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Review Article

FLAXSEED/TUKHM-E-KATAN (*LINUM USITATISSIMUM* LINN.): A REVIEW

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ABSTRACT
Flax/Katan (*Linum usitatissimum* Linn.) an annual herb and a founding crop belongs to the family Linaceae. Flaxseeds are smooth, shiny and dark brown in color with mucilaginous, oily and slightly bitter taste. It is a native of Egypt but also cultivated in India, Holland, Russia and Britannia mainly for the purpose of its oil and fiber and is best adapted to fertile, fine textured, clay soils. Flax was valued in Ancient and Early Modern times as both a food and medicine. The medicinal applications of linseed are mentioned in the works of Hippocrates and Dioscorides as well as in medieval books on medicinal herbs in both Asia and Europe. In Unani system of medicine it is used as an anti-inflammatory, phlegm expectorant, chest cleanser, vesicant, analgesic, lithotriptic and calculus removal, aphrodisiac, spermatogenesis, demulscent and laxative, general tonic, galactagogue, emmenagogue etc. The present review the traditional uses, therapeutic actions and pharmacological properties of the linseed in light of current scientific research.
Keywords: *Linum usitatissimum* Linn, Flaxseed, Soluble flaxseed gum, Unani medicine, traditional uses, pharmacological properties.

INTRODUCTION

Flax/Katan (*Linum usitatissimum* Linn.) belongs to the family Linaceae which is a very large family containing 19 genera and about 290 species[5,2,19,23,42,44,55,64,66,67]. It is also known as Bazar-ul- Katan or Tukhm-e- Katan. In Urdu it is named as Alsi[42,47] while in Persian it is named as Tukhme Katan, Zaghir, Zaghu[42]. In English it is named as Linseed, Flax plant, Common flax[6,42,47,67]. It is an annual herb with 60-120 cm high; stem usually solitary, corymbosely branched, branches ascending towards the apex[23,43]. Its leaves are linear, lanceolate or ovate, attenuated at both ends, acute at the apex and up to 3.8 cm long. Flowers are small about 2.5 cm long, blue, bluish violet or white in terminal panicles in corymbose. Sepals: the 2 outer elliptic, acuminate, with entire membranous margins the 3 inner broader, acuminate, with ciliate margins, all strongly 3 nerved, the middle along reaching the apex. Petals are blue and slightly crenate. Fruits are capsular with 5 cells containing compressed, ellipsoid, smooth, dark brown and shining seeds[6,8,43,67]. Seeds are mucilaginous, oily and slightly bitter in taste[6,43,58]. 10-20 seeds in the capsule, oval lenticular 4-6 mm in length. Surface is smooth, shiny and dark brown[5,63]. A light depression in one edge enclosed in hilum and micropile, from hilum a yellow raphae runs to the chalaza[13]. Flax is a founding crop, being one of the first domesticated plants. Its cultivation likely began in the fertile valleys of the so-called Fertile Crescent in Mesopotamia about 8,000 to 10,000 years ago[18]. Flax was valued in Ancient and Early Modern times as both a food and medicine. It has been cultivated since antiquity, mainly for the purpose of its oil and fiber[19,54,55]. Linseed is a native of Egypt but also cultivated in India, Holland, Russia and Britannia[43,44]. It is best adapted to fertile, fine textured, clay soils[64]. It is extensively cultivated throughout India[23,58] mainly in Madhya Pradesh, Uttar Pradesh, Maharashtra, Bihar, Rajasthan, India and the United Provinces, also occasionally found in wild run[43,47,58]. In India it is sown in the month of Sept-Oct and harvested in march-April. The herb is dried and seeds are collected and used[14].

Chemical Compositions

Flaxseed

It is a leading source of n-fatty acid, α-Linolenic acid (ALA) (52 % of the total fatty acid), and of phenolic compounds commonly known as Lignans (> 500 µg/g, as is bases), in addition to containing hydrocolloidal gum, also referred to as Mucilage (about 8 % of seed weight), and a good quality of protein and fiber[11,45 53]. It also contain 30-40 % of fixed oil and a small quantities of cyanogenetic glycosides (0.05-0.001 %) mainly linustatin, neolinustatin and linamarin; lignans; phenyl propane derivatives including linusitamarin[5,23,63,66]. It also contain amygdalin, resin, wax sugar and ash 3-5 p.c. Ash contain sulphate, chlorides of potassium, calcium and magnesium, β- Carotene forms 22 to 30 % of the total carotenoids[43].

Flaxseed mucilage (Soluble flaxseed gum)

It is a heterogeneous polysaccharides compound of xylose, arabinose, glucose, galactose, galacturonic acid, rhamnose, fucose and glucose. It compromises 8 % of the seed weight[23,54,55,63,64].

Tukhm-e-Katan in view of Unani System of Medicine

Mizaj (Temperament) of Tukhm-e-Katan in light of Unani medicine

Hot[1] and Dry[1] [1,26]
Hot[1] and Dry[0] [12,26,48]
Hot and Dry[2] [51]
Moatadil [26,50]
It is Hot in 1st degree and moderate in yabusat[32]
It is Hot in 1st degree and moderate in Yabusat-wa-Ratubat[12]
Part Used: Seeds, oil and flowers.

