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Therapeutics, phytochemistry and pharmacology of *Tukhm-e-Katan* (*Linum usitatissimum* L.)

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ABSTRACT

The Unani drug Katan comprises of seeds of a plant *Linum usitatissimum* Linn. Which belong to linaceae family, It is one of the most ancient crops cultivated in Egypt. It is also cultivated in India as an oil seed plant. The plant has shown diverse biological and pharmacological activities. It has been used in Unani Medicine and Traditional Systems of Medicine from time immemorial. Its seed and oil are used in various diseases such as asthma, cough, bronchitis, pleurisy, pneumonia, joint pain, renal colic, renal calculi, rheumatic swelling, etc. Keeping in view of the high medicinal importance of the drug in Unani medicine, the present review provides available information on traditional uses, phytochemistry and pharmacological properties of the Unani drug Katan.

Keywords: Flax, Katan, *Linum usitatissimum*, Unani Medicine.

INTRODUCTION

In recent years, considerable research has been done on an array of plants having medicinal values. Katan is a famous Unani drug used in a number of pathological conditions. Although entire plant has medicinal value but its seed and oil are more important and have broad medicinal values. The botanical name of katan is *Linum usitatissimum* Linn. (Family: Linaceae). Katan is an annual herb of about 0.7 m high with blue flowers and a globular capsule. The seed are ovate, flattened and obliquely pointed at one end, about 4-6 mm long and 2-2.5 mm broad. The testa is brown, glossy and finely pitted odorless, taste mucilaginous and oily. If cruciferous seed are present, a pungent odour and taste may develop on crushing and moistening (Evans, 2009). Seeds are sown at the end of March and flower in June. Stems are solitary or few corymbose branched, branches ascend towards the apex. Flowers are of about 2.5 cm across in corymbose, panicles, sepals are 5. The outer elliptic, acuminate with entire membranous margins while the three inner broader acuminate with ciliate margins, all strongly three nerved, and the middle nerve alone reaches the apex (Anonymous, 1992). The seed coat contain mucilage, the surface are studded with fine pits or depression with a ridge just below the apex, having the hilum in the hollow. Seed nuclei or cotyledons are two, large and oily and contained within the external covering, within which is a thin mucous envelope (Khory & Katrak 1993), linseed oil is fixed oil expressed from linseed. It is clear yellowish brown oil, having characteristic odour, and taste bland. Gradually, thickens on exposure to air spread in thin film, a hard transparent varnish (Anonymous 1970). The drug Katan pocess Anti-bacterial, Demulcent, Anti-Inflammatory, Expectorant, Laxative, Analgesic, Diuretic, Emollient, Emmenagogue, Aphrodisiac, Sedative, Lithotriptic, so medicinally used in Renal colic, cystitis, Vesicle Irritation, Renal calculi, Boils, Piles, Leprosy, Burn, Ulcer, Asthma, Gonorrhea, Pleurisy, Pneumonia, cough, Baldness, Joint pain, Gout.

Vernaculars

The plant is known by different vernacular names: Bazrul Katan, Buzruk, Bazen, Katan (Arabic); Tisi, Tusi, (Assamese); Chikna, Tisi (Behar); Masina, Tisi, Alasi (Bengali); Alasi, Javasa, Javas (Bombay); Linho (Brazil); Alashi, Alsi (Canarese); Hou la Tse (Chinese); Alshi, javas (Deccan); Blaebows, Common Flax, Flax, Flix, Linseed, Lint Bells (English); Lin chaud, Lin commun, Lin cultive, Grins de Lin (French); Flachs, Haarlinsen, Lein, Saatlein (German); Linon (Greek); Alshi, Arasi (Gujarati); Alsi, Tisi (Hindi); Lino (Italian); Agasebeeja, Semeegara, Agasi, Kain Atish, Agashi (Kannada); Alish, Kenu (Kashmir); Agastha, Cheruchana-Vittintevilta (Malayalam); Alashi, Javas (Marathi); Atushi, Peso (Oriya); Bazarug, Kuman, Tukhm-e-Katan, Zaghir, Zaghu (Persian); Alish, Alsi, Tisi (Punjabi); Len, Lyon (Russian); Atasi, Atima, Chanaka, Devi, Haimwati, Kshauma, Kshaumi, Kshuma, Madagandha, Madotkata, Malina, Masina, Masrina, Masruna, Nilapushpi, (Sanskrit); Lino (Spanish); Bari Aala (Suryani); Bazrag (Sherazi); Alshi, (Tamil); Atasi, Madanginjalu, Ullusulu (Telugu); Ziggar (Turki); Keten (Turkish); Alsi, Katan (Urdu); Lisfermoon, Lifertus (Unani) (Khan, 1313H; Ghani, 2010; Chopra et al., 1958, Nadkarni, 1982; Khory & Katrak, 1993; Kirtikar and Basu, 1995; Ainslie, 1826; Dayal, 1993; Anonymous, 2007; Jilani, 1933; Ibn Baitar, 2003; Hakim 2002; Ibne Sina, 2007)

Mizaj (Temperament)

The Unani physicians described the temperament of Katan Hot and Dry in first degree (Seed) (Khan, 1313H;Ghani, 2010; Ibn Baitar, 2003; Hakim, 2002; Dymok, 1890), Hot and Wet (Oil), (Ibn-e-baitar, 2003) Hot1° and Equable between Wet & Moist (Mo'atadil) (Baghdadi, 2005; Ibn Sina, 2007).

