



A review on mitigation of various ailments via a bioactive component of *Tribulus terrestris* L. - A medicinally important herb

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Review

Abstract

Background: *Tribulus terrestris* L. is an important traditional therapeutic plant that has been utilized for multiple purposes since the Vedic period and belong to Zygophyllaceae family. It is distributed in sub-tropical regions including India, China, New Zealand, Sri Lanka, and Pakistan. It is used in the Chinese medicine system for eye problems, sexual dysfunction, piles, and vesical calculi. It contains steroids, antioxidants, saponins, flavonoids, phenolics, alkaloids, proteins, and amino acids.

Methods: The review was performed to gain detailed knowledge of this plant. The literature search was carried out by using various platforms like the online database PubMed, Science Direct, Google Scholar, Ayush, e-Charaka, SpringerLink, and books.

Results: *T. terrestris* often referred to as Gokshur or Gokharu, has utilised in Indian, Unani and Chinese medicine to cure various illnesses from long time. The plant is known to have diuretic, aphrodisiac, anti-urolithic, immunomodulatory, hypolipidemic, antidiabetic, cardiogenic, antispasmodic, anti-inflammatory, analgesic, and hepatoprotective activities. It includes flavonol glycosides, flavonoids, steroidal saponins, and alkaloids. Phytochemicals present in plant include protodioscin, terrestrosins A, gitonin, tigogenin, β -sitosterol, and terrestrosins E, spirosta-3,5-diene, stigmasterol, diosgenin, hecogenin, kaempferol. It also possesses anti-cariogenic, antibacterial, anthelmintic, larvicidal, and anticancer activities. The aim of this study is to offer an outline of the pharmacological, medicinal and therapeutic potential of *T. terrestris*.

Conclusion: From an extensive review of this plant, it is found that the plant is a rich source of phytochemicals and has high pharmacological values. Thus, it is concluded that this plant is highly medicinal and can be used as a potent source of drugs that are useful for mankind. The information documented in this paper will be helpful for industrial, medicinal, and commercial use.

Keywords: *Tribulus terrestris*, Gokhru, Ayurveda, Pharmacological activities, Aphrodisiac, Larvicidal

Background

Despite amazing advancements in contemporary medicine, the majority of the globe is familiar with traditional treatment. According to WHO, traditional medications are used by 80% of the population for vital medical services (Qi & Kelley 2014). Due to their low cost and easy access a large population of rural areas uses these medicines to cure many ailments. The work on medicinal plants is being published due to increase in the demand for traditional medicines (Mir *et al.* 2022). Herbal remedies are the oldest form of medicines used in human healthcare system (Jan *et al.* 2021). Traditional medicinal system is rapidly spreading in the developing as well as in industrialized countries. More than 75000 species of plants are being used by ethnic communities for the treatment of various diseases (Jan *et al.* 2021). *T. terrestris* is a medicinally significant plant related to Zygophyllaceae family. It is an annual plant (sometimes perennial). There are 20 different species of *T. terrestris* around the world. Out of these, three species are found in India which are *T. terrestris*, *T. cistoides*, *T. alatus* (Chhatre *et al.* 2014). *T. terrestris* has two forms i.e, sweet (meetha) and bitter (kadwa). Meetha Gokhru is the actual **Gokhru**, which has a tart flavour, but kadwa Gokhru has a pungent, bitter, and gummy flavour. Out of ten materials of "dasmula kwath" one is **Gokhru**. Plant infusion is employed in dealing with gonorrhoea (Ukani *et al.* 1997; Haq *et al.* 2021). It possesses activities like Immunomodulatory, anti-diabetic, antimicrobial, digestion promoting, hypolipidemic, anticancer, cardiogenic, sensory system tonic, hepatoprotective, relaxing, pain relieving, antispasmodic, antibacterial, larvicidal, and anti-cariogenic (Khoja *et al.* 2022). In addition, the plant works as a demulcent and tonic, boosting vigour and consolidating the digestive system. It is also useful for cold, cough, breathing problems, impotence, and cardiac problems (Sivapalan 2016; Abdullah & Syed 2021). This plant is present in loose sandy plains habitats, as well as compact and gravel formations. It can also be found in stony and rocky environment, but only rarely or frequently. *T. terrestris* is prostrate to procumbent silky herb. This species has no erect stem, but four buds emerge above the cotyledonary node and expand into prostrate shoots (Lubna *et al.* 2015). Fruits frequently stick to garments and assortments of creatures and seeds are numerous in woody cocci (Figure. 1) (Akram *et al.* 2011).

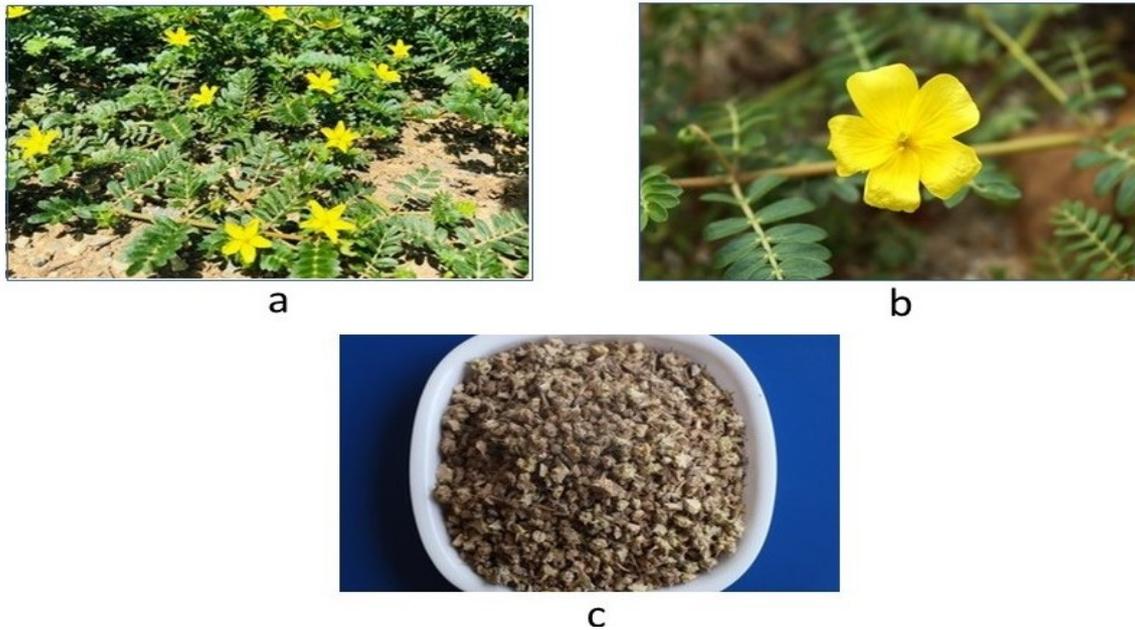


Figure 1. Morphological features of *T. terrestris*: (a) Whole plant (b) Flower (c) Seed.

The flowering and fruiting stage of the plant begins from July to October. Regions, where the plant can be found, include the Mediterranean and subtropic parts of India, China, South America, Pakistan, Mexico, Spain and Bulgaria, Sri Lanka, New Zealand, and South Africa (Tkachenko *et al.* 2020). Except for Antarctica, it is a strong colonizer of all land masses. It grows wild throughout India, particularly in Maharashtra, West Rajasthan, Uttar Pradesh, and Gujarat (Figure 2) (Abdulqawi & Quadri 2021).

