

A COMPREHENSIVE REVIEW ON GOKSHUR (TRIBULUS TERRESTRIS LINN) ACCORDING TO AYURVEDIC AND MODERN ASPECT

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ABSTRACT

Gokshur (Tribulus terrestris Linn.) belonging to the family Zygophyllaceae is found to be growing in subtropical areas around the world. In Ayurveda, *Gokshur* is commonly used as Rasayan (Rejuvenating), Vrisya (Aphrodisiac), and mutral (Diuretic) drug. *Gokshura* contains a number of bioactive chemicals, including saponins, flavonoids, glycosides, alkaloids, tannins and phenolic acid, flavonol glycosides, steroidal. It possesses higher wound healing, diuretic and uricosuric effects. The experimental animal models have revealed diuretic, aphrodisiac, antiurolithic, immunomodulatory, antidiabetic, hypolipidemic, cardio tonic, hepatoprotective, anti-inflammatory, analgesic, antispasmodic, anticancer, antibacterial,

anthelmintic, and anticarcinogenic activities. These studies prove the effect of *Gokshur* on urogenital, musculoskeletal, nervous and cardio-vascular system. This review is an attempt to compile all the information about *Gokshur* mentioned in *Ayurveda* as well as modern science. The present study gives a detailed focus on its botanical details, phytochemistry therapeutic importance and its pharmacological studies.

KEYWORDS: *Gokshura*, *Tribulus terrestris*, ayurvedic, phytochemistry, pharmacology.

INTRODUCTION

Gokshur (Tribulus terrestris Linn.), a deciduous herb of the Zygophyllaceae family, is an important herb from Indian and Chinese 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.^[1] *Gokshur* is mainly planted in the Mediterranean and in sub-tropical regions such as India, China, South America, Mexico, Spain, Bulgaria, and Pakistan. It is a small, prostrate, 10–60 cm high, hirsute or silky hairy shrub. Since the past decades, some plants have been playing important role in disease curing along with artificial medications commonly called medicinal plants. In Ayurveda, *Charaka* identified it as the best drug for *mutrakrichha* (difficulty in urination), as well as *Shotha* (inflammation). The root of *Gokshur* the important ingredients of *Dashamula* spreads on ground and growing widely with aroma of sugarcane. Mainly two varieties mentioned – *Brihat* (*Pedalium murex*) and *Laghu* (*Tribulus terrestris* Linn). According to *Shivadasa Sen*, its bigger variety is best. *Gokshura* is available all over India especially north and south India. The synonyms of *Gokshura* emphasise its diversity.^[2] Leaves are similar to those of gram plant. Many researchers focused on the benefit of *Gokshur* and its effects on female reproductive organs.^[3] *Tribulus terrestris* extract contains many compounds such as alkaloids, flavonoids oil, saponins, resins and nitrates.^[4,5] *Gokshur* is without significant side effects if used at the safe range ‘250-750 mg/day’.^[6] The biological properties of *Tribulus terrestris* extract include diuretic properties, increased release of nitric oxide from endothelium and nerve endings; it relaxes smooth muscles and increases angiotensin converting enzyme (ACE) inhibition.^[7] It also has antioxidant properties.^[5,8] It possesses antihypertensive activity.^[9,10] It is used in folk medicine as tonic, aphrodisiac, analgesic, astringent, stomachic, anti-hypertensive, diuretic, lithontriptic and urinary anti-infective.^[11] The main constituents of *T. terrestris* are saponins, diosgenins, alkaloids and amides.^[12-14] Thus *Gokshur* has multidimensional therapeutic activities due to its vast range of phytochemical constituents and pharmacological activities. Therefore the present study is an effort to gather all information about *Gokshur* according to Ayurvedic and modern aspect, with special reference to its phytochemical and pharmacological activities and guide for future research.

Ayurvedic aspect of gokshur

Gokshur included in following gana (group)

1. **Charka samhita:** Mutravirechaneeya, shodhhar, krumighna, anuvasnopag.^[15]
2. **Sushrut samhita:** Vidarigandhadi, veertarvadi, laghupanchamul, kantakpanchamul, Vatashmaribhedan.^[16]

Gokghur has been included in Nighantus in the Following Vargas

1. **Bhavprakash nighantu, Shodhala nighantu, Shaligrama nighantu:** Guduchyadi Varga.^[17]
2. **Dhanvantari nighantu:** Guduchyadi varga.^[18]
3. **Madanpal nighantu:** Abhayadi varga.^[19]
4. **Aadarsh nighantu:** Laghugokshuradi varga.^[20]
5. **Kaiyedeve nighantu:** Oshadadi varga.^[21]
6. **Raja nighantu:** *Shatahvadi varga.*^[23]
7. **Priya nighantu:** *Haritakyadi varga.*^[24]

Etymology^[20]

Gokshur-Literally the word gokshur means, the spines of the fruit that injures a grazing cow or cattle.

