Comprehensive Review of Tribulus terrestris L.: Phytochemistry, Traditional Uses, and Pharmacological Actions.

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Abstract: Tribulus terrestris L., also known as Puncture vine or Gokhru, is a widely distributed annual plant used extensively in traditional Indian and Chinese medicine for its diuretic, tonic, aphrodisiac, analgesic, and anti-inflammatory properties. The plant's bioactive compounds include steroidal saponins, flavonoids, terpenoids, glycosides, and tannins. Pharmacognostic studies detail the plant's physical characteristics, aiding its identification. Ayurveda attributes multiple therapeutic actions to T. terrestris, including diuretic, aphrodisiac, and anti-inflammatory effects. Modern studies validate its antioxidant, cytotoxic, antibacterial, and antifungal properties. T. terrestris exhibits several pharmacological actions such as Antiurolithiatic, Aphrodisiac, Cardiotonic, Antidiabetic, Antimicrobial, antifungal, Antitumor. In summary, Tribulus terrestris is a valuable medicinal herb with extensive therapeutic applications supported by traditional use and modern scientific research, making it a promising candidate for further medical exploration.

Index Terms: Gokhru, Tribulus, saponins, traditional, cardiotonic.

Introduction:

Tribulus terrestris L. is an annual plant in the Zygophyllaceae family and is referred to as Puncture vine or Devil's horn. The plant is also known as caltrop, goat head, bull's head, and ground burr nut in English. Commonly it is known as Gokhru and used from ancient times in Indian as well as Chinese medicine system(1). In traditional medicine, Gokhru has been used as a diuretic, tonic, aphrodisiac, analgesic, astringent, and stomachic-lithotripter. Additionally, it has been used to treat colicky pain, hypertension, and hypercholesterolemia. Multiple studies have proved the antioxidant, cytotoxic, antibacterial, and antifungal properties of the plant(2,3). Phytochemical studies on T. terrestris (Gokhru) revealed the presence of a variety of chemical substances, including steroidal saponins, terpenoids, glycosides, flavonoids, tannins, phytosterols, and derivatives of amides. The main bioactive substances among them were considered to be steroidal saponins and flavonoids. The plant includes 50 Furostanol saponins and 58 Spirostanol saponins. Protodioscin and protogracillin, among the various kinds of steroidal saponins, have been discovered to have specific biological activities (4). 25 flavonoid's glycosides, like common flavonols which include kaempferol, isorhamnetin, and quercetin, were isolated from Gokhru extract (5).

Overview of Tribulus terrestris:

Tribulus terrestris is a plant that grows annually that belong to the Zygophyllaceae family, and it is well distributed worldwide. It is indigenous to southern Africa and Eurasia's mild temperate and tropical climates. It has unintentionally found its way to Australia and North America. T. terrestris is a hardy and aggressive invasive species that is commonly known as a noxious weed due to its small woody fruit, called a bur, which has long, sharp spines that may penetrate surfaces(6,7).

Taxonomical Classification of Tribulus terrestris:

Kingdom: Plantae
Division: Phanerogams
Subdivision: Angiospermae
Class: Dicotyledonae
Order: Zygophyllales
Family: Zygophyllaceae

Genus: Tribulus (puncturevine)
Species: T. terrestris (Tribulus terrestris L.) (6,8)

GEOGRAPHICAL SOURCE:

Tribulus terrestris has a broad geographical distribution, covering significant areas of Africa, central and south Asia, and south Europe. It has also been introduced to the United States, regions of Canada, and western South America. The plant grows in altitudes ranging from 0 to 3,000 meters above sea level in tropical and subtropical areas, and can be found as high as 3,800 meters above sea level in Tibet (9).

