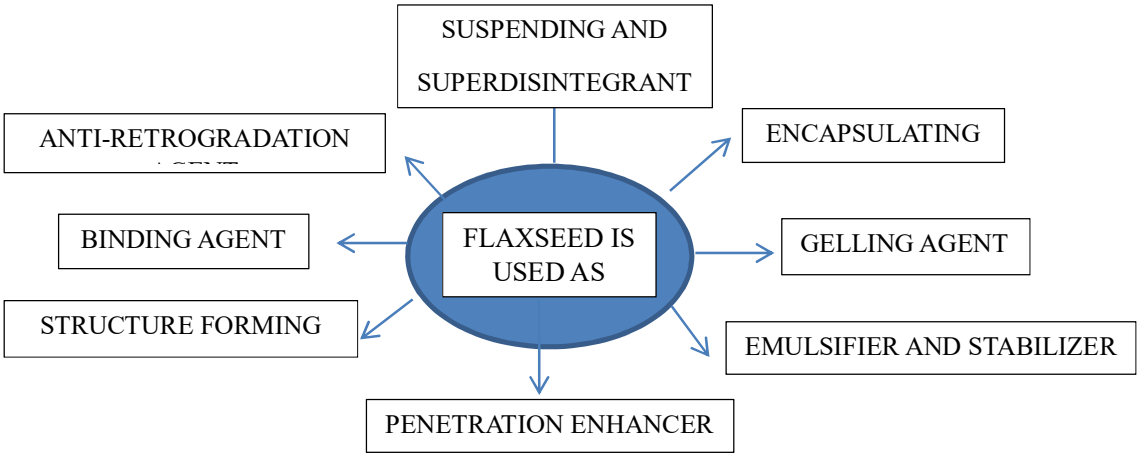


Fig: 1 Uses of flax seed

Use of Flaxseed Mucilage as Binder

To provide cohesion and bonding to solid particles and help them bind together to form tablets under pressure, binders are added to solid pharmaceutical dosage forms. Mucilage is utilized as an adjuvant in controlled-release dosage forms as well as a thickening, binding, dissolving, suspending, and emulsifying agent in pharmaceutical additives.FM is made up of two distinct kinds of polysaccharides: an arabinoxylan, which is neutral, and a pectic-like substance, which is acidic.[21] Mucilage is hydrophilic. L-arabinose, D-xylose, and D-galactose make up the neutral portion in a molar ratio of 5:6.2.1:3. (16). L-rhamnose, L-fucose, L-galactose, and D-galacturonic acid make up the acidic portion in the following ratio: 6:1.1:2.1:4.7 (22).

Physiochemical Characteristics of FM

Organoleptic characterization: Flaxseed mucilage was evaluated for the characterization of color, Odor, taste, and texture.

Table:1. Organoleptic characterization of FM

S.no	Properties	FXM
1)	Color	Light brown
2)	Odor	Nutty
3)	Taste	Nutty
4)	Texture	Smooth

Phytochemical characterization: This is done using an aqueous solution of FM (1 mg/ml). Standard protocol is used for testing for alkaloids, carbohydrates, tannins, starch, and non-reducing sugars (Harborn, 1984). Mucilage, which is made of polysaccharides, should only benefit carbs. The presence of carbohydrates is only detected in the mucilage confirmatory test upon drying, and the moisture level was ascertained by precisely weighing an amount of FXM powder in a hot air oven. Both the moisture content and the drying-related loss are within allowable bounds. This suggests that there is not much moisture in the mucilage.

Swelling index of mucilage: The Gauthami and Bhat (1992), method is used to calculate the swelling index of polysaccharides. Flax seed has a high swelling index, which may help it realize its potential as a binding agent in medication compositions.

Moisture content and drying loss: The mucilage content stays within the usual range. This indicates that low moisture content mucilage is necessary for an excipient to be stored safely.

Relative solubility of mucilage: Mucilage's relative solubility in ethanol, acetone, chloroform, and cold and hot distilled water was ascertained using the technique described by Tadese et al. (2014). In hot water, flaxseed mucilage dissolves easily; in chloroform, it dissolves less readily. Mucilage surface tension: As the concentration of mucilage grew, so did the surface tension. However, in comparison, surface tension decreases when conventional binder PVP solution concentration increases. According to reports, a binder with a low surface tension is crucial for greater polymer penetration and wetting for creating high-quality granules. The findings demonstrate that the granules made using flaxseed mucilage as a binder have satisfactory flow characteristics and that the assessed parameters are within allowable bounds. Therefore, mucilage is a substitute binder in medicine granules (23). The 20 mg prednisolone pill contains flaxseed mucilage as a binder. The purpose of the study was to extract and assess the mucilage from flaxseed used as a binder in prednisolone pills (24). High molecular weight compounds called hydrocolloids are employed as gelling agents. A combination of several hydrocolloids has been used in the study by Saha and Bhattacharya,2010 to examine how foods' viscosity and elasticity are regulated. FSG is low viscosity and has good water binding and retention properties.



The three different percentages 3%, 5%, and 7% of FM were used.

The hardness of the tablet increases with an increase in the concentration of FM

Friability also increases, Flowability also increased

Mucilage of Flaxseed Used as Gelling Agent

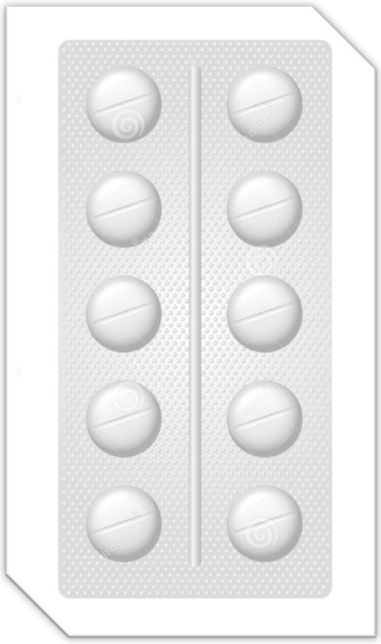
Fig:2. Tablet

The gelling qualities of flaxseed mucilage are weak; however, the inclusion of konjac glucomannan and agar enhances the gel property of FXM, resulting in high structural strength, water retention capacity, and elasticity (25). The gels undergo tests to ascertain their swelling power, moisture affinity, and water solubility index. Additionally, the rheological characteristics of the gel are examined. AG works well as a gelling agent when combined with FSG and KG. The Gelling Agent in Domperidone Tablets is Flaxseed Mucilage:Fourier transform infrared spectroscopy (FTIR) was used to examine the drug excipient compatibility test. By creating a gel layer, the mucilage from flax seeds reduces the amount of domperidone that released from the pill (26).

