



A comprehensive ethnopharmacological review on *Linum usitatissimum* Linn. (*Atasi*)

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Abstract

Linum usitatissimum Linn, popularly known as Flaxseed or Linseed is one of the essential herbs of Ayurveda medicines. It has a strong historical platform of having therapeutical properties to treat various diseases. The present review aimed to provide ethnomedical claims on *L. usitatissimum*. and research efforts carried out on it that validates such claims. Literature was searched through various databases, journals and books through electronic and manual search. *L. usitatissimum* is traditionally used as therapeutics in many different geographical regions globally as well in India. Ethnomedicinally, seed, oil, leaves, and the whole plant are reported to manage 47 various disease conditions, either internally or externally such as rheumatism, digestive complaints, wound, etc. Among all part-used, seed has the maximum number of applications. Plant extracts were experimentally evaluated for nephroprotective, analgesic, antimicrobial Anti-Inflammatory, wound healing, antiulcer, antisecretory, anticholinergic, antihistaminic, anti-cholesterol and cardioprotective activities. Clinical trials were conducted on osteoarthritis and hyperlipidaemia which were confirmed the ethnomedicinal usage of the plant. There is still a lack of good quality clinical evidence in support of ethnic uses. Therefore, in-depth research on efficacy and safety aspects concerning its major compounds of *L. usitatissimum* is desired to validate the traditional claims recorded.

Keywords: *Atasi*, ethno medicine, *Linum usitatissimum* L., traditional practice

Introduction

Traditional medicine and ethnobotanical information play a significant role in scientific research and contribute significantly to the drug preparations manufactured nowadays ^[1]. Many researchers suggested to revisit the historical texts as valuable source of knowledge in a scientific manner for the reinvent codified remedies and the development of modern medicines. ^[2] Traditional medicines have been increasingly used by diverse communities in many parts of the world, due to its important role in maintaining good health with increasing awareness and research. For many people in the developing world, plant based traditional medicine is crucial for their healthcare. WHO also emphasised the incorporation of herbal medicines in primary healthcare system to achieve the goal of "health for all".

Plants have always been considered as the primary source of drugs in traditional and alternative system of medicine in various dosage forms such as crude form, juice, decoction, and crude extracts etc. Medicinal plants played an important role in traditional drug discovery. ^[3] Indian subcontinent known for its rich cultural and plant biodiversity owes its legacy to larger population still living in tribes. The tribal population of India potentiates itself as a huge source of undisclosed ethnomedicinal and ethnopharmacological information in regards to the flora of their surroundings, thereby turning into a big ethnomedicinal resource in rural community. The majority of the India ethnomedicinal knowledge has its roots in the Ayurveda. Ayurveda medicines hugely depended on medicinal plants for the prevention and management of different pathological conditions.

Linum usitatissimum Linn., belongs to family Linaceae, commonly known as *Atasi* in India, is traditionally used by local healers to treat different disease conditions and has been documented by various authors for its ethnomedicinal uses. The plant is extensively cultivated in both temperate and tropical climates e.g. Russia, Egypt, throughout India, United states, south of Europe, Holland and England. In India, it is cultivated chiefly in Bengal, Bihar and the united provinces. ^[4]

L. usitatissimum or flax has been broadly utilized in numerous ethnic worldwide as a primary medicinal plant because of its health benefits in various types of ailments. As per the Ayurvedic classical texts, plant possess has *Madhur* (sweet), *Tikta rasa* (bitter taste), *Guru* (heavy), *Snigdha* (unctuousness) *Guna* (attribute), *Ushna virya* (hot potency), and *Katu vipaka* (pungent bio-transformed rasa). It is used for the management of cough, skin diseases and *Vataroga* (Neuro-musculo-skeletal disorders). Long term use with high dose may cause some untoward effect on vision and semen. ^[5] It is used as an ingredient in many Ayurvedic formulations used internally and externally for therapeutic purposes.

Since the information about the ethnomedicinal uses of the *L. usitatissimum* has been dispersed on different platforms (i.e. journals, books, web-based sources), and under various presentation formats (i.e. glossaries, reviews, notes, surveys), there is a significant need to collect and analyse the information on ethnomedicinal uses and efficacy studies through experimental and clinical researches linked with ethnomedicinal aspect. Hence, in the present review study,

an effort has been made to comprehensive review on its ethnomedicinal aspect, pharmacological experiments and clinical studies on efficacy to validate the ethnomedical knowledge.