Tribulus-is the latin word indicating trouble, pointing to te three-projecting spikes of fruit; in latin ‘terrestris’ means ‘on land’.

Thus, meaning of Tribulus terrestris together can be understood as three spike fruit growing on land.

Synonyms

Ikshugandhi- smell of sugarcane

Gokantak- Prickle causes pain to cattle

Trikantak- Fruits bear three spines

Vanasringara- Thron in the garden

Palankasha- Easily digest the meat

Shwadanshra-Thron prick causes pain equivalent to that of dog bite

Swadukantaka- Sweet thorn

Chanadruma- Leaves like horse gram

Synonym of Gokshura (Tribulus terrestris Linn.) in different Nighantus: in different Nighantus

Bhav prakash Nighantu:^[17] Bhakstaka, gokantak, iksugandhika, ksuraka, palamkasa, svdramastra, svadukantaka, trikantaka, vanasrngata.

Dhanwantar Nighantu:^[18] Gokantak, swadukantak, gokshur, gokshurak vakshak, vakshatak, kantakatri

Kaidev Nighantu:^[21] Gokantak, kantaphala, bhakstaka, swadukantak, swadanstak, byaladanstra, goksharu, gokshur, kshur, saraṅ, shalasringat, trikantak, trik

Madanpala Nighantu:^[19] Gokantak, kantaphala, swadukantak, byaladanstra, gokshur, saraṅga trikantak, trik, khurak, bhākṣyantaka, trikantak, vyaladamstraka, svadamstra, sthulasrngata.

Shaligram nighantu:^[22] Bhākṣyantaka, iksugandhika, vanaṣrngata, lamkaśa, śaranga, vakshatak, khurango, gokshurak khurak, vadra kantik, trik, trikantik, saraṅga, gokshur, gokantak, kantaphala, bhakhhar swadanstak, byaladanstra

Raj Nighantu:^[23] Bhadrakantaka, duscakrama, vyaldantra, mahanga, gokhuraka, kantah, bahukantaka, gokantaka, palankasa, bhaksataka, sthal-srngataka, iksu gandha, trikantaka, sadanga, ksura, kantaphala, ksudra-ksura, canadrumqa, van-srngataka, svadukantah.

Priya Nighantu:^[24] Swadanstak, goksharu, vanaṣrngata.

Sankar Nighantu:^[25] Bhākṣyantaka Nighantu

Aadarsh:^[20] Swadanstak, gokshur, gokshurak, śaranga swadamstra, vanaṣrngata .

Vernacular Names^[17]

Hindi- Gokhru, chota Gokhru, hatheechikar.

Gujrati-Nhana Gokhru, bedha gokharu.

Marathi- Sarate, kate gokhru

Sanskrit- Gokshur, trikantik, swadukantik, chandrum, ekshugandhika, kshvdanshtra

Tamil- Nerinjil, nerunjee.

Telugu- Palleru mullu.

Bengali- Gokshur, gokhuri.

Punjabi- Makhda, makhar.

Kannad- Neglu, neggillumullu

English name: Caltrop

Latin name: *Tribulus terrestris* Linn.

Types^[26]

Laghu goksura (*Tribulus terrestris* Linn)

Brhad goksura (*Pedaliium murex* Linn)

Rasapanchaka of Gokshur^[27]**Rasa:** Madhura**Guna:** Guru, Snigdha**Virya:** Shita**Vipaka:** Madhura**Doshakarma:** Tridosashamak (alleviates Tridosha) mainly Vatapittashamaka (alleviates Vata and pitta)**Karma**

Balya (increases strength), Vatahara (alleviates Vata), mootrala (diuretic), Kaphahara (alleviates Kapha), Rochana (orexogenic), Dipana(stimulates Agni), Vṛishya (aphrodisiac), Ashmarihara (removes urinary stone), Bruhana (nourishing), Bastishodhana (cures bladder ailments), shothahara (cures inflammation), Shwasahar (useful in dyspnea), Kasahar (useful in cough), Hridroghar (cures Cardiac disorders), Pramehahar (useful in Diabetes), Daha nashak (alleviates burning sensation), Arsha (useful in piles) and Rasayan (rejuvenating).

