



TRADITIONAL AND PHARMACOLOGICAL PERSPECTIVES OF GOKHRŪ (TRIBULUS TERRESTRIS AND PEDALIUM MUREX) IN URINARY DISORDERS AND SEXUAL DEBILITY: A REVIEW

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ABSTRACT

Background: *Khār-i-Khasak/Gokhrū* is a valuable medicinal plant in the Unani System of Medicine (USM). *Gokhrū* is classified into two types: *Khār-i-Khasak Khurd* (small caltrop) and *Khār-i-Khasak Kalān* (large caltrop). The small Caltrop (*Tribulus terrestris*) and the large Caltrop (*Pedaliium murex*) belong to the *Zygophyllaceae* and *Pedaliaceae* families. These plants are well-known for their therapeutic benefits. It has medicinal applications in many ancient medical systems, including Unani, Ayurveda, Siddha, and others. **Purpose of review:** This review was to explain in detail the benefits of giving a scientific basis and classical references for the clinical usage of *Gokhrū*. **Materials and Methods:** This review was conducted by thoroughly searching the classical literature, Unani, ethnobotanical, and published research databases of ScienceDirect, PubMed, Web of Science, Google, Google Scholar, ResearchGate, and Elsevier. **Results:** Pharmaceutical businesses utilise this medication to prepare formulations and dietary supplements. It is growing in India, South Africa, the Middle East, Pakistan, Sri Lanka, and Mexico. In India, it is primarily found in Bihar, Andhra Pradesh, Tamil Nadu, the northwestern states, West Bengal, Madras, Gujarat, Awadh, and Rajputana. This plant has abundant therapeutic properties, including anti-ulcerative, anticancer, aphrodisiac, analgesic, stomachic, diuretic, cardiogenic, antibacterial, anti-inflammatory, nephroprotective, antispasmodic, and anti-carcinogenic. This plant is mostly used to treat urogenital problems, kidney disorders such as renal and vesical calculi, gallbladder stones, and sexual disorders such as infertility and erectile dysfunction in both men and women. **Conclusion:** It is concluded that abundant bioactive compounds identified and separated from *Khār-i-Khasak Khurd* and *Khār-i-Khasak Kalān* have potential medicinal values on the male and female reproductive systems, as well as the urinary system (renal and vesical calculi), due to the presence of steroidal saponin compounds, flavonoids, alkaloids, and ursolic acid as the plant's predominant active component.

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INTRODUCTION

Khār-i-Khasak/Gokhrū (small caltrop and large caltrop) is an herbaceous plant from India that belongs to the *Zygophyllaceae* and *Pedaliaceae* families, which has approximately 20 species worldwide. *Gokhrū* is commonly referred to as Tribulus, Puncture vine, small caltrop, Chhota *Gokhrū*, and goat head ^[1,2]. Other names include *Khār-i-*

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Khasak Khurd, *Khasak*, *Hamsul Amīr*, *Akhrasul Ajūz*, and *Zafratul Ajūz* [3,4]. *Gokhrū* grows primarily in Mediterranean countries and subtropical regions worldwide [1].

The word *Tribulus* means “three-pointed caltrops” in Latin, which is indicated for the three-pronged fruit of *Tribulus terrestris* with projecting spikes [5]. It is the most important herbal plant, well-known for its traditional use in various parts of the world to treat multiple ailments [6]. This plant has over 20 species, three of which are found in India: *Tribulus cistoides*, *Tribulus terrestris*, and *Tribulus alatus* [7]. *Gokhrū*, a medicinal plant, is utilised as a food supplement in many nations. *Gokhrū*, an essential medicinal herb, comes in two types: *Chhota Gokhrū/Khār-i-Khasak Khurd* (*Tribulus terrestris*) and *Badā Gokhrū/Khār-i-Khasak Kalān* (*Pedaliū murex* L.) [3,4,8].

Khār-i-Khasak Khurd is used to stimulate hormone synthesis in both men and women. It is also the ripened, dried fruit of *Khār-i-Khasak Khurd*, which is used to cure dysuria and gonorrhoea [9,10]. *Gokhrū* is typically used to treat urinary and renal problems. It also has medicinal properties such as diuretic, aphrodisiac, analgesic, lithotriptic, cardiogenic, antibacterial, anti-inflammatory, anti-spasmodic, stomachic, larvicidal, appetiser, *Muwallid-i-Manī* (spermatogenic), *Mughalliz-i-Manī* (semen inspissant), *Mudirr-i-Hayḍ* (emmenagogue), *Musammin-i-Badan* (adipogenous), and *Kāsir-i-Riyāh* (carminative) [3,4,11]. *Gokhrū* composition and biological activity vary based on growth conditions, soil quality, and harvesting period. Many substances with diverse biological activities and chemical structures have been found in *Gokhrū* extract, including steroidal saponins, flavonoids, tannins, terpenoids, polyphenol carboxylic acids, and alkaloids. The content of *Gokhrū* extract depends on several parameters, including the extraction procedure and whether roots, leaves, or fruits were employed [12].