Material and Methods

Information on Atasi was gathered from various sources, including the scientific databases including PubMed, and Science Direct, Google Scholar, Ayush Research Portal and classical texts of Indian system of medicines. Articles that described the use of *L usitatissimum* (alone or in combination with any other herbs), externally or internally, to treat any disease conditions in human or in animals were included in the review.

Result and Discussion

In the present study, 64 manuscripts were identified and reviewed from various research databases and 20 books related to ethnobotany were reviewed and screened. After the removal of the duplicates yielded a total of 30 articles which in-turn underwent a review.

Habitat

L. Usitatissimum is observed to be used in 12 states of India Viz. Karnataka, Odisha, Madhya Pradesh, Jammu- Kashmir, Maharashtra, Himachal Pradesh, Uttar Pradesh, Rajasthan, Bihar Jharkhand, West Bengal, and Uttaranchal, (Fig.2) and in 7 countries, such as Algeria, Pakistan, Morocco, Ethiopia, Turkey, Nepal and Iraq. (Table 1.)

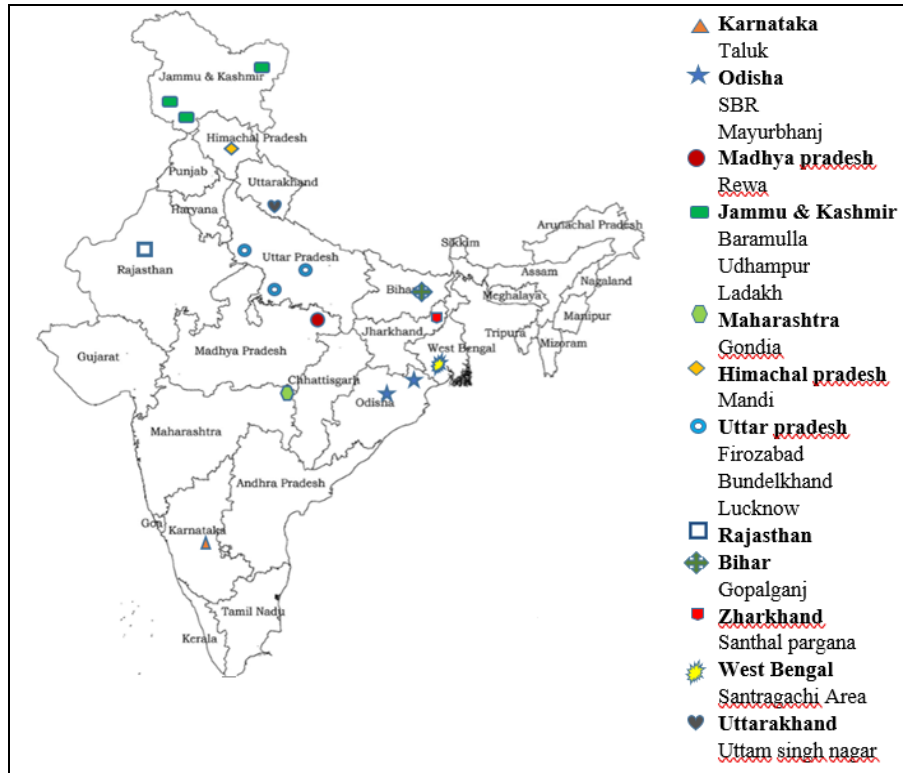


Fig 1: Geographical distribution of ethnomedicinal uses reported on *Linum usitatissimum* L. in India.

Botanical description

L Usitatissimum is stiff, upright annual that grows to be about 1-2 feet tall, the stem usually solitary, cylindrical and has corymbose branches in the upper part, leaves are alternate sessile, linear to lanceolate, and entire. Solitary

flowers at the tip of branches, 5 petals, 5 sepals and 5 stamens. Ovary flask-shaped, 5 cell at the base with a thick axis, fruit capsular, and seeds flattened ovoid with rounded edges and an oblique blunt beak at the upper end. ^[6] (Fig.1. A, B, C, D).