COMMON AND VERNACULAR NAMES:

English: Puncture vine, Small Caltrops
French: Croix de Malte
Spanish: Abrojos
Sanskrit: Gokshur
Marathi: Gokharu, Sarate
Hindi: Gokharu
Gujarati: Bethagokharu, Nanagokharu
Tamil: Nerinjil
Urdu: Khar-e-khasak khurd
Bengali: Gokhri
Kannada: Neggilamullu, Neggilu, Sannaneggilu (6,7)

PHARMACOGNOSTIC FEATURES:

a) **Macroscopy:** Fruit is stalked, pale or greenish yellow, with five ribbed or angled, roughly spherical in shape, and covered in short, stiff, or pubescent hairs. The fruit is surrounded by a pentagonal framework made up of five pairs of prominent, short, stiff spines that point downward and meet in the middle. Ripe fruit splits into five segments, each of which resembles a single fruit. The cocci are semi-lunar or plano-convex in shape, with one chambered, armed with a pair of spines that start from the middle, each containing four or more seeds, and have a slightly astringent taste. (7)
b) **Microscopy:** The transverse section of the fruit shows a rosette of calcium oxalate crystals abundantly present, small epidermal cells of each coccus rectangular, unicellular trichomes in abundance, and 6–10 layers of large parenchymatous cells in the mesocarp. (7)

Properties & Actions mentioned in Ayurveda:

- Rasa (activity-based taste) : Madhura (sweet)
- Veerya (potency): Sheeta (cooling)
- Guna (properties): Snigdha (unctuous), Guru (heavy to digest)
- Vipaka (taste after digestion based on activity): Madhura (sweet)
- Karma (pharmacological actions): Ashmarihara (removes urinary stone), Brumhana (nourishes), Vrusya (aphrodisiac), Vatanut (calms Vata dosha), Vastishodhana (treats bladder problems), (taste after digestion dependent on activity).(5,8)

PHYTOCHEMISTRY:

T. terrestris is a precious herb widely used in alternative medicines and indigenous to different regions worldwide. T. terrestris consists of various compounds with different biological properties and chemical structures, such as steroidal saponins, flavonoids, glycosides, phytosterols, tannins, terpenoids, amide derivatives, amino acids, and proteins. Steroidal saponins and flavonoids are considered the most significant metabolites among the different kinds of constituents, due to their various bioactivities.(10)

The main types of Furostanol and Spirostanol saponins found in T. terrestris include chlorogenin, diosgenin, gitogenin, neohecogenin, hecogenin, ruscogenin, tigogenin, neogitogenin, neotigogenin, and sarsasapogenin. (11)

Following are the types of chemical constituents present in Tribulus terrestris:(12,13)

Steroidal saponins: The chemical constituents of T. terrestris that have been considered to be the most distinctive are Furostanol and Spirostanol saponins. So far, a total of 108 different types of steroidal saponins have been extracted from T. terrestris. There are a total of 58 different types of spirostanol saponins and 50 different types of furostanol

saponins. The steroidal saponins, specifically protodioscin and protogracillin, are believed to provide T. terrestris with distinct and exceptional biological properties.(10)

Steroidal saponins		**Flavonoids**	**Alkaloids**	**Others**
Furostanol	**Spirostanol**			
Protodioscin, Neoprotodioscin, Prototribestin, Terrestrinin A, Terestroside A, Terrestrosin K, Tribufuroside D, etc.	Dioscin, Tribestin, Diosgenin, Tribulosin, Hecogenin, Gitogenin, Tigogenin, etc.	Tribuloside, Kaempferol, Rutin, Quercetin, etc.	Harmine, Harmane, Tribulusterine, Harmalol, etc.	Terrestribisamide, Oleic acid, Palmitic acid, Stigmasterol, Heptacosane, β-sitosterol-D-glucoside,

Table no: 1 Chemical constituents of T. terrestris

Flavonoids: The Flavonoids present in T. terrestris are mostly derivatives of quercetin, kaempferol and isorhamnetin(10). Some of the examples are:

Quercetin derivatives	**Isorhamnetin derivatives**	**Kaempferol derivatives**
iso-quercitrin, rutin, quercetin-3-O-gent, quercetin-3-O-gentr, quercetin-3-O-rha-gent, quercetin-3-O-gent-7-O-glu.	isorhamnetin-3-O-glu, isor-hamnetin-3-O-gent, isorhamnetin-3-O-rutinoside, isorhamnetin-3-O-gentr, isorhamnetin-3,7-di-O-glu, isorhamnetin-3-O-p-coumarylglu, isorhamnetin-3-O-gent-7-O-glu, isorhamnetin-3-O-gentr-7-O-glu.	kaempferol-3-O-glu, kaempferol-3-O-gent, kaempferol-3-O-rutinoside, kaempferol-3-O-gent-7-O-glu, tribuloside.