Afa'al (Action)

In classical Unani literature, various action of the plant *Linum usitatissimum* have been described such as *Dafe-e-Sua'l* (Nabi,1958; Ibn Sina, 2007), *Dafe-e-Tashannuj* (Ibn Sina, 2007; Khan, 1313H), *Habis-ud-Dam* (Hakim, 2002; Ghani, 2010), *Jaali* (Khan, 1313H; Baghdadi, 2005), *Mudrri-e-Baul* (Khan, 1313H; Nabi, 1958; Kareem,1879; Ghani, 2010), *Mudammil-e-Qurooh-e-Gurda-wa-Masana* (Baghdadi, 2005; Khan, 1313H; Hakim, 2002), *Mudirr-e-Labn* (Nabi, 1958; Khan, 1313H; Ghani, 2010), *Mudirr-e-Haiz* (Nabi, 1958; Khan, 1313H), *Mugazzi* (Jilani, 1933), *Mohallil-e-waram* (Khan, 1313H; Ghani, 2010; Nabi, 1958; Baghdadi, 2005), *Moarriq* (Nabi, 1958; Kareem, 1879; Ghani, 2010), *Musakkin-e-Alam* (Ibn Sina, 2007; Baghdadi, 2005; Nabi, 1958; Ghani, 2010;), *Mulattif* (Jilani, 1933), *Mufattit-e-Hisaat*, (Fazlullah, 1918; Ghani, 2010), *Mukhrij-e-Hisat-e-Gurda-wa-Masana* (Khan, 1313H; Kareem, 1879; Ghani, 2010), *Muqawwi-e-Bah* (Baghdadi, 2005; Ghani, 2010), *Muqawwi-e-Basar* (Nabi, 1958), *Muqawwi-e-Aaza* (Nabi, 1958), *Muharriq-e-Bah*, (Ibn Sina, 2007; Baghdadi, 2005; Khan, 1313H), *Mughalliz-e-Mani* (Nabi,1958; Ghani, 2010), *Muwallid-e-Mani*, (Ghani, 2010), *Muqee*, (Ghani, 2010), *Munazij-e-Auraam*, (Baghdadi, 2005; Khan, 1313H), *Mulayyan* (Ibn Sina, 2007; Khan, 1313H; Nabi, 1958), *Mufatteh Sudade Ama'a* (Khan, 1313H; Ghani, 2010), *Qabiz* (Ibn Sina, 2007; Baghdadi, 2005; Khan, 1313H), *Munaffikh* (Ibn Sina, 2007; Baghdadi, 2005; Ghani, 2010), *Mufajjir-e-Auraam* (Ghani, 2010), *Munaffis-e-Balgham* (Ghani, 2010; Anonymous, 2007), *Munaffit* (Baghdadi, 2005; Ghani, 2010), Flower of the plant is *Mufarreh-wa-Muqawwi-e- Qalb* (Khan, 1313H; Hakim, 2002; Gahni, 2010), *Musleh-e-Rehum* (Khan, 1313H; Attar, 1305; Ghani, 2010), *Nafs-ud-Dam* (Khan, 1313H; Kareem,1879), *Nashf-e-Rutubat* (Khan, 1313H; Kareem, 1879).

Figure 1. *Linum usitatissimum* L. plant.

Istemal (Uses)

Katan has been described to be useful in various ailments such as *Balghami Khansi* (Ibn Sina, 2007; Ibn Baitar, 2003; Baghdadi, 2005; Khan, 1313H; Nabi, 1958;Ghani, 2010), *Basoor-e-labniya*, (Ibn Sina, 2007;

Figure 2. *Linum usitatissimum* L. flower.

Ghani, 2010; Khan, 1313H), *Dard* (Ibn Sina, 2007; Jilani, 1933; Nabi, 1958; Ghani, 2010), *Haraq* (Anonymous, 2007), *Kalaf* (Ibn Sina, 2007; Baghdadi, 2005; Khan, 1313H), *Nazaf-ud-Dum* (Ibn Sina, 2007), *Qooba* (Nabi,1958; Ghani, 2010; Khan, 1313H;), *Qurooh-e-Gurda-w-Masana* (Ibn Sina, 2007; Ibn Baitar, 2003; Khan, 1313H), *Qurooh-e-Ama* (Nabi, 1958; Baghdadi, 2005; Khan, 1313H),

Figure 3. *Linum usitatissimum* L. seed.

Qurooh-e-Rehum (Baghdadi, 2005; Ibn Baitar, 2003; Khan, 1313H; Ghani, 2010), *Qurooh-e-Miqaad* (Khan, 1313H), *Sang-e-Gurda-wa-Masana* (Hakim, 2002), *Sa'afa* (Ghani, 2010), *Saalil* (Kareem,1879), *Sozish-e-Baretoon* (Jilani,1933; Ghani, 2010), *Sozish-e-Halq*, (Jilani, 1933; Nabi, 1958; Ghani, 2010), *Suda-e-Warmi* (Khan, 1313H; Kareem,1879), *Surkhi-e-Ain* (Khan, 1313H; Ghani, 2010), *Suzaak* (Jilani, 1933), *Waja-ul-Mafasil* (Ibn Sina, 2007; Khan, 1313H; Ghani, 2010), *Warm-e-Jigar* (Khan, 1313H; Ghani, 2010), *Warm-e-Tihal* (Hakim, 2002), *Amraz-e-Kulliya* (Ibn Baitar, 2003), *Zat-ul-Janab* (Nabi, 1958; Jilani, 1933), *Zat-ur-Riya* (Nabi, 1958; Jilani, 1933), *Zeeq-un-Nafas* (Ghani, 2010; Anonymous, 2007), *Zukaam* (Khan, 1313H; Ghani, 2010).

