



Pharmacological properties of flaxseed, *Linum usitatissimum* Linn., as a potential medicinal plant: An overview

Shweta Gokhale, Alakh. N Sahu

Department of Pharmaceutics, Indian Institute of Technology (Banaras Hindu University), Varanasi, U.P. 221005, India

Received: 25-06-2016 / Revised: 16-07-2016 / Accepted: 24-07-2016 / Published: 31-07-2016

ABSTRACT

India has a great wealth of naturally occurring plant drugs which have great potential and pharmacological activities. Flaxseed, *Linum usitatissimum* Linn. is an annual herb which is used in several traditional medicines to cure various diseases. Flaxseed is a cold temperate herb with erect, slender stems belonging to Linaceae family. Leaves are alternate, lance-like and grayish green with three veins. Stems are slender and fibrous; flowers have five pale blue petals in a cluster. The sepals are lance-like and as long as the pointed fruit. The fruit is like a spherical capsule containing two seeds in each of five compartments. The seeds are oval and flatten with a pointed tip. The seed has both medicinal and nutraceutical properties. This seed has been known to possess 'antidiabetic, antioxidant, estrogenic, antibacterial, cardio-protective activity etc. The texture of it is crisp and chewy, having a pleasant nasty taste. It is richest vegetarian source of Alpha-linolenic acid(ALA), lignans (phytoestrogen) and soluble mucilage, all having benefits in overall health management. These reports show that it should be studied more broadly for its therapeutic benefits. The review summarizes the information about the phytochemistry, pharmacological activity and toxicity of Flaxseed.

Keywords: Flaxseed, linseed, phytochemistry, phytoestrogen, pharmacological activity and toxicity.



INTRODUCTION:

Linum usitatissimum Linn., versatile and blue flowering rabi crop belonging to Linaceae family. The plant is commonly known as Flaxseed or Linseed in English and Alsi, Tisi, Javas, Aksebija in Indian languages. It is a cold temperate herb which was used during ancient times to cure diseases as well as a nutraceutical [1]. Flaxseed is used in Ayurvedic preparations for ages, because of its therapeutic properties. According to Ayurveda, these seeds hot, pungent, heavy, purgative and strengthening properties. Due to its nutty flavor, it is used in bread and bakery products. Flaxseed play a key role in several Ayurvedic protocols like Virechana, which is medicated purgation therapy. Virechana cleanses the sweat glands, colon, kidneys, stomach, liver, and spleen. Flaxseed is beneficial in cardiac disorders, cancer, arthritis, wounds, abscesses, diabetes and digestive disorders. Modern research has discovered that flaxseed possesses antioxidant activity and may be clinically helpful in cardiovascular health [2]. The herb found abundantly in Indian subcontinents,

Flaxseed is being used over centuries and it have a unique characteristic to make you feel satiated when these seeds are eaten before a meal. Thus, it reduces food craving and excessive hunger that occurs in obese people. These seeds can be included in the diet plans for losing weight. Found commonly in Gangetic (North India) and Peninsular (South India) region. Linseed is used in Ayurvedic medicines to treat bronchitis, fever, cough, inflamed lymph nodes etc.

The plant is a food and fiber crop. Cultivated in cooler regions of the world. Leaves are alternate, lance-like and grayish green with three veins, up to 4cm long and 4mm wide. Stems are slender and fibrous; flowers have five pale blue petals in a cluster (3cm in diameter). The sepals are lance-like and as long as the pointed fruit. The fruit is like a spherical capsule (5-9 mm) containing two seeds in each of five compartments [3]. Within 100 days of sowing the plant flower and after two weeks the seed capsules form. The base of the plant turns yellow. Green plant seeds will not be useful and fiber will be underdeveloped. All the parts of plants

have been used for the beneficiary purpose. Other than as medicinal value various parts of the plant have been used to make fabric, dye, paints, varnishes, paper, fishing nets and soaps. Traditionally, it is one out of the five flowers which are offered to Goddess Durga in Durga Pooja. It has anti-inflammatory [4], anti-cancerous [5], antidiabetic, cardio-protective [6], estrogenic [7,8] and hepatoprotective activity [9]. Different types of the bioactive compounds have been isolated from this medicinal plant possesses immense value in medicine.

The aim of the present study was to deliver the literal studies of *L. usitatissimum* with its phytochemical and pharmacological characteristics. Flaxseed is also believed to be a natural liver tonic; it regulates cholesterol by decreasing LDL levels in the liver [10]. It is advocated by Ayurveda as a liver tonic. The extracts of Flaxseed are known to help in strengthening the heart muscles, relieving stress, and hypertension [6]. Flaxseed is also thought to fortify the central nervous system and to quicken individual reflexes [11]. Recently there has been renewed interest in this plant because of its multimodal cardio-protective activity. As there is no single drug till date which alone or in combination offers definite and reliable protection and/or cure from the ravages of atherosclerotic cardiovascular disorders, the time is ripe for evaluating the role of *Linum usitatissimum* Linn. in the overall management of related cardiovascular disorders [12]. The present paper aims to review its ethnopharmacological, phytochemical, pharmacognostical, pharmacological, toxicity and side effects parameters under different conditions.