Gokhrū's beneficial physiological effects on sexual performance, coronary heart disease, preventing ischaemia/reperfusion injury to the heart, and controlling hypertension are all saponins. Nowadays, many sportsmen and non-athletes use products containing *Gokhrū* extracts to increase testosterone levels and strength performance. Athletes are drawn to *Gokhrū* due to its possible ergogenic effects on sports performance, which include enhancing strength, skeletal muscle hypertrophy, and muscle anabolism. *Gokhrū* is also known to work as a testosterone booster. It has been proposed that the saponins in *Gokhrū* are responsible for these effects. By triggering the body's natural synthesis of testosterone and luteinizing hormone (LH), the saponins in *Gokhrū* may have an androgenic/anabolic effect and promote muscle building. *Gokhrū* contains polyphenols and flavonoids, which act as antioxidants by scavenging free radicals in a concentration-dependent manner. *Gokhrū* can reduce inflammation by preventing muscle injury and oxidative damage [1]. Furostanol and spirostanol are the major saponin components identified in this plant, which is known for its medicinal properties [13]. The leaves and flowers have yielded several flavonoids in the past. Tetratriacontanyl octacosanoate and Heptatriaconten-4-one are two recently discovered chemicals from the fruits. Many diseases, including gonorrhoea, dysuria, spasmodic and sexual debility, etc., are treated with an infusion or decoction made from leaves, fruits, and roots [14].

The other type of *Gokhrū* is *Khār-i-Khasak Kalān* (*Pedaliū murex*), which is commonly known as large caltrop, *Dakni-Gokhrū*, *Hast-Chinghār*, and *Gokhrū*. It is also referred to in Sanskrit as *gaja-daunstraka*, *gokshura*, *Tri-Kantak* [3,11,15]. It is a member of the *Pedaliaceae* family. This plant, either whole or in pieces, is used as an antiseptic and to cure illnesses like the common cold and cough [16].

Athletes use *Bara Gokhrū* (*Pedaliū murex* L.) to improve their physical fitness and performance, in addition to using it in herbal remedies to treat illnesses. Numerous scientists have examined a variety of biologically active substances found in these plants (leaves, roots, fruit) extracts [8]. Because it contains diosgenin and vanillin constituents, which are responsible for the *Mudirr-i-Bawl* (diuretic), *Mufattit-i-Haṣāt* (lithotriptic), and emmenagogue properties, it is traditionally used to treat sexual and other reproductive disorders like impotence, *Suzāk* (gonorrhoea), infertility, and *Sur'a al-Inzāl* (premature ejaculation). It helps with vesicular calculi, heart disease, piles, leprosy, coughing, asthma, *Waram al Mathāna* (cystitis), *'Uṣr al-Bawl* (dysuria), *Kathra al-Iḥtilām* (increased nocturnal emission), and appetite. It is also used as a cooling agent in Unani and Ayurvedic medicine. Additionally, it has antibacterial, anti-ulcerogenic, anti-bilious, nephroprotective, hypolipidemic, *Muqawwī-i-Bāh* (aphrodisiac), antioxidant, *Hurqa al-Bawl* (burning micturition), and insecticidal properties [2,3,11,17,18].

MATERIAL AND METHODS

A bibliographic search was conducted to gather available information on *Gokhrū*, including its temperament, pharmacological investigations, actions, and therapeutic uses. Urdu translation of classical books referred to, including *Muḥīt-i-A'zam* of A'zam Khan, *Khaza'in al-Advia* of Najmul Ghanī and *Al Jami'li Mufradāt al-Advia Wa al-Aghzia* of Ibn al-Baitar. WHO international standard terminologies on Unani medicine, the publication by the Geneva World Health Organisation (2022), was used to describe the appropriate Unani terminologies. The different indexed journals were consulted for scientific and English names; the mineral names cited throughout the manuscript were checked against the currently accepted valid names in contemporary reference books, relevant articles, peer-reviewed indexed journals, and other published works on PubMed, ScienceDirect, and Scopus. The keywords used for the search included *Gokhrū*, *Khār-i-Khasak*, *Caltrops*, *Tribulus terrestris*, and *Pedaliū murex*.

Geographical Distribution

Gokhrū/Khār-i-Khasak (*Tribulus terrestris* and *Pedaliū murex*), originating from the Mediterranean region, is primarily found in tropical and subtropical regions of the cosmos. Southern USA, Mexico, South Africa, the Middle East, Pakistan, Sri Lanka, Vietnam, Southern Europe, Spain, Bulgaria, China, and India are just a few of the nations where it is abundantly available. Although it may grow in loamy and clayey soils, sandy soil is the ideal type for its growth. It is mostly cultivated as a weed on wasteland, such as pasture, arid, and roadside areas. In Kashmir, it is often found between 5400 and 11,000 feet above sea level. This plant is found all over India, although it is particularly prevalent in the North-West states, Bihar, Andhra Pradesh, Tamil Nadu, West Bengal, Madras, Gujarat, Awadh, and Rajputana [2,3].

Botanical descriptions

Small caltrop

Khār-i-Khasak Khurd is a tiny, annual herb with a weak stem that is branching and a member of the Zygophyllaceae family. This plant can grow up to 90 cm in length. The plant has fibrous, narrow roots that are 7–18 cm long and 0.3–0.8 cm in diameter. The roots are fractured, astringent, and yellow to light brown, with tiny nodules that have a fragrant smell. Similar to chickpea leaves, the opposite leaves have a fairly spherical shape, are pinnately complex, and have a short stalk with five to six pairs of leaflets that are 6 to 12 mm long. The silky, hermaphrodite, solitary axillary blooms grow from the leaf axils and have five broad yellow petals that range in width from 4 to 10 mm. This plant produces spinous, glabrous, five-cornered, hairy fruits that are covered in greenish-yellow yellow sharp thorns. The fruits are 1 cm in diameter and have five pairs of minutely muricate, woody cocci that contain two pairs of sharp spines, usually one pair longer than the other. The tips of the spines are about 0.5 cm long and nearly meet in pairs [2,8,19].