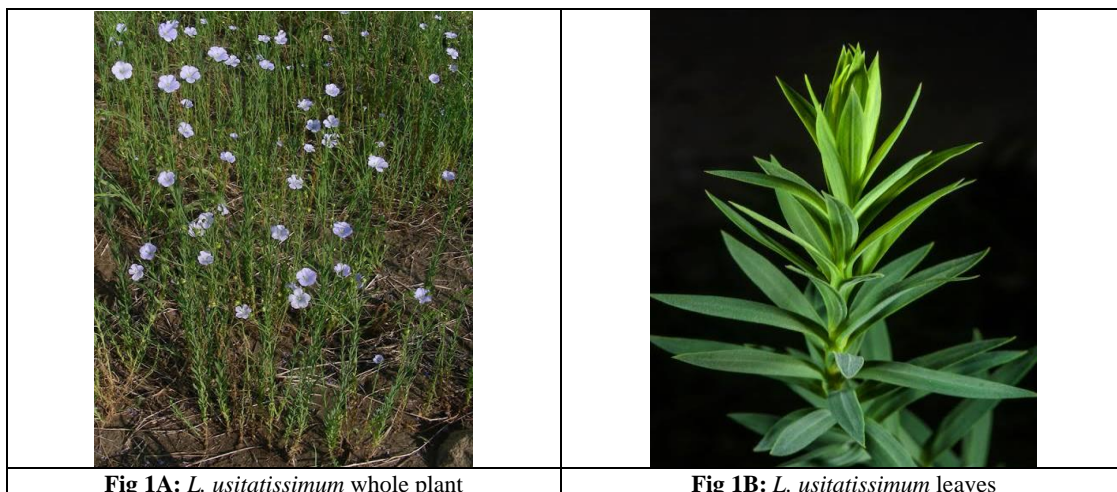


Fig 1A: *L. usitatissimum* whole plant

Fig 1B: *L. usitatissimum* leaves

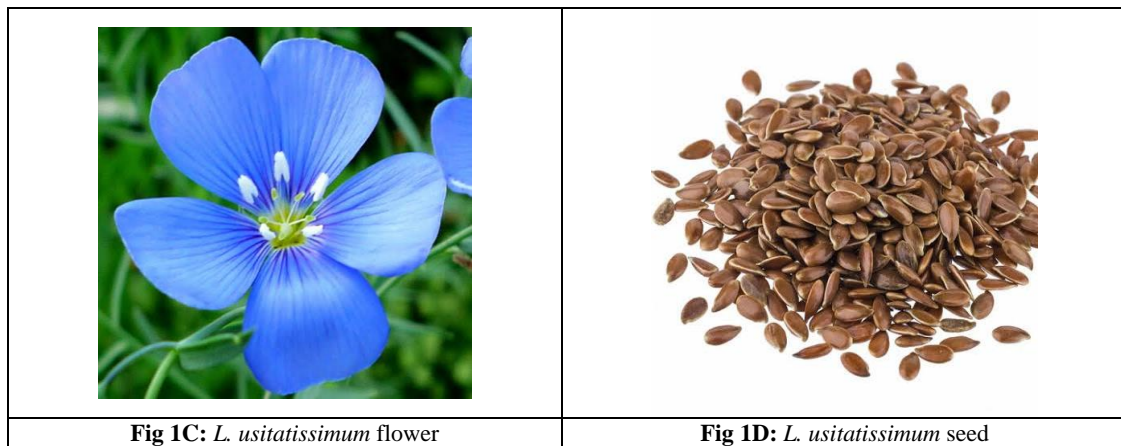


Fig 2

Vernacular Names

L. Usitatissimum is known by 14 names in 20 different languages as follow: Alasi: Odisha, Pakistan, Phesi: Odisha, Alsi: Madhya Pradesh, Firozabad, Rajasthan, J&K, Himachal Pradesh, Uttar Pradesh, Bihar, Uttar Pradesh and, Uttaranchal, Uttarakhand, Telba: Ethiopia, Alshi: Jammu and Kashmir, zriâat al katan: Northern Morocco, Alish: Jammu, Kashmir, Ladakh, Jawas: Maharashtra, Tisi: Bihar, Uttar Pradesh and, Uttaranchal, Keten: Edremit Gulf (Turkey), Tishi: western Nepal, Alasa: western Nepal, Arsi: Uttar Pradesh and, Uttaranchal, Ketani swr: Iraq, (Table 1).

Ethnomedicinal claims

The whole plant of *L. usitatissimum* or its leaves and seeds have been reported to treat many diseases.