SCIENTIFIC CLASSIFICATION:

Kingdom: Plantae
 Division: Angiosperm
 Class: Eudicots
 Sub-class: Rosids
 Order: Malpighiales
 Family: Linaceae
 Genus: *Linum*
 Species: *usitatissimum*

Vernacular Names:

English: Flaxseed, Linseed, Lint Bells
 Sanskrit: Atasi, Uma
 Hindi: Alsi, Tisi
 Marathi: Javas, Alshi
 Bengali: Mashina
 Chinese: Hu ma

Botanical Details: The plant is a food and fiber crop. A cultivated plant has little branching except at the apex. Leaves are alternate, lance-like and grayish green with three veins, up to 4cm long and

4mm wide. Stems are slender and fibrous; flowers have five pale blue petals in a cluster (3cm in diameter). The sepals are lance-like and as long as the pointed fruit. The fruit is like a spherical capsule (5-9 mm) containing two seeds in each of five compartments. The seeds are oval and flatten with a pointed tip (4-6 mm long) [3]. The soils most suitable for linseed are deep loams and containing a large proportion of organic matter. It requires few fertilizers and pesticides. Within eight weeks of sowing, the plant reaches 10-15cm in height and grows several centimeters under its ideal growth conditions up to 70-80cm. Within 100 days of sowing the plant flower and two weeks after the seed capsules form. The base of the plant turns yellow. Green plant seeds will not be useful and fiber will be underdeveloped. Flaxseed comes in two basic forms 1. Brown flaxseed, and 2. Yellow or golden flaxseed (also called as golden linseeds). Flaxseed produces a vegetable oil known as flaxseed oil, which is one of the oldest commercial oils. The texture of linseed is crisp and chewy, having a pleasant nasty taste [13]. It is richest vegetarian source of Alpha-linolenic acid(ALA), lignans and soluble mucilage, all having benefits in overall health management [14]. Other than as medicinal value various parts of the plant have been used to make fabric, dye, paints, varnishes, paper, fishing nets and soaps. Traditionally, it is one out of the five flowers which are offered to Goddess Durga in Durga Pooja.

Distribution: *Linum usitatissimum* Linn, commonly known as Alsi belonging to family Linaceae is cultivated in cooler regions of the world. Linseed is a principal oilseed crop in India and occupies 468.0 thousand ha with the productivity of 349kg/ha. The cultivation of seeds is mainly concentrated in Vidarbha region of Maharashtra (all India coordinated research project on oilseeds, Akola). Linseed is also cultivated in Madhya Pradesh, Rajasthan and Bundelkhand regions. Found commonly in Gangetic (North India) and Peninsular (South India) region.

Macroscopy: Seeds are small, brown and glossy with the slightly pitted surface. Shape elongated-ovoid, flattened, rounded at one end and diagonally pointed at the other. Near one edge a light depression enclosing hilum and micropyle. Embryo consists of yellowish-white, flattened plano-convex cotyledons and a radical filling the seed [1]. The embryo was surrounded with a thin, whitish endosperm. Embryo and endosperm are oily, testa is mucilaginous with a characteristic odour. Taste characteristic and oily when chewed [13].

Microscopy: T.S of seed shows testa with mucilage comprising epidermis from 2-3 layers of

collenchyma. Round cells in a single layer longitudinally extend sclerenchyma. The hynine layer in ripe seeds composed of eradicated parenchyma, and the innermost layer of pigment cells. The basic cells are cylindrical in shape and separated by triangular intracellular space. The sclerenchymatous layer composed of lignified cells with lignified pitted walls. The pigment layer consisting of cells with thickened pitted walls and contain amorphous reddish brown content. The cells of endosperm and cotyledons are polygonal with thickened walls and has aleurone grains and oil globules of fixed oil. Starch is present in unripe seeds only. The powder consists of yellow coloured fiber. Pitted lignified sclerites; the rounded collenchymatous cell was observed. Protein content and fragments of hypodermis were observed. Oil globules with lignified fibers and aleurone grains were observed. Parenchyma with fixed oil and square cells filled with orange-brown mass was found.

Ethnopharmacological considerations: The seeds of Flaxseed have been used in indigenous system of medicine for different ailments. The seeds are said to be hot, pungent, heavy, purgative and strengthening. Its use has been advocated in cancer, arthritis, wounds, abscesses, diabetes, digestive disorders, bronchitis, fever, cough, inflamed lymph nodes etc. as mentioned in Ayurveda ways [15]. The seeds have been attributed to having cardio-protective and hepatoprotective properties. Flaxseed play a key role in several Ayurvedic protocols like Virechana, which is medicated purgation therapy. Virechana cleanses the sweat glands, colon, kidneys, stomach, liver, and spleen.

Laxative and Purgative action: Flaxseed oil acts as a laxative but flax seeds are fried and made into Kashaya, acts as an absorbent and used in Irritable bowel syndrome associated with diarrhoea [16].

Constipation: In constipation and in other diseases where constipation is seen, such as in IBS with constipation, haemorrhoids, etc., 3 – 5 ml of flaxseed oil is administered at night or patient is advised to use it as part of the diet [17].

Inflammation: The effect of L. usitatissimum fixed oil on distinct phases of the inflammatory process: first, an acute phase of local vasodilatation and increased capillary permeability leading to exudation, followed by leucocytes migration. The momentous characteristic of the inflammatory reaction is the transient increase in permeability of small blood vessels to proteins, initially involving the venules, because the delayed phase of increased permeability involves the capillaries as well, and is more relevant to chronic inflammation [4].

Hepato-protective: Supplementation of Omega-3 fatty acid reduces the burden of a number of diseases and have beneficial effects against a number of pathologies. Flaxseed oil is the rich sources of omega 3-fatty acids and is so potent antioxidants. Raw and baked flaxseed products induce hypolipidemic, hypoglycemic and hypocholesterolaemia effects which may be attributed mainly to seed oil rich in alpha linolenic acid [9].