Adverse effects

Improper digestion visual disturbances, decrease blood formation (Ghani, 2010; Kirtikar and Basu, 1995; Ibn-e-baitar, 2003; Khan, 1313H; Kareem, 1879).

Corrective

Kishneez, (*Coriandrum sativum Linn.*) (Khan, 1313H; Kareem, 1879; Anonymous, 1992), Correctives are used for improper digestion; visual disturbances decrease blood formation is *punica granatum* (Anar) and Honey. For refractory error *Coriandrum sativum* is used as corrective. For improper digestion Sikanjibeen is used (Khan, 1313H; Kareem, 1879; Ghani, 2010).

Therapeutic Uses

The oil is used in liniments, and hydrolyzed linseed oil has potentially useful antibacterial properties as' a topical preparation in that is effective against *Staphylococcus aureus* strains resistant to antibiotics (Evans, 2009), the seeds are used internally for gonorrhea and irritation of the genitor-urinary system. The flowers are considered a cardio tonic. Linseed poultice is valuable for gouty and rheumatic swellings; as an emollient (Kirtikar and Basu, 1995). The mucilage is dropped into the eye in irritable conditions of the conjuctiva with honey it is prescribed in cough and colds. Fumigation with the smoke is recommended for colds in the head and hysteria and the tinder is used to staunch haemorrhages (Nadkarni, 1982; Kirtikar and Basu, 1995). The oil mixed with limewater has been a favorite application to burns, the bark and leaves are good for gonorrhea, the bark burnt and applied to wounds, is styptic and heals them. The oil from the seeds removes biliousness and bad blood; useful for internal wounds, and ringworm; causes loss of appetite (Kirtikar and Basu, 1995), An infusion of the seeds known as linseed tea used internally as demulcent and expectorant drink in cold, coughs, bronchial affections and irritation of the urinary organs, cystitis, gonorrhea, strangury, diarrhea, dysentery, and also used as injection to vagina, bladder and rectum. Linseed poultice is a valuable soothing application to ulcerated and inflamed surfaces, boils, carbuncles, threatening abscesses, and to accelerate the maturation of torpid abscesses. It also makes a mild, continuous counter-irritation for deep-seated inflammations such as pneumonia, bronchitis, broncho-pneumonia, pleuritis, pericarditis, peritonitis, arthritis, quinsy, pelvic cellulitis.

The drug *Linum usitatissimum* is described in detail in ethnobotanical and scientific literature. Some pharmacological actions and therapeutic uses are as follows (Table 1).

Linseed oil is valuable remedy for painter'colic and other spasmodic affections of the bowels, and also used in piles (Nadkarni, 1982), the seeds is valuable remedy for diarrhea, catarrh, pneumonia, dysentery, gonorrhea, visceral obstructions, calculus (Ainslie, 1826), as demulcent and diuretic it is used in renal colic, cystitis, vesical irritation, strangury, vesical catarrh and calculi, and its infusion is used in inflammation of the mucous membranes of the respiratory, digestive and urinary, organs also in vesical and renal irritation, ground meal is chiefly used for poultices applied to enlarged glands, boils, gouty and rheumatic swelling, to the chest in pneumonia. The oil is laxative and used in piles (Khory and Katrak, 1995), linseed poultice is useful in gouty and rheumatic swelling, gonorrhoea, and irritation of genitor-urinary system (Chopra et al., 1958).

Phytochemistry

The seed contains about 30-40% of fixed oil, 6% of mucilage (BP swelling index of whole seeds < 4.0), 25% of protein and small quantities of the cyanogenetic glucosides linaamarin and lotaustralin. Other constituents are phenylpropanoid glycosides, flavonoids, the lignin (-)-pinoresinol diglucoside (a tetra hydro furofuran-type lignin), and the cancer chemo protective mammalian lignan precursor secoisolariciresinol diglucoside. Recently 22 different lignans mainly of the artyltetralin type, have been identified from Bulgarian species of Linum, section syllinum (Evans, 2009). Linseed oil of BP quality is a yellowish –brown drying oil with a

characteristic odour and bland taste; it has a high iodine value (<175) as it contains considerable quantities of the glycosides of unsaturated acids. α-linolenic acid, $C_{17}H_{29}COOH$ (36-50%), linoleic acid $C_{17}H_{31}COOH$ (23-24%), oleic acid $C_{17}H_{33}COOH$ (10-18%), together with some saturated acids-myristic, stearic and palmitic (5-11%), (Evans, 2009), Seeds contain 37 to 44 % of a fixed oil which consists of glycerol combined with linoleic acid 30-40%, mucilage 15%,(6% in the testa), proteins, amygdalin, resin, wax, sugar, and Ash 3-5%. Ash contains sulphates and chlorides of potassium, and magnesium, oil lies in the outer skin of the seed and is soluble in boiling water. If ground into a meal the oil is soluble in cold water also Oil contains 10-15% of mineral substances, chiefly phosphates of potassium, calcium and magnesium and about 25% of protein substances (Nadkarni, 1982).

Table 1. Pharmacological actions of *Linum usitatissimum* as described in Ethnobotanical and Traditional literature.