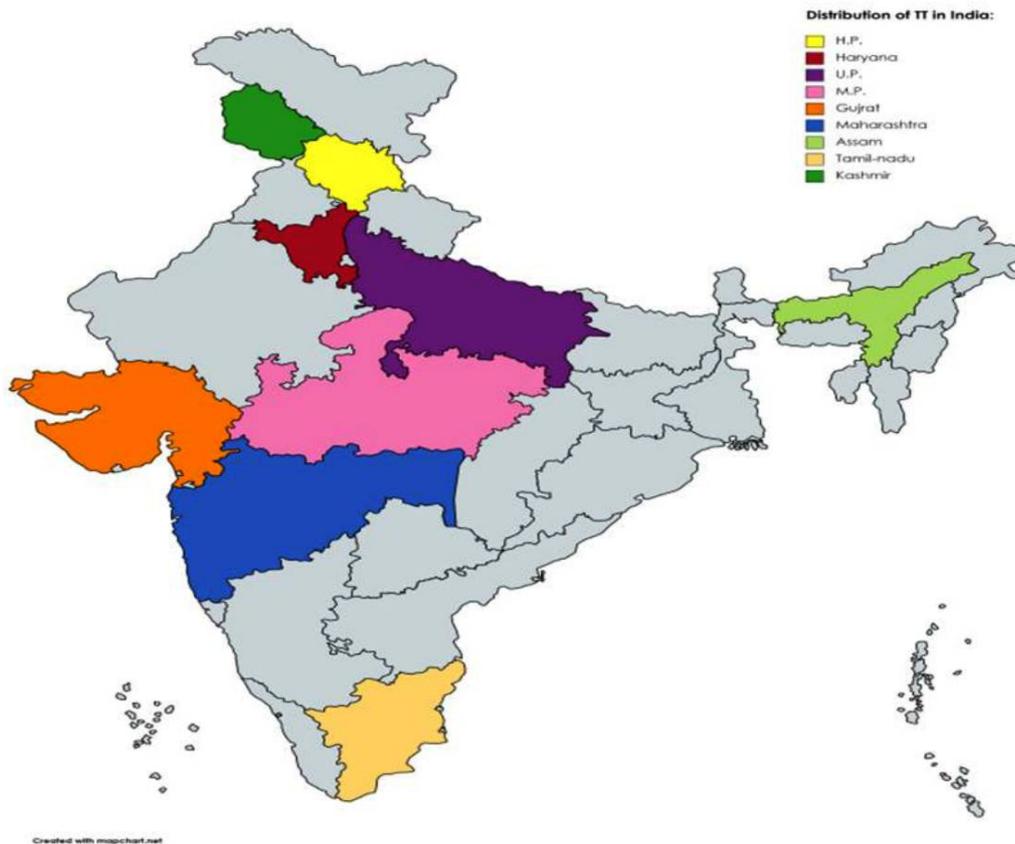


Figure 2. Map showing distribution of *T. terrestris* in India (created with mapchart.net).

The Present study is with aim to provide updated information to understand its ethnobotanical uses through its bioactive components reported in the literature along with various market items and Ayurvedic formulations of *T. terrestris* L. that aid us in our daily lives in many ways.

Materials and Methods

To achieve the framed objectives the databases, Science Direct, Pub Med, Google Scholar, e-charak and AYUSH were investigated for morphology, ethnomedicinal uses, geographical distribution, phytochemistry, pharmacology, Ayurvedic potential, and biomedicine by applying keywords "*Tribulus terrestris*", "**Gokhru**", "biological activities", "ethnomedicine", "phytochemistry", immunomodulator" with the use of OR/AND to connect the terms. English is selected as the primary language for study.

Ethnobotanical Applications

The remedy from this plant is practiced in Indian Ayurvedic tradition as well as in Chinese medicines (Bhandari *et al.* 2013). Upon hydrolysis of saponin produce gitogenin, chlorogenin, steroidal sapogenins-diosgenin, ruscogenin, and 2, 5 D-spirosta-3,5-diene. The entire plant is utilized for various medicinal purposes *viz.* plant leaves are utilized in the treatment of stomach disorders and lithotripter, fruit is considered as tonic, and diuretic, utilized in difficult micturition, calculus affections and is likewise endorsed in Bright's disease. An imbue ment of organic products is given for gout and renal sicknesses and furthermore for cold, cough, asthma, leucorrhoea, and sexual weakness.

The roots of the plant help in curing constipation. Commonly the plant has been utilized for boosting hormonal secretion in both sexes (Sivapalan 2016). The organic products *i.e.*, the fruit of *T. terrestris* has anti-aging property and is used to treat cardiovascular disorders, kidney, and liver diseases (Figure 3). In Peshawar valley, natural products are utilized by ladies to guarantee fertility. In conventional Chinese medicines, mainly fruits of *T. terrestris* known as 'ci ji li' and are utilized as a diuretic and cough expectorant which recovers visual perception/eyesight and for treating stomach distension, skin pruritus, cerebral pain, dizziness, and mammary conduit blockage (Xu *et al.* 2010). In India, the organic products *i.e.*, the fruits of this plant have been utilized traditionally for treating sexual disorders like impotence, infertility, and low moxie in Ayurveda. Fruits are used in Unani medicine to treat

impotence, painful urination, and calculus affection (Table 2). It also helps to cure kidney problems, gravel, and gout when taken as an infusion (Amanullah *et al.* 2021). The herb has uricosuric effects in Pakistan. The plant is suggested as a natural remedy for loose motions and illnesses in South Africa (Jan *et al.* 2021). It is used as cooling medicine by the native people of Omara. In Las Bela the plant is used to cure gonorrhoea. The roots and aerial part are used as aperients by French people. In China, the plant is used to treat cough, asthma, and ophthalmia. The fruits of this plant are used as astringent and tonic. Native people of How Peh and Ho Nan use the seeds to cure diseases related to the bladder (vesicular calculus). People of La Reunion use the leaves as diuretic and astringent. The fruits are used as aphrodisiac. In Gold Coast the plant used to cure whitlow (Gupta 2017).