External Application: Linseed pastes local application is useful in healing wounds and abscesses faster. The oil is applied externally to treat joint and muscle pains, non-healing wounds, skin disorders. Flaxseed oil also helps in speeding up the healing of skin lesions and has proved very effective for everything acne, psoriasis, eczema, and sunburn [18]. It promotes the health of hair and nails and has substances called lignans, which have a beneficial effect on the hormonal system of the body.

Brain health and ADHD: The essential fatty acids present in flaxseed helps in the transmission of nervous impulses. This makes flaxseed oil very useful for numbness and tingling as well as for preventing serious nerve ailments like Parkinson's and Alzheimer's disease. It is very useful in treating intelligence related disorders such as ADHD. Bipolar disorder, depression, menopausal symptoms [11].

Hormone supplement: One important benefit is that flaxseed contains phytoestrogens that can mimic the human sex hormone estrogen. It is useful for infertility, impotence, menstrual cramps, endometriosis and menopausal problems [7,8].

Cardio-protective: It is used in the treatment of cardiac disorders and cholesterol. It acts as a blood thinning agent. Hence, it is useful in preventing and treating atherosclerosis (cholesterol and clot development in blood pipes of the heart) [6]. Omega-3 fatty acids offer protection against heart disease by getting to the membrane of body cells and acting as guards that admit only healthy substances and bar damaging ones. According to Ayurveda the classical description of Flaxseed, it is Madhura and Tikta with Guru (heaviness), Snigdha, Picchila (sticky and slimy) Guna. Katu Vipaka i.e. undergoes pungent taste conversation after digestion. Ushna Veerya (hot potency), balances Vata Dosha and increases Kapha and Pitta Dosha. On the other hand, Flaxseed oil is Teekshna (strong and piercing), Laghu (light to digest), Sara (induces mobility, causes diarrhoea, purgation and relieves constipation) [15].

Benefits of Flaxseed is that it can be Ushna or Agneya (hot), Drukghni or Achakshushya (not good for eyes), Shukraghini (decreases sperm/seed), Vataghni (useful to treat Vata Dosha imbalances such as neuralgia, paralysis, constipation, bloating etc.), Kaphapitta prakopini (increases Kapha and Pitta Dosha), Raktapitta prakopana (not ideal in bleeding disorders such as nasal bleeding, heavy periods etc.). Along with these Flaxseed oil is Balya (improves strength and immunity), Malakrut (increases bulk of faeces), Grahi (absorbent, useful in diarrhoea, IBS etc.), Twakdoshahara (detoxifies skin on external application) and can be useful in Basti chikitsa (enema), Paana (oral consumption), Abhyanga (massage) and Karnapoorana (ear drops) [15].

Flaxseed is recommended as an important cardio tonic which is known to promote healthy functionality of heart and regulate blood pressure [6]. It also helps in the reduction of the corrosive effects of stress and nervousness. Flaxseed with its remarkable medicinal properties helps in maintaining healthy cholesterol levels [9]. Flaxseed is known to possess diuretic property. It is further verified by modern research that flaxseed has antioxidant properties and may be clinically helpful in cardiovascular health. Studies show that it is effective for varieties of heart-related conditions like heart palpitations, rapid heart rate, high cholesterol etc. Researchers characterize these benefits to certain essential fatty acids and lignans that have specific antioxidant properties congenial for the cardiovascular system. Seeds are used very commonly in household preparations. The seeds and flowers are known to regulate cholesterol level by decreasing LDL level in liver. The extract of flaxseed is known to help in strengthening the heart muscles, relieving stress and hypertension. It is also thought to boost the central nervous system and to accelerate individual reflexes. Velioglu et al. (1998) [19] were studied antioxidant activity of flaxseed methanolic extract in β -carotene bleaching method investigated correlation between total phenolics and antioxidant activity; which was found to be statistically significant. Zanwar et al. (2010) [20] assessed in vitro antioxidant activity of ethanolic extract of *L. usitatissimum* by using various methods such as DPPH radical scavenging, reducing power, superoxide scavenging, hydroxyl radical scavenging, hydrogen peroxide scavenging and metal chelating assay and it showed dose-dependent antioxidant activity in different studied models, maximum at 500 μ g/ml. It is concluded that phenolic compounds seem to be the main components responsible for the observed antioxidant activity.

Ischemia regulation: The flaxseed is also known to possess antianginal, decongestive and hypolipidemic effect. James et al. (2007) [21] conclude that flaxseed a nutritional supplement with antioxidant and anti-inflammatory properties can be used to ameliorate acute lung injury in a murine model of Ischemic reperforation injury (IRI). The harmful physiological effects and oxidative damage that result from IRI were repealed in mice prefer a diet supplemented with flaxseed. Flaxseed has potentially multiple mechanisms of action to affect this improvement through both reduced ROS generation and increased ROS detoxification. Bradley et al. (2004) [22] conclude that Dietary flaxseed caused a significant increase in plasma ALA in the rabbits from 2 to 15 g/100 g of total fatty acids. This increase in total fatty acids may be the result of a cholesterol-facilitated uptake of fatty acids by the jejunum. Dietary flaxseed was associated with a shortening of the QT interval. Howiada et al. (2012) [23] conclude that alterations of lipid profile, cardiac and inflammatory markers (II-1 β , PTX 3 and TNF- α) were observed in myocardial ischemia group. Flaxseed supplementation combined with exercise training showed a significant increase of HDL and paraoxonase, HDL-associated enzyme (PON 1), on the other hand, cardiac troponin, II- 1 β and TNF- α levels significantly decreased as compared to the myocardial ischemic group. Receiver Operating Characteristics (ROC) analysis of cTnI, PTX 3, II-1 β and TNF- α revealed a satisfactory level of sensitivity and specificity. Elevation of HDL, the antioxidant PON 1 and the cardio-protective marker PTX 3 emphasizes the protective effects of flaxseed and muscular exercise mutually against the harmful effects of acute myocardial ischemia [24].

