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An Overview on Isolation & Evaluation of Flaxseed Mucilage and its use as a Pharmaceutical Excipients

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Abstract
Flaxseed contains significant concentration of mucilage or gum (a type of hydrocolloid). Flaxseed mucilage (FM) predominantly occurs in the outermost layer of the seed's hull and is known to possess numerous health benefits such as delayed gastric emptying, reduced serum cholesterol, and improved glycemic control. FM is typically composed of an arabinoxylan (neutral in nature) and a pectic-like material (acidic in nature). Similar to gum arabic, FM exhibits good water-binding capacity and rheological properties (similar functionality); therefore, FM can be used as its replacement in foods. In this review, an overview of methods used for FM extraction and factors influencing the extraction yield were discussed initially. Thereafter, food applications of FM as gelling agent/gel-strengthening agent, structure-forming agent, stabilizing agent, fat replacer, anti-retrogradation agent, prebiotic, encapsulating agent, edible coatings and films/food packaging material, and emulsifier/emulsion stabilizer were included. At the end, some limitations to its wide application and potential solutions were added.

Keywords: Flaxseed Mucilage, Encapsulating Agent, Emulsifier, Edible Coating, Fat Replacer, Stabilizing Agent

1. Introduction

Flaxseed also known as linseed, is an annual herb that produces small flat seeds possessing a crispy texture and a nutty taste Flaxseed popularly known as Alsi or Jawas in Indian language is a rabi crop and a member of family Linaceae. Today, it is being cultivated in more than 50 countries, most of which are in the Northern hemisphere. Canada is the main flax producing country, followed by China, United States, and India Flaxseed is thought to be one of the oldest cultivated crops with evidence of cultivation dating back thousands of years Globally, flaxseed is grown either as an oil crop or a fiber crop with fiber linen derived from the stem of fiber varieties and oil from the seed of linseed varieties [1]. Flaxseed has been cultivated and consumed by humans since ancient times owing to its high nutritional value and medicinal benefits. It is an economically important oil-seed crop since it contains about 40% of oil.

Fig 1: Flaxseeds

Anatomically, flaxseed consists of three major parts: an embryo or germ, two cotyledons, and a hull, with approximate proportions of 4%, 55%, and 36%, respectively. Flaxseed hull consists of a thin endosperm and a thick layer of seed coat. The seed is flat and oval with a pointed tip having a smooth-glossy surface, with color ranging from medium reddish-brown to light yellow. The seed colour is determined by the amount of pigment present in the outer seed coat, higher the pigment, the darker will be the color. Flaxseeds vary in dimensions from 3.0 6.4 mm in length, 0.5–1.6 mm in thickness and 1.8–3.4 mm in width (Freeman, 1995). Generally, fibre flaxseeds have lesser dimensions than oily flaxseeds. Prior to design and fabrication of post harvest handling and processing machines, it is necessary to consider some physical properties of the seeds [2]. Physical properties of agricultural materials affect how they are to be handled, processed, stored and consumed. They are required in the design of planting, harvesting, post-harvest handling and processing operations. Gravimetric properties such as seed weight, density and porosity are also important for the design of equipment related to aeration, drying, storage and transport. Bulk density determines the capacity of storage and transport systems, whereas true density is useful for separation equipment. Porosity data is required in modelling and design of various heat and mass transfer processes such as drying, heating, frying, cooling, and extrusion. Flaxseed is rich in fat, dietary fibre, and protein, but poor in starch. Generally, whole flaxseed contains 30–41% fat, 20–35% dietary fibre, 20–30% protein, 4–8% moisture, 3–4% ash, 1% simple sugars. It is also good source of vitamin A, B, C, D, E, minerals, and amino acids. The variation in chemical composition in flaxseed is mainly due to the variation in genetics or cultivars, growth location, time of harvest, and environment, method of processing and analysis [3-6]. Flaxseed, besides its traditional chemical uses, is now gaining recognition as a functional food ingredient for human nutrition products. Awareness about therapeutic nutrition has driven consumer demand for health and functional foods with higher contents of minerals, fiber and antioxidant. Flaxseed has new prospects as a functional food because of consumer’s growing interest for foods with superb health benefits. The health benefits of flaxseed are mainly attributed to presence of certain biologically active components like lignans, alpha-linolenic acid and phenolic acids. Nutraceutical and health benefits of flaxseed have been attributed due to its essential fatty acids, which are omega-6 and omega-3 fatty acids [7-9]. The beneficial health-related effect of flaxseed makes it suitable as an important ingredient in functional foods which are consumed as a part of daily diet. It is enjoying an upsurge in popularity as a result of various reports on its benefits to human health especially in its potential to reduce the risk of certain diseases. The large amount of flaxseed carbohydrate is indigestible and comprises of soluble and insoluble fibre. Soluble fibre of flaxseed is commonly called flaxseed mucilage, or less commonly as flaxseed gum and viscous fibre. It is located in the outermost layer of flaxseed hull, and it is easily leached out to form a viscous layer when flaxseed is wetted [11]. One of the remarkable features of flaxseed is its high mucilage content; representing about 3 to 9% of the total seed. It is composed of 50–80% carbohydrates, 4–20% proteins and 3 to 9% of ash. Flaxseed mucilage is composed of water soluble heteropolysaccharides of high molecular weight. The polysaccharides are composed of galacturonic acid (21–36%), xylose (19–38%), rhamnose (11–16%), galactose (12–16%), arabinose (8–13%) and glucose (4–6%) (Fedeniuk and Biliaderis, 1994; Oomah *et al*., 1995). They are present in an acidic, pectin-like, rhamnogalacturonan I (Naran *et al*., 2008; Cui *et al*., 1994) form and a neutral (galacto)-arabinoxylan form, both differing in ratios according to the cultivar. These heteropolymers, as well as other natural polysaccharides could be widely used in many industries. Flaxseed has been emerging as one of the key sources of bioactive ingredients in the functional food arena. In addition to being one of the richest sources of α-linolenic acid and high-quality soluble fiber, flaxseed is also an essential source of lignans. Flaxseed is rich in total dietary fiber (20–28%) and increased dietary fiber consumption is associated with a lower risk of several types of cancers [12]. Flaxseed mucilage possesses excellent rheological properties including thickening, emulsification and gelling and finds applications as an additive in food industry. Wannerberger reported that mucilage extracted from different flax cultivars exhibit different rheological properties. The functionality of flaxseed mucilage is similar to that of gum arabic. However, the application of flaxseed mucilage in other areas and further development of its products are rarely reported. The intake of flaxseed mucilage reduces blood glucose and cholesterol in diabetics and may suppress postprandial lipemia Bioactive compounds exist in free, bound and soluble conjugated forms which need to be released using optimum experimental parameters like extraction time and temperature and suitable solvents. Phenolic compounds are a group of phytochemicals which are widely distributed in plant kingdom. Basically, phenolics are composed of two main groups: Flavonoids (flavonols, flavones, flavanones, catechins, isoflavonoids, and anthocyanidins) and nonflavonoids (phenolic acids, phenolic alcohols, and stilbenes). Phenolic acids in nonflavonoid group are most important to researchers and food industries due to their reported antioxidant properties as well as their roles in the prevention of many diseases such as cancer and cardiovascular diseases.