Large caltrop

Khār-i-Khasak Kalānis is a succulent, fleshy, annual glandular herbal plant with eight chromosomes (n=8) that grows to a height of 30 to 50 cm. It is also referred to as a huge caltrop and Bara Gokhrū. The simple, ovoid, reticulate, opposing, alternating leaves are 3.2–5.3 cm in length and 1-2.7 cm in width. The plant has white roots with a pleasant scent. The round, solitary, 2.5–3 cm long, bright yellow, axillary, hermaphrodite (bisexual) flowers have a short pedicle and five calyxes with gamopetalous corolla, 5 lobes, 4 stamens, didynamous, 5-celled ovules, 2 lobed styles, and stigma. The glabrous hairs make up the corolla tube. This plant produces indehiscent, meaty, four-angled fruits with conical horizontal trichomes from the angles. The fruits are pale yellowish-brown in hue. The plant has a strong stem. When the plant's leaves and stems are soaked in cold water, they form a thick, tasteless paste with significant therapeutic value. Beginning in June or July, germination thrives at temperatures between 25 to 30°C, and flowering and fruits take place in October or November [2,8].

Scientific classification

The scientific classification of both caltrops is shown in Table 1.

Table 1. Taxonomic classifications of <i>Tribulus terrestris</i> and <i>Pedaliium murex</i> [2]		
Taxonomy	<i>Tribulus terrestris</i>	<i>Pedaliium murex</i>
Kingdom	Plantae	Plantae
Phylum	Spermatophyta	Spermatophyta
Sub-phylum	Angiospermae	Angiospermae
Class	Dicotyledonae	Magnoliopsida
Order	Geraniales	Lamiales
Family	Zygophyllaceae	Pedaliaceae
Genus	<i>Tribulus</i>	<i>Pedaliium</i>
Species	<i>Terrestris</i>	<i>Murex</i>
Common name	Chota <i>Gokhrū</i>	Bara <i>Gokhrū</i>

Mutarādifāt (Vernacular names) of *Gokhrū*

The several vernacular names of both caltrops are shown in Table 2.

Table 2. Vernacular names of <i>Tribulus terrestris</i> and <i>Pedaliium murex</i>	
<i>Tribulus terrestris</i>	<i>Pedaliium murex</i>
Magrib wa Undlus: Ḥamsul ‘Amīr [4]	
Mārwārī: <i>Gokhrū Kāntī</i> [3]	
Persian: Khār-i-Khasak [3,20,21,22], Khārsa Gosha [4,21]	
Shīrazi: Khārsū Hūk [4]	Arabic: Khasak-i-Kabīr [23]
Arabic: Ḥasak [3], Zafratul ‘Ajūz [4,21], Akhrāsul ‘Ajūz [4], Khasak [4,20,22], Ḥamsul ‘Amīr [4,21]	
Ayurveda: Gokshura, Gokshuraka [18]	Ayurveda: Brihatgokshura, Trikantaka, Gokantaka, Bhakshantaka [18]
Bengali: <i>Gokhrū</i> [24], Gokhurī [25]	Bengali: Bad <i>Gokhrū</i> [23]
English: Small Caltrop [21,24,25], Land-Caltrops, Puncture Vine [18]	English: Large Caltrops [23]
Gujarātī: Bīthū <i>Gokhrū</i> [3]	Gujarati: Nahannagokharu, Mitha <i>Gokhrū</i> [23]
Hindi: <i>Gokhrū</i> [4,21], Chhota <i>Gokhrū</i> [25]	Hindi: Hast-Chinghār [3,4], Bara <i>Gokhrū</i> , Farīd Būṭī, Dakshini Gokshur [23]
Punjabi: Kurkundai [25]	Punjabi: <i>Gokhrū</i> Kalān [23]
Sanskrit: Gokshura, [24,25]	Sanskrit: Baṛihata Gokshur [23]
Suryani: Qṭādma, Qūṭīn, Qartū [4]	Sanskrit: Gochūra, Kantakī Achūra, Trikantak [11]
Tamil/Siddha: Sirunenunji, Nerinjil, Nerunjil [18]	Tamil/Siddha: Peru-neranji, Annaineringi [18]
Unani: Ḥusme, ‘Artib [4]	Unani: Khar-i-Khasak Kalān, <i>Gokhrū</i> Kalān [18]
Urdū: Chhota <i>Gokhrū</i> [24], Khār-i-Khasak Khurd [18]	Urdū: <i>Gokhrū</i> [23]

Description of the *Gokhrū* plant in Unani Medicine

It is the fruit of a prickly plant. The rainy season is when the tree grows. It was divided into two categories by Greek physicians: cultivated and wild. Wild *Gokhrū* grows well in both forests and deserts. Its tree spreads out across the ground. Its leaves resemble chickpeas, although they are larger. The branches lie on the ground and are prickly and spherical. There are thorns on the leaves. There is a sour flavour to the dew that collects on its leaves and their surfaces. The fruit, *Gokhrū*, is thorny and has a distinctive triangular shape. The blossom's colour is bright and small. Its leaves are large and thorny, with lengthy branches. The stem is thicker on top and thinner on the bottom.