Flaxseed Used as Emulsifier and Stabilizer

Flaxseed oil-in-water emulsions are stabilized using flaxseed oil cake extract (FOCE) as an emulsifier and stabilizer. The impact of FOCE on several emulsion physiochemical characteristics, including color, stability, rheology, and particle size, is ascertained at different flaxseed oil concentrations. The micro-Biuret method (27) was utilized to certain the protein concentration. The phenol sulfuric reaction was used to determine the amount of carbohydrates present (28). Using a Thermo Scientific Evolution 220 Spectrophotometer, all measurements were assessed. FTIR analysis using an FTIR Spectrometer in ATR mode was used to confirm the presence of compounds in FOCE (29). As can be seen from the rheological parameter, the samples are non-Newtonian fluids. The calculation of the SPAN index provides information regarding the emulsion particle size distribution's breadth. The outcomes are contrasted with the impact of Tween 80, a synthetic

emulsifier, and the individual FOCE components (flaxseed gum and flaxseed protein). The FOCE has high interfacial tension-reduction capabilities and can be utilized to generate bimodal emulsions and FO emulsification. The emulsifying activity of flaxseed gum is higher than that other regularly used emulsifiers, making it a good addition for stabilizing water-oil emulsions (30).



The flaxseed mucilage is used as a gelling agent in Domperidone tablet to develop a novel gastro-retentive sustained drug delivery system

The hardness, friability, weight variation, disintegration time, and thickness are within acceptable limits

the formulation prepared by the exact ratio of FXM, CARBOPOL 934, and HPMC K100 shows a more efficient result than compared with tablet prepared using only CARBOPOL 934 and HPMC K100 M.

Fig: 3. Domperidone Tablet**.**

Flax is Utilized as a Stabilizer in Pickering Emulsions

Pickering emulsions have superior physical stability because of their lower interfacial energy and particles anchored at the oil-water interface (6). However, emulsions stabilized by silica particles have the potential to improve penetration of the skin and dermis by three times and boost temperature absorption efficiency (7). Additionally, it enhances drug deposition to the layers of the epidermis and dermis and skin adherence. Recent studies show disadvantages of inorganic particles can overcome by polysaccharides derived from natural materials. Chitosan is a commonly used natural cationic polysaccharide in developing new formulations because of its biocompatibility (9). Natural polysaccharides with high emulsifying, water-holding, and rheological qualities, including flaxseed gum (FG), are employed as texturing agents in the cosmetic industry (10). Hyaluronic acid is a natural component that is both green and effective when combined with chitosan(cs) because of its high moisturizing properties and biocompatibility (11). DAG which only contains one hydroxyl group, is an excellent emulsifier and interfacial because it interacts with the skin's stratum corneum through hydrogen bonding and van der Waals contact. As a result, it has strong skin penetration and may be utilized as a base oil in cosmetic products (12). The research was done on Pickering emulsions with an internal DAG phase loaded with FA and nanoparticles based on (S-FG or STPP). Pickering emulsions' microscopic appearance, absorption, physiochemical characteristics, skin penetration, and storage stability were all assessed. The project will contribute to the development of environmentally friendly, safe bio-based Pickering emulsions for the topical administration of hydrophobic active agents (13).

Utilizing Flaxseed Protein as an Emulsifier

Precipitation at the isoelectric point was used to create the flaxseed protein solution. According to Kaushik et al, (31). the flaxseed protein is separated into two fractions: water-soluble 1.6-2S albumins and salt-soluble 11-12S globulins, which are known as linin and conlinin. Together with whey protein isolate, flaxseed protein isolate is utilized as an emulsifier. Due to a decrease in the interfacial tension between the oil and

aqueous phases, a rise in FPI concentration results in a high creaming ability to emulsion. However, because flaxseed gum is present in the protein isolate, the same high concentration of FPI in the WPI-FPI emulsion displays a decrease in creaming stability and droplet size. The emulsion's creaming stability can be enhanced at higher concentrations by improving homogenization conditions. Thus far, the bimodal nature has been seen in all emulsions, except for O/W emulsions stabilized by flaxseed protein (32).

Flax as Super Disintegrant and Suspending Flaxseed Mucilage

Acetone and other tests for carbs, fat, protein, reducing and non-reducing sugars, tannins, alkaloids, surface tension, swelling index, and viscosity were used to extract the mucilage from the seed. These findings demonstrate the outstanding flow characteristics of the mucilage in water. The mucilage exhibits good flow qualities as indicated by the angle of repose result and satisfactory results from its pH, surface tension, and physiochemical properties, all of which can be utilized as pharmacological adjuvants. The mucilage isolates from flaxseed produced values comparable to the powdered seeds' swelling index. Because of its great swelling property, it can be utilized in medicinal preparations as a super dissolving and suspending agent (33).

Structure-Forming Agent

Hydrocolloids, including methylcellulose, carrageenan, pectin, guar gum, and HPMC and CMC, are frequently employed as "gluten replacers" in gluten-free products. In gluten-free products, Guar gum and pectin are naturally substituted by flaxseed mucilage, particularly the freeze-dried kind (34).

Anti-Retrogradation Agent

Starch quality is naturally impacted by retrogradation. By adding the FG, the retrogradation of maize starch was suppressed. Following the addition of FG to the starch gel, the starch molecules and FG create hydrogen bonds. Additionally, FG absorbs water to prevent the starch molecules from recrystallizing and rearranging, which increases the texture of gels (35).

Flaxseed as an Encapsulating Agent

Flaxseed protein isolate and flaxseed grain coacervates are utilized as wall materials (36). Lactobacillus casei, a probiotic, is co-encapsulated via FM on an alginate matrix (37). Applying FM and flaxseed soluble protein as a wall material allows lactobacillus acidophilus to be encapsulated by spray drying (38).

Flax Oil Encapsulation

Flax seed is categorized as dry oil due to its 24–44% oil concentration. It contains 55% α linoleic acid, which lowers blood cholesterol levels and has a preventive impact against heart disease and atherosclerosis. Flaxseed oil is encapsulated with gelatin-flaxseed mucilage and oxidized tannic acid (OTA), a tertiary compound with regulated release ability, to prevent exudation, which lowers the oil's nutritional value. It was determined how much oil was present at various percentages of 15%, 30%, and 50% W/W. Encapsulation efficacy (EE) and loading efficacy (EL), SEM, FR-IR, oxidative stability, and release profile of flaxseed oil are all included in the assessment and characterization process.50% concentration shows the maximum oil loading. The peroxide value of the encapsulated oil reveals a lower rate of oxidation during storage than that of the loose oil. There has been no interaction between functional groups of wall materials and the oil, which is physically imprisoned within the complex. It is manipulated from the finding that tertiary complexes can be used in delivery and encapsulating systems for sensitive and functional oils (32).