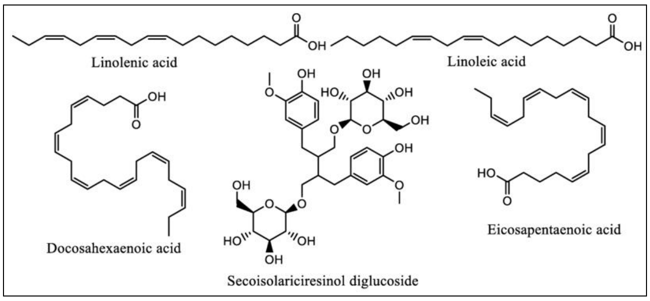

Fig 2: Chemical Constitutents of Flax seed

Williams *et al*. (2013) reported that type and level of bioactive compounds such as phenolic compounds can vary markedly between cultivars, harvest, climatic, agronomic, and postharvest conditions such as food processing. Flaxseed is rich source of different types of phenolic compounds such as phenolic acids, flavonoids, phenylpropanoids and tannins. Reactive oxygen species such as hydrogen peroxide, superoxide anion, and hydroxyl radical can cause damage to biological macromolecules leading to protein oxidation, lipid peroxidation, and DNA base modification and strand breaks that polyphenolic compounds which have the ability to scavenge free lipid, hydroxyl and superoxide radicals, as well as singlet oxygen are possible reasons for DNA damage protection activity. Plant-derived phytochemicals or antioxidants can function as scavengers of free radicals, reducing agents, or metal ion chelators, and they may combat oxidative stress by maintaining a balance between oxidants and antioxidants [12-17]. Consequently, they decrease the incidence of diseases caused by oxidative damage and exert a beneficial effect on human health Chandrasekara and Shahidi. Different solvents and techniques can be used to isolate antioxidants from a plant material, because of diversity of chemical nature of these compounds in the plant matrix. The technique most commonly used for recovery of plant antioxidants is solvent extraction. The yields and antioxidant efficiency of the resulting extracts are affected by chemical nature of the isolated compounds as well as polarity of the solvent. Various polar solvents like methanol, ethanol, and ether have been used to extract phenolic compounds with antioxidant properties from different plant materials. Furthermore, in order to determine phenolic compounds in extracts, various analytical methods such as conventional high performance liquid chromatography (HPLC) and Ultra Performance Liquid Chromatography (UPLC) have been use. The major advantages of UPLC over conventional HPLC are its higher sensitivity, improved resolving power, and shorter retention times. Several processing techniques applied to seeds allow phytate hydrolysis due to enzyme activation during processes such as soaking, germination, fermentation and cooking. Furthermore, several processing and cooking methods have been shown to possibly reduce antinutrients such as phytic acid and trypsin inhibitor, and are known to increase the content of tannins, catechins and polyphenols [18-21]. By applying a variety of heat-processing methods, such as roasting, autoclaving and microwave heating, grains can be prepared for consumption. Many properties of foods such as functional, antioxidant and nutritional value are affected by these processing methods. Processed foods these days require the presence of bioactive ingredients to satisfy the demands of health conscious consumers. Roasting is a simple and convenient process that uses dry heat for short periods of time for improving seed characteristics. Roasted seeds exhibit improved texture, enhanced crispiness and volume due to puffing. However, microwave cooking is becoming a common heating method as the time taken is short. Therefore, the shortcomings of sand roasting like lack of temperature control and contamination with sand can be eliminated by switching over to microwave. Research on cooking and retention of bioactive components show that while a healthy diet may contain an adequate amount of antioxidants, the method by which food is prepared and cooked may be just as important as what is eaten. Hydrothermal application affects the character of changes in the internal structure of the raw material and the extent of change depends on various geometric traits of grain. There have been reports on effect of germination on phenolic compounds and antioxidant activity of flaxseed and microwave assisted extraction of phenolic compounds in flaxseed. Few researchers have studied the effect of soaking on phytase activity and phytic acid hydrolysis from cereals. Alternatively, during the soaking process, the enzyme polyphenol oxidase may be activated, resulting in degradation and consequent loss of polyphenols [16-18].