Properties of Gokshura Mentioned In the Following Nighantus**Bhavprakas nighantu:**^[17] Rasa- Madhura, Guna- Laghu, Ruksha, Virya-Sita**Kaidev Nighantu:**^[21] Rasa- Madhura, Virya-Sita**Madanpala Nighantu:**^[19] Rasa- Madhura, Virya-Sita**Shaligram nighantu:**^[22] Rasa- Madhura, Virya-Sita**Raj Nighantu:**^[23] Rasa- Madhura, Virya-Sita**Priya Nighantu:**^[24] Rasa- Madhura, Virya-Sita Sankar Nighantu[9]: Rasa- Madhura, Virya-Sita**Habitat:**^[17]

It is found in all over *India* also *Bangal, Bihar, Uttar Pradesh, Rajputna, Madras* and all warm regions of both hemispheres.

Traditional Uses

Gokshur is used in folk medicines as a tonic, aphrodisiac, palliative, astringent, stomachic, antihypertensive, diuretic, lithotriptic, and urinary disinfectant. The dried fruit of the herb is very effective in most of the genitourinary tract disorders. It is a vital constituent of Gokshuradi Guggul, a potent Ayurvedic medicine used to support proper functioning of the genitourinary tract and to remove the urinary stones. Gokshur has been used for centuries in

Ayurveda to treat impotence, venereal diseases, and sexual debility. In Bulgaria, the plant is used as a folk medicine for treating impotence. In addition to all these applications, the Ayurvedic Pharmacopoeia of India, Gokshur attributes cardiogenic properties to the root and fruit. In traditional Chinese medicine, the fruits were used for treatment of eye trouble, edema, abdominal distension, emission, morbid leukorrhea, and sexual dysfunction. Gokshur is described as a highly valuable drug in the Shern-Nong Pharmacopoeia (the oldest known pharmacological work in China) in restoring the depressed liver, for treatment of fullness in the chest, mastitis, flatulence, acute conjunctivitis, headache, and vitiligo. In Unani medicine, Gokshur is used as diuretic, mild laxative, and general tonic.^[28]

Therapeutic Uses of Gokshura in Different Nighantus

Bhav prakash Nighantu:^[17] Asmari, Hridroga, Mutral, Shwas, Kasa, Arsha

Dhanvantari Nighantu:^[18] Mutrakrichha, Hridroga, Prameha, Shoola (pain), Tridosashamak, Dipak.

Kaidev Nighantu:^[21] Mutrakrichha, Asmari, Hridroga, Prameha, Shwas, Kasa, Bastidosha, Vrishya, Balya.

Madanpal Nighantu:^[19] Mutrakrichha, Hridroga, Prameha, Shwas, Kasa, Vataroga.

Shaligram Nighantu:^[22] Mutrakrichha, Asmari, Prameha, Daha nashak

Raj Nighantu:^[23] Vrishya, Mutrakrichha, Asmari, Prameha, Rasayana

Nighantu Adarsha:^[20] Vrishya, Mutrakrichha, Asmari, Hridroga, Prameha, Swas, Pradar, Rasayana.

Important Formulations

Gokshuradi Guggulu, Trikantak Ghruta, Drakshadi Choorna, Rasayana Choorna, Gokshuradi Kwatha, Dashamoola Kwatha.

Modern aspect of gokshur

Taxonomical Classification^[29]

Kingdom: Plantae

Division: Phanerogams

Subdivision: Angiospermae

Class: Dicotyledonae

Subclass: Polypetalae

Series: Disciflorae

Order: Giraniales

Family: Zygophyllaceae

Genus: Tribulus

Species: terrestris Linn.

Botanical Description^[30]

Small herb with 2 to 3ft of height.

Branches: Spread from all the sides.

Leaves: Like that of gram plant.

Flowers: Small, yellow colored with five petals.

Fruits: Slightly pentagonal having 2–3 sharp thorns.

Seeds: Many, contain scented oil.

Roots: 10-13 cms long smoky with slightly strong smell and sweet. Flowering occurs in autumn followed by fruiting.