Flaxseed Oil used as a Penetration Enhancer

At various concentrations, flaxseed oil is utilized as a penetration enhancer. When compared to coriander oil, flaxseed oil exhibits a higher flux but a lower one in transdermal patch drug delivery systems. Meloxicam uses flaxseed oil as a permeation enhancer; the oil exhibits maximum flux at higher flaxseed oil concentrations. FT-IR is used to examine the drug-polymer interaction (39).

Flax as Penetration Enhancer in Transdermal Patches

Transdermal patches were made by mixing eudragit and polymers in varying ratios with chitosan, thiolate chitosan, EC, and PVP, and flaxseed and coriander oils as penetration enhancers in varied concentrations (1,2,3,5,6,7,8,9, and 10%). Meloxicam (MLX) was a non-fickian medication. Solvent evaporation

techniques were utilized to develop the MLX patches. The film is taken off and divided into 1.7 cm2 sections once it has dried. The produced patches' homogeneous, smooth, and transparent appearance was assessed using physiochemical parameters. To examine the relationship between the medication and the polymers, FTIR was used. Furthermore, folding endurance, medication content, and moisture content were computed. Using a pharma test dissolving apparatus (PTWS-11/P, Hamburg, Germany), the drug release in vitro was carried out. Using a Fanz diffusion cell device and rabbit skin, in vitro drug permeation was conducted. Skin with an erythematous and oedematous score. A 24-hour in vitro drug penetration investigation was conducted on rabbit skin utilizing flaxseed and coriander oils. The highest flow was seen in flax seed oil at 5% concentration and in coriander oil at 10% concentration. The transdermal patch release pattern has been demonstrated to be controlled by the polymer employed in the patches (33).

Flax Mucilage as a Biocompatible Polymer

As a biocompatible polymer, flax seed mucilage has the potential to be utilized in bone regeneration procedures. It comprises 3.0-9.0% mucilage that contains polysaccharide chains of arabinose (8.0-13.0%), xylulose (19.0-38.0%), rhamnose (11.0-16.0%), glucose (12.0-16.0%), and galacturonic acid (21.0-36.0%) (40). The author treated atherosclerosis using mucilage, a bioactive polymer in which bone repair is essential (41). Biocompatible polymers are selected to facilitate the simple breakdown of polymers in vivo without the need for subsequent operations for removal. Utilizing flaxseed mucilage as a bioactive polysaccharide, composite scaffolds consisting of calcium phosphate embedded in a mucilage matrix were created. The mucilage content of flaxseed ranges from 3.0-9.0% and contains polysaccharide chains of arabinose (8.0-13.0%), glucose (4.0-6.0%), rhamnose (11.0-16.0%), xylulose (19.0-38.0%), and galacturonic acid (21.0-36.0%) (2). By dissolving flaxseed mucilage, calcium phosphate composites and mucilage were formed. After that, samples were separated using centrifugation for 30 minutes at 300 rpm, and any leftover white or off-white material was freeze-dried. FTIR was conducted with a PerkinElmer-FTIR spectrometer; x-ray diffraction was carried out with an Empyrean powder diffractometer; and scanning electron microscopy was used to examine the surface morphology of mineralized scaffolds. Using a PerkinElmer-TGA thermogravimetric analyser, a thermogravimetric analysis was carried out. Cell viability tests on MC3T3-E1 osteoblast cell lines have demonstrated a definite safety profile with minimal toxicity and no need for dosage reduction. Thus, the trial demonstrated the potential of flaxseed mucilage for bone regeneration applications. (3)

Recent Advances in Flax Pharmaceuticals

The function of flax in the controlled release of ketorolac: Ketorolac can be released gradually by using flax seed as an absorption medium. The author created a polymeric matrix for a controlled drug delivery system to prolong the release of ketorolac. As biopolymers, chitosan (chit) and linseed (LS) are combined to create a hydrogel composite that can be utilized as an adsorption material and release ketorolac (42).

Flax Seed Oligosaccharide

Flaxseeds, according to the study, exhibit synergistic effects with proteins, but their high polysaccharide viscosity limits their use in pharmaceutical applications. The author Chenyang used flaxseed oligosaccharides derived from flaxseed gum and reported that, in a dose-dependent manner, FGOS exhibited superior anti-proliferative activity on HepG2 and Hella cells in comparison to Flax seed gum (FG) (43).

Flax in Broiler Meat

Research by D. Mirdula et al. indicates that dietary additions of omega-3 fatty acids, such as ALA, to chickens may affect their growth rates. ALA may help with weight gain; however, the effects may differ according to the makeup of the diet and the amount of ALA consumed. By increasing the feed conversion ratio, omega-3 fatty acids may help hens use their diet more effectively, which could result in improved growth outcomes. The findings demonstrate the consistent size distribution of nano emulsions coated with a whey protein/sodium alginate (WP/SA) combination (44).

Flax with Polyvinyl Alcohol in Wound Healing

Flaxseed (linseed) fibres, in particular, have inherent antibacterial and anti-inflammatory qualities. The polyvinyl alcohol (PVA)-flaxseed mucilage (FM) combination was used in this investigation to create the NF scaffold. Flax seed mucilage has gel-forming and hydrophilic qualities that help seal in moisture and cover wounds in a barrier of defense. An in vitro investigation using human skin fibroblasts was used to

characterize the outcomes. Conversely, the physiochemical characteristics of NFs made of CS and flaxseed mucilage (FM) enhanced with sesame oil and essential oil of Ziziphora clinopodioides were studied. The outcomes demonstrated the extract's successful loading, structural stability, high water-holding capacity, mechanical characteristics, and porosity (45). Like carrageenan, flax seed has excellent water absorption and gel-forming qualities. In a different work, Tayyaba Sadiq et al. created bio-composite hydrogel films from flaxseed gum (FSG) and carrageenan (CGN) utilizing deferoxamine (DFX) as an ion chelator, glycerol as a plasticizer, and potassium chloride as a crosslinker for wound healing (46).

Bigel from Flaxseed

Bigels are a dual-phase system with special qualities like controlled release and enhanced stability. They are made up of two gelled phases: an organic phase and an aqueous phase. Flaxseed meal includes various bioactive substances as well as omega-3 fatty acids. Gum from flaxseed This polysaccharide, which is hydrophilic and forms gels in aqueous conditions, is derived from the mucilage of flaxseed. By causing cancer cells to undergo apoptosis, oral administration of flaxseed oil (FSD) and daubezin (DDZ) has an anticancer effect. The oleo-gel and hydrogel were optimized using central composite design experiments, and the nano-bigel from DDZ&BG was carried out by Bharti Mangla et al. by homogenously mixing the optimized hydrogel with optimal oleo-gel using an ultra-turrax homogenizer after an ultrasonication to make nanogel. The modified bigel formulation showed good rheological and mechanical properties as well as increased drug penetration than plain-gel, according to the solubility and permeability parameter assessment (47).