Demulcent	Evans, 2009, Nadkarni, 1982; Khory and Katrak, 1993; Chopra et al., 1958.
Anti-bacterial	Evans, 2009.
Expectorant	Nadkarni,1982; Khory and Katrak, 1993.
Diuretic	Nadkarni,1982; Khory and Katrak, 1993.
Emollient	Nadkarni,1982 , Kirtikar and Basu, 1995; Khory and Katrak, 1993.
Styptic	Nadkarni,1982
Aphrodisiac	Nadkarni,1982; Kirtikar and Basu, 1995.
Astringent	Nadkarni,1982
Galactogogue	Kirtikar and Basu, 1995
Emmenogogue	Kirtikar and Basu, 1995; Ainslie, 1826.
Anti-diarrhoeal	Ainslie, 1826
Laxative	Khory and Katrak, 1993; Nadkarni,1982
Analgesic	Khory and Katrak, 1993; Nadkarni,1982
Sedative	Bhattacharjee, 2004
Stimulate the kidney	Khory and Katrak, 1993.
Anti –Inflammatory	Khory and Katrak, 1993.
Dilate the local blood vessels	Nadkarni,1982

The spectral analysis of the ethanol extract of flaxseed revealed the presence of seventeen compounds by forming 5 major peaks were Squalene (45.27%), 9, 12, 15, octadecatrienoic acid,(z,z,z)- (24.6%), Pyrrolidine, 1-(1-oxo-7,10-hexadecadienyl)- (17.60%), Oleic acid (10.16%), and Sucrose (9.80%), respectively. The triterpene has also be found to have protective activity

against several carcinogens. Substances related to squalene, including ß-carotene, coenzyme Q10 (ubiquinone) and vitamins A, E, and K (Dharshini et al., 2013). The chromatographic separation of the dried aerial part extracts of *Linum usitatissimum* afforded 8-5' neolignan (dehydrodiconiferyl alcohol-4-ß-D-glucoside), 60 compounds from acetogenins, terpenoids, steroids, and others were identified by the GC/MS from fractions of hexane Lu1, Lu3a and methylene chloride Lu2, Lu3b by comparing the MS spectra with those in NIST library. A sample from hexane fraction Lu1 afforded 24 compounds, representing 95.29% from the sample, with 9,12,15-octadectrinoic acid (80.97%), hexadecanoic acid (10.69%), and selegiline (0.56%) being the major components. Methylene chloride fraction Lu2 afforded 24 compounds, with methyl (z,z,z)9,12,15-octadecadienoate (32.01%), butyl 9,12,15-octadecadienoate (16.29%) and methyl 9-cis,11-trans-octadecadienoate (7.69%), being the major components. Hexane extract Lu3a afforded 19 compounds, representing 75.41% from the sample, with methyl palmitate (38.64%), methyl (Z,Z)7,10-methyloctadecadienoate (9.91%), and methyl (z,z)8,11-octadecadienoate (9.85%) being the major components. Methylene chloride extract Lu3b afforded 14 compounds, representing 4.96% from the sample, with tetracosane (0.54%), eicosane (0.61%), and hexacosane (0.54%) being the major components (*Fatma M.* et al., 2016). Cholesterol (2), compesterol (26), stigmasterol (7), sitosterol (41), 5-dehydro-avenasterol (13) cycloartenol (9) and 24-methyencycloartanol (2%) in seeds characterized by GC-MS (Rastogi & Mehrotra, *1999*) Two new cynogenic glycoside linustatin and neolinustatin, isolated and characterized as 2-[C6-O-ß-D-glucopyranosyl-ß-D-glucopyranosyl-ß-D-glucopyranosyl]-2-methylbutanenitrile respectively (Rastogi & Mehrotra, 2001). Plant contained HCN (0.0486%), isolation of oleic, linoleic and linolenic acids and isofercosterol, from seeds; a new phenyl propanoid glucoside-linusitamarin isolated from defatted seeds and its structure elucidated (Rastogi & Mehrotra, 1998), the most common phytosterol present in Katan in large concentration is ß-sitosterol. Ten compounds were isolated and identified from the roots of *linum usitatissimu* by silica gel column chromatography, as Vanillic acid (1), syringic acid (2), xanthine (3), vitexin (4), isovanillin (5), (E)-3,3'-dimethoxy-4,4'-dihydroxystilbene (6), tachioside (7), beta-sitosterol andstigmasterol (8 and 9) mixture, berberine (10). (Sun et al., 2009),

Pharmacological studies

A number of studies have been carried out on *Linum usitatssmum L.* in recent years showing that it possesses diverse pharmacological effects. Some of the important pharmacological effects are as follows:

Antiarrhythmic effect

A possible antiarrhythmic effect of ALA (α-linolenic acid) and omega-3 fatty acids has been reported (Muzaffarian et at., 2005) while in other study found that antiarrhythmic effects were concentration dependently enhanced by docosahexaenic acid (DHA) and eicosapentaenoic acid (EPA), but not by ALA (Dhein et al., 2005). Higher intake of dietry linolenic acid might be associated with a reduced risk of abnormally prolonged repolarization in men and women (Djousse et al. 2005). The cardio protective effects of typical omega 3 polyunsaturated fatty acids (n-3 PUFAs) is due not through a single mode of action but to a synergism between multiple, inactivate mechanism that involve TG lowering, anti-inflammatory, inflammation-resolving, regulation of transcription factors and gene exertion, membrane fluidity and antiarrhythmic and antithrombotic effects, EPA and DHA have similar yet very distinct cardioprotective properties. Only DHA seem to decrease blood pressure, heart rate and the number of total and small dense LDL particles. n-3 PUFA has the potential to be used for the important or resolution of other inflammatory disease (Yuriko et al., 2009).