Seed of *L. usitatissimum* has been used to cure constipation, and apply seed oil to treat wound among the tribes of Taluk region of Karnataka. [7] Tribal people of Odisha consumed oil of seed to treat Asthma, hives, diseases of intestinal tract, urticaria and hay-fever internally, [8] and roasted seed in joint pain. [27] Seed has been used in the treatment of demulcent, rheumatism and gonorrhoea by the people of Rewa district of Madhya Pradesh. [9] Tribal communities of Jammu and Kashmir used seed powder on abscess [17] and for smooth delivery in labour [13]. Seeds have been reported to cure abscess, arthritis, boils, demulcent, rheumatic pain and as laxative, purgative among ethnic group of Jammu, Kashmir and Ladakh [22]. Seed oil has been reported to cure heart diseases, and skin diseases in local tribe of Firozabad region of U.P. [14] In Lucknow region of Uttar Pradesh, seeds' paste have been applied externally to cure infections [21] and crushed seed poultice applied externally to cure inflammation, ulcers and boils by tribes of Bundelkhand region of same province [25]. Poultice of seed paste has been reported for the treatment of hard boil in Uttar Pradesh. [24] Seed has been used by tribes of Rajasthan for various ailments such as biliousness, backache, leprosy, ulcers, Kidney troubles, Galactagogue and as aphrodisiac and diuretic [16]. Tribal people of Mandi region of Himachal Pradesh used seeds in Gonorrhoea and backache; and laxative in cattles. [19] Seed oil has been reported to cure tympany in

Gondia district of Maharashtra. [23] People of Gopalganj district of Bihar used raw seed in the treatment of cough [26]. Whole plant have been reported to treat Cough, intoxication and wound; [38] found to manage GI problems, cough and cold in Santragachi area of West Bengal. [35] Local community of Udham Singh Nagar region of Uttarakhand applied paste of whole plant to treat wound [36]. Seed and its hot poultice have been reported to treat disease like boils, rheumatism, defective milk production, burns, eczema, gonorrhoea, pneumonia and bronchitis (hot poultice). [18, 20] (Table 1)

L. usitatissimum has been found to be used in other countries too. Raw seed has been reported for the treatment of digestive disorder in south west Algeria. [10] People from Algeria also used whole plant in the treatment of obesity. [37] Seed has been used to cure flatulence by tribal of kurram district Pakistan. [11] People of Kemkem district of northwest Ethiopia have applied cream (made out of mix crushed seed with honey) to cure wound. [12] consumed seed has been consumed with honey by tribal people of northern morocco to cure Stomachic [15]. seed oil on burns and boils and seed poultice has been applied on rheumatic and swellings in western Nepal. [29] It has been reported use of seed in infectious diseases among dwellers of Khyber Pakhtunkhwa region [31]. seed decoction has been administered in bronchitis in Edremit Gulf region of Turkey. [28] Powder of leaves has been used by the people of Kurdistan region of Iraq to treat blood cholesterol, rheumatism, colon problems, antispasmodic, skin burns, gallstones and thyroid problems [34]. (Table 1)

L. usitatissimum seed oil has also been reported to be used for Cooking and burning by local tribes of Santhal Pargana (Jharkhand) [32] and in making of soap, paints and varnish by the people of Uttar Pradesh. [33] (Table 1)

The ethnomedicinal claims showed that seed and its oil have widely been used to manage various ailments by traditional people followed by whole plant and leaves. Plant found to be used externally as well as internally. (Table 1.) Seed, leaves, and whole plant of *L Usitatissimum* are used in 5 different dosage forms such as Oil (7), powder (3), poultice (3), Paste (2), decoction (1) and cream (1). (Table 1)

Table 1: Ethno medicinal use of different parts of *Linum usitatissimum*.