Herbal Trio-Gel from Flax

There are two types of flax seed: golden flax seed and brown flax seed. In conclusion, a brown flax triogel would take advantage of the advantages of brown flaxseed oil while taking into consideration its distinct qualities and color. In this work, the trio-gel is prepared using brown flax seed. Following the supercritical fluid extraction process, carboxymethyl cellulose and Carbopol were individually mixed to create the triogel formulation. Trio-gel characterization was carried out using the antimicrobial, FTIR, SEM, albumin denaturation, and anti-inflammatory assays. Flaxseed trio-gel showed little difference when compared to the usual chlorhexidine gel (48).



Fig.4. Comparative uses of two varieties of flaxseed (49).

Flax Seed Effects on Nano Technology

Since their production is characterized by a variety of spectroscopic techniques, including UV-visible absorption, Powder-XRD, FTIR, X-ray photoelectron spectroscopy (XPS), TEM, and EDS analysis, flax seeds have had a stronger influence on nanotechnology in recent years (50). Additionally, iron nanoparticles' low production costs and low toxicity have made it possible to remove pollutants in-situ in recent years. Flax seed gum has been found to be appropriate for stabilization based on identification, characterisation, and stability testing (51). The density, morphology, peroxide value, and encapsulation efficiency (EE) of flax seed powders have all been measured (52). The water-soluble mucilage that was taken out of the flax seed has a very high potential for hydrocolloid production in gels. Certain bacterial species, including Escherichia coli, Staphylococcus aureus, Klebsiella pneumonia, and Streptococcus pyrogens, are susceptible to the antibacterial action of flax seed, which is utilized in the green synthesis and characterisation of silver nanoparticles. Additionally, the DPPH technique has been used to examine its antioxidant impact (53) Yogurt fortification has been studied with stable flax seed oil-containing Nano emulsions, and low-energy emulsification techniques are also used with flax seed Nano emulsions that have an oil in water phase (54). A green method of stabilizing emulsion has been developed using plant-based particle from the soluble fraction of flax seed mucilage (SFM) and from the complexation of flax seed protein [FP] (54). Recent research has shown that flax seed have been helpful in weight reduction in obese and overweight persons (55).

Anticancer Activity by Nano Technology of Flax Seed

Since cancer is the most common and deadly disease, anticancer medications are used to stop the growth of malignant cells. Doxorubicin is one of the most potent chemotherapeutic drugs available today. Research on the in-vitro and in-vivo anticancer activity of doxorubicin's nano-encapsulation design, which uses grafted melanin as the core and acrylic acid flax seed gum as the shell, has been conducted (56). The abundant fibre polysaccharides in flax seed gum, which is mostly made of rhamnogalacturon and arabinoxylan, lower the risk of colon cancer (57). Several pharmacological and medicinal applications exist for flax seed gum (58). There is confirmed activity of flax seed-AuNPs against cancer cells (59). Flax seeds have demonstrated an inhibitory effect on hepatocellular, colon, and breast cancer (60). The synthetic AuNPs derived from the aqueous extract of flax seed are easy to use, safe, and may have anti-cancer properties in addition to being environmentally friendly (61). Albutrin, globulins, glutelin, and prolamins are among the flaxseed proteins that have anticancer properties. Furthermore, it has been observed that the proteins included in flaxseed can modify the mechanobiology of cancer cells, resulting in altered cellular activity as well as decreased migration and invasion of cancer cells. Proteins from flaxseed can be consumed through food and absorbed in the digestive system. From there, they can travel throughout the body and possibly even reach cancer cells. It is also possible to use targeted medication delivery systems or nanoparticle formulation to directly deliver flaxseed proteins to cancer cells. It has been demonstrated how beneficial flaxseed proteins are for numerous cancer cell lines, including those from the breast, skin, prostate, and colon; this anti-tumor activity causes cell cycle arrest and triggers apoptosis (cell death). In particular, it has been observed that flaxseed proteins improve the efficacy of chemotherapeutic drugs in a variety of cancer cell lines. Additionally, it uses radiation therapy to treat non-small cell lung cancer (NSCLC). Consuming flaxseed on a daily basis has been linked to a lower incidence of acute radiation-induced complications (62).

Antioxidant Activity of Flax Seed by Nano Particles

DPPH, which has a radical scavenging activity (63), is used to measure the antioxidant activity of flax seed. Flax seed priming exhibits a higher level of antioxidant activity (64). According to recent studies, flax seed has a greater capacity for FRAP scavenging than DPPH (65). Several flax seed preparations have demonstrated antioxidant action through their ferrous ion chelating properties (66). To measure the antioxidant activity of plants, 2,2'azino-bis (3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) has been employed (67). The body produces reactive oxygen species and reactive nitrogen species as a result of an ongoing metabolic reaction. Primary and secondary antioxidants are the two categories into which they are split. Providing a hydrogen atom is the fundamental antioxidant's function (chain breaking). Secondary antioxidants have three functions: they bind metal ions that can absorb UV light, they catalyse oxidative processes, and they inhibit enzymes. The overproduction of these species as a result of cellular component damage, such as lipids, proteins, and DNA, disrupts exposure to natural anti-oxidant processes including catalase, glutathione peroxidase, and superoxide dismutase. The creation was connected by these free radicals to an increased risk of cancer and numerous degenerative disorders, including cardiovascular

disease. Flaxseed's antioxidant action has been demonstrated to lower total cholesterol and platelet aggregation (68). Antimicrobial, Fibrinolytic Activity and Anti-inflammatory Activity by Nano Particles of Flax Seed because nanoparticles are harmless, flax seed extract-AuNPs have been shown to exhibit anticoagulant action (69). Flax seed has been shown to have anti-proliferative activity (70), as well as the ability to reduce inflammatory Estrogen receptors, enzyme expression, toxic oestrogen metabolites, prostaglandin E2, and other factors that are linked to the development of ovarian cancer (71). Additionally, some studies have demonstrated the potential protective effects of dietary lignans of flax seed nanoparticles. Nitric oxide, or NO, has the potential to cause cancer; however, the therapy with flax seed will dramatically reduce NO activity (72).