External Morphology

Root: Occurs in pieces, 7-18 cm long and 0.3-0.7 cm in diameter, cylindrical, fibrous, frequently branched, bearing a number of small nodules, fracture fibrous, odor aromatic, taste sweetish and astringent. Transverse section of primary root shows a layer of epidermis followed by 4-5 layers of thin walled parenchymatous cortex. Endodermis is distinct, pericycle enclosing diarchy stele. In mature root, cork is 4-6 layered, cork cambium single layers followed by 6-14 layers of thin walled parenchymatous cells with varying number of fibers distributed throughout. Xylem parenchyma with simple pits and reticulate thickening and xylem fibers few. Starch grains and rosette crystals of calcium oxalate are present in secondary cortex, phloem and medullar ray cell; few prismatic crystals are also present in xylem ray cells.

Fruit: Fruit is stalked, globosely, possessing fire woody wedge shaped cocci, covered with two pairs of short spines, one pair larger than the other. Microscopically the pericarp is differentiated into epicarp, mesocarp and endocarp. Outer surface of epicarp is covered by non glandular trichomes. The endocarp is 3-4 layered, composed of sclerenchymatous cells containing prismatic crystals of calcium oxalate. Vessels have simple pits and some show helical thickening. Fibers are lignified, linear, along with tapering ends.

Dosage: Fruit Powder: 2.5 to 5 gms.

Decoction: 60 – 100 ml.

Parts use: Fruit, root, whole plant.

Phytochemical Composition

The preliminary phytochemical study of *Tribulus terrestris* revealed the presence of saponins, flavonoids, glycosides, alkaloids, and tannins.^[31] isolated and characterized three new compounds, terretribisamide, 25R-spirost-4-en-3, 12dione, and tribulusterine, together with 10 known compounds, N-pcoumaroyltyramine, terrestriamide, hecogenin, aurantiamide acetate, xanthosine, fatty acid ester, ferulic acid, vanillin, p-hydroxybenzoic acid, and β sitosterol, from the dried fruits of *Tribulus terrestris* T.^[32] The alkaloids present are harmane and norharmane. The β -carboline alkaloid, tribulusterine, is present in minor quantities in fruits.^[33] Gas chromatography-mass spectrometry analysis of methanolic extract of the whole plant of *Tribulus terrestris* Linn revealed the presence of α Amyrin as the major constituent and seven minor constituents, which are 3,7,11,15 tetramethyl-2-hexadecen-1-ol, nhexadecadienoic acid, hexadecadienoic acid ethyl ester, phytol, 9,12octadecadienoic acid, 9,12,15octadecatrienoic acid, and 1,2benzenedicarboxylic acid dioctyl ester. Sterols such as β -sitosterols and stigmasterols were also found to be present.^[34]

Steroidal saponins

Spirostanol and furostanol saponins are considered the most characteristic chemicals in TT. To date, 108 kinds of steroidal saponins have been isolated from TT (1–108). Among them, there are 58 kinds of spirostane saponins (1–58) and 50 kinds of furostane saponins (59–108). The steroidal saponins, such as protodioscin and protogracillin, are thought to confer TT unique biological activities.

Flavonoids

The flavonoids of TT are mainly derivatives of quercetin, kaempferol and isorhamnetin. Quercetin (109), isoquercitrin (110), rutin (111), quercetin-3-O-gent (112), quercetin-3-O-gentr (113), quercetin-3-O-rha-gent (114), quercetin-3-O-gent-7-O-glu (115) are flavonoids with quercetin as the basic parent structure. Isorhamnetin (116), isorhamnetin-3-O-glu (117), isorhamnetin-3-O-gent (118), isorhamnetin-3-O-rutinoside (119), isorhamnetin-3-O-gentr (120), isorhamnetin3,7-di-O-glu (121), isorhamnetin-3-O-p-coumarylglu (122), isorhamnetin-3-O-gent-7-O-glu (123), isorhamnetin-3-O-gentr-7-O-glu (124) are flavonoids with isorhamnetin as the basic parent structure. Kaempferol (125), kaempferol-3-O-glu (126), kaempferol-3-O-gent (127), kaempferol-3-O-rutinoside (128), kaempferol-3-O-gent-7-O-glu (129), tribuloside (130) are flavonoids with kaempferol as the basic parent structure.

Alkaloids

Tribulusamide C (131), tribulusterine (132), tribulusin A (133), harmine (134), harman (135), harmmol (136), tribulusimide C (137), terrestriamide (138), N-transcoumaroyltyramine (139), N-trans-caffeoyltyramine (140), terretribisamide (141) are the main alkaloids isolated from the stems, leaves, and fruits of TT. The nuclear mainly belong to β -carboline alkaloids and amide alkaloids.