2. Flaxseed mucilage

The large amount of flaxseed carbohydrate is indigestible and comprises of soluble fibre and insoluble fibre. Soluble fibre of flaxseed is commonly called flaxseed mucilage, or less commonly as flaxseed gum (FG) and viscous fibre. It is located in the outermost layer of flaxseed hull, and it is easily leached out to form a viscous layer when flaxseed is wetted (Susheelamma, 1987). FG is substantially concentrated in the outermost seed coat and it constitutes approximately 8% of dry flaxseed mass. One of the remarkable features of flaxseed is its high mucilage content; located in the outermost layer of the seed's hull, flaxseed mucilage represents 3 to 9% of the total seed (Fedeniuk and Biliaderis, 1994). It is composed of 50–80% of carbohydrates, 4–20% of proteins and 3 to 9% of ash (Cui, 2001; Oomah *et al*., 1995). The polysaccharides are composed of galactose (12–16%), galacturonic acid (21–36%), xylose (19–38%), rhamnose (11–16%), arabinose (8–13%) and glucose (4–6%). Flaxseed mucilage can be further separated into two groups: an acidic fraction (17%) and a neutral fraction (83%) (Dev and Quensel, 1988; Warrand *et al*., 2005). The neutral components are L-arabinose, D-xylose and D-galactose (3.5:6.2:1), whereas the acid components are a mixture of L-rhamnose, L-fucose, L-galactose and D-galacturonic acid (2.6:2:1.4:1.7) (Kaewmanee *et al*., 2014; Qian *et al*., 2012). They are present in an acidic, pectin-like, rhamnogalacturonan I (Naran *et al*., 2008; Cui *et al*., 1994a) form and a neutral (galacto)-arabinoxylan form, both at differing ratios according to the cultivar. The average molecular weights, estimated by gel chromatography, are about 500,000 daltons and 600,000 daltons for the neutral and acidic fractions, respectively (Muralikrishna *et al*. 1987). It has a rheological pattern similar to typical viscoelastic fluids and is comparable to guar gum solutions at similar concentrations (Cui *et al*., 1994a; Fedeniuk and Biliaderis 1994). that soluble fiber is the gel-like mucilage that can be easily extracted from flaxseed by soaking it in water. Flaxseed mucilage is readily soluble at 0.5% concentration. This solubility is better than guar gum and locust bean gum, but slightly lower than Arabic gum. Gums containing a higher amount of acidic polysaccharides exhibit weak rheological properties. In contrast, the level of xylose in the gums reflects the relative amount of neutral polysaccharides, which enhances the rheological properties of the gum by increasing the characters of shear thinning and weak-gel properties (Cui *et al*., 1994a). Flaxseed mucilage is generally obtained by aqueous extraction of the whole seed or meal. Yield, compositional characteristics and rheological properties of the extracted gum are dependent upon the seed:water ratio, pH and time-temperature extraction regime used (Mazza and Biliaderis 1989). Cui *et al*. (1994b) optimised the extraction process in terms of temperature, pH and seed to water ratio. The mucilage exists in two states, one which can be easily separated and the other which tightly adheres to the cell walls. Soaking flaxseed with a water (ratio of 1:13) at 85-95 ºC and pH from 6.5-7.0 for 3 h was found to be the optimum mucilage extraction condition to achieve maximum yield and quality, using response surface methodology. However, higher extraction temperature induced higher protein content and browning in color (Fedeniuk and Biliaderis, 1994). FG is easily extracted by soaking whole flaxseed in water. The main component of FG is a high molecular weight polysaccharide whose glycoside bonds can be degraded by physical, chemical or biological methods, thereby releasing sugar with lower degree of polymerization. Thus, FG could be considered as a suitable source for novel oligosaccharides preparation that flaxseeds with less mucilage were prepared by soaking in water or 0.1 M sodium bicarbonate (NaHCO3) solution for pointed out that the extraction yield of mucilage can vary as a function of environmental factors, such as the climatic condition and crop age. Flax mucilage consumption has health benefits of its own, with implications in diabetes and cardiovascular disease management, colon cancer prevention and reduction in the incidence of obesity that flaxseed is also rich in soluble and insoluble dietary fibre. Further, soluble fibre (mucilage) aids in decreasing cholesterol and optimizing blood sugar levels. Flaxseed has been consumed throughout the world and nowadays, flaxseed is recognized as a good source of soluble fibre, which helps to lower blood cholesterol, insoluble fibre which promotes laxation, α-linolenic acid an essential omega-3-fatty acid important for cardiovascular health and phytoestrogens with estrogen like activity. FG is of special research interest owing to its desirable functional properties, especially its emulsifying properties, and hence making it a useful food additive. Flax mucilage also exhibits surface activity and the ability to stabilize oil/water emulsions and foams and has been used in emulsion preparation in order to enhance stability. It also stabilizes the emulsions by increasing the viscosity and decreasing the interfacial tension. The main advantage of milled flaxseed to be used in bakery products is its protein fractions and carbohydrate (gums) [18-20]. FG has been reported to increase viscosity, stabilize foam and protein based emulsions affecting shear rate as gum Arabic does and showing promise as an improving agent and food thickener in baked goods (Carter, 1993). FG incorporation into food products, such as meat sausage, salad dressing, and dairy dessert have been proposed due to its marked water-holding capacity, swelling, emulsification and rheological propertie. Compared with insoluble dietary fibres, soluble dietary fibres are easier to incorporate into beverages, dairy products, and processed foods as thickeners, emulsifiers, stabilisers, and fat replacers. Fibrous flaxseed hulls contain few amounts of protein and oil but abundant polymeric carbohydrat. Bekhit *et al*. (2018) suggested that sticky mucilage solution can be freeze-dried, vacuum dried or spray-dried to generate a shelf-stable powder product. Also, the mucilage can be used as a emulsifying and thickening agent in food, pharmaceutical and cosmetic applications due to its desirable physical properties. Based on lubrication and moisturising properties of FG solution, these polysaccharides are also suitable for use as laxatives and barium sulphate suspending agents for preparing X-ray contrast suspensions. found that mucilage also can be used in fermented dairy products to support the growth of lactic acid bacteria and favourably modify the product texture at the same time. FG properties are dependent on extraction conditions, drying processes, shear and extrusion, as well as flaxseed cultivar used as a source. The potential utilisation of FG as a commercially viable product requires selection of cultivars that produce consistent FG [17-20].