Development of the Flax Seed as Nano Composites Bio Plastic Film

Glycerol was added as a plasticizer, glutaraldehyde and HCL as a crosslinking agent, and flaxseed gum and cellulose Nano crystals were combined to create a bioplastic Nano composite film. The film with the lowest water solubility was chosen to serve as a benchmark for the creation of nano composites with varying nanocrystalline percentages. Eucalyptus urograndis, hybrid Eucalyptus urophila, and Eucalyptus grandis bleached (kraft pulp) were used to isolate the CN. The Attention Theta line TL 100 optical tensiometer was used to gather the solubility data for water. The mechanical tensile strength and water contact angle of films and nano composites were measured. Additionally, scanning electron microscopy, or SEM, was used. Using an elemental analyser CE instrument EA 110-CHN 10, the C, H, and N content of the films was ascertained. It has been demonstrated that this cross-linking of FG with GLA is more stable in water. This indicates that the culinary, agricultural, and pharmaceutical industries can use flaxseed gum as a bioplastic (73).

Poly-Electrolyte Flaxseed Mucilage Nanoparticles

Using the ionic gelation process and sustained release formulation, a nanoparticle containing flaxseed mucilage (FSM) and chitosan poly-electric complex was created. As a model drug, isonicotinyl hydrazine was employed. It is evident from a study on particle size optimization that low levels of chitosan and flaxseed mucilage support small particle sizes. The dialysis sac was used to determine the INH release profile in vitro. The findings shown that INH is released over a 20-hour period, demonstrating the potential applications of chitosan and FSM in the development of sustained-release formulations (74).

Investigations of Polymeric Nano Particles for Ocular Delivery

The flax seed gum that was extracted from Linnum Usitatissimum was measured and refined using a variety of methods. The flax seed containing nanoparticle polymeric bio adhesive demonstrated a notable bio adhesive quality and a greater corneal penetration than the commercial eye drops. Current research indicates that flax seed containing nanoparticles has been used for glaucoma treatment through ocular delivery since it is biocompatible with the cornea and has demonstrated a longer and better IOP reduction (75).

Iron oxide nano particles using aloe and flax

Mucilage and other polysaccharides found in flax seeds have the potential to stabilize the creation of nanoparticles. Using the green co-precipitation approach, iron salts in aqueous extracts of aloe vera and flaxseed were converted into supra magnetic iron oxide nanoparticles (SPIONS) (76). Iron oxide nanoparticles are employed in cancer treatment, drug delivery, and MRI imaging. Utilizing organic stabilizers such as flaxseed can improve biocompatibility.

Flax Seed Gold Nano Particles (FS-AUNPS)

Using flaxseed's anti-oxidant properties, researchers created flaxseed gold nanoparticles (AuNPs), a green and environmentally acceptable technique of stabilizing produced nanoparticles by using flaxseed as a capping and reducing ligand. Deionized water was utilized to prepare an aqueous extract of flaxseed. Due to the high antioxidant activity of flaxseed, the flaxseed extract converts Au3+ ions to Au0, producing Fs-AuNPs, which are further supported by the solution's distinctive ruby red colour (77).

Flax Seed Nano Particle Activity in Nano ZVI

The flax seed containing nanoparticles has a high absorption of nanoZVI. Additionally, due to its high reactivity and high physical barrier activity.78 nanoparticles have better properties for removing contaminants. Additionally, the flax plant's growth and yield are improved by seed priming, which acts as a catalyst. Recent studies have also demonstrated that nanotechnology has had a greater impact on agriculture. By creating flaxseed gold nanoparticles (AuNPs), the anti-oxidant characteristic of flaxseed was utilized to biologically affect its antioxidant activity. A green and environmentally friendly process that uses flaxseed as a reducing and capping ligand to stabilize the produced nanoparticles. Deionized water was utilized to prepare an aqueous extract of flaxseed. Due to the high antioxidant activity of flaxseed, the flaxseed extract converts Au^{3+}ions to Au0, producing Fs-AuNPs, which are further supported by the solution's distinctive ruby red colour (78), to help mitigate the effects of climate change (79).

Effect of Flax Seed on Microbiome

Recent research on the impact of flax seed on the gut microbiome of female mice has focused on the kinds and quantity of bacteria in the colon. Flax seed is one of the plant's lignan precursors; other plant parts that contain these bacteria include legumes as well as whole grains, vegetables, and seeds (80), Because plant lignans found in flax seeds are edible, the bacterial flora that inhabits the seed converts them into other compounds that are absorbed into the bloodstream. Previous research has demonstrated that postmenopausal women who consume large amounts of lignans in their diets have a lower risk of breast cancer (81), and recent research has demonstrated a connection between the mammary gland miRNA expression and the dietary activity of the caecal microbiome, which has been modified by the flax seed plant's lignans. This is because changes in the breast's miRNA expression may lead to modifications in metabolic processes, which play a significant role in the development of breast cancer (82).

since some studies have also shown that the gut microbiota influences the amount of oestrogen that circulates in the blood, and since bacteria can enter the bloodstream through the colon and travel to other organs, including breast tissues (83). Additionally, because the polysaccharides derived from flax seed have a high identification activity for lipid metabolism, they have been found to be effective in lowering serum blood glucose levels, cholesterol, and total triglycerides. Furthermore, because natural products, prebiotics, and probiotics, modulate the gut microbiota and can help treat diseases, the short-chain fatty acids (SCFA) that these microbiota-metabolized polysaccharides contain can help alter the current ecology of microorganisms. Furthermore, some studies have demonstrated the benefits of flax seed gum and FS meal in preventing obesity, and as a result, some researchers have discovered a relationship between mammalian miRNA and the gut microbiota that can help treat breast cancer (84). The ecologically sustainable production of nanoparticles is utilized to reduce the negative impacts associated with it (85).

