DIURETIC AND LITHOTRIPTIC POTENTIAL OF TRIBULUS TERRESTRIS (KHAR KHASAK) LINN.-A COMPREHENSIVE REVIEW

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ABSTRACT

Tribulus terrestris (family Zygophyllaceae), commonly known as Gokharu or puncture vine, has been used for a long time in both the Indian and Chinese systems of medicine for treatment of various kinds of diseases. Its various parts contain a variety of chemical constituents which are medicinally important, such as Chlorogenin, Tribuloside, Trigogenin and Harmine. Whole plant and seeds are used as traditional herbal medicine to treat various ailments such as diuretic, antiurolithic, aphrodisiac, immunomodulatory, antidiabetic, absorption enhancing, hypolipidemic, cardiotonic, central nervous system, hepatoprotective, anti-inflammatory, analgesic, antispasmodic, anticancer, antibacterial, anthelmintic, larvicidal, and anticariogenic activities. The review highlights only the diuretic and litho-triptic activity, which are mentioned in classical Unani literature.

KEYWORDS: Tribulus terrestris, Unani medicine, Diuretic, Lithotriptic.

INTRODUCTION

Unani system of medicine has employed plant medications as mudir-e-baul(diuretics) for controlling and treating a variety of oedematous conditions associated with ailments of the kidney, heart, abdomen and diabetic nephropathy. Diuretics are generally given as a supportive therapy or first line therapy along with antihypertensive agent. They are indicated in CHF, Cerebral oedema, pulmonary oedema, Ascitis and Renal failure. Diuretics belonging to thiazide and loop diuretics have adverse effect of hypokalemia, which leads to changes in heart function as well as muscular weakness. To prevent such condition, combination of potassium salt or potassium sparing diuretics are indicated. Unani system of medicine has...
also employed Mufatit-e-hisat (Lithotriptic) for crystal excretion, breaking and expelling of stone. Lithiasis is the formation of calculi or stone which is a concretion of material mainly mineral salts in any part of the body. Antilithics are the agents that prevent the formation or promote the dissolution of formed calculi. Lithiasis mostly occurs in any part of the whole urinary tract which includes the kidney ureter and urinary bladder. In this regard Tribulus terristris are in great demand in the developed as well as developing countries because of their wide biological and medical activities, lesser adverse effect and low cost. In addition, presence of potassium would prevent potassium depletion.

The genus Tribulus, belonging to family Zygophyllaceae, comprises about 20 species in the world, of which three species, viz. Tribulus cistoides, Tribulus terrestris, and Tribulus alatus, are of common occurrence in India. Among them, T. terrestris (TT) is a well-patronized medicinal herb by Unani seers as well as by modern herbalists. 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.

**PLANT PROFILE**

**VERNACULAR NAMES**\(^{1, 2, 3, 4, 8, 9, 10, 11, 12}\)

Tribulus terrestris is commonly known as *Khara-khusk, khasak, Ikhwasul ujooj* (Arabic), *Khar-e-khasak* (Persian), *Gokhrur* (Urdu), *Small caltrops or puncture wine* (English), *Ikshugandha* (Sanskrit), *Chota Gokharu* (Hindi); *Bethagokharu* or *Nanagokharu* (Gujarathi); and *Nerinjil* (Tamil).

**Origin and Distribution:** A native of Europe, it grow on dry or Sandy soil along roads and highways. It is now found in the tropics and warm temperate regions of the world. (Medicinal Plants of the world-412).

**BOTANICAL DESCRIPTION**

A variable, prostrate annual herb, up to 90 cm in length, commonly found throughout India, up to an altitude of c.5400 meter. Roots cylindrical, 10-15 cm long, light brown and faintly aromatic leaves peripinnate, fruits globose, consisting of 5-12 woody cocci. The Seeds are several in each coccus with transverse partition between them.\(^66\) The herb is common weed, springing up everywhere soon after the first showers. The herb flowers and fruits almost
throughout the year. The flowering starts within 20-35 days and the fruits matures in 14 days after the formation of seed. About 1.85 tonnes of the drug (fruits, roots and occasionally the entire plants) are reported to be collected from Saharanpur in Utter Pradesh. The leaves and tender shoots are used by the proper class as a proherb, either alone or mixed with other herbs. The flour from the fruits is made into bread and eaten during the times of scarcity. An analysis of green leaves gave the following values: moisture 79.09; protein 7.22; ether extr 0.54; ash 4.63; calcium 1.55; phosphorus 0.08; iron 9.22; and vitamins C 41.53 mg/100g. They are rich in calcium and poor in iron and are valuable as cheap supplements to rice diets in south India, adding to the compensatory value of mixed greens. *(wealth of India 284)*

**PART USED:**
- Fruits[3,6,8,10,11,12]
- Whole Plant[1,2,3,4,7,9,11,12]

**TEMPERAMENT** (Mizaj):
Most of the Unani writers have mentioned in their book that the temperament of drug is Hot and Dry in 1°[8,9,10,12] and Murakkabul quva[3,10].