Others

Other components of TT include organic acids, amino acids and other substances. Organic acids isolated from TT are benzoic acid, vanillic acid, 2-methyl benzoic acid, ferulic acid, succinic acid, palmitic acid monoglyceride, succinic acid, docosanoic acid, Tribulus acid and others. The main amino acids are alanine and threonine. In addition, TT also contains 4-ketopinoresinol, uracil nucleic acid, coumarin, emodin, and physcion.

Pharmacognostical Studies^[35]**a) Macroscopic**

Drug consists of root, 7-18 cm long and 0.3-0.7 cm in diameter, slender, cylindrical, fibrous, frequently branched bearing a number of small rootlets, tough, woody and yellow to light brown in colour, surface becomes rough due to presence of small nodules, fracture fibrous, odour aromatic, taste, sweetish and astringent.

b) Microscopic

Transverse section of primary roots show a layer of epidermis followed by 4-5 layers of thin-walled parenchymatous cortex, endodermis distinct, pericycle enclosing diarch stele, in mature root, cork 4-6 layered, cork cambium single layered followed by 6-14 layers of thin-walled parenchymatous cells with varying number of fibres, distributed throughout, some secondary cortex cells show secondary wall formation and reticulate thickening, fibres found in groups resembling those of phloem, secondary phloem divided into two zones, outer zone characterised by presence of numerous phloem fibres with a few sieve tubes slightly collapsed, inner zone frequently parenchymatous, devoid of fibres often showing sieve tubes and companion cells, phloem rays distinct, few cells get converted into fibres in outer region, cambium 3-5 layered, wood composed of vessels, tracheids, parenchyma and fibres and traversed by medullary rays, vessels scattered, arranged in singles or doubles towards inner side, in groups of three to four on outer side having bordered pits, tracheids long, narrow with simple pits, xylem parenchyma rectangular or slightly elongated with simple pits

and reticulate thickening, xylem fibres few, trachieds elongated with simple pits, medullary rays heterogenous, 1-4 cells wide, starch grains and roseGokshure crystals of calcium oxalate present in secondary cortex, phloem and medullary rays cells, few prismatic crystals also present in xylem ray cells.

Identity, Purity and Strength

Foreign matter Not more than 2 per cent, Appendix 2.2.2.

Total Ash Not more than 13 per cent, Appendix 2.2.3.

Acid-insoluble ash Not more than 3 per cent, Appendix 2.2.4.

Alcohol-soluble extractive Not less than 4 per cent, Appendix 2.2.6.

Water-soluble extractive Not less than 10 per cent, Appendix 2.2.7.

Therapeutic Uses^[36]

The medicinal properties of Brhad Goksura (*Pedalium murex* Linn.) are almost the same as those of Laghu Goksura (*Tribulus terrestris* Linn.) The fresh leaves and stems, briskly agitated in cold water, speedily convert it into a thick mucilage, nearly of the consistence of the white of a raw egg, inodorous and tasteless. An infusion of fresh leaves and stems is used as an esteemed remedy for treating gonorrhoea and dysuria. The juice of the fruits is useful as an emmenagogue. It is employed in puerperal diseases, and to promote the local discharge. The leaves are used as a curry in splenic enlargements. The decoction of the roots is used as an antibilious remedy. It is very useful drug in kidney and urinary troubles specially calculus and dysuria and their allied complications. The fruits are antispasmodic, aphrodisiac and emmenagogue; their decoction is used for the diseases for which the mucilaginous infusion of the leaves is suggested. The juice of the fruits is given in puerperal diseases, and for promoting lochial discharge. A pint of an infusion of the seeds is given daily in spermatorrhoea, impotence and incontinence of urine.