Anti-arthritis effect

The anti-arthritis activity of *Linum usitatissimum* fixed oil on acute and chronic models was studied against castor oil induced diarrhea turpentine oil-induced joint oedema, formaldehyde and Complete Freund's Adjuant induced arthritis in Wistar albino rats. The results suggested that *L. usitatissimum* fixed oil possesses potent antiarthritis activity due to dual inhibition of arachidonate metabolism, resulting in suppressed production of proinflammatory n-6 eicosanoids and decreased vascular permeability (Kaithwas et al. 2010).

Antibacterial activity

The petroleum ether, ethanol, aqueous and chloroform extracts from *Linum usitatissimum* L. seeds subjected to screen antibacterial activity against four types of Gram-positive and negative bacteria: *Staphylococcus aureus, Bacillus cereus, Klebsiella pneumonia, and Pseudomonas aeruginosa* using agar-well diffusion method and comparing their antibacterial activities with the antibiotics Ampicillin, Cefalexin, Chloramphenicol and Tetracycline. The petroleum ether extract demonstrated significant inhibitory effects against all tested bacteria using all extract concentration compared with used antibiotics except chloramphenicol, the clearest activity was seen against K. pneumonia using the extract concentration 50 mg/cm3. Ethanol extract possessed considerable antibacterial activities against the pathogenic bacteria, the highest inhibitory effect was observed against *B. cereus* using the extract concentration 200 mg/cm3, followed by aqueous extract which revealed good inhibitory action against *P.*

aeruginosa using the same concentration. The weakest extract used was the chloroform extract which was only active against *S. aureus* (Firas et al., 2007). The effect of flax seed proteins is investigated on the several species of gram positive and gram negative bacteria, inhibitory effect of flax seed total protein extract on the growth of 10 bacterial species was determined as IC %. The effect is more pronounced on *Salmonella typhimurium* (40%). *Enterococcus foecalis* (45%), *Escherium* (40% and 45%) and *Klebsilla pneumonia* (ATCC: 10031.38%). Also, some antibacterial activity appears on *Staphylococcus epidermidis* (19%) and *Klebsiella pneumonia* (ATCC: 10603, 15%). Flaxseed protein extract showed an antibacterial activity against the most test microorganism, especially gram-negative bacteria. The activity was more pronounced (>50%) for the fractionated and isolated protein. (Tehrani et al., 2014) The antimicrobial activity of hexane, methylene chloride, and butanol extract of *L. usitatissimum* were examined by disc diffusion assay method, using pathogenic microbial species. The activities of hexane, methylene chloride and butanol fraction were comparable to ampicillin. The activities against *E. coli* were 29.2%, 37.5%, and 66.7%, respectively; against *S. aureus* were 45.4%, 36.4% and 63.6%, respectively, and against *C. albicans* were 26.9%, 46.1% and 73.1% respectively (Fatma et al., 2016). Ghaedi et al., (2016) have reported antibacterial and antifungal properties of different extract of *L. usitatissimum* and were screened against two type Gram-positive and negative bacteria: *S. aureus*, *K. pneumonia*, and *A. oryzae*, using agar-well diffusion method and comparing their antibacterial activities with the antibiotics gentamicine, cephalexin, and amphotericin B. *L. usitatissimum* root extract demonstrated significant inhibitory effect against all tested bacterial and fungal. An in vitro antimicrobial assay of ethanol and chloroform extracts was carried out by (Tawheed et al., 2014), by disc diffusion method and showed that chloroform extract are more effective than ethanol extract of seeds against various test microorganism.

Anti-cancerous activity

Thampson et al., (1996) investigated the effect of flaxseed lignan and its oil component in reduction of mammary tumor growth in the last stage of carcinogenesis. And concluded that flaxseed oil and flaxseed (in a dose independent manner) reduced the growth of established tumours at a last stage of carcinogenesis because the mammalian lignan precursor SDG exerted the greatest inhibitory effect on the development of new tumours, Waldschlager et al.,(2005) investigate the effect of flaxseed ligan on hormone receptor positive tumour cell line. They observed an anti-proliferative and a hormone-decreasing effect on the chorion carcinoma cell line jeg3 caused by the flaxseed crude extract. This fraction contains the ligan 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. A cytotoxic activity of butanol, methyline chloride, and hexsane extract of *L. usitatissimum* L. against human tumor cells HePG2 and MCF-7 was assessed by (Fatma et al., 2016). The result indicated that the *in vitro* cytotoxicity against MCF-7, IC_{50} (µg/ml), of the butanol extract was strong, methylene chloride extracts and hexane extract were weak. And butanol extract and methylene chloride extracts were moderate hexane extract was weak against HePG2 cell line.