Local name	Tribes/areas	Dosage form: External (E); internal (I) uses	Therapeutic claims
Seed			
-	Taluk, Karnataka, India	Oil (E) and seed (I)	Oil in Wounds, seed in Constipation [7]
Alasi, Phesi	Odisha, India	Oil (E)	Asthma, hives, diseases of intestinal tract, urticaria, hay-fever [8]
Alsi	Rewa district, Madhya Pradesh, India	-	Demulcent, rheumatism, gonorrhoea [9]
-	South-West Algeria	Raw seed (I)	Digestive disorders [10]
Alasi	Kurram District, Pakistan		Flatulence [11]
Telba	Kemkem District, northwest Ethiopia	Crush, mix with honey then cream (E)	Wound [12]
Alshi	District Baramulla, Jammu and Kashmir	Powder	Smooth delivery [13]
Alsi	Firozabad	Oil	Heart Diseases, Skin Diseases [14]
Zriâat al katan	Northern Morocco	Seed consumed with honey (I)	Stomachic [15]
Alsi	Rajasthan	-	Aphrodisiac, diuretic, biliousness, backache, leprosy, ulcers, Kidney troubles, Galactagogue [16]
Alsi	Udhampur, J&K,	Powder(E)	Abscess [17]
Alsi		Hot poultices(E)	Burns, and eczema, gonorrhea. Poultice of seeds was also used in pneumonia and bronchitis [18]
Alsi	Mandi District, Himachal Pradesh	-	Gonorrhoea, Backache, Laxative in cattle [19]
Alish	-	(E) and (I)	Boils, rheumatism, defective milk production [20]
	Lucknow, Uttar Pradesh,	Paste(E)	Infection [21]
Alish, alsi	Jammu, Kashmir, ladakh	-	Abscess, Arthritis, Boils, Demulcent, Laxative, Purgative, Rheumatic Pain [22]
Jawas	Gondia district, maharashtra,	Oil(E)	Tympany [23]
Alsi	Uttar Pradesh, India	Seed paste poultice (E)	Hard boil [24]
-	Bundelkhand region, Uttar Pradesh, India	Crushed seed poultice(E)	Inflammation, ulcers, boils [25]
Tisi/alsi	Gopalganj district, Bihar (India)	Raw(I)	Cough [26]
	SBR and Mayurbhanj district.	Roasted seed	Joint pain [27]
Keten	Edremit Gulf (Balikesir – Turkey)	Decoction	Bronchitis [28]
Tishi, Alasa	Western Nepal	Seed, and seed oil (E)	Oil for burns and boils, poultice on rheumatic and swellings. [29]
Ketan	-	-	Herpes, eczema, rheumatism [30]
-	Khyber Pakhtunkhwa	-	Infectious diseases [31]
-	Santhal pargana (zharkhand)	Oil	Cooking and burning purpose [32]
Arsi, alsi, tisi	Uttar pradeshand	Oil	Cooking, making soap, paints and varnish [33]
Leaves			
Ketani swr	Kurdistan, Iraq	Powder (I)	Blood cholesterol, rheumatism, colon problems, antispasmodic, skin burns, gallstones, thyroid problems. [34]
Whole plant			
-	Santragachi Area, West Bengal.		GI problems, cough & cold [35]
Alsi	Udham Singh Nagar, Uttarakhand,	paste	Wound [36]
Plant part not specifies			
-	Algeria	-	Obesity [37]
Alsi	India		Cough, intoxication, wound. [38]

Ehtnomedicinal data suggested that *Atasi* has been widely used as medicines amongst folklore and common population since long. Its efficacy data through animal and human experiments linked to the ethnomedicinal uses which validates the claims are presented below:

Pharmacological study

Renoprotective

Study on ethanolic extract of seeds of *L. usitatissimum* (EELU) (400 mg/kg) showed significantly decreased the haemodynamic changes after a period of 4 weeks of renal ischaemia reperfusion injury when administered wister

albino rats. Ethanolic extract was helpful in significantly restoring the levels of renal endogenous antioxidant enzymes, membrane-bound enzymes, levels of blood urea nitrogen and serum creatinine. It also helpful in decreasing the levels of tumour necrosis factor- α and myeloperoxidase activity. A flow-cytometric study validated a significant decrease in cellular necrosis and increase in viability after renal ischaemia reperfusion in EELU-treated rats. [39] (Table 2)

Antimicrobial activities

Antimicrobial activity of *L. usitatissimum* was conducted against seven bacterial and one fungal pathogen using extracted samples from ethyl acetate, n-hexane, butanol and distilled water. Study found that the growth of *Staphylococcus aureus* was inhibited by 56% equally by butanol and ethyl acetate extracted samples in disc diffusion testing method. Similarly, ethyl acetate and butanol extracted samples were found to reduce the growth of *Bacillus cereus* by 44 and 64% respectively. The data also indicated that ethyl acetate inhibited *Erwinia carotovora* up to 42% and 65% inhibition was observed by butanol extracted samples. [40] (Table 2)