It possesses hair-like, fine, clustered hairs. Its fruit is similar to the first variety but tougher, with a few thorns surrounding it and small seeds within. During famines, people consume bread made from green leaves, cooked vegetables, and fruit pulp^[3,4]. Gokhrū is a medicinal plant with two varieties: *Chhota Gokhrū* (*Tribulus terrestris*) and *Barā Gokhrū* (*Pedaliū murex* L.).

Chhota Gokhrū (*Tribulus terrestris*): It is known as *Gokhrū Kanti* in Marwari and *Beto Gokhrū* in Gujarati. This plant can be found in several nations, including South Africa, the Middle East, Pakistan, Sri Lanka, Spain, Bulgaria, and China. This plant can also be found all over India, including Bihar, West Bengal, North India, Madras, Awadh, and Rajputana. This plant expanded across the ground. They feature little yellow flowers and grass-like leaves. The little fruits are found in pairs. They are known as *Gokhrū Kanti* or *Ganti*. Each fruit has three or four exceedingly sharp thorns. It is known as *Khār-i-Khasak Khurd* or *Dakni Gokhrū*^[3].

Barā Gokhrū (*Pedaliū murex* L.) (*P. murex*):” Absolute Gokhrū” refers to the *Barā Gokhrū*. This *Gokhrū* is found in sandy areas in several nations, including Pakistan, Sri Lanka, Spain, Bulgaria, and China. It may also be found all over India, like Ceylon, Gujarat, Kathiawar, and Rajputana, along the sea coast. Its plant is small, measuring approximately a hand long. When its branches and leaves are mixed with water, a large amount of saliva is produced. Its root has the colour of yellow vermilion. The leaves are quite round and thick. It develops fruits that are typically one inch long. There is a thorn in each of their four corners. Their lowest section is rounded on all sides into a corner. The colour of its unripe fruit is green, yellow when ripe, and brown when dried. Its thorns are not as sharp. It’s known as *Khār-i-Khasak Kalān*. persons call it *Vilayati-Gokhar* and claim it is extremely cold; thus, it should be offered with caution to people who are cold-tempered. It is also known as *Hast-Chinghār* in Hindi because when it is put on an elephant’s foot, whenever it pricks an elephant’s foot, it begins to scream^[3].

Ajzā’ Must’mila (Parts used):

- Especially Fruit and root, the entire plant is also used^[25].

Mizāj (Temperament):

- The temperament is Murakkabul Quwā^[3,22] and *BāridYābis*(coldand dry) in the 1st degree^[3,4].
- BāridYābis* (cold and dry) in 2nd degree^[20].

Nafa’ Khāṣ (Main action)

- Mudirr-i-Bawl* (diuretic), *Mufattit-i-Ḥaṣāt* (lithotriptic) and *Muqawwī-i-Bāh* (aphrodisiac)^[3,4,22].

Af’āl (action)

The plant has *Mudirr-i-bawl* (diuretic), *Jālī* (detergent), *Muwallid-i-Manī* (spermatogenic), *Mufattit-i-Ḥaṣāt* (lithotriptic), *Rādi’* (repellent agent), *Mundij* (concoctive), *Muḥallil-i-Awarām* (anti-inflammatory), *Kathrat-i-Hayḍ* (Polymenorrhoea), *Muqawwī-i-Bāh* (aphrodisiac), *Nafkh-i-Mi’da* (flatulence), *Dāfi’-i-Tashannuj* (anti-spasmodic), *Muqawwī-i-Mi’da* (stomachic), *Mulayyin* (laxative/softener) properties^[3,4,11,18,20,21,22].

Isti’mālāt (uses)

The parts of the plant are used to treat various ailments such as *Sozāk /‘Uqūba* (gonorrhoea), *Waja’ al-Khāṣira* (low backache), *Kāsir-i-Riyāh* (carminative), *Qūlanj Rīhī* (gaseous large intestinal colic), *‘Uṣr al-Bawl* (dysuria), *‘Uṣr al-Tamth* (dysmenorrhoea), *Qulā’* (mouth ulcer), *Awrām-i-Litha* (gingivitis), *Waja’ al-Mathāna* (vesicular pain), *Kathra al-Iḥtilā* (nocturnal emesis)^[3,4,11,18,20,21,22].

Tarkīb-i-Iste’māl (method of administration) in various diseases:

- Patients are administered viscous extraction of *Barā Gokhrū* (fruits and leaves), which helps with sensory weakening^[3].
- When cloves, cardamom, sugar, and ghee are combined with *Barā Gokhrū* powder and administered to patients with milk, it helps them gain weight^[3].

Amrād-i-‘Ayn (diseases of the eye)

- The juice of *Gokhrū* mixed with honey can be applied topically to treat eye diseases. The fresh plant can be crushed and applied to the eye to relieve pain^[3,4].

Amrād-i-Dahn (diseases of the mouth cavity)

- The *Gokhrū* decoction and *Maḍmaḍa* (mouth wash) remove the gums’ foul smell while also reducing throat swelling and muscular stiffness^[3,4].

Amrād-i-Ṭiḥāl (splenic diseases):

- The juice of *Barā Gokhrū* leaves, which is beneficial for splenomegaly, is administered to patients^[3].