Afa'al (Actions) of Tukhm-e-Katan

Muhallil-e-Warm (Anti-inflammatory)[1,2,12,26,41,50]
Munaffis-e-Balgham (Phlegm Expectorant)[2,26]
Mukhrij-e-Balgham (Phlegm Expectorant)[2,41]
Munaqqi Sadar (Chest cleanser)[2,50]
Musakkin-e-Alam (Analgesic)[1,12,26,41,50]
Munaffit (Vesicant)[12,26,41]

Mufattite-e-Hisaat (Lithotriptic)[13,26,51]
Mukhrij-e-Hisaat (Calculus removal)[1,2,26,50]
Muqawwi Baah (Aphrodisiac)[6,11,13,14,26,41-43,47,63,65,67]
Mughalliz-e-Mani (Inspissant to semen)[2,13,26,50,51]
Muwallid-e-Mani (Spermatogenesis)[26]
Muqee (Emetic)[26,41]
Mulattif (Demulscent)[2,41]
Mudir-e-Baul (Diuretic)[1,13,26,41,50,51]
Moarriq (Diaphoretic)[26,51]
Mudirr-e-Labn (Galactagogue)[26,51]
Mudirr-e-Haiz (Emmenagogue)[26,51]
Mulayyan (Laxative)[1,29,41,50]
Mufatteh Sudade Ama'a (Deobstruent of intestine)[26]
Qabiz (biryan) (Astringent)[6,12,14,26,42,43,47,61,63,65,67]
Habis-ud- Dam (biryan /roasted) (Styptic/Haemostatic)[26]
Munzij (Concoctive/Maturative)[1,26,39,50]
Muqawwi Aam (General tonic)[26]
Mufajjir Auraam (Resolvent)[26,41,50]
Jaali (Detergent)[1,12,26,41,50]
Mujaffif (Desiccant/Siccative)[2,26,41,50]

Therapeutic Use of Tukhm-e-Katan)

The medicinal applications of linseed are mentioned in the works of Hippocrates, and Dioscorides as well as in medieval books on medicinal herbs in both Asia and Europe. Various medicinal and traditional uses of flax had been recommended by Hippocrates and other historians[4].

Tukhm-e-Katan (Flaxseed)

Balghami khansi (Bronchial Asthma)[2,12,26,31,41]
Zeeq-un-Nafas (Dyspnea)[2,41]
Warm-e-Urooq-e- Khashna (Bronchiolitis)[2,41,50]
Nafs-ud-dam (Hemoptysis)[26]
Sang-e-Gurda (Renal calculus)[2,26,50]
Sang-e-Masana (Vesicle Calculus)[26,50]
Dard (Pain)[12,26,50]
Warm-e-Jigar (Hepatitis)[26]
Warm-e-Tihal (Inflammation of the Spleen)[39]
Zat-Ur-Riya (Pneumonia); Warm-e-Shaob-e-Muzmin (Bronchitis); Warm-e-gilaf-e-Qalb (Pericarditis); Wajaul mufassil (Arthritis)[2,26,50]
Zat-ul-Janab (Pleurisy)[26,39,50]
Sozish-e-Halq (Throat irritation)[26,39]
Wajaul Mufassil (Arthritis)[26,39,50]
Irqunnasa (Sciatica)[26,50]
Niqras (Gout)[26,50]
Qurooh Ama (Intestinal ulcers)[26,39,50,51]
Qurooh-e-Gurda-wa-Masana (Ulcers of kidney and urinary bladder)[26,31,39,51]
Qarha-e-Reham (Uterine ulcer)[26,31,39]
Ikhtenaq-ur-reham (Hysteria)[42]
Awram-e-Zahira-wa-Batina (Inflammation of external and internal organs)[26,31,39,48,50]
Basoor-e-labniya (Acne vagaris)[26,39]
Qooba (Ringworm)[26,39,50,51]
Kalaf (Melasma)[26,31,39,48,50]
Sa'afa (Alopecia)[26]
Surkhi Ain (Redness of eyes)[26,39,50]
Dard-e-Ain (Pain in eyes)[39]
Zoaf-e-Aam (General weakness)[26]
Amraz-e-kulliya (Kidney disease)[14,31]
Ulcer; Local inflammation[14]

Flaxseeds are official in the Indian pharmacopeia as a demulcent, emollient, expectorant, and thermogenic and diuretic. It is astringent after roasting[67]. Flax Seed has been used as a remedy for colds, coughs and irritations of the urinary tract. The whole seed prescribed as a laxative in the same manner as ispaghula (*Plantago ovata*). The mucilaginous infusion, Linseed Tea as it is called, is used internally as a demulcent in cold, coughs and bronchial affections, inflammation of the urinary tract, gonorrhea and diarrhea. Crushed linseed is applied in the form of a poultice for the relief of local inflammations and ulcers, boils and carbuncle; linseed poultice retain heat better than most other substitutes and they dilate the local blood vessels, relax the tissue, and thereby relieve the tension and pain hence they act as a good supportive. Linseed poultice is also useful in bronchitis and other deep-seated inflammations and has been recommended for gouty and rheumatic swellings[6,14,43,42,47,61,63,65,67].

Loab-e-Tukhm-e-Katan (Flaxseed mucilage)

It is a hydrocolloid with good water-holding capacity and also exhibits "week gel" like properties. It occurs mainly at the outermost layer of hull[6,54]. The fiber-rich hull is able to release mucilaginous material (soluble gum) easily when soaked in water (soaking in water for 24 h) as a white fibrous mass which becomes friable when completely dry and now it becomes a significant source of soluble fiber for both its availability and low viscosity[14,38]. It is used in cosmetic and pharmaceutical industries as demulcent or emollient.