Table no: 2 Flavonoids present in T. terrestris

TRADITIONAL USES:

T. terrestris is used in herbal remedies for several purposes, including diuretic, lithotriptic, antihypertensive, astringent, stomachic, tonic, aphrodisiac, palliative, and urinary disinfection(2). In most of genitourinary tract disorders, the dried fruit of the plant is highly effective. It is an essential component of Gokshuradi Guggul, an effective Ayurvedic remedy which helps the genitourinary system work normally and by getting rid of urinary stones(5). In Ayurveda, T. terrestris has been utilized for centuries to cure sexual debility, impotence, and venereal disorders. The Indian Ayurvedic Pharmacopoeia lists the root and fruit for their cardiotonic properties in addition to all these other uses. The fruits were used to treat eye problems, edema, abdominal distension, emission, morbid leukorrhea, and sexual dysfunction in traditional Chinese medicine. The oldest published pharmaceutical work in China, Shern-Nong Pharmacopoeia, states that T. terrestris is most valuable drug for treatment of vitiligo, mastitis, flatulence, headaches, acute conjunctivitis, and chest fullness. It also states that T. terrestris helps in restoring the depressed liver. T. terrestris is used as a diuretic, a general tonic, and a mild laxative in Unani medicine(8,14).

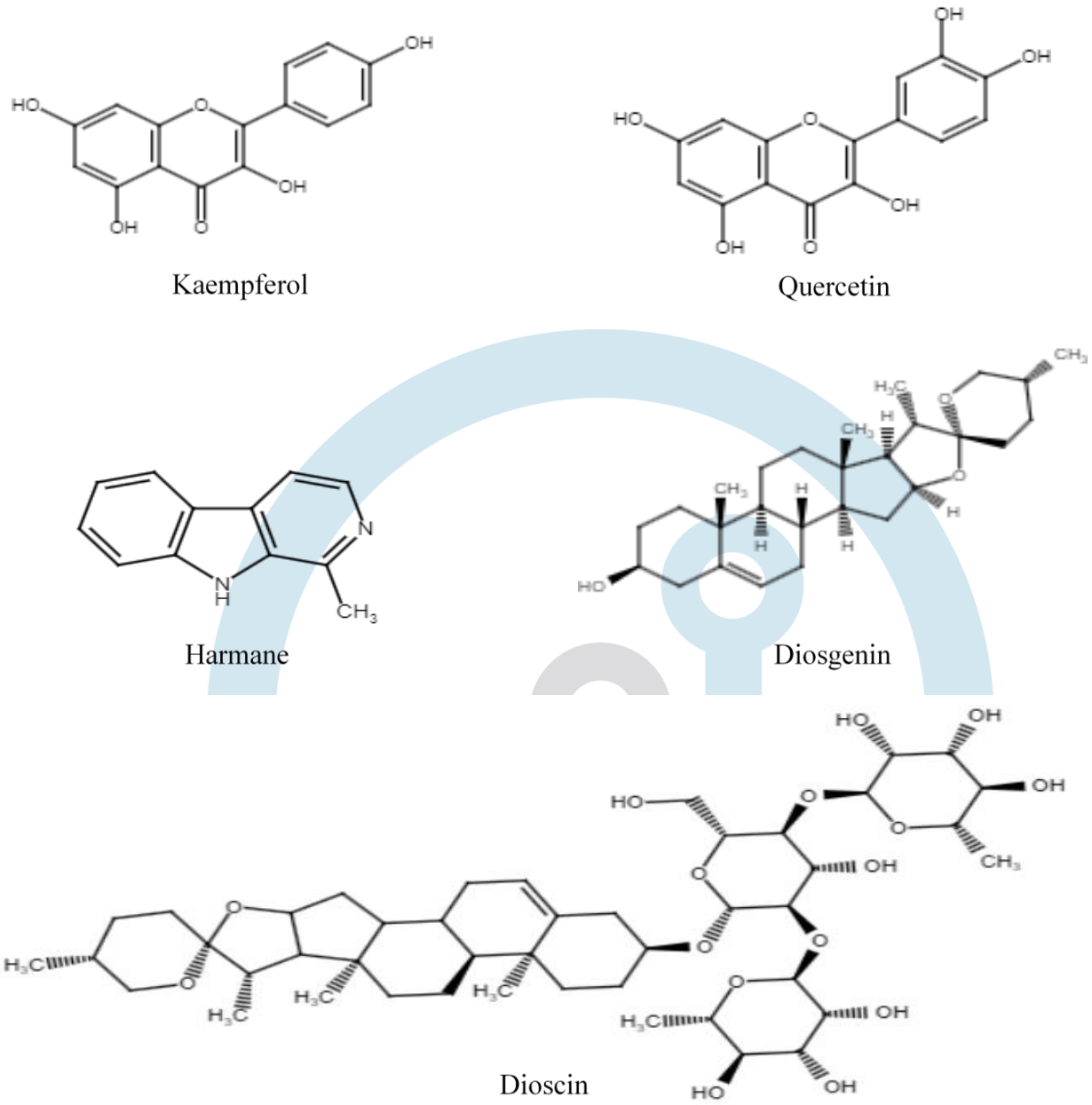

Figure no: 1 Chemical structures of some chemical constituents present in *Tribulus terrestris*

PHARMACOLOGICAL ACTIONS:

T. terrestris has been used for a long time to treat a variety of diseases in traditional Chinese and Indian systems of medicine, especially to enhance sexual function, prevent and treat cardiovascular problems, and control diabetes. Additionally, it possesses antitumor, anti-inflammatory, antibacterial, antioxidant, hepatoprotective, and anti-inflammatory properties(10).

1. **Antiurolithiatic activity:** The effectiveness of the ethanolic extract of Gokhru was evaluated against experimentally induced urolithiasis in albino rats. The extract was administered orally at doses of 25, 50, and 100mg/kg daily for 4 months. It exhibited antiurolithiatic activity which was dosage dependent, almost completely reduced the occurrence of stones, and showed the potential to prevent hyperoxaluria(15,16).

2. **Aphrodisiac activity:** A study was done to investigate the effect of orally administering the Tribulus terrestris extract on the isolated corpus carvenosal tissue of rabbits. The objective was to discover the mechanism via which protodioscin (PTN), a constituent of Tribulus terrestris, exhibits its pharmacological effects. The penile tissues obtained from the sacrificed animals were tested for their response to various pharmacological agents and electrical field stimulation (EFS). The results showed that the tissues exhibited relaxation in response to Acetylcholine, nitroglycerin, and EFS,

with increases of more than 10%, 24%, and 10% respectively compared to their control values. However, there was no effect on the contractile response to noradrenaline and histamine. These results reveal that PTN has pro-erectile activity. The increased relaxation effect has been attributed to the elevation of nitric oxide production from the endothelium and nitrergic nerve endings, which could explain its purported aphrodisiac potential(17).