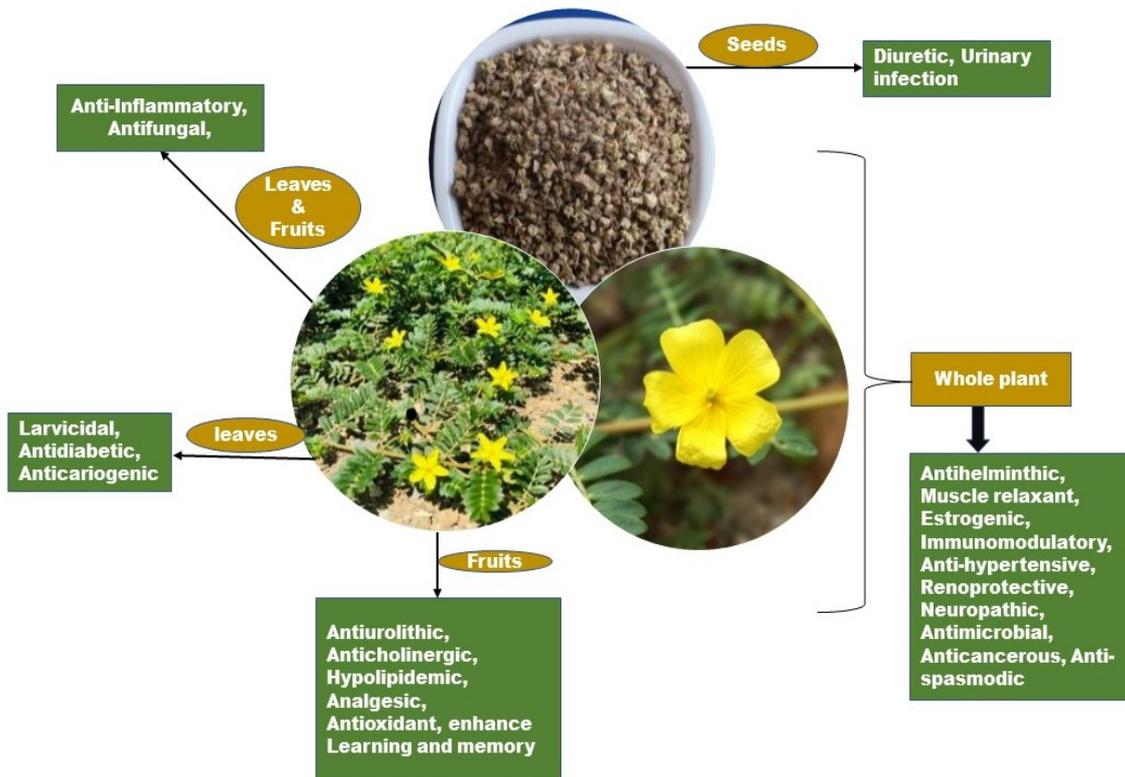


Figure 3. Different parts of *T. terrestris* used to treat various disorders

Table. 2 Ethnobotanical applications of *T. terrestris*.

Plant part	Ethnobotanical applications
Leaves	Different formulations were prepared which are utilized as stomachic and lithotripters as well as to cure cold, cough, asthma, etc.
Fruits	Tonic is prepared which is used to cure kidney problems, stomach diseases, eyesight, and cold.
Fruits	Utilized traditionally in the treatment of sexual disorders like infertility and impotence.
Fruits	Used to treat cardiovascular infections, liver disorders, and also as an antiaging medicine.
Roots	The plant is suggested as a natural tonic for loose motions, illnesses of the throat, eye problems, and also as a cardio tonic.
Whole plant	Used as diuretic and uricosuric drug.

Ayurvedic Potential

In Ayurveda, products of *T. terrestris* are regarded as **Gokshura**. Aside from *T. terrestris* different types of species of this plant are *T. lanuginosus* and *T. subramanyamii* and additionally openly exchanged and devoured for the sake of Gokshura (Balasubramani *et al.* 2010). It has additionally appeared to have pain-relieving (torment mitigating), calming, and cancer-prevention agent impacts. The plant has also been used to treat ailments such as Mutrakrucha, Mutraghat, Alpamutrata, Mutrashmari (Figure 4), Shwas, and Shotha (Shelke *et al.* 2014).

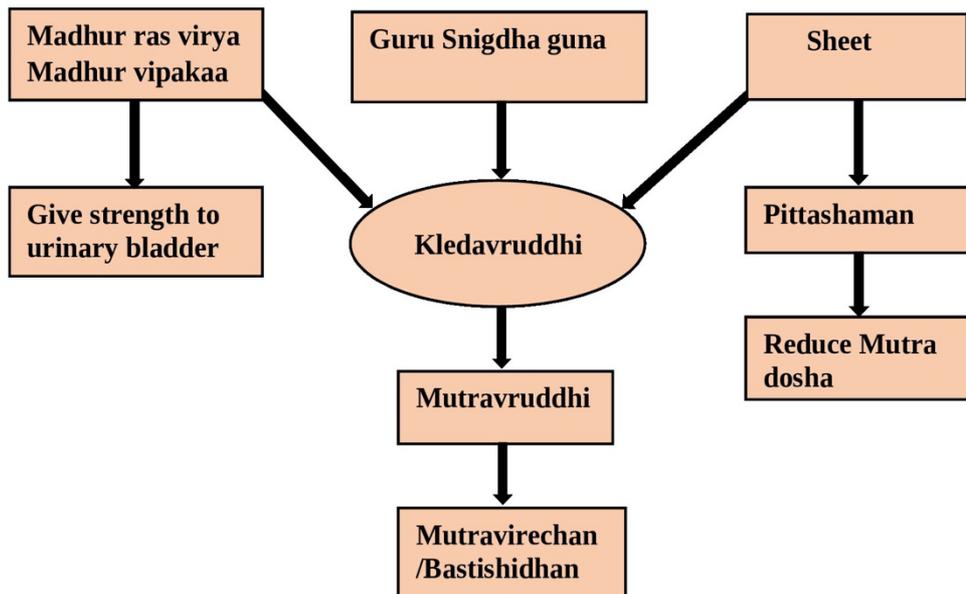


Figure 4. Flow chart showing activity of *T. terrestris* on Mutrachruchcha

As a result, it is an Ayurvedic wonder medication that causes an increase in urination frequency at high dosages and a decrease in urination frequency at low dosage. *T. terrestris* used in trayodashang guggulu which is a significant Ayurvedic polyherbal. A herbal formulation called trayodashang guggulu is utilized in the medication to treat different fiery conditions like joint inflammation (Dadoriya *et al.* 2020). Laghupancamula a compound which is originally known as Kaniyapancamula, Vidarigandhadi, and Khuddakapancamula involves five plants *i.e.*, Salaparni, Priniparni, Brihati, Kantakari, and Goksura. It is utilized in the customary Ayurvedic framework for the therapy of Sotha (irritation), Sula (agonizing conditions), Vrana (wound), Rasayana (Rejuvenator), Jwara (fever), Gulma (cancer), and other ailments (Agrawal 2018). An Ayurvedic formulation prepared from *T. terrestris* along with other herbs is used against hair problems (Pandey *et al.* 2013).

Phytochemicals

T. terrestris is rich in potentially important natural compounds. The plant contains 12.06 percent crude protein, 2.61 percent ether extract, 27.78 percent crude fibre, 40.83 percent N-free extract, and 16.72 percent total ash, calcium, phosphorus, and total digestive nutrients on a dry basis. Carboline alkaloids, flavonoids, harman, and hermine are all found in the plant (Amanullah *et al.* 2021). With all species, the potency of the dynamic fixes varies according on the location of the plant; for the most part, the above-ground territories, such as the leaves and fruits, have larger concentrations. Terrestrosins, F-gitonis, desgalacto-tigonis, desgluolanatigoneis are the major elements of this plant's fruits, which when hydrolyzed generate diosgenins, hecogenins, and neotigogenin. Through hydrolysis rough saponins, gitogenin, tigogenin, neotigogenin, and neogitogenin, hecogenin, neohecogenin, manogenin and neomanogenin are released. Glucose, rhamnose, rutin, resin, fixed oil, essential oil, chlorogenin, and gitogenin have been found in *T. terrestris* fruits. Kaempferol, campesterol, 13-sitosterol, and stigmasterol are all found in the herb's blooms. The plant's seeds are said to contain harmine and roots have been desoluted of sitosterol, stigmasterol and neotigogenin. Phytochemicals present in plant include Protodioscin, terrestrosins A, tigogenin, terrestrosins E, Fgitonin, β -Sitosterol, spirosta-3,5-diene, stigmasterol, ruscogenin, diosgenin, hecogenin, terrestrosins B, and Kaempferol (Akram *et al.* 2011). These isolated phytochemicals can be modified with few chemical synthesis reactions which lead to drug discovery for anticancer properties (Sharma *et al.* 2014).