Flaxseed tea

Uncrushed flaxseeds are soaked in water for 30 minutes. Seeds are then removed while the water is warmed moderately. It is useful against dyspnea, asthma, dysphonia, bad cough and bronchitis (Ankit Goyal, Vivek Sharma *et al*-2013). As rich source of dietary fiber (accounting 28 %), both soluble as well as insoluble fibers add a high amount of dietary fiber adds bulk to waste products in the gut and increases bile movement in the gastrointestinal movement and exhibits natural laxative effect hence, useful in the treatment of constipation, intestinal inflammations, lesions and ulcers, irritable bowel syndrome and diverticular disease and Low glycemic index foods containing soluble fiber not only prevent certain metabolic ramifications of insulin resistance but also reduce insulin resistance. Soluble fiber and other components of from flaxseed mucilage delays gastric emptying could potentially affect insulin secretion and its mechanism of action in maintaining plasma glucose homeostasis and reduces serum cholesterol[5,23,49]. Besides physically coating the digestive track, gum/mucilage induce a reflex causing relaxation in the gut and respiratory and urinary tracks as well. It is also recommended for the use in food products as a water-soluble emulsifying agent, thickener or binder. It may be employed as a substitute of acacia gum in stabilization of emulsions and is a useful base for eye ointments. It is also suitable for use in water paints and in the manufacture of soluble fibers[14,49,64].

Miqdar (Doses) mentioned in Unani classical literature

5 g-12g[41]
10 ½ g[26]
14 g[26]
10 g[51]

10-15 g of seed is given in kidney disease; 40 g in menopausal syndrome; 35-50 g daily in crushed form or may be incorporated into muffins or breads in hypercholestremia; 500-600 mg of seed extract in diabetes type-2. In conclusion the general recommendation for daily intake has been 1–3

table spoons per day for ground flaxseed or 1-2 tablespoonfuls flaxseed oil daily may use for decrease platelet aggregation[23].

Muzir mentioned in Unani literature (Toxicity)

Digestion[26,51]
Eye[1,13,51]
Khusiya i.e. testes[51]

The toxic effect of this drug is due to its cyanogenic glycosides which may cause prussic acid poisoning in humans. Although no health hazards or side effects are known in conjunction with the proper administration of designated therapeutic dosages. People with diarrhea, irritable bowel syndrome, diverticulitis, or inflammatory bowel disease (Crohn's disease or ulcerative colitis) should avoid flaxseed due to its possible laxative effects. Nausea, vomiting, and abdominal pain are reported in two individuals shortly after taking flaxseed products by mouth; these reactions may have been caused by allergy. The use of large quantities of the drug as a laxative with too little fluid intake can lead to an ileus. Its Fiber can also cause flatulence and bezoars, if taken with an inadequate amount of water[59]. It may also prolong bleeding time (Blood thinning medications) and may leads to hypoglycemia in diabetics during medication. Therefore, if anyone taking medicines for diabetes, including insulin, they should use flaxseed (ALA) only under your doctor's supervision. Flaxseed may change hormonal levels and change the effects of oral contraceptives or HRT. If anyone taking oral contraceptive or HRT, ask your doctor before taking flaxseed[22,54].

Musleh mentioned in classical Unani literature (Correctives)

Kishneez (*Coriandrum sativum*)[1,13,26,39,51]
Sikanjabeen (A syrup obtained by mixing vinegar and honey)[26,39,51]
Shahad/Asl-e-Khalis (Honey)[1,13,26,51]
Anar (*Punica Granatum*)[26]
Gulqand (A preparation made of rose petals or petals of some other flowers and powdered sugar, mixed together in ratio of 1:3)[26].

Badal (Substitute) of Tukhm-e-Katan

Tukhm-e-hulba *(Trigonella Foenum-graecum)*[1,26,41,51]
Tukhm-e-baqilla (*Vicia Faba*)[26]

Murakkabat (Compound formulation of Tukhm-e-Katan)

- Lauq-e- Katan[13,29,30,39,40,52,60]
- Qairooti Bazar-e-Katan[2,7,40]

Research Reports

There are various studies regarding the consumption of the flaxseed. It is being traditionally used in Ayurveda comes under ICMR guidelines in the category of clinical evaluation of traditional Ayurveda, Siddha, Unani (asu) remedies and medicinal plants and relevant guidelines of ICMR were followed during experimentation. The Clinical and large-scale population studies show that flax improves laxation, lowers blood cholesterol, aids in blood glucose control, endotoxic shock and blocks inflammation. Because it has an anti-inflammatory effect, eating flax regularly may help prevent and treat chronic diseases in which inflammation plays a role–chronic diseases like heart disease, stroke, diabetes, cancer, obesity, the metabolic syndrome, and Alzheimer disease[18]. The available literatures suggest that the flaxseed and its oils supplementations are well tolerated with negligible side effects[28].

Anti-inflammatory, Analgesic and Antipyretic activities

Fixed oil of *Linum usitatissimum* as Anti-inflammatory, analgesic and antipyretic activity of was evaluated in the study conducted by Gaurav Kaithwas *et al*-2011. The results showed that the fixed oil of Linum inhibited PGE2, leukotrienes, histamine, bradykinin and also arachidonic acid induced inflammation. It showed an excellent peripherally acting analgesic activity in comparable to aspirin against acetic acid induced writhing in mouse. It was also found to have a significant antipyretic activity in typhoid paratyphoid vaccine induced pyrexia[24]. Another study was conduct by Singh S, Nair V *et al* in 2008 in order to evaluate the anti-inflammatory activity of plant lipids containing alpha-linolenic acid. Two groups of fatty acids are essential to the body, the omega-6 (n6) series derived from linoleic acid (18:2, n-6) and the omega-3 (n3) series derived from alpha-linolenic acid (18:3, n-3). Fatty acids provide energy, are an integral part of the cell membranes and are precursors of prostaglandins, thromboxanes and leukotrienes collectively known as eicosanoids. Eicosanoids participate in development and synthesis of immunological and inflammatory responses. The fixed oils (1, 2, 3 ml/kg) containing alpha-linolenic acid, obtained from the seeds of Linseed (*Linum usitatissimum*), Soyabean (Glycine max) and Holy basil (*Ocimum sanctum*) were screened for their anti inflammatory activity using carrageenan, leukotrienes and arachidonic acid induced paw edema models in rats and the anti inflammatory effects were compared with the standard drug indomethacin. Significant inhibition of paw edema was produced by all the oils in the highest dose (3 ml/kg) in all the models. While *O. sanctum* oil produced the maximum percentage inhibition in leukotrienes induced paw edema, *L. usitatissimum* oil produced maximum percentage inhibition in carrageenan and arachidonic acid induced paw edema models. The results of this study suggestive that oils with higher alpha-linolenic acid content (*L. usitatissimum* and *O. sanctum*) produced a greater inhibition of paw edema suggesting that modulation of the course of inflammatory disorders may be achieved by altering the eicosanoids precursor (i.e. poly unsaturated fatty acids: PUFA) availability through dietary manipulation.

