P-ISSN: 2618-0723
E-ISSN: 2618-0731

Impact Factor: RJIF 5.16
www.extensionjournal.com

International Journal of Agriculture Extension and Social Development

Volume 5; Issue 1; Jan-Jun 2022; Page No. 83-87

Received: 02-10-2021
Accepted: 09-11-2021

Indexed Journal
Peer Reviewed Journal

Phytopharmacological characters of *Tribulus terrestris*

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Abstract

Tribulus terrestris (family Zygophyllaceae), commonly referred to as Gokshur or Gokharu or puncture vine, has long been used in both Indian and Chinese medicine systems to treat various ailments. Its various components contain a variety of chemicals that are important for healing, such as flavonoids, flavonol glycosides, steroidal saponins, and alkaloids. Contains diuretic, aphrodisiac, antiurolithic, immunomodulatory, antidiabetic, enhances absorption, hypolipidemic, cardiotonic, central nervous system, hepatoprotective, anti-inflammatory, analgesic, antispasmodic, anticancer, antibacterial, anthelmintic, larvicidal, and anticariogenic activities. Over the past few decades or so, extensive research has been done to confirm its biological functions and pharmacies for its quotes. The purpose of this review is to build a further research site on the phytochemical and pharmacological properties of this plant to further research. This will help ensure its traditional consumption and its added value, ultimately leading to higher revenue from the plant.

Keywords: *Tribulus terrestris*, Pharmacology, saponin

Introduction

The genus Tribulus, belonging to family Zygophyllaceae, comprises about 20 species in the world, of which one species, viz. *Tribulus terrestrisare* is very common in Sidhi district (M.P.) India. Trease, *et al.* (2002) [1] The *T. terrestris* is a well-patronized medicinal herb by Ayurvedic seers as well as by modern herbalists. Duke, *et al.* (2002) [2] The plant is used individually as a single therapeutic agent or as a prime or subordinate component of many compound formulations and food supplements. It is an annual shrub found in Mediterranean, subtropical, and desert climate regions around the world, *viz.* India, China, southern USA, Mexico, Spain, and Bulgaria (Nadkarni, 1927 and The Wealth of India (CSIR, 1972) [3, 4].

Taxonomical classification

Kingdom	:	Plantae
Division	:	Phanerogams
Subdivision	:	Angiospermae
Class	:	Dicotyledonae
Subclass	:	Polypetalae
Series	:	Disciflorae
Order	:	Giraniales
Family	:	Zygophyllaceae
Genus	:	*Tribulus*
Species	:	*terrestris* Linn.

Distribution

Tribulus terrestris is commonly known as Gokshur (Sanskrit); puncture vine, land (or small) caltrops (English); Gokharu (Hindi); Bethagokharu or Nanagokharu (Gujarathi); Nerinjil (Tamil); and Khar-e-khusak khurd (Urdu). It is distributed along a wide geographic perimeter. It is found all over India up to 11,000 ft in Kashmir, Ceylon, and all warm regions of both hemispheres. It is a common weed of the pasture lands, road sides, and other waste places, chiefly in hot, dry, and sandy regions including West Rajasthan and Gujarat in India (Kokate, *et al.* 2007) [5].

Botanical description *T. terrestris*

Small prostrate, 10-60 cm tall, hirsute or silky hairy shrub. Leaves opposite, usually uneven, paripinnate; pinnae from five to eight pairs, lanceolate elliptical or oblong. The flowers are yellow in colour. Its carpel fruits are characteristic, stellate, round, compact, five-cornered, and covered with very bright yellow prickles. There are several letters in each crocus with opposite divisions between them. Seeds are naturally oily. When young, the root is thin, fibrous, cylindrical, usually branched, carrying a large number of small rootlets and light brown. The fruits and roots are widely used as a traditional medicine to treat various ailments. Root occurs in pieces, 7-18 cm long and 0.3-0.7 cm wide, cylindrical, fibrous, regular branches, carrying large, small, hard, woody, yellowish-brown rootlets, with a painful surface due to the presence of nodules. small; fibrous fracture; sweet smell; sweetish astringent taste. The fruit of the tree is known as “Chih - hsing” in China or goats in the USA. The winged fruit looks like a separate cow's hoof, hence the name go - ksura (cow hoof). The fruits are pale yellow and have a backbone. They are globose, consisting of five cocci, almost glabrous, muriculate, triangular, woody, each with two pairs of strong

spinal cords, one pair longer than the other. The tips of the spines almost double together form a pentagonal structure around the fruit. The exterior of the schizocarp is hard. There are several seeds in each coccus, which have a distinct difference between them. The aroma of the fruit is delicious and the taste is a little sour.