Steroidal Saponins

The most characteristic compounds in *T. terrestris* are spirostanol and furostanol saponins (Fig. 5). There are 108 different steroidal saponins, fifty types of furostane saponins, and fifty-eight types of spirostane saponin are isolated from *T. terrestris* (Figure. 5). Protodioscin, betasitosterol, dioscin, and protogracillin are steroidal saponins that give *T. terrestris* its particular biological properties (Zhu *et al.* 2017). Tribestin, Tribulosin, Terrestrinin C, Terrestrinin G, Terrestrinin F, Terrestrinin D, 26-O- β -d-glucopyranosyl-(25S)-furost-4-en-22 α ,26-diol-3,6,12-trione are present (Dinchev *et al.* 2008).

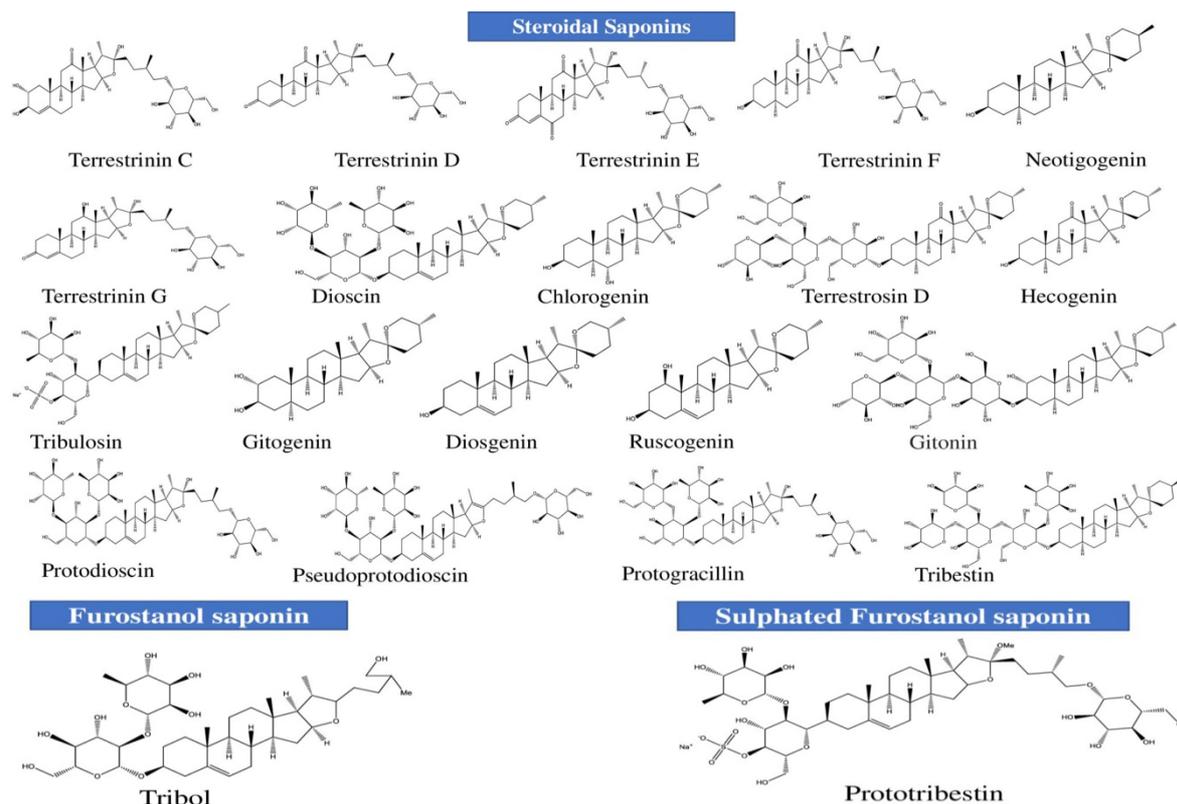


Figure 5. Structures of some of the steroidal, furostanol, and Sulphated saponins present in *T. terrestris*.

Novel furostanol saponin

Tribol, (25R)-furost-5(6)-ene-3 β ,16,26-triol-3-O- α -rhamnopyranosyl-(1 \rightarrow 2)-[α -rhamnopyranosyl-(1 \rightarrow 4)]- β -glucopyranoside), a novel furostanol saponin was extracted from the herb and its structure was reported to be as through 1D and 2D-NMR technique (Figure 5) (Conrad *et al.* 2004). Tribol, Spirostanol saponin 2, sitosterol glucoside, and saponin 3 are present in the aerial part of Bulgarian origin of *Tribulus* (Akram *et al.* 2011). Terrestroside A and 3-O- β -D-xylopyranosyl(1 \rightarrow 3)- β -D-xylopyranosyl(1 \rightarrow 2)]- β -D-glucopyranosyl(1 \rightarrow 4)-[α -L-rhamnopyranosyl(1 \rightarrow 2)]- β -D-galactopyranosyl)-26-O- β -D-glucopyranosyl-5a-furost-22-methoxyl-3 β ,26-diol, Novel FS-Tribol, Protodioscin, and Prototribestin were isolated from the plant (Wie-Hua *et al.* 2008).

Sulfated Furostanol saponin

Methylprototribestin and prototribestin were the two novel sulfated saponins (26-O-beta-glucopyranosyl-22alpha-hydroxy-(25R)-furost-5-ene-3beta,26-diol-3-O-alpha-rhamnopyranosyl-(1 \rightarrow 2)-beta-4-O-sulfo-glucopyranoside) (Figure 5) isolated from the plant (Kostova *et al.* 2002).

Flavonoids

The flavonoids (present in plant are mostly quercetin, kaempferol, isorhamnetin (flavonoid aglycones), Quercetin-3-O-gent, Rutin, and quercetin-3-O-gent-7-O-glu (Fig. 6) (Zhu *et al.* 2017). Astragalin, isoquercetin, and isorhamnetin-3-O-rutinoside are flavonoid glucoside. Tilioside is a flavonoid-p-coumaroyl glucoside present in the plant (Hashim *et al.* 2014).

Alkaloids

The principal alkaloids identified from the whole plant comprise tribulusterine, terretribisamide, terrestriamide, Tribulusin A, and harmine. Other alkaloids present are N-trans-coumaroyltyramine, harman, harmol, tribulusimide C, tribulusin, and N-trans-caffeoyltyramine (Fig. 7) (Zhang *et al.* 2012; Zhu *et al.* 2017).