Antidepressant Activity

Rath B.P *et. al*-2012 conducted a study to evaluate the antidepressant activity of extract of *Linum usitatissimum* in wistar rats. Locomotors activity, forced swimming test and tail suspension test were used for assessing antidepressant activity. They reported the less significant antidepressant activity in comparison to standard drugs Fluoxetine, Chlorpromazine and Imipramine.

Anti hyperglycemic activity

In a study, the effect of ethanolic extract of seeds of *Linum usitatissimum* (EELU) was evaluated in hyperglycemia associated oxygen reactive species (ROS) production in peripheral blood mononuclear cells and pancreatic cells (PBMNCs) and pancreatic antioxidant enzymes in alloxan induced diabetic rats. The result showed that treatment of the EELU (200 mg and 400 mg/kg) significantly reduced serum glucose level in both acute and sub acute study[9].

Anti-oxidant activity

The anti-oxidant activity of ethanolic extract of *Linum usitatissimum* EE-LU (100, 200, 300, 400 and 500 µg/ml) was evaluated by Anand A. Zanwar *et al*-2010 in an *in-vitro* model. The results indicated significant dose dependent inhibition against DPPH radical, reducing power, superoxide anion radical scavenging, hydroxyl radical scavenging, metal chelating and hydrogen peroxide scavenging by EE-LU and α-tocopherol. The study conducted by Arvind Lal Bhatia *et al* was a pilot study that explores the anti oxidative properties of linseed (*Linum usitatissimum*) oil in its prophylactic action against oxidative stress induced by a radiomimetic drug, cyclophosphamide. Oral administration of linseed oil (0.1 mL/kg of body weight/day) for 20 days prior to an acute dose of cyclophosphamide (75 mg/kg) significantly inhibited the augmented level of malondieldehide, conjugated dienes, and hydroperoxides in the mouse brain. The cyclophosphamide-induced decline in the levels of reduced glutathione, glutathione peroxidase, and alkaline phosphatase was also significantly prevented by linseed oil in mouse blood. Similarly, the increased activity of acid phosphatase and oxidized glutathione was significantly inhibited by linseed oil. Results clearly indicate the prophylactic action of linseed oil against cyclophosphamide- induced oxidative stress[9].

Anti-peptic ulcer activity

In a recent study, Esmaeilzadeh Mahdi *et al*-2013 evaluated the anti-peptic ulcer action of the water extract of whole seed of *Linum usitatissimum* Linn. They reported that the extract was observed to show significant spasmolytic activity and protective effect against experimental ulcerogenesis[21]. In another study both flaxseed oil and flaxseed mucilage was found to have significant protective activity against ethanol induced gastric ulcer. The results show that pretreatment of rats with flaxseed oil and flaxseed mucilage significantly reduced the number and length of gastric ulcers induced by ethanol. Flaxseed oil was more effective than flaxseed mucilage in reducing the number of ulcers. The reduction in ulcer severity (cumulative length in mm) provided by an oral dose of flaxseed oil (5 ml/kg) was more prominent than that obtained by ranitidine (50 mg/kg). This study indicates that both flaxseed oil and flaxseed mucilage can provide a cytoprotective effect against ethanol-induced gastric ulcers in rats[20]. Gaurav Kaithwas and Dipak K. Majumdar in 2010 had planned a study with an aim to evaluate the antiulcer activity of *Linum usitatissimum* fixed oil against aspirin, indomethacin, ethanol, reserpine, serotonin and stress-induced gastric ulceration in rats and histamine induced gastric ulceration in guinea pigs. Attempts were also made to evaluate the *in vitro* anticholinergic and antihistaminic activity and *in vivo* antisecretory and antiulcer activity of oil following pylorus ligation in rats. *L. usitatissimum* fixed oil exhibited significant antiulcer activity against different ulcerogens in experimental animal models. The fixed oil significantly inhibited acetylcholine and histamine-induced contraction of guinea pig and rat ileums, respectively, suggesting its anti cholinergic and antihistaminic activity. The oil also exhibited significant inhibitory effect on gastric secretion/total acidity and aspirin-induced gastric ulceration in pylorus-ligated rats. The lipoxygenase inhibitory, histamine antagonistic and antisecretory (anti cholinergic) effects of the oil could probably have contributed towards antiulcer activity. *L. usitatissimum* fixed oil may be considered to be a drug of natural origin which possesses significant antiulcer activity. The present observation is the first experimental data showing antiulcer activity of *L. usitatissimum* fixed oil[24].