Properties and actions mentioned in ayurveda

Rasa (taste based on activity)	:	Madhura (sweet)
Guna (properties)	:	Guru (heavy to digest), Snigdha (unctuous)
Veerya (potency)	:	Sheeta (cooling)
Vipaka (taste after digestion based on activity)	:	Madhura (sweet)
Karma (pharmacological actions)	:	*Brumhana* (nourishing), *Vatanut* (pacifies Vata-dsha), *Vrusya* (aphrodisiac), *Ashmarihara* (removes urinary stone), *Vastishodhana* (cures bladder ailments).

Chemical Constituents

Preliminary phytochemical studies of *Tribulus terrestris* revealed the presence of saponins, flavonoids, glycosides, alkaloids, and tannins. Usman, *et al.* (2007) [6] according to literature data, the saponin composition and the saponin content of *Tribulus terrestris* from different geographic regions is different. Kostova *et al.* (2005) [7] studied the chemistry and bioactivity of saponins in *Tribulus terrestris*. They reported that furostanol and spirostanol saponins of tigogenin, neotigogenin, gitogenin, neogitogenin, hecogenin, neohecogenin, diosgenin, chlorogenin, ruscogenin, and sarsasapogenin are commonly found in this plant. In addition, the four sulfated saponins of tigogenin and diosgenin were also isolated. The most common are furostanol glycosides which include protodioscin and protogracillin, whereas protodioscin dominates saponin and spirostanol glycosides in small quantities. Xu *et al.* (2010) and Wu *et al.* (1999) [8, 9] found that the quantity of main flavonoids is about 1.5 times that of main saponins. This indicated that the flavonoid contents in *Tribulus terrestris* should be studied, developed, and further used. Bhutani *et al.* (1969) [10] isolated kaempferol, kaempferol-3-glucoside, kaempferol-3-rutinoside, and tribuloside [kaempferol-3-β-d-(6″-p-coumaroyl) glucoside] from leaves as well as fruits and identified them by spectroscopic analysis. Louveaux *et al.* (1998) [11] detected 18 flavonoids (caffeoyl derivatives, quercetin glycosides, including rutin and kaempferol glycosides) using high-performance liquid chromatography (HPLC) in four Tribulus species leaf extracts. Yang *et al.* (2011) [12] optimized the extraction condition using orthogonal experiment. Matin Yekta *et al.* (2008) [13] isolated three flavonoid glycosides, *viz.* quercetin 3-O-glycoside, quercetin 3-O-rutinoside, and kaempferol 3-O-glycoside from the aerial parts of *T. terrestris* L. var. orientalis (Kerner) G. Beck in the northeast of Iran.

Traditional Uses

Tribulus terrestris is used in traditional medicine such as tonic, aphrodisiac, palliative, astringent, stomachic, antihypertensive, diuretic, lithotriptic, and urine antibiotic. The dried fruit of the tree is very effective in many problems of the genitourinary tract. It is an important component of Gokshuradi Guggul, a powerful Ayurvedic medicine used to support the proper functioning of the genitourinary tract and to release urine stones. *Tribulus terrestris* has been used for centuries in Ayurveda to treat impotence, venereal diseases, and sexual dysfunction. In Bulgaria, this plant is used as a traditional medicine to treat infertility. In addition to all of these applications, Ayurvedic Pharmacopoeia of India links cardiotonic features to root and fruit. In traditional Chinese medicine, the fruit was used to treat eye problems, edema, stomach upset, diarrhea, sick leukorrhea, and sexual dysfunction. *Tribulus terrestris* is described as a very important drug in Shern - Nong Pharmacopoeia (a well-known medical practice in China) in restoring the depressed liver, to treat asthma, breast inflammation, constipation, acute conjunctivitis, headache, and vitiligo. In Unani medicine, *Tribulus terrestris* is used as diuretic, mild laxative, and general tonic (Khare, 2007) [14].