Amrād-i-Nizām-i-Bawl (diseases of the urinary system)

- For the treatment of dysuria, combine 5-6 g of dry *Gokhrū* with the same weight of Misri and drink it with water or milk^[3].
- Giving patients 2.5 to 7.5 tolas of *Chhota Gokhrū* (fruits and leaves) three to four times a day helps reduce chronic bladder inflammation^[3].
- It licked the *Gokhrū*, mixed it with honey, and then gave it goat’s milk to remove the stones^[3].
- Patients are administered *Barā Gokhrū* fruits and leaves of viscous extraction, which help with urinary blockage, bladder and urinary tract irritation^[3].

Amrād-i-Nizām-i-Tānāsul (diseases of the genital system)

- For the treatment of dysuria, semenorrhoea, and premature ejaculation, combine five to six grammes of dry *Gokhrū* with the same weight of Misri and drink it with water or milk^[3].
- Gokhrū* has a potent aphrodisiac effect when it is boiled three times in milk, dried three times, and then eaten as a powder^[3,4].
- The urinary tract irritation and gonorrhoea can both be treated with fresh leaf water^[3].
- A potent aphrodisiac effect can be obtained by repeatedly soaking chana in water containing *Gokhrū* leaves or fruits, then drying and consuming them^[3,4].
- Chhota Gokhrū* has potent aphrodisiac qualities and is given to patients in combination with *Satāwar*

(*asparagus racemosus*)^[3].

- It is used to treat gonorrhoea and general weakness. The patient was given 15 *raṭṭī* (1 *raṭṭī* = 125 mg) of caltrop powder along with black pepper and Misri^[3].
- Patients are administered *Barā Gokhrū* fruits and leaves of viscous extraction, which help with gonorrhoea and premature ejaculation^[3].
- When patients are given a decoction of caltrop fruits, their menstrual flow begins to normalise^[3].
- The sufferers' puerperium benefits from the *Barā Gokhrū* fruit decoction^[3].
- Chronic gonorrhoea can be cured by giving the patient a *Barā Gokhrū* decoction along with *jawakhār* (potassium carbonate)^[3].

Amrāḍ-i-Raham (disease of the uterus):

- When administered to patients, *Chhota Gokhrū* powder helps in the treatment of infertile ladies^[3].
- When the components of *Chhota Gokhrū* are soaked in water for two hours and subsequently filtered for the patient, it helps in the treatment of gonorrhoea^[3].

Animal poisons

- The 7 g *Gokhrū* fruits or juice is given to patients; it's useful for insect and snake bites^[4].
- The juice of *Gokhrū* is beneficial for scorpion bites^[4].
- The effects of lethal herbal medicines are neutralised when 9g of *Gokhrū* is consumed with alcohol^[4].

Miqdār-i-Khūrāk (dose):

The therapeutic dose of *Khār-i-Khasak* is mentioned as;

- 6-12 g^[20,22].
- 7-17.5 g^[4].

Maḍarrat (adverse effect): Excessive use can produce harmful effects such as *Amrāḍ-i-Ra's* (disease of the head)^[3,22], *Tihāl* (spleen)^[3,4,20].

Muslih (corrective): *Bādām* (*Prunus amygdalus*), *Ravghan Kunjad* (*Sesamum indicum*) and *Dūdh* (Milk), *Gulqand* (Rose petal jam)^[4,20,22].

Badal (substitute): *Tukhm-i-Kakrī* (*Cucumis sativa*),^[20] *Kāknaj* (*Physalis alkalangi*)^[3,4].

Murakkabāt (compound formulations)

In Unani Medicine, several compound formulations are prepared by adding both caltrops as an ingredient, as mentioned in Table 3.

Kīmiyāwi ajzā' (chemical constituents) present in *Gokhrū/ Khār-i-Khasak* plant

Extensive phytochemical studies on the plant (*Tribulus terrestris* and *Pedaliium murex*) confirmed the presence of several phytoconstituents such as alkaloids, flavonoids, saponins and glycosides, etc., as mentioned in Table 4.

Tribulus terrestris

The plant contains saponins that, when hydrolysed, create sapogenins such as diosgenin, gitogenin, chlorogenin, ruscogenin, 25-D-spirosta-3, and 5-diene. Flavonoids such as rutin, quercetin, kaempferol, kaempferol-3-glucoside, rutinoid, and tribuloside have been identified from the plant's leaves and fruits. Harman and harmine are two carboline alkaloids found in seeds. The herb has also been reported to contain Harmol. An unidentified saponin has been shown to effectively cure angina pectoris in patients with coronary heart disease. Several investigations have established its diuretic (more effective than furosemide), proerectile aphrodisiac, hypotensive, hypolipidemic, and hypoglycemic properties (40-67% in diabetic mice)^[18].

Pedaliium murex

The stems and fruits include flavonoids pedaliin (pedalitin 6-O-glucoside), diometin, dinatin, and their derivatives. The fruits contain nonacosane, tritriacontane, triacontanoic acid, sitosterol-beta-D-glucoside, rubusid acid, and luteolin as main ingredients. Leaves and fruits generate phenolic acids, which include caffeic, protocatechuic, p-coumaric and ferulic acids. Flowers provided dinatin, quercetin, and quercetin-7-glucoside. Aqueous extract from the fruit has been shown to reduce crystallisation in urinary lithiasis in vitro. Uric acid is 45% more soluble in aqueous extract than in pure water. The plant extracts indicate diuretic activity^[18].