Anticoagulant and antiplatelet

Allman et al., (1995) studied to compare the effects of supplementing a low fat diet with an alpha-linolenic acid-rich oil with a linoleic acid-rich oil on platelet composition and function and concluded that consumption of alpha-linolenic acid-rich oils have protective effects against cardiovascular disease, over linoleic acid-rich oil and have ability to decrease the tendency of platelets to aggregate. Nordstrom et al., (1995) has been studied to compare the flax seed oil to a linoleic acid control in patients with rheumatoid arthritis (N=22) reported that flax seed oil decreased collagen-stimulated platelet aggregation and bleeding time. Conversely, a crossover study in which 10 healthy volunteers consumed both a standardization diet with no supplementation and one supplemented with flax seed oil found that flax seed oil had no effect on bleeding time, prothrombin time, or partial thromboplastin time (Kelley et al., 1993), though a recent review concludes that available clinical data do not support the existence of any such clinically relevant interaction (Bays et al., 2007).

Anti-estrogenic and weak estrogenic

Richter et al. (2010) was investigated that potential phytoestrogens isolated from flaxseed significantly stimulate estrogen production in MCF7 breast cancer cells and also observed a down-regulation of ERB receptor expression and down-regulation of PR expression in MCF7 cells after treatment. The expression of ERα was also significantly altered in MCF7 cells after stimulation with extracts. A down-regulation of ERα expression was also observed. Brooks et al. (2004) concluded that supplementation of flaxseed alters the estrogen metabolism in post-menopausal women. And showed that dietary supplementation with 25 g ground flaxseed significantly alters the metabolism of estradiol in favour of the less biologically active estrogen metabolic (2OHEI) in postmenopausal women.

Antidiabetic

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 cell (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 (Bhatia et al., 2006). A study analyzed the effect of flaxseed by double-bind, randomized, crossover trail 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. (Pan et al., 2007) On the other hand Rhee et al. (2011) analyzed the effect flaxseed supplementation on the 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, Antioxidant have been reported to diminish inflammatory response, insulin resistance, and diabetes development. Thakur et al. (2009) have studied the effect of flaxseed gum on reduction of blood glucose and cholesterol particularly LDL in Type 2 diabetes patients have shown that 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 (5g) as per the recommendations (ADA) result showed decreased in fasting blood sugar and LDL. Mitra et al., (2009) have studied the effect of flaxseed gum, like guargum, in reducing the blood glucose level in non insulin dependent diabetes mellitus (NIDDM). And observed that flax gum-containing therapeutic diet reduced TLC, LDLC, and FBS significantly, the changes in other parameter were not statistically significant. Hussein et al. (2012) have been concluded that flaxseed oil administration has a beneficial effect on decreasing insulin resistance in diabetic rats through the scavenging of free radicals and increase in superoxide dismutase.

Anti-diarrhea

The effects of Flaxseed in infectious and non-infectious diarrhea were investigated. The result suggested that the *Linum usitatissimum* (Flaxseed) extract exhibit antidiarrheal and antispasmodic activities by virtue of its antimotility and antisecretory effects which are mediated possibly through inhibition of ca+ + channels, thus Flaxseed extract proved effective against both enteric and non enteric pathogens causing diarrhea (Palla et al., 2015).

Antidepressant activity

Extract from seed of *Linum usitatissimum* subject to evaluate the antidepressant activity in wistar albino rats. Locomotors activity, forced swimming test and tail suspension test were used for assessing antidepressant activity. Show less significant antidepressant activity in comparison to standard drugs Fluoxetine, Chlorpromazine and Imipramine (Rath et al., 2012).

Anti-inflammatory

Fixed oil of *Linum usitatissimum* as Anti-inflammatory, analgesic and antipyretic activity was evaluated and 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 (Kaithwas et al., 2011), Another study was conducted to evaluate the anti-inflammatory activity of plant lipids containing alpha-linolenic acid. The fixed oil (1, 2, 3, ml/kg) containing alpha-linolenic acid, obtained from the seed of Linseed (*Linum usitatissimum*). Soyabean (Glycine max) and Holy basil (Ocimum santum) screened for their anti inflammatory activity using carrageenan, leukotrienes and arachidonic acid induced paw edema was produced by all the oils in the highest dose (3 ml/kg) in all the models. *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 cource of inflammatory disorders may be achieved by altering the eicosanoids precursor (Singh et al., 2008) in a study Kaihwas et al., (2013) have investigate the effect of *Linum usitatissimum* fixed oil against different phase of acute inflammatory reaction, namely protein exudation, peritoneal capillary permeability, and leukocyte migration. The fixed oil exhibited dose-dependent inhibition of protein exudation vascular permeability, comparable to standard aspirin. The oil also inhibited the leukocyte migration in pleural exudates in a dose dependant manner.

Antilipidemic

Jankins et al.,(1999) have studies the health aspects of partially defatted flaxseed, including effects on serum lipids, oxidative measures, and ex vivo androgen progestin activity, and concluded that partially defatted flaxseed is effective in lowering LDL cholesterol concentration, the flaxseed gum is likely the major active ingredient in flaxseed responsible for the lipid-

lowering action. No effect on lipoproteins, ex vivo serum androgen or progestin activity.