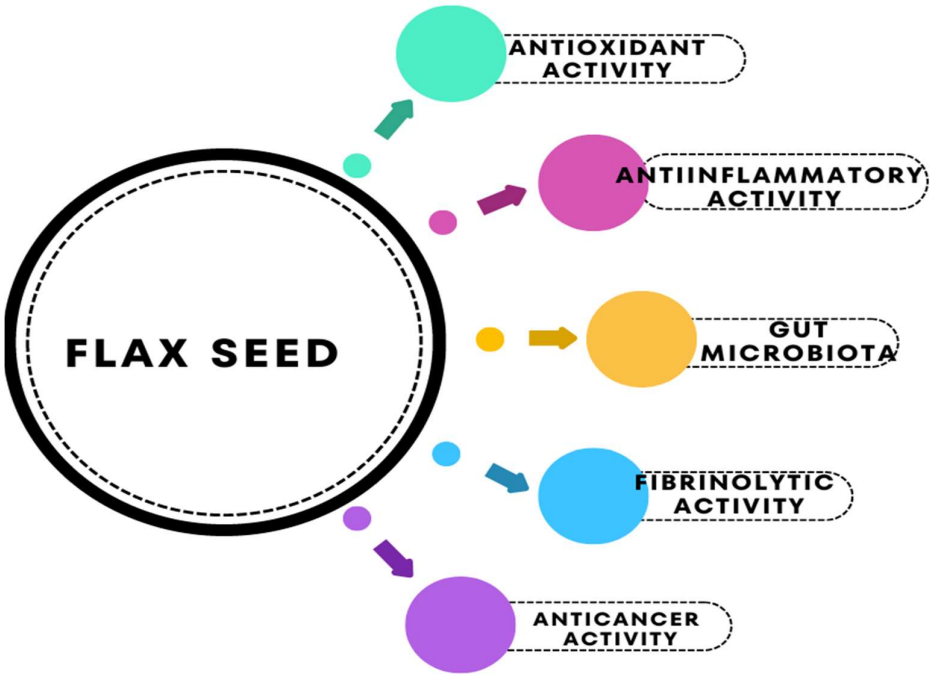


Fig.5. Pharmacological Activities of Flax Seed

Flax seed extract has demonstrated both an antibacterial and antioxidant activity that combats gram-positive and gram-negative bacteria (86). Additionally, a yogurt-based Nano emulsion referred to as fortified yogurt has been proposed as a way to meet daily requirements for omega-3 intake (87), Additionally, the most notable health benefits of flax seed's nano emulsion are its ability to prevent neurological diseases, treat microbial infections, and improve cardiovascular health (88). The FP-SFM nano assemblies show good promise as food grades and feature a protective layer at the interface that inhibits and resists the production of flocculation and coalescence (89).

Activity of Flax Seed on Human Health

Flax Seed's Role in Sex Hormones

A person's food, lifestyle, level of physical activity, genetics, and environment all influence how sex hormones are made and metabolized. The verification indicates that the phytoestrogens, including lignans, found in flaxseed have an impact on the level of sex hormones. Secoisolariciresinol Diglucoside, the main lignan found in flaxseed, is converted by intestinal bacteria into the mammalian lignans enterolactone and enterodiol. Because lignan and sex hormones share the similar structure, they can inhibit aromatase activity and promote the synthesis of sex hormone-binding globulin (SHBG) in the liver and adipose tissue. Additionally, lignan may bind to testosterone and increase biliary excretion of that hormone. The precise impact in supplementation of flaxseed on sex hormones was unclear, while the lignan components of the seed may preserve sex hormones while also influencing the incidence of linked disorders. Previous research shown that postmenopausal women's metabolism of Estrogen may be altered by flaxseed consumption. While some research indicates that flaxseed has no discernible impact on adult sex hormones, other studies indicate that supplementing with flaxseed enhanced SHBG in subjects under 50 years old and in males with PCOS and TT (90). Both oestrogenic and antiestrogenic actions are associated with phytoestrogen. The most interesting chemical phenomenon about lignan is that it can function as weak agonists (promoters), partial agonists (agonists), or antagonists (blockers) for endogenous oestrogen and xenoestrogens, which are synthesised oestrogens found in many commercial skincare, cosmetic, and cleaning products. They function at the receptor level by poorly binding (91).

Flax Seed's Role in Cardiovascular Diseases

Because flaxseed contains omega-3 fatty acids and β-linolenic acid (ALA), it has heart-healthy properties. It preserves gene transcription and expression, changing the production of enzymes and modifying a number of coronary heart disease risk variables, such as blood pressure and serum triglycerides. Of the approximately 35% oil in flaxseed, 55% is α-linolenic acid (ALA). The rabbit model showed that the combination of very little ALA, flaxseed oil, flax lignan complex (FLC), and secoisolariciresinol Diglucoside (SDG) decreased the development of hypercholesteremia atherosclerosis by 46%, 69%, 0%, 73%, and 34%, respectively. Additionally, it was observed that the progression of atherosclerosis was slowed down by these compounds. It demonstrates that lignan raises serum HDL cholesterol and lowers serum total and low-density lipoprotein (LDL) cholesterol (92). The research indicates that a 10% decrease in the serum level of total cholesterol can reduce the incidence of cardiovascular disease by 30%. Additionally, it has been shown that adding whole flaxseed to the diet of patients with hyperlipidaemia and hypertension, along with following a healthy diet for eight weeks, can lower anthropometric parameters (WC and WHR) and improve participant profiles (TG, CHO, and LDL) (93).

Risk Factors for Heart Disease

Blood pressure: Flaxseed lowers blood pressure, especially when consumed for 12 weeks or longer, according to an analysis of fifteen studies published in the clinical nutrition. Level of cholesterol: According to research, eating roughly three tablespoons of roasted flaxseed powder on a daily basis for three months significantly reduced the total cholesterol levels of fifty persons with elevated cholesterol. raises the levels of HDL, or good cholesterol, while lowering those of LDL, or bad cholesterol (94).

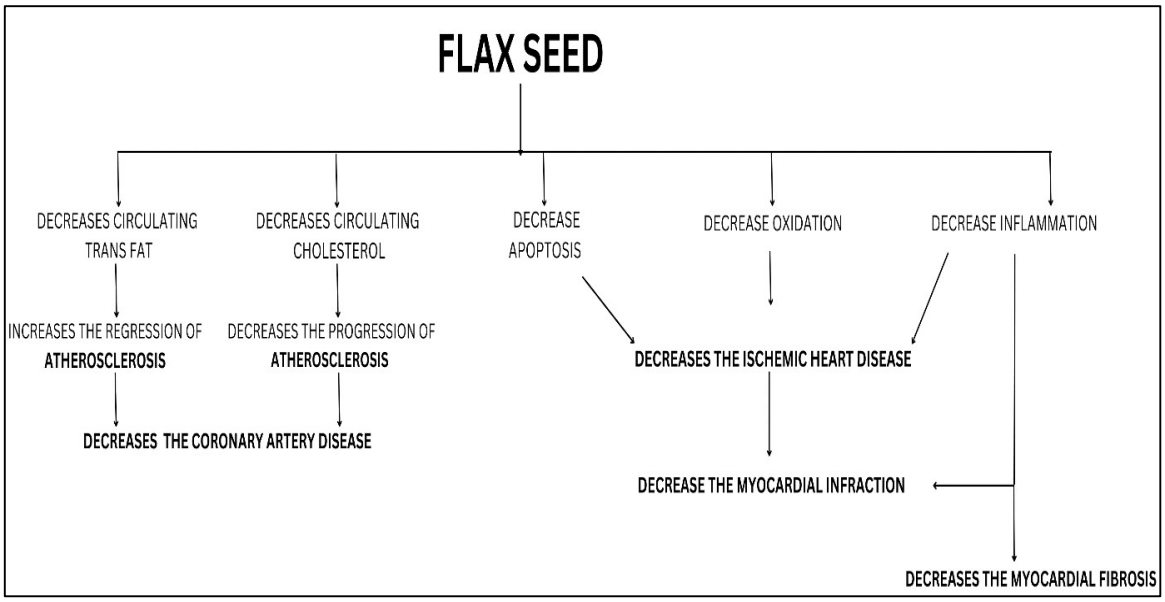


Fig.6. Health benefits of flaxseed (95).