Pharmacological Activities

Diuretic activity: The diuretic properties of *Tribulus terrestris* are due to large quantities of nitrates and essential oil present in its fruits and seeds. The diuretic activity can also be attributed to the presence of potassium salts in high concentration. Al-Ali *et al.* (2003) [15] tested the aqueous extract of *Tribulus terrestris* prepared from its fruit and leaves in rat diuretic model and strips of isolated Guinea pig ileum were used for the contractility test. The aqueous extract of *Tribulus terrestris*, in oral dose of 5 g/kg, elicited a positive diuresis, which was slightly more than that of furosemide. Sodium and chloride concentrations in the urine were increased. The increased tonicity of the smooth muscles, which was produced by *Tribulus terrestris* extract, together with its diuretic activity helped in the propulsion of stones along the urinary tract. Chhatre *et al.* (2012) [16] The diuretic action of *Tribulus terrestris* makes it useful as an anti-hypertensive agent.

Aphrodisiac activity: Singh *et al.* (2012) [17] evaluated the acute and repeated dose administration of lyophilized aqueous extract of the dried fruits of *Tribulus terrestris* (LAET) at doses of 50 and 100 mg/kg of body weight as a sexual enhancer in the management of sexual dysfunction in male rat. A dose-dependent improvement in sexual behavior was observed with the LAET treatment, which was more prominent on chronic administration of LAET. A significant increase in serum testosterone levels too was observed. These findings confirm the traditional use of *Tribulus terrestris* as a sexual enhancer in the management of sexual dysfunction in males.

Antiurolithic activity: An ethanolic extract of *Tribulus terrestris* fruits was tested in urolithiasis induced by glass bead implantation in albino rats by Anand *et al.* (1994) [18]. It exhibited significant dose-dependent protection against deposition of calculogenic material around the glass bead, leukocytosis, and elevation in serum urea levels. Subsequent fractionation of the ethanol extract led to decrease in activity. Various other biochemical parameters in urine, serum, and the histopathology of urinary bladder were restored in a dose-dependent manner. A novel antilithic protein having cytoprotective potency and of molecular

weight ~ 60 kDa was purified from *Tribulus terrestris*. Aggarwal *et al.* (2012) [19] tested the activity of *Tribulus terrestris* on the nucleation and growth of calcium oxalate (CaOx) crystals as well as on oxalate-induced cell injury of NRK 52E renal epithelial cells.

Immunomodulatory activity: Saponins isolated from the fruits of *Tribulus terrestris* demonstrated dose-dependent increase in phagocytosis, indicating stimulation of nonspecific immune response. An alcoholic extract of the whole plant of *Tribulus terrestris* exhibited a significant dose-dependent increase in humoral antibody titre and delayed type hypersensitivity response, indicating increased specific immune response (Tiwari *et al.* 2011) [20].

Antidiabetic activity: Saponin from *Tribulus terrestris* possesses hypoglycemic properties. *Tribulus terrestris* ethanolic extract at 2 g/kg body weight produced protective effect in streptozotocin-induced diabetic rats by inhibiting oxidative stress. Ethanolic extract of *Tribulus terrestris* exhibited 70% inhibition of α-glucosidase at 500 µg/ml using maltose as the substrate and 100% inhibition of aldose reductase at a dose of 30 µg/ml using dl-glyceraldehyde as the substrate (Amin *et al.* 2006 and Lamba *et al.* 2011) [21-22]. Significant decrease in postprandial blood glucose levels in mice was found after administration of saponin from *Tribulus terrestris*. *Tribulus terrestris* produced coronary artery dilation and improved coronary circulation. Ayurveda is therefore recommended in the treatment of angina pectoris and other heart problems for diabetes. Therefore, *Tribulus terrestris* may be helpful in treating diabetes by lowering blood sugar, lipid levels, and its antioxidant properties.

Absorption enhancer: Ethanolic extract of *Tribulus terrestris* enhanced the absorption of metformin hydrochloride, a Biopharmaceutics Classification System (BCS) class III drug, in everted sac technique using goat intestine, due to the presence of saponins in the extract (Ayyanna *et al.* 2012) [23].