Phytochemical Studies: According to World Health Organization, medicinal plants would be the best source to get a variety of drugs. Medicinal plants contain some organic compounds which give definite physiological action on the human body and these bioactive substances include tannins, alkaloids, carbohydrates, terpenoids, steroids, flavonoids and phenols [25]. The bio-active phyto compounds are synthesized by primary or rather secondary metabolism of living organisms. Secondary metabolites are chemically and taxonomically extremely diverse compounds with obscure function. They are widely used in the human therapy, veterinary, agriculture, scientific research and countless other areas. Medicinal plants containing active chemical constituents with high antioxidant property play an important role in the prevention of various degenerative diseases and have possible benefits to the humanity [26]. A large

number of phytochemicals belonging to several chemical classes have been shown to have inhibitory effects on all types of microorganisms in vitro. Botanical medicines or phytomedicines refer to the use of seeds, berries, leaves, bark, root or flowers of any plant for medicinal purposes by a significant number of people. Knowledge of the chemical constituents of plants is necessary because such information will be important for the synthesis of complex chemical substance [27-29]. Flaxseed is a rich source of fats, protein, and dietary fibers. It has around 41% fat, 20% protein, 28% total dietary fibers, 7.7% moisture, and 3.4% ash. It was valued because of the abundance of fats; provide a mixture of fatty acids [30]. Fatty acids are organic constituents found in all type of food. Linseed is rich in polyunsaturated fatty acid. Amino acids act as the building blocks of protein. Phenolics are phytoconstituents having different functions, adding color to the flowers and attracting insects [31]. They have anticancerous and antioxidant property [32-34]. Flaxseed has three types of phenolics: Phenolic acids, 8-10g/kg of flaxseed [35]. Flavonoids, 35-70mg/100g of flaxseed [36]. Lignans, it is a rich source of SDG found in amount 1-26mg/g of seed [37]. Flaxseed also contains water and fat-soluble vitamins in minor amounts. Vitamin-E is present in the form of gamma-tocopherol, which is an antioxidant that prevents cell protein and fats from oxidation, increase sodium excretion in the urine, which helps in lowering blood pressure and decreases the risks of cardiac diseases [38], some varieties of cancer and Alzheimer's disease [39-40]. It also contains Vitamin-K in the form of phylloquinone, plays a significant role in the formation of several proteins essential for blood clotting and bone development.

Flaxseed Lignans: Phytoestrogens are phytochemicals having estrogen-like activity in humans and animals. The major phytoestrogens are lignans, flavonoids, coumestans, and isoflavones [41]. Lignans are widely distributed in plants, and play a significant role in plant growth and act as antioxidants in animal metabolism. They are similar to the natural and synthetic estrogens in their chemical structure. They can serve as a weak estrogen, binding to estrogen receptors present on the cell membrane. They can also act as an estrogen antagonist, by preventing estrogen binding to the receptor [42]. Lignans which are present in linseed are matairesinol, SDG, Secoisolariciresinol (SECO), pinoresinol, etc. They are metabolized into mammalian lignans enterodiol and enterolactone by colon bacteria. Mammalian lignans are produced only in human intestine and are biologically active. The major lignan present is SDG, presents as a complex of five SDG bound together. Lignans have antioxidant, anticancerous,

antiviral effects, can activate gene expression and protect against hormones related disorders like osteoporosis [41-42]. Diet with a high amount of lignan maintains coronary health, cognitive function in menopause, reduce risks of prostate, breast and uterine cancer [43]. SDG act as an antioxidant by scavenging free radicals which are continuously produced in our body by oxidation of fats, carbohydrates, proteins and alcohol. Free radicals damage cells, and cause many disorders like atherosclerosis, Cancer, and Alzheimer's disease [44]. Mammalian lignans bind to the receptor present on the cell membrane. They activate the receptor pregnane-X responsible for the metabolism of bile acids, steroidal hormones, and several drugs [45]. Sex hormone binding globulin (SHBG) is stimulated by enterolactone, which binds with sex hormones and decreases their concentration in the bloodstream, reducing their activity [44]. Higher plasma concentration of SHBG lowers the risk of Type-2 diabetes by 80% in women and 52% in men [46]. Low level of SHBG in menopausal women associated with breast cancer [47]. SDG protect against breast cancer also by decreasing the production of estrogen by inhibiting aromatase enzyme [48].

Minerals: The milled flaxseed also contain large amount of calcium (236mg/100g), potassium (831mg/100g), magnesium (431mg/100g), phosphorus (622mg/100g), sodium (27mg/100g) and in very low amount copper, zinc, iron and manganese [13].

Anti-cancerous activity: Richter et al. (2010) [49] investigated the effect of phytoestrogens extracted from flaxseed on estradiol production and expression of ER/PR in MCF7 breast cancer cell. They had concluded that lignan extracts stimulate the production of estrogen in MCF7 cells. They also observed a down-regulation of ER β receptor expression and down-regulation of PR expression in MCF7 cells after treatment. The expression of ER α was also much altered in MCF7 cells after stimulation with extracts A down-regulation of ER α expression was also observed. Thompson et al. (1996) [50] investigated the effect of flaxseed lignan and its oil component in reduction of mammary tumor growth in the last stage of carcinogenesis. They concluded that flaxseed oil and flaxseed (in a dose independent manner) reduced the growth of established tumours at a late stage of carcinogenesis because the mammalian lignan precursor SDG exerted the greatest inhibitory effect on the development of new tumours. In contrast to the new tumours, the size of established tumours was inversely related to the level of urinary mammalian lignans indicating that the lignans produced by SDG played a role in the

reduction of established tumor growth. Waldschlager et al. (2005) [51] investigated the effect of flaxseed lignan on hormone receptor positive tumor cell line. They observed an anti-proliferative and a hormone-decreasing effect on the chorion carcinoma cell line Jeg3 caused by the flax-seed crude extract. This fraction contains the lignan matairesinol and the isoflavone biochanin A. estrogenic or anti-estrogenic effect of phytoestrogens depend on the level of endogenous estrogens. Phytoestrogens may act as antagonists in pre-menopausal women and replace endogenous estrogen in the post menopause.