Flax Seed's Role in Anticancer

Proteins from flax seeds have a number of health advantages. Albutrin, globulins, glutelin, and prolamins are among the flaxseed proteins that have anticancer properties. Furthermore, it has been documented that flaxseed proteins alter the mechanobiology of cancer cells, resulting in altered cellular behaviour as well as decreased migration and invasion of cancer cells. Proteins from flaxseed can be consumed through food and absorbed in the digestive system. From there, they can travel throughout the body and possibly even reach cancer cells. It is also possible to use targeted medication delivery systems with nanoparticle formulation to directly deliver flaxseed proteins to cancer cells. These proteins are also delivered to the skin cancer cells through topical administration. It has been demonstrated how beneficial flaxseed proteins are for numerous cancer cell lines, including those from the breast, skin, prostate, and colon; this anti-tumour activity causes cell cycle arrest and triggers apoptosis (cell death). In particular, it has been observed that flaxseed proteins

improve the efficacy of chemotherapeutic drugs in a variety of cancer cell lines. Additionally, it uses radiation therapy to treat non-small cell lung cancer (NSCLC). Consuming flaxseed on a daily basis has been linked to a lower incidence of acute radiation-induced complications (96).

Flax Seed's Role in Breast Cancer

Food flaxseed has been extensively researched because of potential link to breast cancer. According to several research, omega-3 fatty acids are mostly linked to a lower risk of breast cancer. According to certain research on animals, ALA can decrease growth, size, and cell proliferation while also increasing or regulating the effectiveness of tamoxifen in reducing tumour growth, cell proliferation, and cell death (apoptosis). Diets containing 5 or 10% flaxseed daily prevented Mice injected human breast cells from growing ER+. This also occurred with the ER-growth. Additionally, it lowers the ER-breast tumour's metastasis. Pre-menopausal women may also benefit from breast cancer treatment, which primarily targets post-menopausal women and lowers their risk of developing the particular form of cancer (97).

Flax Seed's Role in Diabetes

Flaxseed consumption lowers the risk of developing diabetes. One important hepatic enzyme involved with the synthesis of glucose is phosphoenol pyruvate carboxykinase, whose activity is decreased by flaxseed contain lignan SDG. Flaxseed supplementation lowers blood sugar levels in people suffering type 2 diabetes and prediabetes. Rats having type-1 diabetes demonstrate an antihyperglycemic effect from flaxseed's lignan content. Oral SDG supplementation reduced the risk of developing diabetes in female rats by 80% prior to the onset of the disease. When compared to other age groups, flaxseed has a particularly positive effect of type 2 diabetes in individuals between the ages of 25 and 45. It also helps to maintain a healthy BMI, WC, and WHR in both men and women (98). When compared to other age groups, flaxseed has a particularly positive effect of type 2 diabetes in individuals between the ages of 25 and 45. It also helps to maintain a healthy BMI, WC, and WHR in both men and women (99).

Flax Seed's Role in Anti-Oxidant

The antioxidant activity of the SDG's hypoglycaemic effect in type 2 diabetes may be the reason for its suggestion. Lignan aids in lowering the harm caused by free radicals, which are linked to a variety of illnesses and ailments (100). Flaxseed is an abundant source of antioxidants.100 The body produces reactive oxygen species and reactive nitrogen species as a result of an ongoing metabolic reaction. Primary and secondary antioxidants are the two categories into which they are split. Providing a hydrogen atom is the fundamental antioxidant's function (chain breaking). Secondary antioxidants have three functions: they bind metal ions that can absorb UV light, catalyse oxidative processes, and inhibit enzymes. The overproduction of these species as a result of cellular component damage, such as lipids, proteins, and DNA, disrupts exposure to natural anti-oxidant systems including catalase, glutathione peroxidase, and superoxidase dismutase. The creation was connected by these free radicals to an increased risk of cancer and numerous degenerative disorders, including cardiovascular disease (101). It has been demonstrated that flaxseed's antioxidant action lowers both total cholesterol and platelet aggregation (102).

Flax Seed's Role in Skin Health

Omega-3 fatty acids play a crucial part in the physiology of skin health. When supplementing with flaxseed oil, the skin condition can be much improved (103). It is acknowledged that the primary bioactive component with an impact on the skin and aging is a-linolenic acid. The addition of flaxseed oil supplementation resulted in notable reductions in skin roughness, sensitivity, scaling, & trans epidermal water loss (104).

Flax Seed's Role in Nervous System

The oil from flax seeds is used to treat certain cases of depression and helps older people's mental health. About 55–60% of the total fatty acid in flax seed oil is omega-3 fatty acid. It is beneficial for preserving brain health since the lining of every brain cell is made up of lipids and cell membranes, which make up 60% of the brain (105). Compare puff wheat and flax seed to the participants in the case study. The effects of flaxseed on physical and mental exhaustion in children and adolescents with increased body weight are evaluated through the use of the Multidimensional Fatigue Inventory, which takes into account factors like depression, anxiety, and stress. The A group ate 20 g of flaxseed and the B group ate 25 g of puff wheat for four weeks. They examined fatigue, mood fluctuations, and appetite, as well as height, weight, and waist circumference. The developer discovered a significant reduction is mental weariness in the group that

received puffed wheat. However, daily flaxseed consumption had no effect on overall weariness. Motivation or physical exercise had little effect on depression or anxiety levels (106).

Flax Seed's Role in Osteoporosis

Osteoporosis is a skeletal illness characterized by reduced bone mass and density and microarchitectural damage to bone tissue. It is a huge public problem that currently affects over 75 million people worldwide. Flax oil performs poorly in terms of IL-4 and IL-8 validation. Flaxseed is one of the best sources of lignan phytoestrogens. Several research have used improved techniques to discover and evaluate phytoestrogens in flaxseed. According to previous research, phytoestrogen prevents glucocorticoid-induced osteoporosis while also producing additional negative effects. It produces serum calcium, phosphorus, and other relevant parameters. In the current study, feeding diets containing glucocorticoids resulted in a significant decrease of feed intake, body weight gain, and feed efficiency ratio, which was balanced with the healthy control group fed a basal diet. It demonstrates that incorporating flaxseed into the eating regimen had no clinically significant influence, since there was no weight increase or BMI. According to the findings, it is possible the dietary supplementation of flaxseed can help prevent glucocorticoid-induced bone loss. Some of the associated adverse effects were also reduced (107).