Rheumatoid Arthritis

In a double-blind, placebo-controlled randomized study flaxseed vs. safflower was evaluated in 22 patients with rheumatoid arthritis. The groups were followed up after 3 months and showed no improvement in the clinical subjective findings (pain, global assessment, functional status), or laboratory parameters (C-reactive protein, erythrocyte sedimentation rate). Therefore, the author concluded that flaxseed did not prove to be beneficial in patients with rheumatoid arthritis. Dahl WJ *et al* had investigated whether a flax supplement taken orally or baked in a bakery product would affect the physiological responses characteristic of soluble and insoluble fiber, i.e. laxation and glycemic response, respectively. In Study 1, 26 healthy young adults consumed up to 15 g of fiber from a proprietary flax fiber supplement or as a psyllium supplement for 2 weeks once usual fecal weights were established. Changes in dietary fiber intake and acceptability of both products were evaluated. An increase in fecal weight was found with both fiber treatments. Supplemental fiber at intakes of 9.0 g/day (flax) and 10.4 g/day (psyllium) gave fecal bulking capacity of about 2.9 and 4.8 g of fecal weight/g of fiber, respectively. In Study 2, the effect of flax bread versus control white bread on glycemic response was studied. Eleven fasting subjects completed four test periods (duplicate trials to each bread) under standardized glycemic testing conditions. Paired t tests were used to analyze test compared with control peak blood glucose values (6.6 +/- 0.9 mmol/L compared with 6.9 +/- 0.7 mmol/L, $P < .05$, respectively) and area under the curve (AUC) (669 +/- 53 compared with 693 +/- 57, $P = .015$, respectively). Peak blood glucose values and AUC were improved by ingestion of flax fiber in healthy subjects. In conclusion, a flax fiber supplement provides the benefits of soluble and insoluble fiber[15].

Cancer

A pilot study was done at dietary fat restriction and flaxseed supplementation in 25 prostate cancer patients. The patients were asked to take 30 g/day of ground flaxseed and to have a low fat diet of 20 % of total kilocalories or less. The study lasted an average of 34 days and there was a significant decrease in total testosterone (422 ± 122 ng/dL to 360 ± 128 ng/dL), total cholesterol (201 ± 39 mg/dL to 174 ± 42 mg/dL) and free androgen index (36.3 % ± 18.9 % to 29.3 % ± 16.8 %) ($p< 0.05$), a decrease in the mean proliferation rate (7.4 ± 7.8 historic controls vs. 5.0 ± 4.9 for treated patients, $p = 0.05$), the distribution of the apoptotic indexes differed significantly ($p = 0.01$) and the proliferation rat and apoptosis were significantly associated with the number of days on the diet ($p = 0.049$ and $p = 0.017$).

Hyperlipidemia and oxidative stress

A study conducted by David J.A. Jenkins *et al*-1999 with an objective to evaluate the health aspects of partially defatted flaxseed in relation to serum lipids, indicators of oxidative stress, and ex-vivo sex hormone activities. In this study 29 hyperlipidemic subject (22 men and 7 postmenopausal women) completed 2-weeks treatment periods in a randomized, crossover trial. Subjects were given muffins that contributed app. 20 g fiber/d from either flaxseed (app. 50 g partially defatted flaxseed/d) or wheat bran (control) while they consumed self-selected National Cholesterol Education

Program Step II diets. Both muffins had similar macronutrient profiles and the treatment phases were separated by ≥ 2 wks. The results of this study shows that the partially defatted flaxseed reduces total cholesterol (4.6 ± 1.2 %; P = 0.001), LDL cholesterol (7.6 ± 1.8 %; P < 0.001), Apo-lipoprotein A-I (5.8 ± 1.4 %; P = 0.005), but it had no effect on serum lipoprotein ratios at week 3 compared with the control. There were no significant effects on serum HDL cholesterol, serum protein carbonyl content, or ex vivo androgen or progestin activity after either treatment. Unexpectedly, serum protein thiol groups were significantly lower (10.8 ± 3.6 %; P = 0.007) at 3 week after the flaxseed treatment than after the control, suggesting increased oxidation. These data indicate that partially defatted flaxseed is effective in lowering LDL cholesterol[17]. Another study was carried out using 80, 32-weeks old, single comb white leghorn (SCWL) laying hens which were subjected to 4 dietary treatments, namely Control, 5 % flaxseed endosperm-rich fraction (ERF), 10 % ERF and 20 % ERF. At the end of the 4th week, all groups were examined hematologically and histopathologically. There was a linear relationship between feed consumption and decrease in body weight. The decrease in body weight of the birds was directly proportional to the concentration of ERF in the diet. Packed cell volume (PCV) and red blood cell (RBC) counts had a negative significance (P < 0.05) linear relationship with the ERF level. There was a decrease in PCV and RBC counts as ERF increased in the diet. Broadly, the livers of birds fed with 20 % ERF were enlarged, pale in color, soft in consistency and were hemorrhaged with fat and fibrin deposits[33].