Anti-inflammatory activity: Kaithwas et al. (2013) [4] investigated the effect of fixed oil present in flaxseed on distinct phases of inflammation. *L. usitatissimum* fixed oil demonstrated a significant dose-dependent inhibition of protein exudation (i.e., the rise in protein concentration in peritoneal fluid) and inhibited the vascular permeability shown by inhibition to dye leakage.

Weak estrogenic and anti-estrogenic activity: Richter et al. (2010) [49] investigated that potential phytoestrogens isolated from flaxseed significantly stimulate estrogen production in MCF7 breast cancer cells. They also observed a down-regulation of ER β receptor expression and down-regulation of PR expression in MCF7 cells after treatment. The expression of ER α was also significantly altered in MCF7 cells after stimulation with extracts A down-regulation of ER α expression was also observed. Jennifer et al. (2004) [52] concluded that supplementation of flaxseed alters the estrogen metabolism in post-menopausal women. This study showed that dietary supplementation with 25 g ground flaxseed significantly alters the metabolism of estradiol in favour of the less biologically active estrogen metabolite (2OHE1) in postmenopausal women. Our study showed for the first time that changes in urinary lignan excretion with flaxseed supplementation are positively related to significant changes in 2OHE1:16OHE1.

Anti-ulcerogenic action: Dugani et al. (2012) [53] investigated the effect of mucilage and fixed oil on the gastric lesions induced by ethanol. Their study provides clear evidence that consumption of the products of flaxseed (oil and mucilage) have gastro-protective effect against ethanol-induced gastric ulcers.

Anti-bacterial activity: Tehrani et al. (2014) [54] investigated the effect of flaxseed proteins on the several species of gram positive and gram negative bacteria. Inhibitory effect of flaxseed total protein extract on the growth of 10 bacterial species was

determined as IC %. The effect is more pronounced on *Salmonella typhimurium* (40 %), *Enterococcus faecalis* (45 %), *Escherichia coli* (40 % and 45 %) and *Klebsiella pneumonia* (ATCC: 10031, 38 %). Also, some antibacterial activity appears on *Staphylococcus epidermidis* (19 %) and *Klebsiella pneumonia* (ATCC: 10603, 15 %). These bacteria, by the reduction of protein concentration, the inhibitory effect on bacterial growth inversely increased (e.g., 22 % to 40 % by reducing protein concentration from 250 μ g/ml to 50 μ g/ml for *Salmonella typhimurium*). The steep slope of inhibitory effect was also rising sharper on some bacteria (e.g., *Klebsiella pneumonia* (ATCC: 10031, from 8 % to 38)). Flaxseed protein extract showed an antibacterial activity against the most test microorganisms, especially gram-negative bacteria. The activity was more pronounced (>50%) for the fractionated and isolated protein.

Laxative: Tarpila et al. (2003) [17] investigated the efficacy of ground flaxseed on constipation in irritable bowel syndrome patients. The study concludes that Ground flaxseed contains insoluble fiber 33.2 % and soluble fiber 11 %. Flaxseed as bulk laxative proved to be more effective than psyllium. This is due to the presence of a larger amount of insoluble fiber in flaxseed. Psyllium contains mostly water-soluble fiber (47 g/ 100 g). Its effect seems to be faster than the effect of flaxseed on constipation. The additional laxative effect caused by the 20 % of residue oil that is left in ground flaxseed after cold-pressing. Psyllium does not contain any oil. Therefore, they introduced ground flaxseed as "oil fiber" instead of traditional bulk-laxative.

Plasmogen: Herper et al. (2006) [55] investigated the effect of flaxseed oil which was found to increase the cardio-protective fatty acids in humans. The conclusion of the study showed the increase in plasma fatty acids EPA (eicosapentaenoic acid) and DPA (docosapentaenoic acid) by 60% and 34%, while no increment was seen in olive oil groups. This is because flaxseed is the rich source of ALA which acts as a precursor in the synthesis of EPA and DPA.

Antidiabetic: Pan et al. (2007) [56] analyzed the effect of flaxseed by double-blind, randomized, crossover trial study on Type 2 diabetic patients. Flaxseed supplementation act to increase the blood lipid level and phytoestrogen present in seeds improve the glycemic control in people. On the other hand, Rhee et al. (2011) [57] analyzed the effect of flaxseed supplementation on obese glucose intolerant patients and concluded that the active ingredient of flaxseed (lignan,

Secoisolariciresinol Diglucoside (SDG)) has significant antioxidant effects by inhibiting DNA scissions and lipid peroxidation and decreasing ROS. Antioxidants have been reported to diminish inflammatory response, insulin resistance, and diabetes development.