Antibacterial Activity

The study was carried out to evaluate the antibacterial activity of *L. usitatissimum* extracts (alcoholic and aqueous) against three species of bacteria (*Shigella flexneri*, *Salmonella typhimurium* and *E. coli*) obtained from stock cultures by the agar diffusion method. These extracts inhibited maximum zone against *Shigella flexneri*. Data suggested that alcoholic extract of *L. usitatissimum* showed better inhibitory effects against all bacterial species compared to aqueous extract. According to the study, flaxseed extracts may be a potent source of antibacterial chemicals and a promising alternative to antibiotic therapy. [41] (Table 2)

Analgesic and anti-inflammatory activity

Analgesic activity of the plant was examined by hot plate test model wherein 192 mice were randomly designated into 4 sets of 6 groups of 8 mice including control (normal saline), positive control (morphine), morphine plus naloxone, experimental groups (200 and 500 mg/kg extract), and extract along with naloxone group, each of which received 500 mg/kg. The analgesic activities were evaluated at 5, 15, 30, and 60 minutes, respectively. Both the doses showed analgesic activity, the 200 mg/kg possessed higher effects ($P < .05$). [42] (Table 2)

For the anti-inflammatory evaluation xylene test was used for which, 48 mice were randomly designated into 6 groups of 8 each including: control, dexamethasone as positive control (15 mg/kg), and experimental groups (42, 85, 170, and 340 mg/kg, respectively). At 170 mg/kg dose level, extract performed better anti-inflammatory activity ($P < .05$). *L. usitatissimum* might be used as analgesic and anti-inflammatory agent due to the presence of phenolic, flavonoid, and flavonol compounds. [42] (Table 2)

Wound healing activity

A study was done to determine the wound healing activity of flaxseed oil on induced incision wound. The ointments from flaxseed oil were made in two concentrations—0.75 and 1.5 percent and applied to the wounds. In the period of

re-epithelization, treated mice demonstrated a considerable decrease in inflammatory cells. Flaxseed oil greatly speeds up the healing of wounds, making it a promising natural remedy for skin wounds. [43] (Table 2)

Antiulcer, antisecretory activity, anticholinergic and antihistaminic activity

study was to Anti-ulcer activity of fixed oil was evaluated against aspirin-, indomethacin-, ethanol-, reserpine-, serotonin- and stress-induced gastric ulceration in rats and histamine- induced gastric ulceration in guinea pigs. *in vitro* anticholinergic and antihistaminic activity and *in vivo* antisecretory and anti-ulcer activity of oil were also evaluated through pylorus ligation in rats. *L. usitatissimum* fixed oil exhibited significant antiulcer activity against different ulcerogens. Significant inhibition of acetylcholine- and histamine-induced contraction of guinea pig and rat ileums, respectively, suggested its anticholinergic and antihistaminic activity. The oil also exerted inhibitory effect on gastric secretion and aspirin-induced gastric ulceration in pylorus-ligated rats. Antiulcer activity of the fixed oil can be explained by the lipoxigenase inhibitory, histamine antagonistic and antisecretory (anticholinergic) effects. [44] (Table 2)

Anti-cholesterol and anti-oxidant activity

in-vitro antioxidant activity of flaxseeds was evaluated through DPPH free radical scavenging and total antioxidant potential assay.

Phenolic compound content of the flaxseeds was found as 0.059 mg Gallic Acid Equivalent g^{-1} and antioxidant potential was 1.037 mg mL^{-1} . The results indicated that flaxseed could probably reduce or control the cholesterol levels and oxidative damage. [45] (Table 2)

Anti-cholesterol activity by flaxseeds was observed up to 20 min wherein maximum inhibition was found as 93.04%, which was significantly comparable to positive control drug simvastatin (95.1%). Study suggested flaxseed might decrease the cholesterol levels and oxidative damage.