Type II diabetes and Dyslipidaemia

A study conducted by Goutam Thakur on the effect of flaxseed gum on reduction of blood glucose and cholesterol particularly LDL in Type 2 diabetes patients have shown the that the use of flaxseed mucilage in these patients has reduced the clinical symptoms of DM associated with Dyslipidaemia. In study 60 patients of Type 2 diabetes were fed for 3 months a daily diet, along with 6 wheat flour chapattis containing flaxseed gum (5 g), as per the recommendations American Diabetic Association (ADA). The blood biochemistry profile (BBP) on being monitored before starting the study and at monthly intervals showed fasting blood sugar (FBS) in experimental group decreased from 154 ± 8 mg/dl to 136 ± 7 mg/dl (p = 0.03) while the total cholesterol (TC) reduced from 182 ± 11 mg/dl to 163 ± 9 mg/dl (p = 0.03). Result showed decrease in LDL from 110 ± 8 mg/dl to 92 ± 9 mg/dl (p = 0.02)[28]. Another study designed by Soren Toubro the principal investigator to evaluate "Effect of Whole Flaxseeds and Flaxseed Mucilage on Lipid Absorption, Glucose and Insulin Metabolism and Appetite Regulation". The primary purpose of this study is prevention. It is a randomized multiple crossover trial in 18 healthy males aged 18-40 years each are required to complete a total of five iso-caloric meal tests lasting approximately 8 ½ hours. Test meals will be given as breakfast meals, in which different fractions are incorporated into baked products. Appetite will be registered using visual analogue scales during 7 hours after the test meal and a total of 10 blood samples will be drawn to evaluate TAG in chylomicrons, plasma LDL, HDL and total cholesterol, plasma TAG, insulin, glucose and appetite hormone levels. At the end of the test an *ad libitum* meal will be served and food intake registered. The recruitment status of this study is unknown because the information has not been verified recently. A study conducted by Mitra A, Bhattacharya D in 2009 in order to find out whether flaxseed gum, like guargum, is effective in reducing the blood glucose level in non insulin dependent diabetes mellitus (NIDDM). In this study 20 NIDDM patients were fed, for 3 months, 5 chapattis each containing 5 g flaxseed gum and 25 g wheat flour. Blood biochemistry of these patients when on normal monitored diet for the preceding 3 months, before initiation of therapy with flax gum, was measured monthly using standard procedures and monthly therefore, after the initiation of therapy. 20 other (non-diabetic) patients subjected to identical conditions acted as controls. It was observed that flax gum-containing therapeutic diet reduced TLC, LDLC, and FBS significantly. In fact the statistical analysis of the data confirmed that flax gum caused significant reduction of TLC (p = 0.025), LDLC (p = 0.030) and FBS (p = 0.045). The changes in other parameters were not statistically significant. The conclusion from this study is that flaxseed gum is an inexpensive, abundant, natural material with no side effects. It is helped in curing various diseases by lowering the recognized risk factors like TLC, LDLC, and FBS. In diabetes, this is a useful nutraceutical for its effects in controlling blood sugar and Dyslipidaemia[49].

Hypercholesterolemic atherosclerosis

K. Prasad *et al*-1998 had reported that antiatherogenic activity of flaxseed is not due to its α-Linolenic acid. For this purpose he planned a study on CDC-flaxseed (Type II flaxseed), which has similar oil and lignans content but has very little (2-3 % of the total oil) α-Linolenic acid and this CDC-flaxseed is going to be investigated on high cholesterol diet induced atherosclerosis and serum lipids (total cholesterol (TC), triglycerides (TG), High Density Lipoprotein cholesterol (HDL-C), low density lipo-protein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C)) in rabbits. In this study the rabbits were assigned to four groups: group-I, Control; group-II- Type II flaxseed diet (7.5 g/kg orally daily); group-III- 1 % cholesterol diet; group-IV- 1 % cholesterol diet Supplement with Type II Flaxseed (7.5 g/kg orally daily). Blood samples were collected before (0 time) and after 4 and 8 weeks of the experimental diets for measurement of serum lipids. Aorta was removed at the end of 8 weeks for assessment of atherosclerotic plaque. Serum (TC), (LDL-C), TC/(HDL-C), and LDL-C/(HDL-C) were lower in group IV as compared to group III by 14 and 31 %, 17 and 32 %, 28 and 34 % and 24 and 32 % respectively, at 4 and 8 weeks. HDL-C was not affected by Type II flaxseed in Hypercholesterolemic rabbit. TG and VLDL-C were markedly increased in group IV as compared to group III. Type II flaxseed reduced the development of atherosclerosis by 69 %. Histological changes in the atherosclerotic regions were qualitatively similar in groups III and IV. These results are indicating that the reduction in Hypercholesterolemic atherosclerosis by Type II flaxseed is due to a decrease in serum TC and LDL-C and not due to its α-Linolenic acid[37].

Cardiovascular disease (Hypertension in Dyslipidaemia)

GK Paschos *et al*-2007 had planned a study entitled "Dietary supplementation with flaxseed oil lowers blood pressure in dyslipidaemic patients" with an objective to examine the effect of increased ALA intake on blood pressure in man. It was design as a prospective, two-group, parallel-arm to examine the effect of a 12-week dietary supplementation with flaxseed oil, rich in ALA (8 g/day), on blood pressure in

middle-aged dyslipidaemic men (n¼ 59). The diet of the control group was supplemented with safflower oil, containing the equivalent n-6 fatty acid (11 g/day linoleic acid (LA); n¼ 28). The Arterial blood pressure was measured at the beginning and at the end of the dietary intervention period. The study shows that supplementation with ALA resulted in significantly lower systolic and diastolic blood pressure levels compared with LA (P¼ 0.016 and P¼ 0.011, respectively, from analysis of variance (ANOVA) for repeated measures). In Conclusion GK Paschos *et al* had observed a hypotensive effect of ALA, which may constitute another mechanism accounting in part for the apparent cardio protective effect of this n-3 fatty acid[27]. P.M. Gala *et al* had designed a Comparative study for evaluation of ground flaxseed (*Linum ussitatissimum*), flax oil and atorvastatin on endothelial cells in terms of nitric oxide (NO) release and their interaction with monocytes. In this study, Rats (n = 32) were randomized into test and control groups. The test groups received either atorvastatin (50 mg/kg orally), flax oil (1.8 g/kg) or ground flaxseed mixed in diet (2.34 g/kg) for 21 days, following which blood was collected to separate sera for further study. Human umbilical vein endothelial cells (HUVECs) were incubated with sera samples and NO release was estimated. To study interaction of HUVECs with monocytes, co-culture of HUVECs and smooth muscle cells were incubated with sera in presence of LDL. Supernatants were separated and using Neuroprobe chamber chemotaxis of monocytes towards supernatants was counted as monocytes migrated per HPF. Co-culture supernatants were incubated with HUVECs and monocytes to count the number of adherent monocytes to HUVECs. Under the results of this study they analyzed that Atorvastatin significantly increased NO release by HUVECs (46.92 + 10.19 μM/ml). Maximum NO release however was seen when HUVECs were incubated with sera of rats given ground flaxseed (138.66 + 17.21 μM/ml vs flax oil: 123.91 + 17.94 and atorvastatin; P < 0.001). Flaxseed and Flax oil reduced chemotaxis and adhesion of monocytes to HUVECs and the results were comparable to atorvastatin. In conclusions they mentioned that all the three agents prevented interaction of monocytes with endothelial cells. Moreover, significantly higher release of NO from endothelial cells was seen with ground flaxseed mixed with diet than flax oil and atorvastatin. Hence, this study has proves the beneficial effects of flax seed, a cheap and easily available alternative for flax oil, on endothelial cells[56].