Nephroprotective: Clark et al. (2000) [58] concluded that dietary phytoestrogens have a beneficial role in chronic renal disease. Flaxseed has been shown to limit or reduce proteinuria and renal pathological lesions associated with progressive renal failure. In short-term clinical studies, the omega-3 polyunsaturated fatty acids, derived from flaxseed, seem to diminish cyclosporine-induced kidney toxicity and the attendant complication of hypertension; to inhibit inflammatory and atherogenic mechanisms in lupus nephritis, and to preserve renal function and reduce proteinuria. Hall et al (1993) [59] showed that flax lignans were highly protective “in a dose-dependent fashion, with a significant delay in the onset of proteinuria with preservation in glomerular filtration rate and renal size.” The study suggests that flax lignans may have a therapeutic role in lupus nephritis.

Radioprotective Activity: Solomidou et al. (2012) [60] investigated the effect of flaxseed lignan SDG as a radioprotective in lungs. Flaxseed has potent anti-inflammatory, antifibrotic and antioxidant properties in acute and chronic lung injury. This study evaluated the lignan complex of flaxseed-enriched in Secoisolariciresinol Diglucoside with respect to lung radioprotective and tumor radiosensitizing efficacy. flaxseed induced radiosensitizing effects in metastatic lung cancer. Importantly, protection of normal tissue does not prevent tumor cell death by radiation treatment.

Modern research and flaxseed: Modern clinicians are just beginning to use flaxseed for coronary artery disease, heart failure, high cholesterol and inflammation. The herbs part includes a variety of polyphenols, which probably account for much of its activity. They include Lignans (SDG, SECO, matairesinol, pinoresinol and lariciresinol), flavonoids and phenolic acids. Other than these flaxseed contains fatty acids (ALA and LA), Vitamin K, Vitamin E, zinc, calcium, potassium, and magnesium. Flaxseed seems to improve cardiac muscles function and pumping of the heart. Flavonoids contribute to antioxidant action and strengthening veins. Ischemia patients, in particular, may benefit from flaxseed. It is particularly effective in coronary heart failure. It also benefits in cardiomyopathy or weakening of the lower heart muscles and may help in recovery from heart attack.

Toxicity and side effects: Flaxseed when to consume in excessive quantity cause few side effects like gastric disturbance, bloating, internal bleeding, stomach pain, nausea, loose stool, prostate cancer risk etc. [61-62]. The consumption of flaxseed is precautions in pregnancy, lactation, bleeding disorder, low blood pressure, bipolar disorder, food allergy, gastric obstructions etc.

Flaxseed consists of cyanogenic glycosides, a group of a natural substance found in plants which release cyanide on degradation with enzymes and organic acids [63]. Thiocyanate is a breakdown product of cyanogenic glycosides, it acts as a goitrogen, it blocks the uptake of iodine from the thyroid gland [64]. Excess consumption of cyanogenic glycosides results in the swelling of the thyroid gland to trap much more iodine and forming a goiter or lump in the neck [65]. In a model of mouse skin cancer, six common cyanogenic glycosides decreased the tumors by 13-33% and had a potency comparable to that seen with the anticancer phenolic compound found in green tea [66]. Flaxseed also contains phytic acid and oxalate that binds with calcium, copper, magnesium and zinc to form insoluble complexes in the intestine [65]. Phytic acid lowers blood glucose and reduces the incidence of colon cancer [67]. It also possesses some interaction with drugs like glimepiride, glipizide, clopidogrel, diclofenac, ibuprofen, dalteparin, heparin, warfarin, naproxen and aspirin [68].

Discussion: Present review provides a broad information about the chemical constituents, ethnopharmacology along with the scientifically proven medicinal uses of *L. usitatissimum*. Several fatty acids, vitamins, phytoestrogens, proteins, flavonoids etc. have been reported in flaxseed. The plant shows various type of activities such as antioxidant, antidiabetic, antihypertensive, laxative etc. due to the presence of investigated active chemical constituents. The pharmacological studies so far have been performed in-vivo and in-vitro. Therefore, there is a need of investigation and quantification of phytoconstituents and pharmacological profile.

Conclusion and future strategies: The herbal remedies have been employed in a various medical system for the treatment and management of diseases. The plant has been used in the different system of traditional medicines in the treatment of diseases and human ailments. The plant contains alpha-linoleic acid, lignans, flavonoids, calcium, zinc, magnesium, sodium, Vitamin K, Vitamin E etc. it has been reported as cardio-protective, hepatoprotective, antidiabetic, anti-inflammatory, anti-cancerous, estrogenic, antioxidant properties.

The efficacy of Flaxseed is much more popular as cardio-protective and antioxidant.

It can be considered as an important drug for hypertension, coronary artery disease and ischemic cardiomyopathy. Its action in different cells of the cardiovascular system needs more research. Further, a well-developed study to evaluate its toxicity from its long-term use is another priority. Studies will provide a scientific basis for its medicinal use. As the overall scenario is changing regarding the use of non-toxic plant products, development of modern drugs should be emphasized. Clinical trials should be conducted to support its therapeutic use. The current review is

therefore carried out to provide requisite phytochemical and pharmacological details about the plant. The plant is cultivated in different parts of India on a small scale. However, systematic information on different aspects of the species is still not provided. In this review, an attempt has been made to present maximum information.

Acknowledgement: Department of Pharmaceutics, IIT- BHU for providing laboratory and library facilities is highly acknowledged. The financial assistance in the form of fellowship by the University Grants Commission, New Delhi, India for this research work is thankfully acknowledged.