2.1 Flaxseed characteristics

Flax is a blue flowered annual oilseed crop, which belongs to the family Linaceae. Flax plant is native to western Asia and Mediterranea and is widely cultivated all over the world primarily for its seeds and fiber. Flax has been cultivated since at least 5000 BC, but today it is mainly grown for its. It is grown as a crop in very cool climate region of the world except the arctic and the tropics. Globally, large amounts of flaxseed are produced with a total output of 1.173 million tons in 2014 (FAO, 2017). Flaxseed, popularly known as Alsi, is used as food and for medicinal purposes in India. The important flaxseed growing countries include Canada, India, China, United States, and Ethiopia with Canada being the world's largest producer. In India it is mainly cultivated in states of Madhya Pradesh, Maharashtra, Chattisgarh and Bihar. Flaxseed is formed in a capsule containing up to ten seeds of variable weight and size, according to the genotype. At maturity, the capsule opens and releases its seeds into the environment. Its development is typical of dicots, with the plantlet showing two cotyledons. Anatomically, flaxseed comprises of three layers viz. cotyledon, endosperm and spermoderm from inside to outside. Flaxseed oil is distributed mainly in the cotyledon and endosperm while the lignans and mucilage exist in the spermoderm portion. The seed is oval and flat with a pointed tip and it has a smooth glossy surface. The color of flaxseed, range from medium reddish brown to light yellow, according to different varieties of flaxseed (Freeman, 1995). The seed colour is determined by the amount of pigment present in the outer seed coat, higher the pigment, the darker will be the color of the seed. The oily flaxseeds generally have greater dimensions than fibre flaxseeds. The seeds have a crisp and chewy texture and a pleasant, nutty taste. Physical properties of agricultural materials affect how they are to be processed, handled, stored and consumed and so are required in the design but the study was mainly concentrated on a commercial sample of flaxseed. The geometric mean diameter of flaxseed has been reported to be lower than and higher than that of sesame seeds. Gravimetric properties such as thousand seed weight, bulk density, true density and porosity are also important for the design of equipment related to aeration, drying, storage and transport. Bulk density determines the capacity of storage and transport systems, whereas true density is useful for separation equipment. Thousand seed weight is a useful parameter in determining the equivalent diameter which can be used in cleaning using aerodynamic forces and in the theoretical estimation of seed volume. Baryeh (2002) reported that porosity value depends on true and bulk densities. Porosity is defined as the volume fraction of the air or the void fraction in the sample. Porosity depends on geometry and surface properties of the material [22-26].