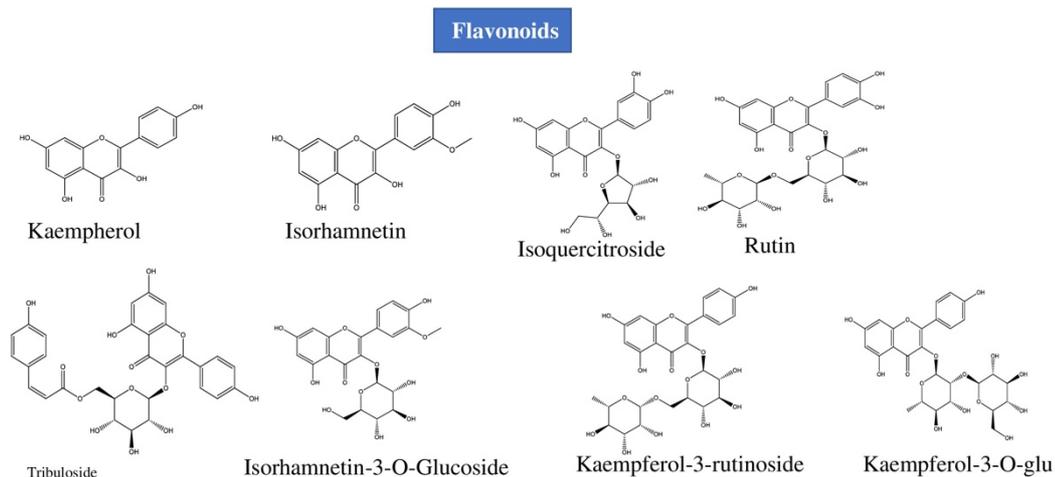


Figure 6. The structures of the flavonoids present in *T. terrestris*

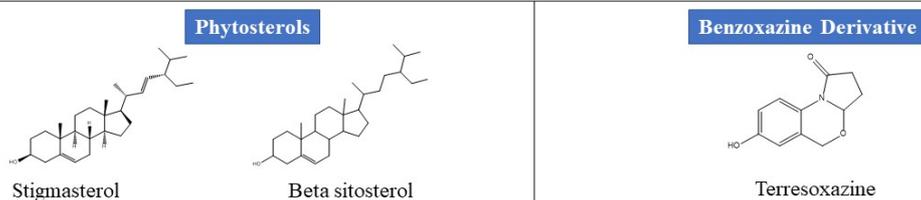
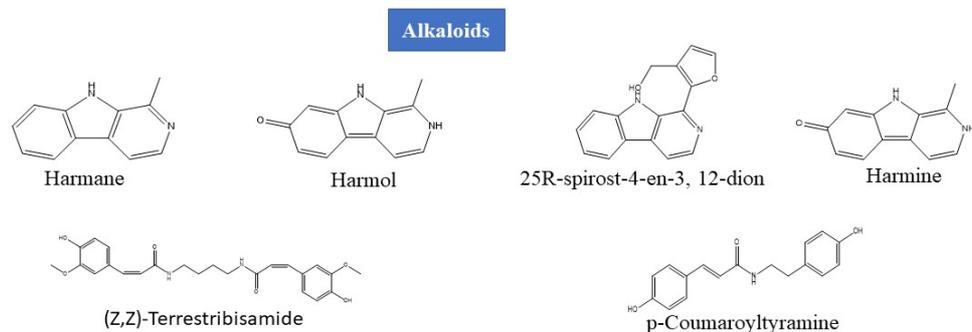


Figure 7. The structures of the alkaloids, Benzoxazine derivative, and phytosterols present in *T. terrestris*

Acids

Ferulic acid, Benzoate, vanillic acid, palmitic acid, tribulus acid, and succinic acid are identified (Figure. 8). The amino acids alanine and threonine are the most common. *T. terrestris* also contains emodin, coumarin, and physcion, 4-ketopinoresinol (Zhu *et al.* 2017; Thakur *et al.* 2020).

Market Products

Various natural enhancers are popular over the world with signs chiefly to boost moxie, sexual execution in both genders, and athletic performance. In the market there are a variety of *T. terrestris* items for varied purposes. Expanded utilization of supplements made up of *T. terrestris* has additionally been seen in athletes as they consistently look for normal hotspots for boosting their exhibition. It is a class of over-the-counter supplements that are commonly prescribed as human vitality boosters (Table 1). Although numerous studies have not confirmed such anabolic effects, the plant is widely advertised as games dietary and can boost the level of testosterone. Its dehydroepiandrosterone, androgenic metabolites, and dihydrotestosterone, result in increased strength and bulk (Pokrywka *et al.* 2017).

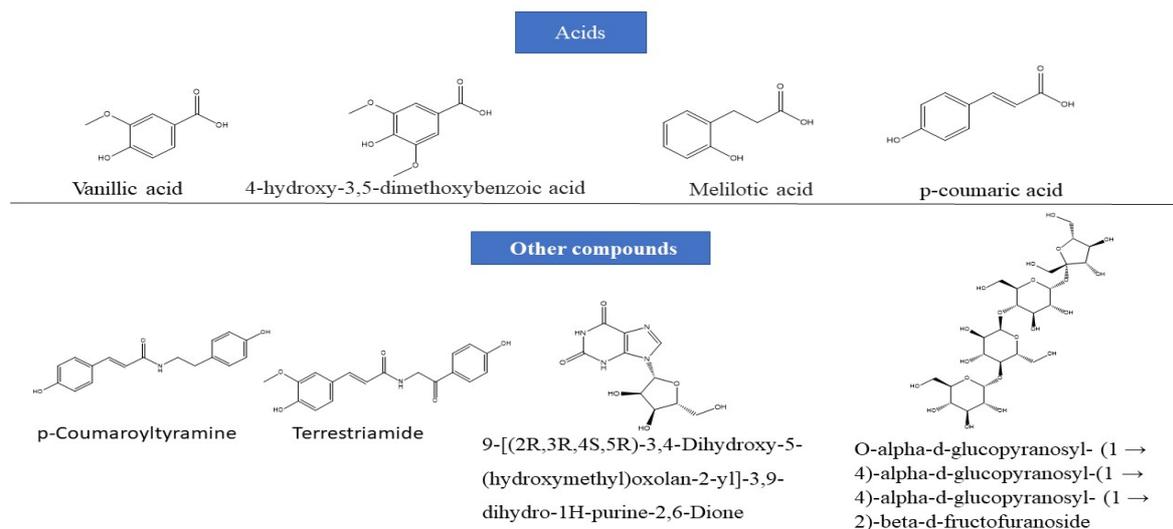


Figure 8. Some of the skeletal structures of acids and other compounds

Table 1. List showing some market products of *T. terrestris* as of Dec. 22.