REFERENCES

1. Tanna I et al. Pharmacognostical and Phytochemical evaluation of Atasi (*Linum usitatissimum* L.). *Indian J Tradit Know* 2013; 12: 688-92.
2. Bloedon LT et al. Flaxseed and cardiovascular risk factors: results from a double-blind, randomized, controlled clinical trial. *J Am Coll Nutr* 2008; 27 :65-74.
3. Pradhan RC et al. Supercritical CO₂ extraction of fatty oil from flaxseed and comparison with screw press expression and solvent extraction processes. *J Food Process Eng* 2010; 98(4): 393-7.
4. Kaithwas G, Majumdar DK. Effect of *L. usitatissimum* (flaxseed/linseed) fixed oil against distinct phases of inflammation. *ISRN inflammation* 2013; 2013: 1-4.
5. Kitts DD et al. Antioxidant activity of the flaxseed lignan secoisolariciresinol diglycoside and its mammalian lignan metabolites enterodiol and enterolactone. *Mol Cell Biochem* 1999; 202: 91-100.
6. Tuteja S et al. Pharmacokinetic interactions of the microsomal triglyceride transfer protein inhibitor, lomitapide, with drugs commonly used in the management of hypercholesterolemia. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy* 2014; 34: 227-39.
7. Yusuf S et al. Telmisartan to prevent recurrent stroke and cardiovascular events. *New Engl J Med* 2008; 359: 1225-37.
8. Ziegler RG. Phytoestrogens and breast cancer. *Am J Clin Nutr* 2004; 79: 183-4.
9. Shakir KF, Madhusudhan B. Hypocholesterolaemia and hepatoprotective effects of flaxseed chutney: Evidence from animal studies. *Indian J Clin Biochem* 2007; 22: 117-21.
10. Khanchandani R. Role of omega-3 fatty acid in hepatoprotection against carbon tetrachloride induced liver injury in albino rabbits. *Journal of Biomedical and Pharmaceutical Research* 2015; 3.
11. Boyles S, Agus ZS. Recent Posts. *Eur J Obstet Gynecol Reprod Biol* 2014; 2:10.
12. Swingle KF. Evaluation for anti-inflammatory activity. *Anti-inflammatory Agents: Chemistry Pharmacology* 1974; 2:33-122. (in press)
13. Carter JF. Sensory evaluation of flaxseed of different varieties. *InProc. Flax Inst* 1996; 56: 201-203.
14. Jiang Y et al. Modulation of chloride channel functions by the plant lignan compounds kobusin and eudesmin. *Front Plant Sci* 2015; 6 (1041): 1-11.
15. Goyal A et al. Flax and flaxseed oil: an ancient medicine & modern functional food. *J Food Sci Tech* 2014; 51: 1633-53.
16. Cunnane SC et al. Nutritional attributes of traditional flaxseed in healthy young adults. *Am J Clin Nutr* 1995; 61: 62-8.
17. Tarpila S et al. Efficacy of ground flaxseed on constipation in patients with irritable bowel syndrome. *Curr Top Nutraceutical Res* 2004; 2:119-25.
18. O'Neill W et al. Flaxseed (*Linum usitatissimum*) supplementation associated with reduced skin test lesional area in horses with *Culicoides* hypersensitivity. *Can J Vet Res* 2002; 66: 272-7.
19. Velioglu YS et al. Antioxidant activity and total phenolics in selected fruits, vegetables, and grain products. *J Agric Food Chem* 1998; 46: 4113-7.
20. Zanzwar A et al. Cardio-protective activity of flax lignan concentrate extracted from seeds of *Linum usitatissimum* in isoprenaline induced myocardial necrosis in rats. *Interdiscip toxicol* 2011; 4: 90-7.
21. Metcalf RG et al. Effects of fish-oil supplementation on myocardial fatty acids in humans. *Am J Clin Nutr* 2007; 85: 1222-8.
22. Ander BP et al. Dietary flaxseed protects against ventricular fibrillation induced by ischemia-reperfusion in normal and hypercholesterolemic rabbits. *J Nutr* 2004; 134: 3250-6.
23. Nounou HA et al. Effect of flaxseed supplementation and exercise training on lipid profile, oxidative stress and inflammation in rats with myocardial ischemia. *Lipids Health Dis* 2012; 11: 1-10.
24. Wald NJ et al. Homocysteine and ischemic heart disease: results of a prospective study with implications regarding prevention. *Arch Intern Med* 1998; 158: 862-7.
25. Yadav RN, Agarwala M. Phytochemical analysis of some medicinal plants. *J Phytol* 2011; 3: 10-14.
26. Hakkim FL et al. Antioxidant property of selected *Ocimum* species and their secondary metabolite content. *J Med Plants Res* 2013; 2: 250-7.
27. Mojab F et al. Phytochemical screening of some species of Iranian plants. *Iran J Pharm Res* 2010; 2: 77-82.
28. Parekh J, Chanda S. Antibacterial and phytochemical studies on twelve species of Indian medicinal plants. *Afr J Biomed Res* 2007; 10: 175-181.
29. Parekh J, Chanda S. Phytochemical screening of some plants from western region of India. *Plant Archives* 2008;8(2):657-62.
30. Katare C et al. Flax seed: a potential medicinal food. *Journal of Nutrition & Food Sciences* 2012; 2: 1-8.
31. Amarowicz R et al. Antioxidant activity of hydrophobic phenolic fractions of flaxseed. *Food/Nahrung* 1997; 41: 178-80.
32. Murphy PA, Hendrich S. Phytoestrogens in foods. *Adv Food Nutr Res* 2002 Dec 31;44: 195-246.