2.2 Nutritional composition and health benefits of flaxseed

Proximate composition is often the basis for establishing the nutritional value and overall acceptance of the consumers and also important in determining the quality of raw material. Flours rich in fats are useful in improving palatability of food products in which they are incorporated by being good flavour enhancers. Flaxseed has been reported to contain relatively high contents of ash, fat, protein and dietary fiber. Flaxseed proteins could be considered a good source of functional ingredients with antibacterial and antioxidant activities and a potential use in the prevention of lipid oxidation in food products. Flaxseed is a rich source of lipids (30–40%), proteins (20–25%), dietary fiber (20–28%), minerals, and vitamins with an amino acid profile comparable to that of soya bean. Flaxseed also known as linseed, is enjoying an upsurge in popularity as a result of reports on its health benefits to humans and therefore, its potential to reduce the risk of certain diseases. Flaxseed is grown for its seeds, fibre and also as an ornamental plant in gardens. It also contains high level of lignans and omega 3 fatty acids. Flaxseed oil is a dietary source of omega-3 fatty acid and is rich in polyunsaturated fatty acids. Flaxseed is made up of approximately 45% lipid and 55% meal on a dry basis. Flaxseed lipid is the main source of nutrient for seed germination. Microscopically, flaxseed lipid is stored in oil droplets (1.3 µm diameter), composed of 0.1% free fatty acids, 1.3% encasing protein, 9% phospholipids, and 98% neutral lipid. Flaxseed has a unique fatty acid profile. It is high in polyunsaturated fatty acids (73% of total fatty acids), moderate in monounsaturated fatty acids (18%), and low in saturated fatty acids (9%). indicated that linoleic acid, an omega-6 fatty acid, constitutes about 16% of total fatty acids, while alpha-linolenic acid constitutes about 57%, the highest of any seed oil. Further, the average yield of linseed oil pressed from the seeds was 35–50% of the seed weight. The most frequently found fatty acids in linseed oil are: stearic acid (2.5%), palmitic acid (6%), linoleic acid (13%), oleic acid (19%), and alpha-linolenic acid (55%). reported that the oil content as well as fatty acid composition often changes due to crop adaptation to regional growing seasons as well as environmental effects. In addition to it, several clinical research studies in humans have aimed at assessing the efficacy of linseed bioactivity in health and disease. Many research reports suggest the valuable impact of a diet high in alpha-linolenic acid from linseed oil on decreasing markers of oxidative stress and inflammation associated with risk of many common chronic diseases (e.g. atherosclerosis). Alpha-linolenic acid (ALA) forms almost 51-55 g/100 g of the total fatty acids of flaxseed oil, making flaxseed as a leading plant source of omega-3 fatty acids. Linolenic acid is the predominant fatty acid in the lipids of flaxseed, and studies have showed its beneficial effect on the growth and development of children as well as on reducing the risk of stroke, cardiovascular and inflammatory disease, and immunological disorders. Most of the flaxseed protein is stored in its cotyledons as the main nitrogen reserve for germination and post-germination of the embryo. Similar to soy protein, flaxseed protein is high in asparagine, glutamic acid, leucine, and arginine. However, flaxseed protein is poor in sulphur-containing amino acids, which are methionine and cysteine [25]. The protein content in flaxseed has been reported between 10.5% and 31%. Khategaon cultivars grown in India are reported to have protein content of 21.9%. Hull fraction contains lower protein levels and dehulling increases protein level of flaxseed protein level from 19.2% to 21.8%. Albumin and globulin type proteins are the major proteins in flaxseed. Flaxseed albumin comprised 20% of meal protein. Globulin fraction makes up to 73.4% and albumin constitutes about 26.6% of total protein. The sensory characteristics of foods are attributed by the functional properties which play an important role in the physical behaviour of food or its ingredients during preparation, processing and storage (Enwere and Ngoddy, 1986). These functional properties include texture, foaming, emulsification, gelation, water and oil absorption and viscosity. The bulk density of a material is important in relation to its packaging. Water absorption capacity is an important processing parameter affecting the viscosity of the food products. Oil absorption capacity is an indication of the rate at which the protein binds to fat in food formulations and it is attributed mainly to the physical entrapment of oils (Singh et a. The enhanced ability of a flour to absorb and retain oil and water may be useful to improve binding of the structure, mouthfeel, enhance flavor retention and to reduce fat and moisture losses from the food products [27]. Foaming capacity is important for use of flour in leavening food products such as baked food items, biscuits and cakes. Emulsifying properties are important functional properties of food proteins. Various chemical and physical factors are involved in the formation, stability, and textural properties of protein–fat–water emulsions. Least gelation concentration can be defined as a measure of the minimum amount of flour that is needed to form gel in a given volume of water. Many food industries intensify on the desirable functional properties in order to improve them to meet their requirements. The functional properties of different proteins can be employed to figure out the fact that how flour proteins can be used to enrich, fortify, or replace more expensive protein sources which are used traditionally. Approximately one third of all proteins and enzymes contain strongly bound elements in their structures, especially transition metals such as copper, cobalt, iron, manganese, molybdenum. Biochemical processes in enzymes and proteins, including activation of substrate, transport and storage, are performed by these elements. Due to the high content of proteins, flaxseed is expected to be a rich source of these elements. In biological systems, minerals take part in proteins, lipids and carbohydrate metabolism, as well as in cellular and skeletal structure and play a role in osmotic pressure and acid/base regulation [28]. The determination of the levels of elements is vital for human dietary intake of essential minerals or for the evaluation of human exposure to toxic elements. Numerous techniques have been employed for trace elemental analysis in food such as Atomic Absorption Spectrometry (AAS) and Flame Atomic Absorption Spectrometry (FAAS). Plants absorb minerals not only through soil but these can also be absorbed through their leaves by sources such as atmospheric dust, rain, fertilizers and plant protection products, described the quantification of trace elements bound to proteins in flaxseed samples after removal of the lipid fraction. Several extraction media were studied for this purpose and the defatted samples were digested using a cavity microwave oven to permit quantitation of Cu, Fe and Zn by FAAS. The separated protein fractions were also isolated using a trisaminomethane buffer and mineral contents quantified by graphite furnace AAS (GFAAS). According to Naozuka and Oliveira (2007), metal ions have high affinity for sulfur containing amino acids or charged groups such as methionine, cysteine, glutamic acid, arginine, aspartic acid and lysine. also reported that high concentrations of these constituents in flaxseed as an indicator of elements being linked to the protein phase. Minerals are among the micronutrients that must be obtained through diet (Reddy and Bhatt, 2001). Minerals are needed by the body in different amounts, depending on the element, to maintain good health. The terms trace minerals or trace elements can refer to essential, non-essential, or toxic elements which are found in very small amounts in human body. Iron (Fe), zinc (Zn) and calcium (Ca) are essential nutrients that are often lacking in human diets, either due to insufficient intake or to poor absorption of food. In developing countries, deficiencies of Fe and Zn lead to much suffering and death. In industrialised countries, chronic Ca deficiency is one of the important causes of reduced bone mass and osteoporosis in the elderly [23]. Flaxseed contains three bioactive components, namely ALA, dietary fibres and lignans which synergistically show health benefits such as reduction in the risk of occurrence of breast cancer cardiovascular disease and menopausal symptoms osteoporosis and diabetes. According to various reported researches, flaxseed consumption has been shown to cause a reduction in postprandial glucose absorption, serum cholesterol levels and an improvement in glucose tolerance (Hutchins *et al*., 2013; Thakur *et al*., 2009). One of the studies on mice has shown that flaxseed intake helped to reduce growth in some specific types of tumours. The health benefits from flaxseed can be credited mainly to its abundance in dietary fibre, high quality proteins, omega-3 fatty acids, and antioxidants. Flower observed that flaxseed intake might be associated with decreased risk of breast cancer and its daily ingestion of 25 g increased the tumor apoptotic index and therefore, reduced cell proliferation among breast cancer patients [22]. Also, flaxseed is a good source of fibre, minerals and vitamins and is a food with functional properties to prevent or lower the risk of cardiovascular diseases and cancer observed that flax lignin compounds have antioxidant activity and can be regarded as anti-cancer, with cardiovascular protective bioactivities.