3. **Cardiotonic activity:** The saponins found in the plant Tribulus terrestris show the ability to dilate the coronary artery and enhance the flow of blood in the coronary circulation. A clinical trial was conducted on 406 patients who had coronary heart disease. The results revealed that the overall rate of successful remission of angina pectoris was 82.3%, and the rate of improvement in ECG was even higher at 52.7% compared to the control group's rate of 35.8% (18).
Tribulus Terrestris plays an essential role in treatment of cardiovascular diseases, such as in the treatment of anti-myocardial ischemia and myocardial ischemia-reperfusion injury. GSTT exhibits a protective effect in myocardial ischemia-reperfusion injury. In rats, GSTT decreased LDH, MDA, TNF-α, and IL-6 levels, enhanced SOD and apoptosis, and improved cardiomyocyte structure(19).
In addition, GSTT has the potential to improve coronary blood flow and enhance heart function, while also increasing adenosine triphosphate (ATP) activity in cases of myocardial ischemia-reperfusion injury(20).
The methanol extract of T. terrestris (METT) fruits, mostly composed of ferulic acid, phloridzin, and diosgenin, had an impact on mitochondrial dysfunction in a cell-based (H9c2) model of myocardial ischemia. The extract protects the mitochondria by utilizing its antioxidant capabilities(21).

4. **Antidiabetic activity:** The gross saponins of T. terrestris (GSTT) exhibited inhibitory effects on α-glucosidase. Additionally, it exhibited inhibitory effects on a postprandial elevation of blood glucose levels and ameliorated symptoms of insulin-dependent diabetes (22). The results of animal studies revealed that GSTT effectively reduced postprandial blood glucose levels in both normal rats and type 2 diabetic rats when sucrose was administered through the GI tract. However, GSTT had no effect on postprandial blood glucose levels in rats when glucose was administered through the GI tract(23). Scientific investigations have demonstrated that the water extract of T. terrestris (WETT) possesses antidiabetic properties. The levels of fasting blood glucose, 2-hour postprandial glucose, glycosylated hemoglobin, and lipid profile in diabetic women who administered a daily dose of 1000 mg of T. terrestris extract for three months were lower compared to those in the placebo group(24).

5. **Antimicrobial and antifungal:** The antimicrobial and antifungal properties of organic and aqueous extracts derived from T. terrestris fruits, roots, and leaves were studied. It was shown that the extracts' ability to form a complex with bacterial cell walls and extracellular soluble proteins may be the basis of their antibacterial activity(25). In addition, lipophilic flavonoids can interfere with microbial membranes. The antifungal action of T. terrestris is linked to a variety of chemical compounds present in its extracts, including saponins (26).

6. **Antitumor activity**: According to Costa-Lotufo et al. (2005), T. terrestris has been shown to have specific anticancer effect on human cancer cells in vitro(27). Saponins found in extracts of T. terrestris, which are structurally similar to diosgenin, have the potential to inhibit cancer cell line growth, block cell cycle, and activate apoptosis. Ukani et al. (1997) discovered that T. terrestris exhibits a protective effect against UVB-induced carcinogenesis(28). The mechanism by which T. terrestris saponins regulate cell death shows its potential for a possibility for the development of a novel anticancer drug.

7. **Action on Central Nervous System:** Deole et al discovered that Swiss Albino mice showed antidepressant and anxiolytic effects after receiving a dose of 260 mg/kg of Rasayana Ghana tablet. This tablet includes three potent rejuvenating herbs, which are Tinospora cordifolia, Emblica officinalis, and T. terrestris, which are present in equal quantities. Study revealed that harmine, a β-carboline alkaloid found in T. terrestris, is a key active ingredient responsible for above mentioned activities. Harmine functions as a monoamine oxidase inhibitor, leading to an elevation in dopamine levels within the brain(29).

8. **Anti-Inflammatory Activity:** In lipopolysaccharide-stimulated RAW264.7 cells, Oh et al. found that the activity of COX-2 (cyclooxygenase-2) and iNOS (inducible nitric oxide synthase) was inhibited by the ethanolic extract of T. terrestris. Additionally, it inhibited the production of proinflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-4, in a macrophage cell line(30).

Conclusion:

In conclusion, Tribulus terrestris is a valuable medicinal herb with a broad spectrum of therapeutic applications validated by both traditional use and contemporary scientific research. Its rich phytochemistry and diverse pharmacological actions make it a promising herbal drug for further exploration in modern medicine.

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