33. Simmons CA et al. The effect of a flaxseed oil-enhanced diet on the product quality of farmed brook trout (*Salvelinus fontinalis*) filets. *J Food Sci* 2011; 76(3): S192-7.
34. Dashwood RH. Frontiers in polyphenols and cancer prevention. *J Nutr*. 2007; 137: 267S-9S.
35. Oomah BD et al. Phenolic acids in flaxseed. *J Agric Food Chem* 1995; 43: 2016-9.
36. Wang SY, Lin HS. Antioxidant activity in fruits and leaves of blackberry, raspberry, and strawberry varies with cultivar and developmental stage. *J Agric Food Chem* 2000; 48: 140-6.
37. Muir AD. Flax Lignans Analytical Methods and How They Influence Our Understanding of Biological Activity. *J AOAC Int* 2006; 89: 1147-57.
38. Daun JK, Przybylski R. Environmental effects on the composition of four Canadian flax cultivars. *InProc. Flax Inst* 2000; 58: 80-91.
39. Sen CK et al. Tocotrienols: vitamin E beyond tocopherols. *Life sciences* 2006; 78: 2088-98.
40. Morris MC et al. Relation of the tocopherol forms to incident Alzheimer disease and to cognitive change. *Am J Clin Nutr* 2005; 81(2): 508-14.
41. Martin JH et al. Does an apple a day keep the doctor away because a phytoestrogen a day keeps the virus at bay? A review of the anti-viral properties of phytoestrogens. *Phytochemistry* 2007; 68(3): 266-74.
42. Benassayag C et al. Phytoestrogens as modulators of steroid action in target cells. *J Chromatogra B* 2002; 777: 233-48.
43. Hedelin M et al. Dietary phytoestrogen, serum enterolactone and risk of prostate cancer: the cancer prostate Sweden study (Sweden). *Cancer Causes & Control* 2006; 17(2): 169-80.
44. Herman C et al. Soybean Phytoestrogen Intake and Cancer Risk. *J Nutr* 1995; 0022-3166: 757S-770S.
45. Jacobs MN et al. Lignans, bacteriocides and organochlorine compounds activate the human pregnane X receptor (PXR). *Toxicol Appl Pharmacol* 2005; 209(2): 123-33.
46. Ding X et al. Variants on ESR1 and their association with prostate cancer risk: a meta-analysis. *Asian Pac J Cancer Prev* 2012; 13(8): 3931-6.
47. Golan A et al. Ovarian hyperstimulation syndrome: an updated review. *Obstet Gynecol Surv* 1989; 44(6): 430-40.
48. Wang LQ. Mammalian phytoestrogens: enterodiol and enterolactone. *J Chromatogra B* 2002; 777(1): 289-309.
49. Richter DU et al. Effects of phytoestrogen extracts isolated from flax on estradiol production and ER/PR expression in MCF7 breast cancer cells. *Anticancer Res* 2010; 30: 1695-9.
50. Thompson LU et al. SHORT COMMUNICATION: Flaxseed and its lignan and oil components reduce mammary tumor growth at a late stage of carcinogenesis. *Carcinogenesis* 1996; 17: 1373-6.
51. Waldschläger J et al. Flax-seed extracts with phytoestrogenic effects on a hormone receptor-positive tumour cell line. *Anticancer Res* 2005; 25: 1817-22.
52. Brooks JD et al. Supplementation with flaxseed alters estrogen metabolism in postmenopausal women to a greater extent than does supplementation with an equal amount of soy. *Am J Clin Nutr* 2004; 79: 318-25.
53. Dugani AM et al. Comparative effect of flaxseed oil and fish oil in acetic acid induced colitis in rats. *LJPCP* 2012; 1: 1-7.
54. Tehrani MH et al. Extraction and purification of flaxseed proteins and studying their antibacterial activities. *J Plant Sci* 2014; 2: 70-6.
55. Harper CR et al. Flaxseed oil supplementation does not affect plasma lipoprotein concentration or particle size in human subjects. *J Nutr* 2006; 136: 2844-8.
56. Pan A et al. Effects of a flaxseed-derived lignan supplement in type 2 diabetic patients: a randomized, double-blind, cross-over trial. *PLoS One* 2007; 2: 1-7.
57. Rhee Y, Brunt A. Flaxseed supplementation improved insulin resistance in obese glucose intolerant people: a randomized crossover design. *Nutrition journal* 2011; 10: 1-7.
58. Clark WF et al. A novel treatment for lupus nephritis: lignan precursor derived from flax. *Lupus* 2000; 9: 429-36.
59. Hall AV et al. Abrogation of MRL/LPR lupus nephritis by dietary flaxseed. *Am J Kidney Dis* 1993; 22(2): 326-32.
60. Christofidou-Solomidou M et al. Radioprotective role in lung of the flaxseed lignan complex enriched in the phenolic secoisolariciresinol diglucoside (SDG). *Radiat Res* 2012; 178: 568-80.
61. Martin KR. Targeting apoptosis with dietary bioactive agents. *Exp Biol Med* 2006; 231: 117-29.
62. Lampe JW. Spicing up a vegetarian diet: chemopreventive effects of phytochemicals. *Am J Clin Nutr* 2003; 78: 579S-83S.
63. Vetter J. Plant cyanogenic glycosides. *Toxicol* 2000; 38(1): 11-36.
64. Dorea JG. Maternal thiocyanate and thyroid status during breast-feeding. *J Am Coll Nutr* 2004; 23(2): 97-101.
65. Potter SM, Pertile J. Soy protein concentrate and isolated soy protein similarly lower blood serum cholesterol but differently affect thyroid hormones in hamsters. *J Nutr* 1996; 126: 2007-11.
66. Fukuda T et al. Anti-tumor promoting effect of glycosides from *Prunus persica* seeds. *Biol Pharm Bull* 2003; 26(2): 271-3.
67. Daun JK et al. Structure, composition, and variety development of flaxseed. *Flaxseed in human nutrition*. 2003 (Ed. 2); 2:1-40.
68. Ratnayake WM et al. Chemical and nutritional studies of flaxseed (variety Linott) in rats. *J Nutr Biochem* 1992; 3: 232-40.