Evaluation Studies of Flax Seed

Software has been utilized to ascertain the genotype variation in flax seed quantitative data, and the ANOVA technique has also been employed to determine flax seed quantitative data (108). The flax seed underwent physical, chemical, and biological analysis. The results of the chemical analysis revealed the presence of oil and linolenic acid, indicating that the flax seed was routinely ingested. The flax seed is also available in raw and conventional, arbitrary forms (109). Flax seed's liposome content has been used as a skin-protective activity. The liposome cream was assessed for PH, organoleptic properties, viscosity, and microscopy testing. Additionally, recent research has demonstrated that tamarind seed oil and flax seed were entrapped in the liposome formulation, which has a strong protective effect against skin damage (110). Flax seeds include oil, lignans, protein, vitamins, and fibre. These nutritional components are assessed using a variety of methods, including chromatography, mass spectroscopy (MS), UV-visible spectroscopy, evaporative light scattering (ELSD), and flame ionization detection (FID) (111).

The nutritional and biological qualities of unleavened flat breads have been enhanced by the use of flax seed flours, and the biological activities have assessed the quality of the protein and amino acids (112), The content of unsaponifable matter, total tocopherols, fatty acid content, total flavonoids, and phenolics have all been studied (113), as the consumption of flax seed has increased significantly in pregnant women recently and as flax seed consists of secoisolariciresinol diglycosides (SDG). PUFA has a rich fatty source that is necessary for the human diet but can be susceptible to oxidation. It is a precursor of lignan and is transformed by the bacterial flora found in the human colon into significant mammalian lignans (114). Since linum usitatissimum has been assessed using a variety of techniques and has some Physico-chemical properties assessed, it has the potential to function as binders, stabilizers, and disintegrants in both liquid and solid formulations (115). Women's menopausal climacteric symptoms have been lessened by the FS meal and extracts, and the variance has been calculated using the Kupperman index (116).

Since flax seeds are rich in macro- and micronutrients and are primarily grown for their oil and fibre, they are useful in preventing malnutrition. Flax seed is also used in medicine for purposes such as expectorant, demulcent, and emollient, as well as polishes and lubricants (117), Additionally, natural polymers with low allergic reactions, chemical flexibility, non-toxicity, and biodegradability have been applied in a variety of biopharmaceutical applications. In fact, modern naturapolyceutics concepts integrate natural polymers in drug delivery systems (118).

The flax seed is functioning as a chemo preventive. Studies have been conducted on the sensory evaluations such as flavor, consistency, and appearance, as well as the biological evaluations such as blood analysis, histopathological examination, serum analysis, liver and kidney function evaluation tests, and statistical analysis such as ANOVA is used to analyze the variance of treatments and lipid content such as HDL/LDL, triglycerides, and cholesterol level examined in the groups of rats (119).

The FS oil has been microencapsulated using a modified starch-containing emulsion by spray drying, and the fatty acid's moisture content activity, water holding capacity, fatty acid composition, distribution of microcapsule size of the microcapsules, and crystallinity have been determined (120) and the crude oil exhibits lower stability and oxidative stress properties compared to the microcapsules, which are uncrackable. Under vacuum storage has been used to prevent microcapsule oxidation (121); the complexing activity of both polyanions and chitosan has been significant in effectively limiting the drug's release from entrapment (122);

And the evaluation of certain content, such as size, shape, and color, is crucial in the description of the FS because, as of late, the primary objectives of research are to support breeding programs. and image analysis's importance has grown recently (167), along with the evaluation of phenotypic character alterations and the identification of any visual changes. Changes in FS resulting from soil, climate, cultivating region, and geographic characterization are also assessed (123), and plant characterization has been accomplished by image analysis (124).

Evaluation of Flax Seed Extract on the Anti-Depressant

Due to the fact that flax seed (FS) containing lignans contains Di phenolic compounds, which may help prevent or treat cancer. Recent studies have also looked into the management and treatment of neurotic disorders (125). A thorough analysis of flax seed also revealed the presence of flavonoids, which are alkaloid compounds, phenolic elements, phytosterols, and amino acids. Moreover, an extract from flax seeds has been found to have more sucrose (126). Additionally, researchers have discovered that the immobility period for flax seed extract is shorter than that of imipramine because the omega-3 fatty acids in the extract help regulate neuronal receptors, control oxidative stress in the brain, ensure optimal brain function, and treat a number of neuropsychiatric disorders (127). Because of this, studies have shown that when extract concentration rises, so does treatment effectiveness due to the existence of omega-3 content in FS, because flax seed has a higher cleansing activity and has been shown to be beneficial in lowering microbial counts, as well as for improving flax seed extraction, Because of this, studies have shown that when extract concentration rises, so does treatment effectiveness due to the existence of omega-3 content in FS (128).

Evaluation of Flax Seed Activity on the Skin

In addition to providing a barrier to the skin, the FS also helps to prevent skin irritation and damage (129). Tocopherol, vitamin B, and vitamin C included in the FS also help to protect the skin from sun damage (130). Ph studies have been carried out for liposomal preparation, and rheological investigations have also been performed to analyze the properties of flow for the liposome formulations using rheometer equipment (131). The liposomal formulation's storage stability is between 4 and 25 degrees Celsius.

Evaluation of Flax Seed on the Artificial Tear

The negative effects of dry eye illness on visual performance and quality of life include ocular discomfort and impaired vision. (132-135) Artificial tears that contain lipids to safeguard ocular cell surfaces from hyperosmotic stress include lipids like castor oil, mineral oil, and salts such as Na+/K+ or organic osmolytes, along with humectant polymers like carboxymethyl cellulose (CMC), hyaluronic acid, or polyethylene glycol that help hydrate and lubricate the ocular surface. In comparison to artificial tears (Refresh optive advanced ROA), this study assesses the safety and effectiveness of a nano-emulsion artificial tear (OM3) that contains CMC, glycerin, flaxseed oil, castor oil, and 3 Osmo protective substances (levocarnitine, erythritol, and trehalose). Evaluation study results lend support to the use of OM3, a novel nano-emulsion tear formulation free of preservatives, in conjunction with trehalose and the oil of flaxseed to treat dry illnesses (136).

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