Product Name	Price	Country of Origin	Usage
Natural Gokshura extract, 800mg capsules	Rs.800	India	Body strengthening, Urinary health and Digestive health
<i>T. terrestris</i> Seeds, Grade Standard: A-1, Seed	Rs.3,500/Bag	India	Enhance libido, keep the urinary tract healthy and reduce swelling
Mysha Nutrition <i>T. terrestris</i> capsule	Rs.999/Bottle	India	Muscle growth
Planet Ayurveda Gokshura Powder (100g)	Rs.899/100g	India	Better functioning of urinary, reproductive and nervous system.
<i>T. terrestris</i> Capsule, 90 Capsule,	Rs.165/bottle	India	Boost sex drive
<i>T. terrestris</i> 1000 mg	749.25	India	Increase Stamina
<i>T. terrestris</i> 625 CAPS	\$16.99	USA	Strength booster
Bulgarian <i>T. terrestris</i> , 90 capsules	\$ 60.75	USA	For kidney disorders
Ojio <i>T. terrestris</i> extract	400/kg	India	Pharmaceutical and healthcare
Vuaxo Herbals Advance Gokshura Macaroot capsules	Rs.611/Bottle	India	Men's wellness
Fushi Wellbeing Gokshura 60 capsules	£ 8.99	UK	Support Men health
<i>T. terrestris</i> extract	525/kg	India	Pharmaceuticals, healthcare and cosmetics
Divya Patanjali Gokshradi Guggul	Rs.40/20g	India	Cure renal and Urinary Tract Infection
Jarrow Formulas <i>T. terrestris</i> Complex 60 Tablets	\$14.95	USA	Enhances energy and Recuperation
<i>T. terrestris</i> Extract Capsules Herbal Bodybuilding Supplement	Rs.175/Bottle	India	Boost energy

Pharmacological activities

The main pharmacological activities such as anti-helminthic, anti-conceptive, and anti-estrogenic. Other important activities are antifertility, antimicrobial, chemopreventive, hypoglycemic, and antioxidant as well as anti-cancer (Kumari *et al.* 2022). Saponins are important active components that are used for treating cardiac diseases (Huang *et al.* 2004). Every part of the plant has distinctive pharmacological activities including a sexual enhancer, mitigating, antimicrobial, antibiotic, and immunomodulatory (Figure 9).

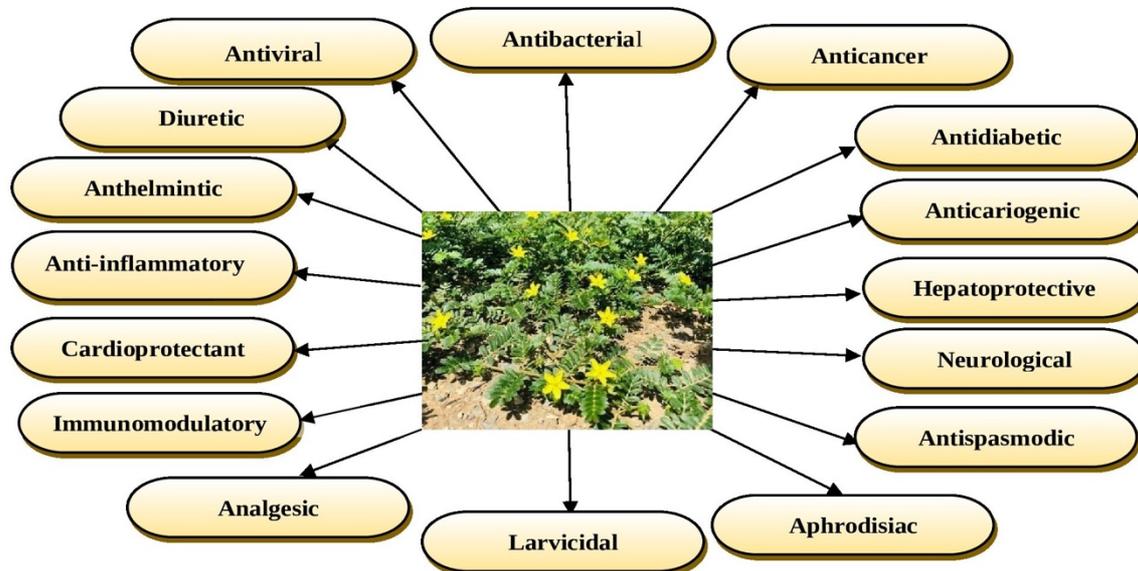


Figure 9. Various pharmacological activities of *T. terrestris*

The herb is frequently utilized for infertility and loss of moxie. *T. terrestris* is an immunomodulator, hepatoprotective, hypolipidemic, anthelmintic, and anticarcinogenic (Shahid *et al.* 2016). The existence of wide range of antibiotic chemicals in the plant could explain the plant's effectiveness against bacteria (Mitra *et al.* 2012).

Antidiabetic activities

Diabetes mellitus comprises chronic hyperglycemia, which consequences from a deformity in insulin activity (Sharma & Kumar 2020). The gross saponins of plant showed the restraint exercises of a post-prandial expansion in glucose there in blood and enhancement in insulin-subordinate diabetes manifestations (Zhu *et al.* 2017). Clinical preliminaries demonstrated that the aqueous extract has anti-hyperglycemic and anti-hyperlipidemic effects. The plant significantly reduced serum levels of fatty substances, glucose and cholesterol. The decoction made from *T. terrestris* inhibited gluconeogenesis in mice (Samani *et al.* 2016). In an experiment on animal, it was demonstrated that gross saponins of plant inhibit the postprandial rise in glucose level of blood and show improvement in the symptoms related to diabetes. The gross saponins of plant show inhibitory effect against α -glucosidase (Ercan & SN 2016).

Anticholinergic and Anticholesterolemic effects

Gastric administration of a saponin fraction of dried root to the rabbits slowed the formation of carbohydrate, protein and liver lipid dystrophy vs. cholesterol-loaded animals. The dried fruit, which was given to the mice via gastric intubation, was loaded with *Bombyx mori* containing preparation of *Mentha arvensis*, *Aconitum sinense*, *Alpinia species*, and *Sophora flavescens* was found to have anticholinergic properties.

Diuretic activities

The diuretic properties of *T. terrestris* are because of huge amounts of oil and nitrates presence in the fruits and seeds (Deshpande *et al.* 2018). The aqueous extract from fruits and leaves was tested on rat model and for contractility test strips of isolated ileum of Guinea pig was used. In the oral portion of five mg/ml the watery concentrate of *T. terrestris* evoked a positive diuresis when tested on Wistar male rodents despite its diuretic action, the plant extract had generated a contractile movement in the ileum of Guinea pig. The plant extract creates expanded toning of the smooth muscles, along with its diuretic movement helping to push the stones along the urine parcel (Al-Eisa *et al.* 2022). On albino mouse the diuretic potential of plant was tested. Potassium salt

concentration was high credit to the diuretic effect and the diuretic action was confirmed with minimum side effect (Ahmed *et al.* 2020).

Antirolithic activity

In Unani medical system the plant is known to inhibit the formation of kidney stones. In traditional medicine system the plant is used to treat urinary diseases like urolithiasis (Akram *et al.* 2011). An ethanolic concentrate of natural products of *T. terrestris* was tried in kidney stone disease instigated by glass globule implantation in albino rats. It displayed a critical portion of subordinate insurance against the statement of calculogenic substance round the glass leukocytosis, dot and rise in serum levels of urea. The resulting fractional process of the ethanol extricates prompted a diminishing in action (Anand *et al.* 1994).