Immunocompetence

Darshan S Kelley *et al*-1991 have examined the effect of dietary ALA on the indices of immunocompetence in 10 healthy free-living men (age 21-37 years) who consumed all meals at the western human nutrition research center for 126 days and found that the overall, flax diet tended to suppresses the cell-mediated- immunity without affecting the humoral immunity. There was a stabilization period of 14d at the start when all 10 subjects consumed basal diet (BD) and there were two intervention periods of 56d each. Five of the subjects consumed the basal diet and another five consumed flax-seed-oil-diet (FD) during each intervention period. Feeding of FD suppressed the proliferation of peripheral blood mononuclear cells when they were cultured with phytohemagglutinin-P (p = 0.041) and concanvalin A (p = 0.054) and the delayed hypersensitivity response to seven recall antigens (NS). Concentrations of immunoglobulin in serum, C3, C4, Salivary IgA, the numbers of Helper cells, suppressor cells and the total T and B cells in the peripheral blood were not affected by the diets[16].

Infant allergies and respiratory diseases

In a paper "Role of dietary long-chain polyunsaturated fatty acids in infant allergies and respiratory diseases" Lynette P. Shek *et al* during had examine the role PUFAs consumption during pregnancy and early childhood and its influence on allergy and respiratory diseases as the long-chain polyunsaturated fatty acids have been reported to have immunomodulatoray effects. Decreased consumption of omega-6-PUFAs, in favor of more anti-inflammatory omega-3-PUFAs (flax is rich in ALA which is a biological precursor to omega-3-fatty acid) in modern diets, has demonstrated the potential protective role of allergic and respiratory diseases. PUFAs act via several mechanisms to modulate immune function. Omega-3-PUFAs may alter the T helper cell balance by inhibiting cytokine production which in turn inhibits immunoglobulin E synthesis and T helper 2 cell differentiations. PUFAs may further modify cellular membrane, induce eicosanoids metabolism, and alter gene expression[46].

Oxidative lung damage, inflammation, fibrosis and thoracic radiation injury

Flaxseed is one such dietary supplement, a whole grain that is non-toxic and has both anti inflammatory and antioxidant properties due to its high concentrations of omega-3 fatty acids and lignans. In a study, James C. Lee, Ryan Krochak *et al*-2009 demonstrates that FS, a non-toxic nutritional supplement with antioxidant properties, can prevent oxidative reactions in lung cells and tissues induced by radiation. Long term post-XRT fibrosis and inflammation were also improved with FS feeding prior to and after XRT. This normal tissue radioprotection does not come at the expense of tumor protection, suggesting that dietary FS may be clinically useful in increasing the therapeutic index of thoracic radiation therapy. Antioxidant cell and tissue protection from radiation using FS and FS-derived SDG was also demonstrated. Thus, the use of FS in the realm of radiation pneumonopathy is novel and has potential implications for more effective radiotherapy of thoracic malignancies[36]. Another study conducted by Paul Kinniry *et al* in 2006 on acute lung injury. In this study, Paul Kinniry *et al*. evaluated the diets with high FS content in experimental murine models of acute lung injury and inflammation. The kinetics of lignan accumulation in blood, following 10 % FS supplementation, was determined using liquid chromatography tandem mass spectrometry. Mice were fed isocaloric control and 10 % FS-supplemented diets for at least 3 wk and challenged by hyperoxia (80 % oxygen), intra tracheal instillation of lipopolysacharide, or acid aspiration. Bronchoalveolar lavage was evaluated for white blood cells, neutrophils, and proteins after a 24 h post intra tracheal challenge of hydrochloric acid or lipopolysacharide, or after 6d of hyperoxia. Lung lipid peroxidation was assessed by tissue malondialdehyde concentrations. The plasma concentrations of the FS lignans, enterodiol and enterolactone, were stable after mice had eaten the diets for 2 wk. Following hyperoxia and acid aspiration, Bronchoalveolar lavage neutrophils decreased in FS-supplemented mice (P ¼ 0.012 and P ¼ 0.027, respectively), whereas overall alveolar white blood cell influx tended to be lower (P ¼ 0.11). In contrast, neither lung injury nor inflammation was ameliorated by FS following lipopolysacharide instillation. Lung malondialdehyde levels