2.3 Antioxidant potential

Different solvents and techniques can be used to isolate antioxidants from a plant material, because of diversity of chemical nature of these compounds in the plant matrix. The technique most commonly used for recovery of plant antioxidants is solvent extraction. The yields and antioxidant efficiency of the resulting extracts is affected by chemical nature of the isolated compounds as well as polarity of the solvent. Various polar solvents like methanol, ethanol, and ether have been used to extract phenolic compounds with antioxidant properties from different plant materials. Extractions of flaxseed phenolics have usually been carried out with organic solvents and sometimes mixed with water. In order to determine phenolic compounds in extracts various analytical methods have been used. The speed and cost of analysis, and efficiency improvement is always desirable in any application of liquid chromatography [24]. High-performance liquid chromatography (HPLC) is used normally for separating non volatile, high-molecular mass constituents, namely normal phase, and is widely used to separate classes of constituents according to the number and nature of polar functional groups. However, reversed-phase high-performance liquid chromatography (RP-HPLC) is used to separate individual components that belong to one constituent class. Other methods of quantifying polyphenolic compounds include spectrophotometric analysis. The free radical scavenging activity is one of the known methods by which antioxidants inhibit lipid peroxidation. The degree of discoloration indicates the free radical scavenging potential of the antioxidant extract, which is produced by the hydrogen donating ability. Moreover, their antioxidant activity is determined by various *in vivo* and *in vitro* assays. Antioxidant activity of these compounds can be accounted to their redox properties that play crucial roles in adsorbing as well as scavenging free radicals, quenching oxygen and decomposing peroxides. Hydroxyl radicals are short-lived, most damaging radicals within the body formed from hydrogen peroxide and superoxide radicals and oxidize biological macromolecules including proteins, lipids and nucleic acid. Transition metals can generate hydroxyl and superoxide radicals and lead to lipid peroxidation, DNA damage and protein modification. Chelating agents may inactivate these metal ions and therefore, potentially inhibit the metal-dependent processes (Finefrock *et al*., 2003). Sample extracts with metal chelating activity have ability to convert metal ions into insoluble metal complexes or generate steric hindrance, which can prevent the interactions between metals and lipid intermediates, thus inhibiting lipid oxidation process. DPPH (2, 2-diphenyl-1-picrylhydrazyl) radical scavenging activity has been widely used to evaluate antioxidant activity of phenolic compounds extracted from different plants because of its ease of use and stability. The reducing power activity of a compound may be considered as an important indicator of its antioxidant activity. Reducing agents are considered as electron donor compounds and can further reduce the oxidised intermediates of the lipid peroxidation reactions therefore they may be primary or secondary antioxidants. Metal chelating activity is one of the numerous methods used to evaluate antioxidant activity of foods and to explain the function of antioxidants (Amarowicz *et al*., 2000). Recently, these characteristics have been upgraded in the new generation of ultra performance liquid chromatography (UPLC) to provide both qualitative and quantitative information. UPLC is an advanced form of liquid chromatography in which mobile phase delivery systems operating at high back pressures are used [28-29]. The major advantages of UPLC over conventional HPLC are its higher sensitivity, improved resolving power, and shorter retention times. Researchers have reported the identification and quantification of phenolic compounds using UPLC in different raw materials such as in fenugreek seeds and bitter melon, and in various spices. In a study by Hung *et al*. (2011) the researchers presented the first report on application of UPLC for rapid quantification of phenolic acids in cereal grains replacing the traditional HPLC system. Phenolics are important secondary metabolites in plants, which are not only involved in the processes of growth, reproduction and colouring shades in the fruits and flowers of the plant species, but also play an important role against diseases caused by parasites, pathogens and predators (Liu, 2007, 2013). Phenolic acids are derivatives of cinnamic and benzoic acids (Onyeneho and Hettiarachchy, 1992). Ferulic and vanillic acid are the most dominant phenolic acids in Linaceae family (Siger *et al*., 2008) and are found together with other phenolic compounds including p-hydroxybenzoic and chlorogenic acids. Phenolic compounds are the phytochemicals which are abundantly found in cereal grains, fruits, vegetables, medicinal plants and agri wastes. Phenolic compounds are mostly found in the outer layers of plants, such as peels, shell and hull and they contain large amounts of polyphenolic compounds to protect the inner component. Basically, flaxseeds contain three different types of phenolic compounds–phenolic acids, flavonoids and lignans. Phenolic compounds may be affected by multiple factors, such as genetics, environmental stress (drought, temperature, and light), and agronomic conditions [30].

3. Material, Method, and Properties of Flaxseed Mucilage Gel [31-36]

Flaxseed mucilage gel is created from the mucilaginous substances found in flaxseeds (*Linum Usitatissimum*). This gel is rich in polysaccharides, mainly composed of water-soluble fibers, which provide excellent hydration and emollient properties. Below is an outline of the materials and method for preparing flaxseed mucilage gel, along with a description of its properties.

3.1 Materials for Flaxseed Mucilage Gel

1. **Flaxseeds (*Linum Usitatissimum*):** Whole, ground, or cracked flaxseeds can be used, but whole flaxseeds are most commonly used for mucilage extraction. Flaxseeds contain mucilage, a natural gum-like substance, which, when mixed with water, forms a gel. This is the key ingredient in the formulation.
2. **Water (Distilled or Purified):**
   - Acts as the solvent for extracting mucilage from the flaxseeds. The ratio of water to flaxseed affects the final gel's viscosity.
3. **Preservative (Optional):** To prevent microbial growth, especially when storing the gel for a longer period. Commonly Phenoxyethanol, Ethylhexylglycerin, or other broad-spectrum preservatives.
4. **Glycerin (Optional):** Acts as a humectant to enhance the gel's moisture-retention properties, providing additional hydration to the skin.
5. **Essential Oils (Optional):** Added for fragrance or therapeutic properties. Common options include lavender, tea tree, and chamomile essential oils.
6. **pH Adjuster (Optional):** Used to adjust the pH of the gel to be more skin-friendly (generally pH 4.5–5.5). Common Adjusters are widely used Citric acid or lactic acid.