Cardio protective activity

Cardioprotective activity of flax lignan concentrate (FLC) was evaluated in isoprenaline (ISO) induced cardiotoxicity in male Wistar rats. marker enzymes in serum (lactate dehydrogenase (LDH), creatine phosphokinase-MB isoenzyme (CK-MB) and aspartate transaminase (AST)) and haemodynamic parameters were recorded. FLC at the dose of 500 mg/kg decreased these biochemical changes (LDH, CK-MB and AST) significantly compared with ISO group. Cardiotoxic effect of isoprenaline was less in FLC pre-treated animals, which was verified in histopathological study. In isoprenaline induced cardiotoxicity, a cardioprotective effect of FLC was confirmed by haemodynamic, biochemical alteration and histopathological findings. [46] (Table 2)

Clinical study

Hyperlipidemia

A pilot clinical trial was done to determine whether flaxseed supplementation could improve the profiles of lipids and inflammatory mediators in patients with severe hyperlipidemia resistant to conventional lipid-lowering pharmacotherapy and requiring lipoprotein apheresis. Six patients received 10-week dietary supplementation with flaxseed (28 g/d) in the form of biscuits followed by a 10-

week wash out-period and a 10-week period of whole wheat placebo supplements. Flaxseed supplementation was well-tolerated by the patients and significantly decreased total cholesterol and low-density lipoprotein (LDL) levels. There alteration was observed by flaxseed administration on lipoprotein (a) (Lp(a)), C-reactive protein (CRP), and interleukin 6 (IL-6). The finding suggested that flaxseed can induce a cholesterol- and LDL lowering effect in patients treated with lipoprotein apheresis. However, randomised control trial is warranted to confirm the efficacy.⁴⁷ (Table 2) In another single arm clinical study, 30 obese patients of with hyperlipidaemia was administered with flaxseed powder for a period of 40 days in the dose of 3 g. twice a day with luke-warm water. Flaxseed powder significantly reduced the total cholesterol and LDL-Cholesterol and

increased HDL-Cholesterol levels with no significant change on Triglycerides and VLDL Cholesterol. ^[48] (Table 2)

Osteoarthritis

randomized, double-blind, placebo-controlled clinical trial was conducted to determine the efficacy of linseed oil on pain and clinical symptoms of the knee Osteoarthritis. Experimental group received 20 drops every 8 hours to rub on the knees for 6 weeks whereas the placebo control group received the liquid paraffin in the same way. The study showed the activities of daily living, sport and recreation, and knee-related quality of life in the linseed group significantly improved compared to placebo group. ^[49] (Table 2)

Table 2: Experimental and clinical studies conducted on *L. usitatissimum* in accordance to Traditional Use.

Sr. no.	Reported research activities	Ethnomedicinal claims
Pharmacological study		
3	Renoprotective effect	Kidney trouble
4	Antimicrobial activities, Antibacterial Activity	Infection
5	Analgesic and Anti-Inflammatory activity	Joint pain, Backache, Swelling, inflammation
6	Wound healing activity	Wound, Burn, skin diseases, Leprosy, eczema,
7	Antiulcer, antisecretory activity, anticholinergic and antihistaminic activity	Ulcer
8	Anti-cholesterol and antioxidant	Blood cholesterol
9	Cardioprotective activity	Heart disease
Clinical Study		
1	Hyperlipidaemia	Obesity
2	Osteoarthritis	Arthritis

Conclusion

L. usitatissimum has been used for its therapeutic and nutritional potential since from the ancient Ayurveda. It is evident from this review that *L. usitatissimum* possesses many ethnomedicinal uses in many tribes of India. *L. usitatissimum* has been reported to have numerous pharmacological effects to treat various disorders including rheumatism, wounds, eczema, cough, ulcer, constipation, asthma, urticaria, digestive disorder, heart diseases, galactagogue, arthritis, laxative etc. Some of them were examined and validated by animal expectation and clinical trials. Plant extracts were experimentally evaluated for nephroprotective, analgesic, antimicrobial Anti-Inflammatory, wound healing, antiulcer, antisecretory, anticholinergic, antihistaminic, anti-cholesterol and cardioprotective activities. Clinical trials were conducted on osteoarthritis and hyperlipidaemia which were confirmed the ethnomedicinal usage of the plant. Now, the road ahead is to establish the active therapeutic compound with specific mode of actions, which might be responsible for the medicinal properties of the plant. Further clinical trial is required focusing pharmacodynamic, pharmacokinetic and safety profiles to validate its efficacy reported through preliminary animal experimentations.

Acknowledgement

The authors are thankful to the Director, ITRA, Jamnagar for providing library and other facilities to carry out the research work.

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