Hypolipidemic activity: The aqueous extract of the fruits of *Tribulus terrestris* was evaluated for their hypolipidemic activity in Wistar albino rats. A dose of 580 mg/kg of the extract was found to decrease cholesterol-induced hyperlipidemia, with a decrease in cholesterol, triglycerides, low density lipoprotein (LDL), very low density lipoprotein (VLDL), and atherogenic index (AI), and an increase in high density lipoprotein (HDL) levels in the blood. Hypolipidemic activity may be due to the presence of phenolic compounds leading to increased lipoprotein lipases in the muscles and decreased activity in the adipose tissues, thus indicating that plasma triglycerides are utilized for energy production by the muscle and not for energy storage by the adipose tissue (Khan *et al.* 2011) [24].

Activity in cardiac disorders: *Tribulus terrestris* showed significant effect in the treatment of various cardiac diseases including coronary disease, myocardial infarction, cerebral arteriosclerosis, and the sequelae of cerebral thrombosis. Zhang *et al.* (2010) [25] evaluated the protective effect of tribulosin from *Tribulus terrestris* against cardiac ischemia/reperfusion injury to study the underlying mechanism in rats. Tribulosin protected myocardium against ischemia/reperfusion injury through protein kinase C epsilon activation. *Tribulos* in treatment resulted in a significant reduction of malondialdehyde, aspartate transaminases, creatine kinase, lactate dehydrogenase activity, and myocardial apoptosis rate. It increased the activity of SOD. Crude saponin fraction of this plant has shown significant effects in the treatment of various cardiac diseases including hypertension, coronary heart disease, myocardial infarction, cerebral arteriosclerosis, and thrombosis.

Central nervous system (CNS) activity: Swiss Albino mice demonstrated antidepressant and anxiolytic activity on administration of 260 mg/kg dose of Rasayana Ghana tablet comprising three potent well-established rejuvenator herbs, *viz. Tinospora cordifolia* (stem), *Emblica officinalis* (fruit), and *Tribulus terrestris* (fruit and root), present in equal quantities in the tablet. It was suggested that harmine, a β-carboline alkaloid present in *Tribulus terrestris*, is one of the main active constituents that contributes to the above-mentioned activities. Harmine is an inhibitor of monoamine oxidase which helps to increase level of dopamine in the brain (Deole *et al.* 2011) [26].

Hepatoprotective activity: The *Tribulus terrestris* extract (250 mg/kg) showed a remarkable hepatoprotective activity against acetaminophen-induced hepatotoxicity in *Oreochromis mossambicus* fish. The elevated biochemical parameters and decreased level of reduced glutathione enzymes were normalized by treatment with *Tribulus terrestris* extract (250 mg/kg) for acetaminophen-induced toxicity in freshwater fish (Kavitha *et al.* 2011) [27].

Anti-inflammatory activity: The ethanolic extract of *Tribulus terrestris* inhibited the expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in lipopolysaccharide-stimulated RAW264.7 cells. It also suppressed the expression of proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-4 in macrophage cell line. Thus, the ethanolic extract of *Tribulus terrestris* inhibits the expression of mediators related to inflammation and expression of inflammatory cytokines, which has a beneficial effect on various inflammatory conditions (Oh *et al.* 2012) [28].

Analgesic activity: The analgesic activity of *Tribulus terrestris* was studied in male mice using formalin and tail tests. Studies have shown that the methanolic extract of *Tribulus terrestris* at a dose of 100 mg / kg produced an analgesic effect. This analgesic effect of *Tribulus terrestris* release may be mediated locally and / or around. The effect of excretion is lower than morphine and higher than acetylsalicylic acid (aspirin) in both studies. Previous treatment of animals with an opioid receptor antagonist, naloxone, did not alter the analgesic effect of the extract in both experiments; therefore, the involvement of opioid receptors in the analgesic effect of *Tribulus terrestris* is not included. However, other mechanisms responsible for the analgesic effect of *Tribulus terrestris* are yet to be

investigated. The results of the ulceogenic study show that the gastric ulcerogenecity of *Tribulus terrestris* is lower than indomethacin in mice (Heidari *et al.* 2007) [29].

Antispasmodic activity: The lyophilized saponin mixture of the plant exhibited a significant decrease in peristaltic movements of rabbit jejunum preparation in a dose-dependent manner. These results showed that the saponin mixture may be useful for smooth muscle spasms or colic pains (Arcasoy *et al.* 1998) [30].