Antioxidant activity

Antioxidant potential of flaxseed and their phenolic constituent have been studies, in both *in vitro and in vivo* models. In most of the studies, antioxidant potential of whole flaxseed or their extract has been tried to correlate with their phenolic content. The anti-oxidant activity of ethanolic extract of *Linum usitatissimum* EE-LU at dose (100, 200, 300, 400, 500 µg/ml) was evaluated by Zanwar et al., (2010) in an in-vitro model. The result indicated significant dose dependent inhibition against DPPH radical scavenging, reducing power, superoxide anion radical scavenging, hydroxyl radical scavenging, hydrogen peroxide scavenging, metal chelating by EE-LU and α-tocopheral maximum at 500 µg/ml. authors concluded that phenolic compounds seem to be the main components responsible for the observed antioxidant activity. Fatma et al., (2016), reported the anti-oxidant activity of hexane, methylene chloride and butanol fraction by ABTS method. A control experiment and another one using ascorbic acid as a reference antioxidant material were conducted. The result showed that Butanol has highest scavenging activity. The scavenging effect of the extracts and standard on the ABTS radical decreased in following order: ascorbic acid > butanol > methylene chloride > hexane fraction. The another study conducted by Bhatia et al., (2006) that explore the anti oxidative properties of linseed oil in its prophylactic action against oxidative stress induced by a radiomimetic drug, cyclophosphamide. Oral administration of linseed oil at dose (0.1 ml/kg of BW/day) for 20 days prior to an acute dose of cyclophosphamide (75 mg/kg) significantly inhibited the augmented level of malondeldehide, conjugated diens, and hydroperoxide in the mouce brain. The cyclophosphamide induced decline in the level of reduced glutathione, glutathione peroxide, and alkaline phosphatase was also significantly prevented by linseed oil in mouse blood. The results clearly indicate the prophylactic action of linseed oil against cyclophosphamide induced oxidative stress. Velioglu et al., (1998) was studies antioxidant activity of flaxseed methanolic extract in ß-carotene bleaching method. And investigated the correction between total phenolics and anti-oxidant activity: which was found to be statistically significant. A study conducted by Kazakova et al., (2015) that compare the anti-oxidant activity of the extract of flaxseed and its alkaline hydrolysate in two model system: lipid auto-oxidation of tricyglycerol of sunflower oil (TGSO) in a homogeneous lipid media and during ß-carotene-linoleate emulsion system. In addition to pure lignans were tested. And concluded that flaxseed extracts, its alkaline hydrolysate and SDG (secoisolariciresinol diglucoside), are not able to inhibit effectively lipid autooxidation in TGSO model. Both extract act as natural antioxidant in a ß-carotene-linoleate emulsion system. SECO (secoisolariciresinol) exhibited a stronger activity then SDG. A study reported that oral administration of flaxseed oil significantly increased the activity of antioxidant enzyme glutathione peroxide, superoxide dismutase and catalase in liver tissue of rats with oxidative stress. These effects were amplified by co-administration of flaxseed oil with vitamin E. therefore, intake of flaxseed and vitamin E produced high antioxidant activity and may be beneficial for reducing the oxidative stress.(Hala M. et al., 2013). The *in vitro* antioxidant activities of hydroalcoholic extract of *Linum usitatissimum* L. was estimated using DPPH assay. And result showed that the shoot of extract of *L. usitatissimum* had the highest antioxidant activities (Ghaedi et al., 2016). The antioxidant activity of ethanol extract of seed of *L. usitatissimum* was determined by DPPH method and hydrogen peroxide method. The result is obtained for antioxidant assay by both methods. According to DPPH method, the IC_{50} value of ethanol extract of flaxseed is 256, 313 µg/ml while it is 33.718 µg/ml according to hydrogen peroxide method, (Tawheed et al., 2014). In another study it was demonstrated that dietary flaxseed supplementation increase antioxidant defenses through both reduced ROS generation and increase ROS detoxification (Lee et al., 2008). Bhatia et al. (2007) studied radioprotective and antioxidant potential of flaxseed oil against radiation-induced hepatotoxicity in mice. Prophylactic effect of flaxseed oil supplementation after exposure of single dose of gamma radiation was assessed by estimating biochemical parameters such as lipid peroxide, reduced glutathione, total protein, AST, ALT, and alkaline phosphatase. Result showed that radiation-induced deficits in body and organ weight were significantly reduced or prevented in flaxseed oil pretreated mice; and the observed protective effect could be due to omega-3 fatty acids and phytoestrogenic lignans. Sargi et al., (2013) have evaluated the antioxidant capacity of the seeds with ABTS, DPPH, and FRAP methods, and showed that brown flax and perilla seeds have higher antioxidant capacity. Waszkowiak et al. (2015) have been comparing the antioxidant activity of ethanolic extracts and aqueous extract. The results show that ethanolic extraction give extract rich in antioxidant lignans; aqueous extacts have lower antioxidant activity than ethanolic.

Anti-ulcer activity

Madhi et al. (2013) evaluated the spasmolytic and indomethacin-induced ulcer protective effect of the water extract of whole seed of *Linum. Usitatissimum* in gunia pig and mouse stomach, and show significant spasmolytic effect and protective effect against experimental ulcerogenesis ($p< 0.01$), both effect was observed to increase with increase in the soaking period ($p <0.01$). In another study both flaxseed oil and flaxseed mucilage was found to have significant protective activity against ethanol induced gastric ulcer.

The result 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 provided by an oral dose of flaxseed oil (5ml/kg) was more prominent than that obtained by ranitidine (50 mg/kg) (Dugani et al., 2008). Kaithwas et al., (2010) evaluated the antiulcer activity of *L. usitatissimum* L. 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, suggestive 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.

Cardiovascular

Prasad et al., *(2009*) have studies the Cardiovascular of effect of Flaxseed and its components and concluded that flaxseed with very low ALA, Flaxseed lignan complex (FLC) secoisolariciresinol diglucoside (SDG) suppress the development of atherosclerosis, FLC and SDG slow progression of atherosclerosis but do not regress atherosclerosis. And the lipid lowering effects of flaxseed are variable, flaxseed with very low ALA, SDG, and FLC significantly reduce serum lipids. SDG, and FLC raise serum HDL-C. Flaxseed oil does not affect serum lipids. But in high doses suppresses inflammatory mediators and decreases platelet aggregation and increase bleeding time.