were lower in hyperoxic mice than in unchallenged mice (P ¼ 0.0001), and decreased with FS treatment following acid aspiration (P ¼ 0.011). Dietary FS decreased lung inflammation and lipid peroxidation, suggesting a protective role against pro oxidant- induced tissue damage *in vivo*. The lung is an organ particularly susceptible to oxidative stress and this study shows here the first supporting evidence to indicate that dietary supplementation with FS can ameliorate oxidative tissue damage and inflammation in certain forms of experimental acute lung injury[57]. Dietary flaxseed (FS) is a nutritional whole grain with high contents of omega-3 fatty acids and lignans with anti-inflammatory and antioxidant properties. James C. Lee, Faiz Bhora *et al* -2008 evaluated FS in a murine model of pulmonary ischemia-reperfusion injury (IRI) by dietary supplementation of 0 % (control) or 10 % (treatment) FS before IRI. Mice fed 0 % FS undergoing IRI had a significant decrease in arterial oxygenation (PaO_2) and a significant increase in Bronchoalveolar lavage (BAL) protein compared with sham-operated mice. However, mice fed 10 % FS undergoing IRI had a significant improvement in both PaO_2 and BAL protein compared with mice fed 0 % FS undergoing IRI. In addition, oxidative lung damage was decreased in 10 % FS-supplemented mice undergoing IRI, as assessed by malondialdehyde levels. Immunohistochemical staining of lungs for iPF2α-III F2 isoprostane, a measure of lipid oxidation, was diminished. FS-supplemented mice had less reactive oxygen species (ROS) release from the vascular endothelium in lungs in an ex vivo model of IRI, and alveolar macrophages isolated from FS-fed mice had significantly reduced ROS generation in response to oxidative burst. Pulmonary micro vascular endothelial cells produced less ROS in a flow cessation model of ischemia when pre incubated with purified FS lignan metabolites. Pharmacological inhibition of heme- oxygenase-1 (HO-1) resulted in only a partial reduction of FS protection in the same model. We conclude that dietary FS is protective against IRI in an experimental murine model and that FS affects ROS generation and ROS detoxification via pathways not limited to up regulation of antioxidant enzymes such as HO-1. Hence, Dietary flaxseed enhances antioxidant defenses and is protective in a mouse model of lung ischemia-reperfusion injury[35]. Flax seed use in preventing thoracic X-ray radiation therapy (XRT)-induced pneumonopathy has never been evaluated. With this aim James C. Lee, Ryan Krochak *et al*-2009 had planned a study to evaluated FS supplementation given to mice given before and post-XRT. FS-derived lignans, known for their direct antioxidant properties, were evaluated in abrogating ROS generation in cultured endothelial cells following gamma radiation exposure. Mice were fed 10 % FS or isocaloric control diet for three weeks and given 13.5 Gy thoracic XRT. Lungs were evaluated at 24 hours for markers of radiation-induced injury, three weeks for acute lung damage (lipid per oxidation, lung edema and inflammation) and at four months for late lung damage (inflammation and fibrosis). FS-Lignans blunted ROS generation *in vitro*, resulting from radiation in a dose-dependent manner. FS-fed mice had reduced expression of lung injury biomarkers (Bax, p21, and TGF-beta1) at 24 hours following XRT and reduced oxidative lung damage as measured by malondialdehyde (MDA) levels at 3 weeks following XRT. In addition, FS-fed mice had decreased lung fibrosis as determined by hydroxyproline content and decreased inflammatory cell influx into lungs at 4 months post XRT. Importantly, when Lewis Lung carcinoma cells were injected systemically in mice, FS dietary supplementation did not appear to protect lung tumors from responding to thoracic XRT. Hence, this study further justify that Dietary FS is protective against pulmonary fibrosis, inflammation and oxidative lung damage in a murine model. Moreover, in this model, tumor radioprotection was not observed. FS lignans exhibited potent radiation-induced ROS scavenging action. Taken together, these data also suggest that dietary flaxseed may be clinically useful as an agent to increase the therapeutic index of thoracic XRT by increasing the radiation tolerance of lung tissues[36]. Due to the interest in functional foods the aim of the present study, was to investigate breads supplemented with functional components. One was bread supplemented with inulin, linseed and soya fiber (prebiotics bread). The other was prebiotics antioxidant bread (pre-aox-bread), which additionally contained green tea powder, herbs and tomato paste. The effects of these two breads on immunological and anti oxidative parameters were compared with control bread (placebo). Twenty smokers and eighteen non-smokers were enrolled in the randomized parallel study, which consisted of a control period and an intervention period, each lasting for 5 weeks. Daily intake of bread and nutrients did not differ between the intervention and the control period. Most of the twenty-three investigated immunological parameters measured in peripheral blood were unaffected. However, the percentage of CD19 increased after intervention with prebiotics bread, whereas intercellular adhesion molecule-1 (ICAM-1) and CD3 + NK + ($P < 0.05$) decreased in both intervention arms. The ferric reducing ability of plasma (FRAP) was increased after consumption of the pre aox-bread for non-smokers (1256 v. 1147 micromoles/l; $P = 0.019$) and remained unchanged for smokers consuming the pre-aox-bread[62].

CONCLUSION

Flaxseed is undoubtedly the nutraceutical food of the 21st century given its unlimited potential in preventing and/or reducing the risk of several major diseases, including diabetes, lupus nephritis, atherosclerosis and hormonally dependent cancers. Apart from this flaxseed has been shown to decrease tumors of the colon and mammary gland as well as of the lung and its omega 3s inhibits the activity of ALOX5, an enzyme that exacerbates lung inflammation and Causes asthma. The Clinical and large-scale population studies show that flax improves laxation, lowers blood cholesterol, aids in blood glucose control, endotoxic shock and blocks inflammation. Because it has an anti-inflammatory effect, eating flax regularly may help prevent and treat chronic diseases in which inflammation plays a role–chronic diseases like heart disease, stroke, diabetes, cancer, obesity, the metabolic syndrome, and Alzheimer disease. The scientific studies have proved the claims of traditional system of medicine and the use of flaxseed as a dietary supplement is increasing in parallel with the research on its multitudinous effects on human health. For this reason, further detailed clinical research appears worthwhile to explore the full therapeutic potential of this drug in order to establish it as a standard drug.

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