3.2 Method to Prepare Flaxseed Mucilage Gel

1. Preparing the Flaxseed Gel:

1. Measure the Ingredients 10 grams of whole flaxseeds.200 milliliters of distilled water (for a thicker gel, reduce the amount of water).Thoroughly wash the flaxseeds to remove any dirt or dust. In a saucepan, combine the flaxseeds with the water. Heat the mixture over medium heat while stirring occasionally. The heat will help the mucilage to dissolve from the seeds into the water, forming a gel-like consistency. Continue stirring to prevent the seeds from settling and burning. This process should take about 10–15 minutes. Once the mixture has thickened and achieved a gel-like consistency, remove it from the heat. Strain the gel through a fine mesh sieve or cheesecloth to separate the flaxseeds from the mucilage gel. Allow the gel to cool to room temperature. If using a preservative, add it according to the manufacturer's instructions (usually 0.5%–1% of the total weight). Add a few drops if you want to enhance the moisturizing effect of the gel. Add a few drops (typically 0.5%–1%) of your chosen essential oil if desired. If necessary, use a pH adjuster to bring the pH to around 4.5–5.5. Transfer the cooled gel to an airtight container. Store the gel in the refrigerator for up to 1–2 weeks for maximum freshness.

3.3 Properties of Flaxseed Mucilage Gel:

1. Hydration & Moisture Retention:

High Water Content: The gel can hold a large amount of water, making it an excellent moisturizer. It helps the skin retain moisture, making it beneficial for dry or dehydrated skin.

Humectant Properties: Flaxseed mucilage attracts and retains moisture, keeping skin or hair hydrated for longer periods.

2. Emollient & Soothing:

Calming Effect: The gel has a softening effect on the skin, making it suitable for treating irritation, redness, and inflammation. It can also be used for minor burns or skin conditions like eczema and psoriasis due to its soothing properties.

Softens Skin: The gel's emollient nature softens rough patches of skin, making it ideal for use in moisturizers, lotions, or after-sun care.

3. Anti-inflammatory & Antioxidant:

Flaxseed Compounds: Flaxseeds contain lignans and omega-3 fatty acids (particularly alpha-linolenic acid, ALA) which have anti-inflammatory and antioxidant effects. These compounds can help soothe irritated skin and reduce redness.

Skin Protection: The antioxidants present in flaxseed mucilage may help protect the skin from free radicals, which are responsible for premature aging.

4. Thickening Agent:

Gel Consistency: Due to its high content of mucilage, flaxseed gel acts as an effective natural thickener. It is commonly used in skincare products, hair gels, and even food as a plant-based thickening agent.

Stable Texture: The gel retains its consistency at room temperature, making it suitable for use in various cosmetic and pharmaceutical formulations.

5. Hair Care Benefits:

Hair Conditioning: Flaxseed mucilage gel can be used as a natural hair gel to add hold without the use of synthetic chemicals. It helps to define curls and manage frizz.

Scalp Health: The soothing properties of flaxseed mucilage may help calm an irritated scalp and promote hair growth by improving scalp hydration.

6. pH Balanced:

- **Skin-Friendly:** The mucilage gel is naturally close to the skin's pH level (around 4.5–5.5), making it suitable for use in personal care products without causing irritation or dryness.

7. Biodegradable & Eco-friendly:

Natural Source: Being plant-derived, flaxseed mucilage is biodegradable and an environmentally friendly ingredient. It is often used in formulations where sustainability is a key consideration.

3.4 Applications of Flaxseed Mucilage Gel

1. Cosmetic Use:

- Moisturizers, serums, and body lotions.
- Face masks, soothing gels, or after-sun products.
- Hair gels, conditioners, and treatments for frizz control.
- Anti-aging and anti-inflammatory creams.

2. Food Use:

- **Vegan Egg Substitute:** Flaxseed mucilage can replace eggs in recipes like baking (about 1 tablespoon of flaxseed gel equals one egg).
- **Thickener for Sauces, Soups, and Dressings**.

3. Pharmaceutical Use:

- Used as an emollient in creams and ointments for soothing skin conditions.
- Can be incorporated into topical treatments for its anti-inflammatory and hydrating properties.

4. Applications of Flaxseed Mucilage Gel as a Pharmaceutical Excipient [33-37]

Flaxseed mucilage gel is a naturally occurring polysaccharide gel extracted from flaxseeds known for its gelling, thickening, and stabilizing properties. Its composition primarily consists of mucilage (a water-soluble fiber), which has many valuable characteristics making it a useful excipient in pharmaceutical formulations. Below are the key pharmaceutical applications of flaxseed mucilage gel as an excipient:

1.) Binder in Tablet Formulations: Flaxseed mucilage gel can act as a natural binder in the preparation of tablets. Binders help hold the ingredients of a tablet together and improve its mechanical strength, ensuring that the tablet doesn't crumble during storage or handling.

Advantages

- **Natural and Safe:** Unlike synthetic binders, flaxseed mucilage is a natural substance, making it suitable for use in herbal or natural pharmaceutical products.
- **Mild & Non-irritating:** Being derived from a plant, flaxseed mucilage is generally well-tolerated, making it safe for patients, including those with sensitivities to synthetic excipients.

Example Use: In the formulation of herbal tablets, flaxseed mucilage can be used to bind plant powders or active ingredients into a solid dosage form.

2.) Controlled Release Formulations: The gel formed by flaxseed mucilage can be used in controlled or sustained-release drug delivery systems. Mucilaginous polysaccharides like those found in flaxseeds have the ability to swell and form gel matrices that can control the release of active pharmaceutical ingredients (APIs) over time.

Advantages

- **Slow Drug Release:** Flaxseed mucilage can slow down the release of drugs, providing extended therapeutic effects, reducing the frequency of dosing.
- **Biodegradable and Biocompatible:** Being a plant-based excipient, flaxseed mucilage is naturally biodegradable, which is an important feature in controlled-release formulations.
- **Minimal Side Effects:** The natural composition reduces the likelihood of side effects commonly associated with synthetic excipients.
- **Example Use:** Flaxseed mucilage gel can be used as a matrix material for controlled-release tablets or capsules, especially for hydrophilic drugs that benefit from a slower release profile.

3.) Disintegrant in Tablet Formulations: As a disintegrant, flaxseed mucilage can aid in the breakdown of tablets after ingestion. It absorbs water and swells, promoting the disintegration of tablets in the gastrointestinal tract and ensuring faster dissolution and absorption of the active drug.