**TRADITIONAL MEDICINAL USES:** *(Medicinal Plants of the world-412)*

**India**
1. Hot water extract of the dried plant is taken orally for renal Urinary Calculi.
2. Water extract of the fruit is taken orally as a tonic and diuretic.
3. Infusion of the dried fruit is taken orally as a treatment of urolithiasis and as a diuretic for gout.

**Nepal:** Hot water extract of the fruit is taken orally as a diuretic.

**Peru:** Hot water extract of the dried aerial part is taken orally as a diuretic.

**Thiland:** Hot water extract of the dried root is taken orally as a diuretic.

**Turkey:** Decoction of the seed is taken orally to pass kidney stone.

**PHARMACOLOGICAL PROPERTIES MENTIONED IN UNANI LITERATURE**
- Diuretic *(Mudir-e-baul)*[1,2,3,4,6,7,8,9,10,12]
- Lithotriptic *(Mufatit-e-hasat)*[1,2,3,4,8,9,10,11,12]
- Anti-inflammatory *(Muhalil-e-auram)*[3,4]
- Analgesic *(Musakkin-e-alam)*[4]
- Cooling agent *(Mubarrid)*[1,4,6]
- Haemostyptic *(Habis-e-dam)*[4]
- Aphrodisiac *(Muqavi bah)*[1,3,4,5,6,7,8,9,10,12]
- Tonic *(Muquvi)*[1,4,6,7]
- Emmenagogue *(Mudir-e-haiz)*[3,8,10]
- Appetizer *(Mushtahi)*[4]
- Munzij-e-Maddah[1,3] etc.
THERAPEUTIC APPLICATION MENTIONED IN UNANI LITERATURE
A number of Unani scholars have shared their valuable experiences for Khar Khasak (Tribulus terrestris) as a lithotriptic and diuretic in various Unani texts. Although the list is very exhaustive, it will be worthwhile to pen down a few of them here:

1. The plant which was also known to the old Greek physicians is used in south Europe as an aperients and diuretic.\(^1\)
2. Plant and dried spiny fruits are used in decoction or infusion form, in cases of disease of the genitourinary system such as dysuria, gonorrhoea, gleet, chronic cystitis, calculus affection, urinary disorders and incontinence of urine.\(^1\)
3. Sheerah-e-khar-e-khasak is useful in cystitis and burning micturition\(^{17, 24}\). (Tibbe akbar, Al-akserr)
4. Khar Khasak kla is used as a breaking of kidney stone.(Alhavi 123)
5. Arq Khar khasak is used as a lithotriptic, when grow in dry places.(Alhavi 124)
6. Seed of Khar khasak breaks kidney stone.(Alhavi 131)
7. Alhavi quote with reference to Galen, use of Sharbat Khar khasak is beneficial for renal and bladder stone.(Alhavi 131)
8. Fruit of Khar khasak kla breaks kidney stone.
9. Fresh white lime 14gm, 7gm and 3.5 gm for Obese, overweight and weak patients respectively with Joshanda Khar Khasak, is taken regularly for a few days to help in expelling urolithiasis. (Alhavi 132)
10. Fruits and root decoction thrice a day is taken regularly for a fortnight to help in expelling kidney stone. (IJTK)

PHARMACOLOGICAL ACTIVITIES AND CLINICAL TRIALS
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. Ali et al. 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. Saurabh et al. evaluated the different extracts of Tribulus terrestris fruits, viz. aqueous, methanolic, Kwatha-high strength, Kwatha-low strength, and Ghana powder, for diuretic activity in rats. Kwatha-high strength showed diuretic effect comparable to that of the reference standard frusemide and also exhibited additional advantage of potassium-sparing effect. The diuretic action of TT makes it useful as an anti-hypertensive agent. (Pharmacogn Rev. 2014 Jan-Jun; 8(15): 45–51.)

- Alkaloid fraction of dried fruit, taken orally by adults, produced weak activity. The ether extract, administered intravenously to anesthetized dogs, produced diuresis and increased the creatinine renal clearance, but had little effect on chloride clearance. Ethanol (95%) extract of the entire plant, administered orally to dogs at a dose of 20 mg/kg, was an active. Etanol (95%) extract of the seed, taken orally by adults was active. Hot water extract of the plant administered intraperitoneally to male rat at a dose of 0.2ml/animal, was active. The duration of action was 60 minutes. (Medicinal plants of the world -2-417)

- The fruits are credited with diuretic and tonic properties and are used for the treatment of calculus affections and painful micturition. The diuretic activity has been subject of detailed study in both human beings and animals. In dogs the fruits showed activity comparable to that of urea, but in rats the activity was less. The diuretic effect of the seeds as well as the aqueous extract of the ashes obtained by burning of the seeds has been studied in albino rats: an isotonic solution, their action was found to be comparable to that of potassium chloride. Besides the potassium content of the fruits, the diuretic effect has also been ascribed to the alkaloidal fraction present in the seeds. The observation has been supported by clinical trials; the use of alkaloidal fraction in case of ascites and oedema showed mild diuretic action. (The wealth of India-284)