Anticancer activity

The plant is effective against liver cancer. The aqueous extract can block the HepG2 cell proliferation and initiate apoptosis by inhibiting NF- κ B (Chhatre *et al.* 2014). The anticancer properties of plant have been described by different cell lines for example mouse sarcoma 180 (ASC), BEL-7402 liver malignant growth cell line, Bcap-37 breast carcinoma cell line, SK-MEL, KB, and SK-OV-3 (Sun *et al.* 2004). The motivation behind malignant growth anticipation is to create a setback for the beginning of malignancy, movement from precancerous injury or repeat after therapy, as an option in contrast to therapy of malignancy cases after clinical manifestations have shown up. The chemopreventive capability of this plant against DMBA-incited skin carcinogenesis in Swiss albino rat has been assessed. Their investigation exhibited that the oral organization of the *T. terrestris* remove at pre, peri and post-initiation stages showed a huge decrease in tumor occurrence and the aggregate number of papillomas and a critical expansion in the normal ideal time frame. Nonetheless, it was seen that the root concentrate of plant has more chemopreventive potential than the fruit, in skin papillomagenesis in Swiss albino rat (Kumar *et al.* 2006).

Aphrodisiac property

The plant contains active phytochemicals *viz.* protodioscin, dioscin, and diosgenin which show the effect on sexual performance and used in the treatment of sex related disorders. They increase the testosterone level in men and also affect the level of progesterone and estrogen. This plant is used to treat problems related to menopause and premenstrual syndrome in women. Sterols like β -sitosterols prevent prostate cancer (Akram *et al.* 2011). Investigation of phytochemical and pharmacological examinations in people and creatures uncovered a significant job for *T. terrestris* in treating the sexual disorders. It is used to treat erectile dysfunction in males. *T. terrestris* is tested on primates, rats and rabbits for its hormonal impacts on them to recognize its advantage in the management of sexual disorders (Gauthaman & Ganesan 2008). Blood tests were analyzed for testosterone levels utilizing a radioimmunoassay. Because of the occurrence of protodioscin *T. terrestris* enhanced a portion of the sex hormones was examined (Tyagi *et al.* 2008). Wister rats were emasculated, separated into five groups, each group has six animals, and given subcutaneous infusions of *T. terrestris* extract once daily for 14 days. There were decreases in the post-ejaculation interval, mounting, and a surge in mounting frequency, and ejaculation latency after the strong and sub-acute therapies with the plant extract. The presence of protodioscin (a steroidal saponin present in *T. terrestris*) was shown to have a favorable effect on the female reproductive system (Ghanbari *et al.* 2021).

Anti-inflammatory activity

The plant Extract was reported to contain N-trans- p -caffeoyl tyramine that had noticeable anti-inflammatory properties. In lipopolysaccharide-promoting RAW264.7 cells, N-trans-caffeoyl tyramine inhibited the production of nitric oxide, TNF, IL-10, and IL-6. Additionally, N-trans- p -caffeoyl tyramine significantly inhibited the activity of acetylcholinesterase *in vitro* and *in vivo* (Ko *et al.* 2015). Moreover, it was found to suppress the production of proinflammatory cytokines including interleukin-4 and tumour necrosis factor- α in the macrophage cell line. As a result, the ethanolic plant extract reduces inflammatory cytokines and mediators and has a positive impact on a variety of inflammatory disorders (Lee *et al.* 2017). In carrageenan induced rat paw model plant extract showed inhibition of rat paw volume. 30 minutes prior to carrageenan injection plant extract and COX-inhibitor (diclofenac sodium) was injected. After 1-4 hours it was observed that histamine, kinins, and serotonin are inhibited by carrageenan and reduced the paw volume (Zhu *et al.* 2017).

Antispasmodic activity

In an experiment, the lyophilized saponin combination of *T. terrestris* significantly decrease the peristaltic movements of jejunum of rabbit. This lyophilized material came from the dried and powdered plant from which saponins were extracted. These outcomes presented that the saponin blend might be helpful for spasms in muscles

or colic strain (Arcasoy *et al.* 1998). The plant can be used to manage the BPH (Benign prostatic hyperplasia) and the prostate gland has smooth muscles, the antispasmodic activity of the drug is valuable in reduction of tone of the prostate (Tarique *et al.* 2022).

Larvicidal activity

With an LC₅₀ of 64.6 ppm, a *T. terrestris* leaf extract of petroleum ether is known to have exceptional larvicidal efficacy against *Aedes aegypti* mosquito larvae, the third instar larvae that transmit dengue fever. Acetone extract of leaves and seeds displayed sturdy larvicidal possessions 100 percent mortality in the 3rd-instar larvae (Singh *et al.* 2008). The primary vector of lymphatic filariasis, malaria and dengue fever are *C. quinque-fasciatus*, *A. stephensi* and *A. aegypti* respectively. Different extracts of plant were tested for larvicidal activity by calculating the mortality percent of the disease vectors. It was observed that fruit has more larvicidal potential as compared to leaves (Zhu *et al.* 2017).

Hypolipidemic activity

In an experiment, rabbit was given diet rich in cholesterol and the vascular endothelium of intestinal blood vessels was examined. Supplementing the diet with the herb was found to lesser blood lipid profiles, lessen endothelial cell surface abrasions and partly repairs the dysfunctioning of endothelial which was caused by hyperlipidemia (Tuncer *et al.* 2009). The hypolipidemic activity is due to the presence of phenols. The aqueous extract was used to investigate the hypolipidemic activity on the rats. There was decrease in cholesterol-induced hyperlipidemia when the dose 580 mg/kg of extract was used. There was decrease in VLDL (Very Low Density Lipoprotein), LDL and increase in HDL (Chhatre *et al.* 2014).

Immunomodulatory activity

From the fruit of this plant, saponins were isolated and showed a dose-dependent rise in the phagocytic index in rats and the alcoholic extract made from the entire plant, significantly improves the humoral antibody titer and delayed-type hypersensitivity reaction. Thereof, plant possesses immunomodulatory activities (Tilwari *et al.* 2011). There is dose dependent increase in the humoral antibody when alcoholic extract of plant was used. Hypersensitive response was delayed indicate the specific immune response (Chhatre *et al.* 2014).

Analgesic activity

In male mice, the analgesic effects of *T. terrestris* were investigated by means of tail flick trial. The methanolic extracts of plant show an analgesic effect at a dosage of 100 mg/kg. The extract had a lesser impact than morphine and a larger effect than acetylsalicylic acid. In different assays, treatment of rats with the (opioid receptor) antagonist naloxone had no effect on the analgesic effect of the extract; hence, opioid receptor participation in the pain-relieving action of the plant extract is ruled out (Heidari *et al.* 2007). The methanol extract showed analgesic effect on albino mouse and formalin and tail flick assay was used. Percolated extract of plant at different dosage (50, 100, 200, 400, 800 mg/kg of body weight) were given to mouse. 100 mg/kg was the most effective dosage (Azam *et al.* 2019).

Antioxidant activity

In spleen cells, aqueous extract of plant fruit scavenged ROS generated by γ -radiation. It had mitogenic action in spleen cells (Pandey *et al.* 2007). Plant possesses antioxidant activity with DPPH, H₂O₂, superoxide scavenging activity, and FRAP assay. Butanol extract is rich in saponins and show notable quenching of NO and H₂O₂. From the Callus of plant diosgenin was obtained which has great antioxidant activity (Zhu *et al.* 2017).