Medicinal Uses

Tribulus terrestris Linn has been used as a diuretic, tonic and aphrodisiac, urinary disorders, hyperuricemia, and impotence. Tribulus has been shown to enhance sexual behaviour in an animal model. *Tribulus terrestris* Linn has long been a constituent in tonics in Ayurveda medicine, where in it is used as an aphrodisiac, also used diuretic and nervine in tonic, where as in Unani medicine to inhibit the formation of kidney stone. *T. terrestris* contains three groups of active phytochemicals: Dioscin, protodioscin, diosgenin and similar. These substances have effect on sexual performance and may treat various sexual disorders, they

regulate sexual energy level and strength by increasing the percentage of free testosterone level for men and they affect pregnenolone, progesterone and estrogen. The hormone balancing effects of Bulgarian *Tribulus terrestris* for women makes this herb suitable for premenstrual syndrome and menopausal syndrome.^[37,38] Sterols like betasitosterols or stigma substances. These protect the prostate from swelling and in combination with the X steroidal saponins, protect the prostate from cancer. Steroidal saponins currently referred to as X steroidal saponins.^[39] These X steroidal saponins affect the complete immune system.^[40] They have been demonstrated to possess antibacterial and anti-viral effects. Bulgarian *T. terrestris* may be used internally and externally to treat herpes, and virus infections such as influenza and the common cold. *Tribulus terrestris* was found to be a rich source of calcium.^[41] Instead of being a testosterone precursor, it leads to the production of the Lutenizing Hormone. When LH levels are increased, the natural production of testosterone also increases. LH is a hormone that also deals with sex drive. *T. terrestris* increases sperm count as well as motility levels when it is taken for 30 days. This is a good supplement for men and women to increase their sex drive. Most experts recommend experimenting with 750 to 1,250 mg per day.^[42]

Pharmacological Activities

Diuretic activity

The diuretic properties of *Gokshur* 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. The aqueous extract of *Gokshur* 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 *Gokshur*, 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 *Gokshur* extract, together with its diuretic activity helped in the propulsion of stones along the urinary tract.^[43] The different extracts of *Gokshur* 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.^[44] The diuretic action of *Gokshur* makes it useful as an anti-hypertensive agent.

Aphrodisiac activity

Gokshur is emphasized to be a *vajikara dravya* (Aphrodisiac).^[18] Studies reported that, furastanolic type of saponin present in *Tribulus terrestris* increases the amount of luteinizing hormone (LH), motivate spermatogenesis and results in stimulation of Testosterone. These activities may help in improving the quality and quantity of sperm significantly.^[45] Furostanol saponin extract from *Tribulus terrestris* shows positive effect on spermatogenesis of rams during breeding season with increase in count of spermatozoids, time of viability and sperm motility.^[46]

Antiuro lithic activity

An ethanolic extract of *Tribulus 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.^[47] 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*.^[48] 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 TT extract not only has a potential to inhibit nucleation and growth of the CaOx crystals but also has a cytoprotective role. *Tribulus terrestris* was found to inhibit stone formation in various models of urolithiasis using sodium glycolate and ethylene glycol.^[49] 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 antiuro lithic activity of *Gokshur* is attributed to its GOX inhibition. Quercetin and kaempferol, the active components of *Gokshur*, were found to be non-competitive and competitive inhibitors of GOX, respectively.^[50]

Immunomodulatory activity

Saponins isolated from the fruits of GOKSHUR demonstrated dose-dependent increase in phagocytosis, indicating stimulation of nonspecific immune response. An alcoholic extract of the whole plant of GOKSHUR exhibited a significant dose-dependent increase in humoral

antibody titre and delayed type hypersensitivity response, indicating increase specific immune response.^[51]

Antidiabetic activity

Saponin from *Gokshur* possesses hypoglycemic properties.^[52] *Gokshur* significantly reduced the level of serum glucose, serum triglyceride, and serum cholesterol, while serum superoxide dismutase (SOD) activity was found to be increased in alloxan-induced diabetic mice. The decoction of *Gokshur* showed inhibition of gluconeogenesis in mice.^[53,54] *Gokshur* ethanolic extract at 2 g/kg body weight produced protective effect in streptozotocin-induced diabetic rats by inhibiting oxidative stress. Ethanolic extract of *Gokshur* exhibited 70% inhibition of α -glucosidase at 500 μ g/ml using maltose as the substrate and 100% inhibition of aldose reductase at adose of 30 μ g/ml using dl-glyceraldehyde as the substrate.^[55] A significant decrease in the postprandial blood glucose level of rats was found after administration of saponin from *Gokshur*. *Gokshur* produced dilation of coronary artery and improved the coronary circulation. It is therefore recommended in Ayurveda for the treatment of angina pectoris and other cardiac complications of diabetes. Thus, *Gokshur* could be beneficial in the treatment of diabetes by lowering blood glucose, lipid levels, and by its antioxidant mechanism.