Immunocompetence

Kelly et al., (1991) have studied 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 hormonal immunity.

Infant allergies and respiratory diseases

Shek et al. (2012) have investigate the Role of dietary long-chain polyunsaturated fatty acid (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 immunomodulatory effects. Decreased consumption of omega-6-PUFAs, in favor of more anti-inflammatory omega-3-PUFAs 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-fatty acids may alter the T helper 2 cell differentiations. PUFAs may further modify cellular membrane, induce eicosanoids metabolism, and alter gene expression.

Laxative

The effect of ground flaxseed on constipation in irritable bowel syndrome patients was investigated. And concluded that flaxseed contains insoluble fiber 33.2 % and soluble fiber 11 %. Flaxseed as bulk laxative proved to be effective more then psyllium. This is due to the presence of large amount of insoluble fiber in flaxseed. Psyllium contains mostly water soluble fiber (47g/ 100g). 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. (Tarpila et al., 2004) In a other study Jiqu et al., (2012) investigate the Laxative effects of partially defatted flaxseed meal on normal and experimental constipated mice, and concluded that partially defatted flaxseed meal has the ability to promote intestinal motility, stimulate intestinal transit as well as increase stool frequency and weight. And suggested that partially defatted flaxseed meal may be a usefull laxative to facilitate fecal output in normal and constipation condition,

Nephroprotective

In a study showed that flax lignans were highly protective in a dose dependent manner, with a significant delay in the onset of proteinuria with preservation in glomerular filtration rate and renal size and also suggests that flax lignans may have therapeutic role in lupus nephritis. (Hall et al.,1993). Clark et al. (2000) concluded that dietary phytoestrogens have a beneficial role in chronic renal disease. Flaxseed has been shown to limit or reduced proteinuria and renal pathological lesion associated with progressive renal failure.

Pharmacokinetic

Studies were conducted to characterize the pharmacokinetic and bioavailability of ß-sitosterol from seeds of Tukhm-e-katan, using HPTLC in male albino rabbits. After single oral administration of refluxed residue of Tukhm-e-katan in olive oil (1g kg^{-1}) the blood samples was collected at different time interval, the result indicated that a marker from Tukhm-e-katan at R_F = 0.48 was detected in rabbit plasma after half an hour of ingestion of the plant refluxed extract. The marker reached maximum concentration at 6 hrs post dose and was not detectable in plasma after 8 hrs post dose. (Sunita et al., 2011)

Plasmogen

Herper et al. (2006) investigated the effect of flaxseed oil which was found to be increase the cardio-protective fatty acid in humans. The conclusion of 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 act as precursor in the in the synthesis of EPA and DPA.

Protective effects

Hala et al. (2013) have studies the protective effect of flaxseed oil and vitamin E on potassium Bromate-induced oxidative stress in male rats and concluded that oral administration of flaxseed oil improve hepatorenal function, normalize serum total cholesterol and triglycerides, reduces tissue lipid and triglyceride, reduces tissue lipid peroxidation and enhances the activity of tissue antioxidant enzymes, and these effects are amplified by coadministration of flaxseed oil with vitamin E.

Radioprotective activity

Radioprotective effect of flaxseed oil was studied against radiation induced hepatotoxicity in mice. Prophylactic effect of flaxseed oil supplementation after exposure of single dose of gamma radiation was assessed. Result showed that the radiation induced deficits in body and organ weight were significantly reduced or prevented in flaxseed pretreated mice. (Bhatia et al., 2007), Solomidou et al., (2012) investigated the effect of flaxseed lignan SDG as a radioprotective in lungs and evaluated the lignan complex of flaxseed enriched in secoisolariciresinol Diglucoside with respect to lung radioprotective and tumor radiosensitizing efficacy. And concluded that flaxseed lignan complex supplementation potentially protects normal lung parenchyma against radiation injury and may also be clinically useful in narrowing the limitation of radiation therapy in thoracic malignancies. Lee et al. (2009) demonstrates that flaxseed 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 flaxseed feeding prior to and after XRT. and suggesting that flaxseed successfully and preferentially provides protection of normal lung parenchyma while not radio protecting established lung tumors.

Safety study

Sunita et al. (2011) have investigate the safety evaluation of *Tukham-e-katan* refluxed residue was monitored by conducting acute toxicity, and concluded that it was not toxic at 2g / kg dose.

CONCLUSION

Katan (*Linum usitatimum*) has been in use since times immemorial to treat wide range of indication. It has been subjected to quit extensive phytochemical, experimental and clinical investigations. The plant contains alpha-linoleic acid, lignans flavonoids, calcium, zinc, magnesium, sodium, Vitamin K, Vitamin E etc. Experimental studies have demonstrated its anti-cancerous, estrogenic, anticoagulant, antidiabetic, anti-inflammatory, antimicrobial, antioxidant, hepatoprotective, nephroprotective, and radioprotective. The efficacy of *Tukhm-e-Katan* is much more popular as cardio-protective and antioxidant. The scientific studies have proved most of the claims of traditional medicines. However, further, detailed clinical research appears worthwhile to explore the full therapeutic potential of this plant in order to establish it as a standard drug.

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