Antibacterial activity

T. terrestris had been examined for antibacterial activity. *H. pylori* strains were sensitive to 1000 mg mL⁻¹ of the plant's entire extract using the method (*in vitro* cup plate). The *C. albicans* ACS1, ERG11, ERG1, ERG2, ACS2, ERG6, ERG25, ERG26, and ERG27 genes were suppressed by GSTT. These genes are directly engaged with the ergo sterol synthesis pathway. Different extracts of plant were prepared. The methanolic extract showed the maximum inhibition zone for *B. cereus*, *S. aureus* and *E. coli*. Ethanol extract showed inhibitory activity against *S. sanguis*, *S. mutans*, *A. viscosus*, and *E. coli* (Kiran *et al.* 2012).

Antifungal activity

The *in vitro* MICs of the compounds were determined with the of methods defined by the National Committee for Clinical Laboratory Standards. *C. krusei* and *C. parapsilosis* were tested in each assay (Zhang *et al.* 2006). The saponins derived from plant has antifungal efficacy and investigated against *Candida albicans*, fluconazole-

resistant yeast. The findings revealed that saponins from *T. terrestris* exhibit antifungal activity *in vitro* and *in vivo* reducing the pathogenicity of fungus and killing them by damaging the membrane of cell (Amanullah *et al.* 2021).

Anticariogenic activity

The ethanol extract of plant fruit has anti-cariogenic activity (0.1-0.5 mg/ml) against *Streptococcus mutans*, the microbe that causes tooth caries, which is substantial. The ethanol extract inhibits the production of acid, growth, adhesion, and water unsolvable glucan synthesis of *S. mutans* (Chhatre *et al.* 2014).

Central Nervous System (CNS) activity

Swiss Albino rats displayed antidepressive as well as anti-anxiolytic effects after receiving the Rasayana Ghana pill (260 mg/kg). Three effective, well-known herbs are included in the tablet in equal amounts: *T. terrestris* (fruit and root), *Tinospora cordifolia* (stem), and *Embllica officinalis* (fruit). Harmine an alkaloid found in *T. terrestris* has been proposed as one of the key active elements involved in the above-mentioned actions. Harmine is a monoamine oxidase inhibitor that helps to raise dopamine levels in the brain (Deole *et al.* 2011). The neuroprotective property of the plant extract was studied in chloride-induced Alzheimer's disease in mice. The biochemical and behavioral parameters were observed which showed improvement that can be connected to antioxidant activity of plant extract and chelating properties of flavonoids (Ştefănescu *et al.* 2020).

Activity in cardiac disorders

The plant's crude saponin fraction has been demonstrated to be effective for treating a variety of cardiac ailments, myocardial infarction as well as hypertension, and congestive heart failure. Saponins from the plant are known to help dilate coronary arteries and improve coronary circulation, according to study investigations. In an active diagnosis including 406 patients, the complete efficacious frequency of angina pectoris remission was 82.3 percent, and the TFR of ECG enhancement was 52.7 percent higher, which is why the herb *T. terrestris* was advised (Hashim *et al.* 2014). Various studies have discovered that fruit extract from *T. terrestris* plant has antihypertensive properties. In 2K1C hypertensive mice the antihypertensive activity of *T. terrestris* was studied by evaluating systemic and local ACE activity in the aorta, heart, and kidney. GSTT can protect cardiocytes that have been affected by ADR, which may be dependent on the ability to withstand reactive oxygen species. In Chinese traditional medicine formulation "Xin-nao-shutong" contain saponins and is used to treat cardiovascular disorders (Zhang & Yang 2010).

Activity to Improve Athletic Abilities

The testosterone and corticosterone levels, as well as the corticosterone and testosterone ratio, are commonly used to assess athletic weariness. Herbs are being utilized to boost athletic performance in a variety of ways, including stimulating epinephrine effects, stimulating testosterone effects, and increasing corticotropin and cortisol production. Because of their chemical structures *T. terrestris* contains protodioscin, gitonin and tribulosaponins A, which are thought to imitate actions similar to testosterone in humans (Bucci 2000). The major consequence is a boost in testosterone's anabolic and androgenic properties due to the stimulation of endogenous testosterone synthesis (Saudan *et al.* 2008). Androgen receptor is the receptor of testosterone. IGF-1 is related to muscle strength, muscle skeletal system, and metabolic rate. Gross saponin extract suppress the overtraining induced rise in IGF-1R in the liver and increase the AR in gastrocnemius. Gross saponin improves the exercise performance (Zhu *et al.* 2017).

Radioprotection

The aqueous extract of plant roots provides considerable radioprotection. The aqueous root extract of the plant when given orally (800 mg/kg) to the mouse for seven days prior to gamma radiation produced significant radioprotection. The extract pretreatment protected mice's livers from radiation damage by reducing lipoperoxidation and preventing radiation induced glutathione depletion (Manish *et al.* 2008).

Anti-arthritis activity

The presence of flavonoids may explain the anti-arthritis activity. Surface charge neutralization is a property of these flavonoids. *T. terrestris* treatment inhibits leukocyte migration, which could be good for joint preservation. The presence of steroidal glycosides may explain the action (Mishra *et al.* 2013). The methanol extract of plant fruit was studied for anti-arthritis properties in mouse. Using FCA induced arthritis in rats, the anti-arthritis activity of plants was evaluated (Mishra *et al.* 2013).

Conclusion

In this review research, we managed to focus and assemble information on the morphological, ethnobotanical, phytochemical, Ayurvedic potential, market products, and pharmacology of *T. terrestris*. The plant has long-term use in Ayurveda, dating back to the Vedic era. The plant may be used for various medical purposes. It can be used for various disorders. It has anti-diabetic, antioxidant, antibacterial, antiviral, analgesic, aphrodisiac, immunomodulatory, anticancer, hepatoprotective, hypolipidemic, anti-spasmodic, anti-helminthic, anti-inflammatory, anticariogenic, larvicidal, absorption enhancer, CNS, and cardiac properties. *T. terrestris* is quite effective in a variety of disorders. There are substantial scientific reports and data available on *T. terrestris*. As a result, it is regarded as a significant plant with a wide range of pharmacological properties that is extremely valuable to humans. Furthermore, much investigation is necessary to uncover the plant's hidden properties, the particularly whole mechanism of action of its active ingredients, which are responsible for the aforementioned activities. It can be concluded that more study is needed to determine the clinical consequences of *T. terrestris*.

Declarations

List of Abbreviations: WHO (World Health Organization), *T. terrestris* (*Tribulus terrestris*), i.e. (that is), g (gram), Kg (kilogram), DMBA (7,12-Dimethylbenz [a]anthracene), TNF (Tumor necrosis factor), IL-10 (Interleukin 10), LC 50 (Lethal concentration causing death in 50%), PPM (Parts Per Million), ROS (Reactive Oxygen Species), mg (milligram), mL (milliliter), NF-κB (nuclear factor kappa-light-enhancer of activated B cells), LDL (low density lipoprotein), ACS (acetyl-CoA synthetase), HDL (high density lipoprotein), GSTT Gross saponin of *Tribulus terrestris*, ECG (Electrocardiogram), MICs (minimal inhibitory concentrations), FCA (Frund's complete adjuvant), ACE (Angiotensin Converting Enzyme), ADR (Cardiocytes impaired by Adriamycin), TFR (total effective rate), RK (Ruchika Kumari), M (Manisha), PK (Palak Thakur), AC (Ashun Chaudhary).

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