Scientific studies of *Tribulus terrestris*

Diuretic activity

Its fruits and seeds contain significant amounts of nitrates and essential oils, which give it its diuretic qualities. Another explanation for the diuretic action is the high concentration of potassium salts. Ali *et al.* (2003) used strips of isolated Guinea pig ileum for the contractility test and a rat diuretic model to

Table 3. *Murakkabāt* (Compound) preparations containing *Khār-i-Khasak/Gokhrū*

S.N.	Compound formulations	Dose	Action and therapeutic uses	Reference
1.	Halwa Maghz Sar-i-Kunjashk	25-35 g	It has aphrodisiac and spermatogenic properties; it helps in the treatment of premature ejaculation, semenorrhoea and sexual debility.	26,27
2.	Jawārish Kāfūr	5-10 g	It has stomachic and carminative properties; it helps for the treatment of perverted digestion, flatulence and dyspepsia.	26
3.	Jawārish Zarūni Ambarī	5 g	It has been tonic for the kidney, liver and bladder properties; it is helpful for the treatment of weakness of the kidney, gout and urinary incontinence.	26

4.	Lubūb Al-Asrār	5-7 g with milk or water	It has aphrodisiac, tonic for the brain and heart properties; it helps in the treatment of spermatogenic disorders.	27
5.	Ma'jūn Alkalī	10 g	It has been a renal tonic, aphrodisiac and nervine tonic; it is helpful for the treatment of weakness of the kidney, urinary bladder and sexual debility.	26,27
6.	Ma'jūn Nishād Angaiz	6 g with milk or water	It has aphrodisiac, tonic for vital organs and nerve properties; it helps in the treatment of premature ejaculation, decreased libido, sexual debility and weakness of vital organs.	28
7.	Ma'jūn Sa'lab	7-12 g with milk	It has aphrodisiac and nervine tonic properties; it helps in the treatment of decreased viscosity of semen and semenorrhoea.	27
8.	Ma'jūn Supari Pāk	12-24 g with milk or water	It has aphrodisiac properties; it helps in the treatment of premature ejaculation, leucorrhoea, and conception of pregnancy.	27
9.	Qurs-i-Suzāk	4 tablets	It has a vulnerary agent, diuretic and anti-burning micturition properties; it helps in the treatment of urinary tract ulcer, burning micturition and retention of urine.	28
10.	Sufūf Bījband	12 g with milk	It has aphrodisiac and semen inspissant properties; it helps in the treatment of premature ejaculation.	27
11.	Sufūf Dārchīnī	12 g with milk	It has aphrodisiac properties; it helps in the treatment of leucorrhoea and semenorrhoea.	27

Table 4. Chemical compounds were identified in both caltrop plants.

<i>Khar-i-Khasak Khurd/Tribulus Terrestris</i>		
Class	Compound	Reference
Alkaloids	tribulusamide C, tribulusterine, tribulin A, harmine, harman, harmmol, tribulusimide C, terrestriamide, <i>N-trans</i> -coumaroyltyramine, <i>N-trans</i> -caffeoyltyramine, and terrestribisamide	29,30,31
Steroidal saponins	Spirostane, spirostanol, furostanol, furostane saponins, Protodioscin, protogracillin,	2,32
Steroidal sapogenins	diosgenin, gitogenin, chlorogenin and ruscogenin	32
Steroidal glycosides	neohecogenin glucoside of tribulosin, six-glycoside quercetin, eight glycosides of iso-hamnein, four glycosides of kaempferol	33
Flavonoids	kaempferol, kaempferol-3-glucoside, kaempferol-3-rutinoside, and tribuloside. Isorhamnetin, isorhamnetin-3-O-glu, isorhamnetin-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 with isorhamnetin	2,34,35
<i>Khar-i-Khasak Kalān/Pedalium Murex</i>		
Flavonoids (fruits, leaves and flowers)	Pedalitin, Diosmetin, Dinatin, Quercetin, Kaemoferol, Luteolin.	36,37,38
Steroids/saponins (fruits)	β-sitosterol d-glucoside, Sitisterol, Diosgenin.	39,40
Terpenoids (fruits)	Rubusic acid, Lupeol acetate, Ursolic acid	41,42
Alkaloids (fruits)	Isatin (2,3-Dioxo-2,3-dihydroindole, 2,3-Diketoinoline, 2,3-Dioxoindoline, 2,3-Indolinedione, o-Aminobenzoylformic anhydride)	43
Hydrocarbons (fruits)	Hexatriacontanoic acid, Hentriacont-yllic Acid, Heptatriacontan-4-one, Tetratriacontanyl octacosanoate	40
Phenols (fruits)	Vanillin, Caffeic Acid, Ferulic acid, Protocatechuic acid.	40,44,45
Amino acid (fruits)	Threonine, Aspartic Acid, Glutamic Acid, Histidine	43

test the *Tribulus terrestris* (TT) aqueous extract made from its fruit and leaves. A positive diuresis was produced by the TT aqueous extract at an oral dosage of 5 g/kg, which was marginally greater than that caused by furosemide. Urine's concentrations of sodium and chloride increased. The diuretic action of TT extract, together with the enhanced tonicity of the

smooth muscles it produced, assisted in the passage of stones along the urinary system [46]. Chhatre *et al.* (2012) tested the diuretic efficacy of various TT fruit extracts, including aqueous, methanolic, Kwatha high strength, Kwatha low strength, and Ghana powder, on rats. Kwatha high strength demonstrated a diuretic effect equal to the reference standard frusemide, as

well as an extra potassium-sparing benefit ^[47]. TT's diuretic activity makes it an effective anti-hypertensive medication.