Effect on sexual function

Morphine, an opioid drug, reduces hormone levels and fertility, and causes sexual activity disorders. *Tribulus terrestris* (TT) is a traditional herbal medicine used to enhance sexual activities. They randomly divided 48 rats into four groups: i. control, ii. TT-treated iii. Addicted and iv. TT-treated addicted in this experimental study. Administration of oral water-soluble morphine was done for 21 days to induce addiction, after which the treated groups 2 and 4 received plant-mixed pelleted food (6.25%) orally for four weeks. Sex hormone and gonadotropin levels of all rats' sera were determined by radioimmunoassay and Elisa kits at the end of the treatment period. The data obtained were statistically analyzed using the one-way analysis of variance, followed by post-hoc Tukey test. $P < 0.05$ was considered significant.^[56] The authors found that TT caused a considerable increase ($P < 0.05$) in the hormones in the treated addicted group and oral consumption of TT could markedly antagonize the reduction of sex hormones and gonadotropins (except for FSH) due to morphine addiction.^[57]

Effect on erectile dysfunction

The hormonal effects of *Tribulus terrestris* (TT) in primates, rabbit and rat to identify its effectiveness in the management of erectile dysfunction (ED). They found that *Gokshur* may be useful in mild to moderate cases of ED as it increases some of the sex hormones, possibly due to the presence of protodioscin in the extract. The hormones testosterone and DHT were increased significantly, which could possibly be due to the presence of steroidal glycosides, among them PTN, as one major active principle in. In this study *Gokshur*, it was confirmed that the PTN containing *Tribulus terrestris* -extract increases the levels of T, DHT and DHEAS and that the effect was more pronounced in hypogonadal state.^[57] Protodioscin is a phytochemical agent derived from *Tribulus terrestris* L plant, which has been clinically proven to improve sexual desire and enhance erection via the conversion of protodioscine to DHEA (De-Hydro-Epi-Androsterone).^[58]

Effect on female sexual dysfunction

Female sexual dysfunction (FSD) is a multifaceted and multifactorial condition. An increased incidence of FSD is especially associated with the decline of estrogen. Consequently, menopause is a critical phase for FSD complaints. In this context, medicinal plants may be a therapeutic option. *Tribulus terrestris* may help with desire disorder studies. *Lepidium meyenii* should be studied further.^[59]

Spermatogenic effect

The effect of *Tribulus terrestris* extract on the primary spermatocyte in rat. The researchers found that *Tribulus terrestris* can probably balance the functions of the male reproductive system and can be used in treatment of male infertility, while affecting the testis spermatocyte. The studies show that *Tribulus terrestris* plant increases secretion of luteotropic hormone from pituitary gland due to containing saponins. Luteotropic hormone is also a special stimulant for production of testosterone and hence can improve sexual function in forms of increased sperm production, improved erectile function and increased libido. Furostanol is one of the saponins in *Tribulus terrestris* with stimulant effect on spermatogenesis. This material significantly improves the quality and quantity of sperm.^[60]

Estrogenic effect

The saponins fraction of the dried entire plant was active when administered by gastric intubation to female rats.^[61]

Fertility promotion effect

In this experimental study, thirty five mature male Wistar rats with average weight of 180 ± 10 g and age of 2-3 months were randomly divided into five groups of seven each. Group I served as a control and group II as a experiment group (normal saline, 2.5 ml) and groups III, IV and V were treated with three different doses of oral *Tribulus terrestris* extract (2.5, 5 and 10 mg/kg body weight, respectively) once daily for 8 weeks. After the last treatment, the rats were sacrificed and their testis was removed, fixed and studied using light microscope. The treatment produced an improvement in total sperm count and motility. The saponin fraction of the dried entire plant was active when administered by gastric intubation to female rats. *Tribulus terrestris* increases body ability to produce muscular mass and physical strength. Furthermore, it causes production of red blood cells and improvement in circulation and oxygen transportation.^[59]

Anti-hypertensive property

Gokshur showed significant effect in the treatment of various cardiac diseases including coronary disease, myocardial infarction, cerebral arteriosclerosis, and the sequelae of cerebral thrombosis. The protective effect of tribulosin from *Gokshur* against cardiac ischemia/reperfusion injury to study the underlying mechanism in rats. Tribulosin protected myocardium against ischemia/reperfusion injury through protein kinase C epsilon activation.^[62] Tribulosin treatment resulted in a significant reduction of malondialdehyde, aspartate transaminases, creatine kinase, lactate dehydrogenase activity, and myocardial apoptosis rate. It increased the activity of SOD. Crude saponin fraction of this plant has shown significant effects in the treatment of various cardiac diseases including hypertension, coronary heart disease, myocardial infarction, cerebral arteriosclerosis, and thrombosis. It also has been shown that the aqueous extract of *Gokshur* fruits has significant acetylcholinesterase (ACE) inhibitory effects in vitro. Methanolic and aqueous extracts of *Gokshur* are shown to possess significant antihypertensive activity by direct arterial smooth muscle relaxation and membrane hyperpolarization in spontaneously hypertensive rats.^[63] *Gokshur* also appears to protect the heart cells and may even improve the heart function following a heart attack.^[64]