**ANTIUROLITHIASIS ACTIVITY**

- Ethanol (95%) extract of the dried fruit, administered intragastrically to rat at a dose of 25.0mg/kg, was active vs. seed induced crystallithiasis. (Medicinal plants of the world -2-416)

- Ethanol(95%) extract of the dried entire plant, in combination with Cucumis melo, Carum carvi, Pimpinella anisum, Zea mays, Foeniculum vulgare, Laurus nobilis, and Prunus avium, was taken by 300 patients with kidney and uretral stones. 67% of the patients passed stones, 18% transferred and there was a decrease in volume of stone in 11%. 98% of the patients reported relief from colic.
An ethanolic extract of *Teribulus terrestris* fruits was tested in urolithiasis induced by glass bead implantation in albino rats by Anand et al. 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 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. The experiments revealed that Tribulus terristris extract not only has a potential to inhibit nucleation and growth of the CaOx crystals but also has a cytoprotective role. Tribulus terristris was found to inhibit stone formation in various models of urolithiasis using sodium glycolate and ethylene glycol. (Pharmacogn Rev. 2014 Jan-Jun; 8(15): 45–51.)

Glycolate oxidase (GOX) is one of the principal enzymes involved in the pathway of oxalate synthesis converting glycolate to glyoxylate by oxidation and finally to oxalate. The antiurolithic activity of Tribulus terristris is attributed to its GOX inhibition. Quercetin and kaempherol, the active components of Tribulus terristris, were found to be non-competitive and competitive inhibitors of GOX, respectively. (Pharmacogn Rev. 2014 Jan-Jun; 8(15): 45–51.)

Aqueous extract of the plant administered to sodium glycolate fed rats produced a significant reduction in urinary oxalate secretion and a significant increase in urinary glyoxylate excretion as compared to in sodium glyoxylate fed animals. (World Journal of Pharmacy and Pharmaceutical Sciences)

Evaluation of diuretic potential of Tribulus terrestris in albino rats has been observed. The diuretic effect was attributed to the presence of potassium salt in high concentration and this action with minimal side effect of Tribulus terrestris in albino rat was confirmed.(Mohd Jameel IRJP)

The ethanolic extract of the plants was tested for activity against artificially induced urolithiasis in albino rats by administration of oral dose at 25, 50 and 100 mg/kg daily for 4 months. It exhibited dose dependent antiurolithic activity and almost completely inhibited stone creation along with anti hyperoxalluria potential. (Mohd Jameel IRJP)
CHEMICAL CONSTITUENT

- The fruits contain $^{1,2,6,9,10,12}$
  - Alkaloid in trace (0.001%)
  - Fixed oil (mainly unsaturated fatty acid)-3.5%
  - An essential oil- small quantity
  - Resins
  - Fair amount of nitrates
- Chlorogenicin, Tribuloside, Trigogenin isolated from fruits.$^{[93]}$
- The alkaloid, Harman, has been reported from the herb, and harmine from the seeds. The plant contains saponins, which on hydrolysis, yield steroidal saponins: diosgenin, gitogenin, chlorogenin, ruscogenin and 25 D–spirosta-3,5-diene. Saponins having high haemolytic index are present in leaves and roots, but absent in stems or seeds; three saponins in leaves and two in roots have been identified. Kaempferol, Kaempferol-3-glucoside, Kaempferol-3-rutinoside, and a new flavonoid tribulosides have also been isolated from the leaves and fruits. (The wealth of India 284)

RECOMMENDED DOSE OF TRIBULUS TERRISTRIS

5-7gm$^{[8,9,10,12]}$

- **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.

CONCLUSION

*Tribulus terrestris*, have great significance in the traditional system of medicine especially Unani, Ayurvedic and Chinese for the treatment of various properties especially diuretics and Lithotriptic. The whole plant and seed of *Tribulus terrestris* has been explored exhaustively for its mentioned in classical unani literature, clinical trials, phytochemical and pharmacological activities such as diuretic, antiuricithic. Considering the available literature *Tribulus terrestris*, the plant could have a potential as a herbal medicine for effective Urinary tract infection, Congestive heart failure, Ascitis, Urolithiasis and blood pressure control due to its diuretic activity (potassium sparing). It is also important to mention here that the diuretic properties of this drugs are acting as adjuncts to this antibacterial activity by decreasing the bacterial index through frequent clearing the tract and also preventing the stasis in the tract for certain length of time, thus the bacteria could not get proper time for growth and multiplication. Though *Tribulus terrestris* has been used extensively over the centuries and
currently scientific evidence with respect to its pharmacological activities is also being generated, more studies at the molecular level are needed to further understand the mechanism by which it modifies the disease condition. The pharmacological experiments performed on the plant must be extended to the next level of clinical trials to generate novel drugs. This will help Tribulus terrestris in achieving a status of medicine or to be prescribed as a dietary supplement in various disease conditions.

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