Aphrodisiac activity

The impact of *Tribulus terrestris* (TT) extract on the rat primary spermatocyte was examined by Jashni *et al.* (2012). While TT affects the testis spermatocyte, the researchers discovered that it can likely balance the activities of the male reproductive system and be utilised to treat male infertility. According to studies, the saponins in *T. terrestris* plants cause the pituitary gland to secrete more luteotropic hormone. Because luteotropic hormone is a unique stimulant for testosterone production, it can enhance sexual performance by increasing libido, sperm production, and erectile function. One of the saponins in *Tribulus terrestris* that has a spermatogenesis-stimulating function is furostanol. The amount and quality of sperm are greatly increased by this substance ^[48]. The impact of TT aqueous extract on the reproductive system of mature albino female mice was investigated by Adaay and Mosa (2012). The researchers found that TT significantly increased the diameter of mature follicles, the number of developing follicles, the height of endometrial lining cells, and the width of endometrial glands at both dose levels (100 and 200 mg/kg/day) ^[49]. According to Adaikan *et al.*, oral administration of TT extract at 2.5, 5, and 10 mg/kg body weight for eight weeks produced a pro-erectile impact on the smooth muscle of the rabbit corpus cavernosum *ex vivo*. Nitroglycerine significantly relaxed the smooth muscle tissue of the corpus cavernosum by 24%. Similarly, when the rabbits received the TT treatment mentioned above, a 10% relaxation was observed with both acetylcholine and electrical field stimulation. Its claims as an aphrodisiac may be explained by the increased release of nitric oxide from the endothelium and nitrergic nerve endings, which results in the greater relaxing effect seen ^[50]. To treat sexual dysfunction in male rats, Singh *et al.* assessed the acute and recurrent administration of lyophilised aqueous extract of the dried fruits of TT (LAET) at doses of 50 and 100 mg/kg of body weight as a sexual enhancer. Sexual behaviour improved with the LAET treatment in a dose-dependent manner; this effect was more noticeable after long-term LAET administration. Serum testosterone levels were also found to have significantly increased. These results support the long-standing practice of using TT as a sexual enhancer to treat male sexual dysfunction ^[51].

Immunomodulatory activity

A dose-dependent increase in phagocytosis was seen by saponins extracted from *Tribulus terrestris* (TT) fruits, suggesting that they stimulated a nonspecific immune response. A substantial dose-dependent rise in humoral antibody titre and a delayed type hypersensitivity response were observed in an alcoholic extract of the entire TT plant, suggesting an elevated specific immune response ^[52].

Absorption enhancer

Because *Tribulus terrestris* (TT) contains saponins, its ethanolic extract improved the absorption of metformin hydrochloride, a class III medication according to the Biopharmaceutics Classification System (BCS), in the everted sac technique utilising goat intestine ^[53].

Hypolipidemic activity

The hypolipidemic effect of the *Tribulus terrestris* (TT) fruit aqueous extract was assessed in Wistar albino rats. The extract was shown to reduce cholesterol-induced hyperlipidaemia at a dose of 580 mg/kg, increasing blood levels of high-density lipoprotein (HDL) and decreasing triglycerides, cholesterol, low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), and atherogenic index (AI). The presence of phenolic compounds may cause hypolipidemic activity by increasing the activity of lipoprotein lipases in the muscles and decreasing that of adipose tissues. This suggests that the muscles use plasma triglycerides for energy production rather than for storing energy ^[54].

The lipid profile and vascular endothelium of the abdominal aorta in New Zealand rabbits given a diet high in cholesterol were examined to determine the pleotropic effect of TT at a dose of 5 mg/kg/day for 8 weeks. The herb was found to dramatically reduce the serum lipid profile, reduce endothelial cell surface damage and ruptures, and partially restore endothelial dysfunction brought on by hyperlipidaemia ^[55].

The preventative and therapeutic effects of TT saponins on diet-induced hyperlipidaemia in mice were investigated. Serum total cholesterol (TC) and LDL cholesterol levels decreased, indicating the preventative impact. Additionally, it raised the liver's SOD activity while lowering TC and triglycerides. By considerably lowering the liver and serum TC, it demonstrated a therapeutic effect ^[56].

Hepatoprotective activity

In *Oreochromis mossambicus* fish, the *Tribulus terrestris* (TT) extract (250 mg/kg) demonstrated an impressive hepatoprotective effect against acetaminophen-induced hepatotoxicity. When freshwater fish were treated with TT extract (250 mg/kg) for acetaminophen-induced toxicity, the raised biochemical parameters and decreased level of reduced glutathione enzymes returned to normal ^[57].

Analgesic activity

Tribulus terrestris (TT) was investigated in male mice using the tail flick test and formalin. A dose of 100 mg/kg of TT methanolic extract exhibited an analgesic effect, according to the study. The TT extract's analgesic action could be mediated centrally or peripherally. The extract had a greater effect than acetylsalicylic acid (aspirin) and a lower effect than morphine in both tests. The analgesic effect of TT is not thought to be mediated by opioid receptors because pretreatment of rats with the opioid receptor antagonist naloxone did not alter the extract's analgesic effect in either test. However, more research is needed to determine the various processes underlying TT's analgesic action. In the stomach of rats, TT has a lower gastric ulcerogenicity than indomethacin, according to the findings of ulcerogenic research ^[58].