Advantages

- **Efficient Tablet Breakdown:** Flaxseed mucilage facilitates rapid disintegration, improving the bioavailability of poorly soluble drugs.
- **Natural Option:** It provides a natural alternative to synthetic disintegrants like sodium starch glycolate or croscarmellose sodium.
- **Example Use:** In tablet formulations, flaxseed mucilage can be added in small amounts to improve the disintegration time, especially in the case of herbal or nutraceutical formulations.

4.) Emulsifying Agent in Oral and Topical Formulations: Flaxseed mucilage can act as an emulsifying agent, helping to stabilize emulsions (mixtures of oil and water). This property is valuable in both **oral formulations** (e.g., liquid syrups, suspensions) and **topical formulations** (e.g., creams, lotions).

Advantages

- **Stabilizes Oil-in-Water Emulsions:** Flaxseed mucilage helps disperse oil droplets evenly in water, preventing separation and ensuring consistent dosing of active ingredients in oral liquid forms.
- **Topical Use:** In topical creams or lotions, flaxseed mucilage improves the uniform distribution of hydrophobic ingredients, enhancing the texture and performance of the product.
- **Example Use:** In pharmaceutical emulsions, flaxseed mucilage can serve as a stabilizing agent for the formulation of herbal-based or natural emulsions.

5.) Thickening Agent in Liquid Formulations: Flaxseed mucilage gel can be used as a thickening agent in liquid pharmaceutical preparations such as syrups, suspensions, and gels. It increases the viscosity of the formulation, providing a more stable and palatable product.

Advantages

- **Natural and Non-toxic:** Being plant-derived, it is a safe alternative to synthetic thickeners like xanthan gum or hydroxyethyl cellulose.
- **Improves Palatability:** Thicker syrups and suspensions

are often more palatable, making them more acceptable to patients, particularly children or the elderly.
- **Example Use:** In oral suspension formulations, flaxseed mucilage can help improve the suspension stability and ensure that the active ingredients do not settle.

6.) Excipient in Herbal and Nutraceutical Formulations: Flaxseed mucilage is commonly used in the preparation of **herbal medicines** and **nutraceuticals** as a safe and effective excipient. Its natural origin makes it ideal for products marketed as organic or plant-based.

Advantages
- **Plant-Based and Biocompatible:** Ideal for use in herbal medicine, where natural excipients are preferred to synthetic alternatives.
- **Provides Consistency:** It can help maintain a consistent texture and structure in herbal liquid formulations, pastes, and gels.
- **Example Use:** Used as a base in oral pastes or gel formulations that deliver herbal or nutraceutical compounds.

7.) Suspending Agent in Oral Suspensions: Flaxseed mucilage is highly effective at suspending particles in oral liquid formulations. It can prevent the settling of active ingredients in suspensions, ensuring uniform distribution of the drug or nutrient.

Advantages
- **Improves Stability:** By preventing sedimentation, flaxseed mucilage ensures that the active ingredient is evenly distributed, reducing the need for shaking before use.
- **Gentle on the Stomach:** The mucilage's soothing properties may also help mitigate gastrointestinal irritation caused by some active ingredients.
- **Example Use:** In the formulation of suspensions for liquid dosage forms, flaxseed mucilage helps keep the active compound evenly dispersed.

8.) Wound Healing and Topical Applications: Flaxseed mucilage has moisturizing, anti-inflammatory, and soothing properties, making it useful in topical pharmaceutical formulations for wound healing, skin care, and as an emollient.

Advantages
- **Hydrating:** Its gel-forming ability can provide a moisturizing layer on the skin, promoting wound healing by maintaining the appropriate moisture levels.
- **Soothing and Anti-inflammatory:** Flaxseed mucilage's anti-inflammatory properties can help reduce redness and irritation in burns, cuts, and other skin conditions.
- **Example Use:** Used in creams, ointments, or gels for topical wound care, eczema, or minor burns.

9.) Gel-Based Drug Delivery Systems: Flaxseed mucilage can be used in gel formulations for local drug delivery. The gel's viscosity and gelling properties make it suitable for **topical gel formulations** where controlled release of a drug is required.

Advantages
- **Controlled Release:** The gel can hold active ingredients within its structure and gradually release them over time.
- **Targeted Delivery:** Flaxseed mucilage gels can be used in targeted delivery applications, such as in the treatment of localized skin conditions, where the drug is needed only at a specific site.
- **Example Use:** Used in the development of topical gel formulations for skin conditions like acne, eczema, or localized pain relief gels.

5. Conclusion

Flaxseed mucilage, a natural polysaccharide derived from the seeds of *Linum usitatissimum*, has garnered significant attention as a potential pharmaceutical excipient due to its unique physicochemical properties, such as its water retention capacity, gel-forming ability, and biocompatibility. The mucilage can be effectively isolated from flaxseed using various methods, such as hot water extraction, and its purity and yield are influenced by factors like extraction conditions and the method of separation.

As an excipient, flaxseed mucilage has shown promise in various pharmaceutical applications, including in the formulation of controlled-release drug delivery systems, tablets, and capsules. Its mucoadhesive properties are particularly beneficial in the development of topical and oral dosage forms, enhancing drug absorption and bioavailability. Moreover, its natural origin makes it an attractive alternative to synthetic excipients, offering advantages such as biodegradability, safety, and low toxicity.

Future research should focus on optimizing the extraction and purification processes of flaxseed mucilage, exploring its interactions with other excipients and active pharmaceutical ingredients, and assessing its long-term stability and effectiveness in various drug formulations. In conclusion, flaxseed mucilage holds considerable potential as a multifunctional excipient in the pharmaceutical industry, contributing to the development of more sustainable, effective, and patient-friendly drug delivery systems.

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7. Conflict of Interest

None.

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