Anticancer activity: Chemopreventive potential of the aqueous extract of the root and fruit of *Tribulus terrestris* at 800 mg/kg on 7,12-dimethylbenz (a) anthracene (DMBA) and croton oil induced papillomagenesis in Swiss albino male mice depicted significant reduction in tumor incidence, tumor burden, and cumulative number of papillomas, along with a significant increase in the average latent period in mice treated orally with *Tribulus terrestris* suspension continuously at pre-, peri-, and post-initiation stages of papilloma genesis, as compared to the control group treated with DMBA and croton oil alone. The root extract of *Tribulus terrestris* exhibited better chemo preventive potential than the fruit extract at the same concentration (800 mg/kg body weight) in skin papilloma genesis in mice (Kumar *et al.* 2006) [31].

Antibacterial activity: All parts (fruits, stems, leaves, and roots) of Turkish and Iranian *Tribulus terrestris* showed antibacterial activity against *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, in contrast to the aerial parts of Yemeni *Tribulus terrestris* which had no detectable antibacterial activity against these bacteria, while only the fruits and leaves of Indian *Tribulus terrestris* were active exclusively against *E. coli* and *S. aureus*. These different results relating to the antibacterial activity of *Tribulus terrestris* may be due to using different geographic sources of the plant, types of strains, and assay methods. The methanolic extract of fruits of *Tribulus terrestris* was found to be most active against gram-positive and gram-negative bacteria, while moderate activity was observed in its petroleum ether extract and chloroform extract (Mohammed, 2008) [32].

Anthelmintic activity: The methanolic extract of *Tribulus terrestris* was found to be more effective than the petroleum ether, chloroform, and water extracts for *in vitro* anthelmintic activity on the nematode Caenorhabditis elegans. Further bioactivity-guided fractionation confirmedtribulosin and β-sitosterol-d-glucoside to be the active components with ED50 of 76.25 and 82.50 µg/ml, respectively (Kiran *et al.* 2011 and Deepak *et al.* 2002) [33, 34].

Larvicidal activity: The petroleum ether extract of the leaves of *Tribulus terrestris* exhibited better larvicidal activity against the third instar larvae and adults of the mosquito, Aedes aegypti, which is the vector of dengue fever, with LC_{50} of 64.6 ppm as compared to the crude ethanol and acetone extracts (Singh *et al.* 2008) [35].

Anticariogenic activity: The ethanolic extract of fruits of *Tribulus terrestris* (0.1-0.5 mg/ml) possesses significant anticariogenic activity against *Streptococcus mutans*, the pathogen responsible for dental caries. The growth, acid production, adhesion, and water-insoluble glucan synthesis of *S. mutans* were significantly inhibited in the presence of the ethanol extract of *Tribulus terrestris*. Further studies are necessary to elucidate the active constituents of *Tribulus terrestris* responsible for such activities (Oh *et al.* 2011) [36].

Recommended dose of TT in Ayurveda

- Fruit: 3-6 g of the drug in powder form; 20-30 g of the drug for decoction
- Root: 20-30 g of the drug for decoction (Ayurvedic Pharmacopoeia of India, 1989) [37].

Important formulations

Gokshuradi Guggulu, Trikantak Ghruta, Drakshadi Choorna, Rasayana Choorna, Gokshuradi Kwatha, Dashamoola Kwatha (Ayurvedic Pharmacopoeia of India, 1989) [37].

Conclusion

Tribulus terrestris, a common weed, is a great help in traditional medicine programs, namely. Ayurveda, Chinese, Siddha, and Unani. *Tribulus terrestris* is also a popular remedy in traditional medicine in many countries for a number of diseases. The whole plant of *Tribulus terrestris* has been thoroughly tested for its phytochemical and medicinal properties such as diuretic, aphrodisiac, antiurolithic, immunomodulatory, antihypertensive, Antihyperlipidemic, antidiabetic, hepatoprotective, anticancer, anthelmintic, antibacterial, analgesic, analgesic. Considering the available literature of *Tribulus terrestris*, this plant can be effective as an effective herbal medicine for its potency due to its potassium sparing function, Antihyperlipidemic activity, and cardioprotective activity. Although *Tribulus terrestris* has been widely used for centuries and currently scientific evidence of its medicinal properties is also being produced, further research at the cellular level is needed to improve understanding of its pathogenesis. Plant drug testing should be extended to the next level of clinical trials in order to produce new drugs. This will help *Tribulus terrestris* to achieve the drug status or to be prescribed as a dietary supplement in the treatment of various diseases.

Acknowledgement

Authors are thankful to authority of colleges for providing necessary facilities to carryout this work.

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