Antispasmodic activity

The plant lyophilised saponin mixture significantly reduced the peristaltic motions of the prepared rabbit jejunum in a dose-dependent manner. According to these findings, the saponin mixture might help with colic or smooth muscle spasms ^[59].

Scientific studies of *Pedaliium murex*;

Nephroprotective activity

According to Shelke *et al.* (2009), an ethanolic extract of *P. murex* fruits is a superior nephroprotective to the common medication Cystone when it comes to preventing kidney damage in Wistar rats from cisplatin and cadmium chloride^[60]. It was administered orally at a dose of 250 mg/kg during the experiment. Significant alterations in body weight, blood creatinine, and urea level showed that the extract considerably reduced the cisplatin-induced nephrotoxicity. Another study indicated that an aqueous fruit extract was beneficial against renal damage caused by cadmium chloride, with notable alterations in kidney lipid peroxidation, glutathione, catalase, urine to serum creatinine ratio, blood urea nitrogen, and urine protein^[61].

Antiproliferative activity

According to reports, *Pedalium murex* fruits are high in vitamin C and flavonoids, two powerful antioxidants that can reduce oxidative cell damage and provide protection against all phases of carcinogenesis^[62]. The fruits have antiproliferative properties, and research has shown that a methanolic fruit extract at a greater concentration (1000 µg/ml) significantly inhibited the growth of the A549 lung cancer cell line, lowering the cell viability %^[63]. The presence of alkaloids in *P. murex* fruits may also be the cause of the antiproliferative effect.

Antioxidant activity

According to Patel *et al.* (2011), the ethyl acetate fraction derived from *P. murex* fruits possesses strong free radical scavenging properties, suggesting its significance for human health^[64]. In vitro antioxidant activity experiments demonstrate that the ethyl-acetate fraction has a higher reducing power and antioxidant capacity than other fractions. Additionally, it is said to have a strong ability to scavenge the activity of a variety of free radicals, including DPPH, nitric oxide, hydrogen peroxide, and hydroxyl radicals^[65].

Anti-inflammatory and analgesic activity

Ethanolic extract of *P. murex* fruit is reported to have anti-inflammatory and analgesic effects^[66]. Its anti-inflammatory effect was proved by the experiment conducted in Lambda-carrageenan induced paw oedema in Wistar albino rats at a dose of 200 and 400 mg/kg, P.O. These doses resulted in significant anti-inflammatory activity from 15 to 180 min as compared to the positive control Diclofenac sodium^[67].

Antimicrobial activity

It has been stated that *P. murex* roots, leaves, fruits, and flowers all have antibacterial properties. According to Prabhakaran *et al.* (2016), ethyl acetate extract of flowers is effective against human pathogenic bacteria, including *Salmonella typhi*, *Escherichia coli*, *Enterococcus faecalis*, *Bacillus cereus*, *Bacillus subtilis*, and *Lactobacillus*^[68]. While methanolic extracts of fruits and leaves are known to be active against bacterial pathogens such as *Streptococcus pyogenes*, *Enterococcus faecalis*, and *Klebsiella pneumoniae*^[14,69,70], ethanolic extracts of fruits have demonstrated action against the fungal pathogen *Trichophyton rubrum*^[71].

Aphrodisiac activity

It is commonly known that *Pedalium murex* has aphrodisiac properties. Fruit extract in ethanol is said to be an effective

aphrodisiac that promotes conception. However, male rat models at varying doses of extract, namely 200 and 400 mg/kg, P.O., have demonstrated that petroleum ether extract of fruits can also improve aphrodisiac activity and treat ethanol-induced germ cell damage and sterility^[72]. In rats, it markedly improved sperm motility, litter size, total body weight, percentage of pregnancy, mating, and mounting behaviour. Additionally, it was found to considerably raise testosterone, total cholesterol, and total protein^[17]. Histopathological analysis of the testes of the rats treated with 400 mg/kg, P.O. of the extract showed that the luminal spermatozoa and germinal cells were significantly restored and recovered^[73].

Insecticidal activity

According to reports, *P. murex* root extract exhibits insecticidal action against *Spodoptera litura* larvae in the third, fourth, and fifth stages. At an extract concentration of 8%, the highest death rate was observed^[74]. Food consumption index, growth rate, estimated digestibility, and the efficiency of swallowed and digested food conversion were all decreased. This could be because the extract contains tannin and saponins^[14,75].

CONCLUSION

In conclusion, the *Khār-i-Khasak Khurd* and *Khār-i-Khasak Kalān* plants are utilised in a variety of Unani products and formulations to treat a range of illnesses because of their well-being in therapeutic phytochemical elements. The *Khār-i-Khasak Khurd* plant is mostly used to treat kidney and urogenital problems, including gall-bladder and renal stones, according to published pharmacological research. The *Khār-i-Khasak Kalān*, on the other hand, possesses aphrodisiac properties and is mostly used to treat sexual issues in both males and females, including erectile dysfunction, premature ejaculation, impotence, and infertility. Both plants have several characteristics and are used to treat a variety of other illnesses, including cough, skin conditions, heart problems, and asthma, since they contain similar chemical ingredients, and also act as an anticancer, aphrodisiac, antimicrobial, anti-inflammatory, antioxidant, nephroprotective, antidiabetic, and antifungal agent. Both of these plants have substantial therapeutic significance and may be studied further to create new herbal and Unani remedies for human health.

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