Vasodilator effects of methanolic and aqueous extracts of *Tribulus terrestris*

Phillips et al (2006) concluded that methanolic and aqueous extracts of *Tribulus terrestris* possess significant antihypertensive activity in spontaneously hypertensive rats. The

antihypertensive effects appeared to result from a direct arterial smooth muscle relaxation possibly involving nitric oxide release and membrane hyperpolarization.^[65]

Cardiotonic activity

Water extract of fruit showed cardiotonic activity on cat papillary muscle, frog and rabbit hearts. Ethanol (95%) extract of the entire plant caused increase in the rate and amplitude of frog heart.^[61]

Cardiovascular effect

Ethanol (95%) extract of dried plant decreased the force of contraction of rabbit heart.^[61]

Antidepressant and anxiolytic activity activity

Swiss Albino mice demonstrated antidepressant and anxiolytic activity on administration of 260 mg/kg dose of Rasayana Ghana tablet comprising three potent well-established rejuvenator herbs, viz. *Tinospora cordifolia* (stem), *Emblica officinalis* (fruit), and *Gokshur* (fruit and root), present in equal quantities in the tablet. It was suggested that harmine, a β -carboline alkaloid present in *Gokshur*, is one of the main active constituents that contributes to the above-mentioned activities. Harmine is an inhibitor of monoamine oxidase which helps to increase level of dopamine in the brain.^[66]

Hepatoprotective activity

The *Gokshur* extract (250 mg/kg) showed a remarkable hepatoprotective activity against acetaminophen-induced hepatotoxicity in *Oreochromis mossambicus* fish. The elevated biochemical parameters and decreased level of reduced glutathione enzymes were normalized by treatment with *Gokshur* extract (250 mg/kg) for acetaminophen-induced toxicity in freshwater fish.^[67]

Antiinflammatory activity

The ethanolic extract of *Gokshur* inhibited the expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in lipopolysaccharide-stimulated RAW264.7 cells. It also suppressed the expression of pro inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α) and interleukin (IL)-4 in macrophage cell line. Thus, the ethanolic extract of *Gokshur* inhibits the expression of mediators related to inflammation and expression of inflammatory cytokines, which has a beneficial effect on various inflammatory

conditions.^[68] The methanolic extract of *Gokshur* showed a dose-dependent inhibition of rat paw volume in carrageenan-induced inflammation in rats.^[69]

Analgesic activity

Analgesic activities of *Gokshur* were studied in male mice using formalin and tail flick test. The study indicated that the methanolic extract of *Gokshur* at a dose of 100 mg/kg produced analgesic effect. This analgesic effect of the *Gokshur* extract may be mediated centrally and/or peripherally. Effect of the extract was lower than morphine and higher than acetylsalicylic acid (aspirin) in both tests. Pre-treatment of animals with opioid receptor antagonist, naloxone, did not change the analgesic effect of the extract in both tests; therefore, the involvement of opioid receptors in the analgesic effect of *Gokshur* is excluded. However, the other mechanisms responsible for the analgesic effect of *Gokshur* remain to be investigated. The results of ulcerogenic studies indicate that the gastric ulcerogenicity of *Gokshur* is lower than indomethacin in the rat's stomach.^[71]

Antispasmodic activity

The lyophilized saponin mixture of the plant exhibited a significant decrease in peristaltic movements of rabbit jejunum preparation in a dose-dependent manner. These results showed that the saponin mixture may be useful for smooth muscle spasms or colic pains.^[71]

Anticancer activity

Chemopreventive potential of the aqueous extract of the root and fruit of GOKSHUR at 800 mg/kg on 7,12-dimethylbenz (a) anthracene (DMBA) and croton oil induced papillomagenesis in Swiss albino male mice depicted significant reduction in tumor incidence, tumor burden, and cumulative number of papillomas, along with a significant increase in the average latent period in mice treated orally with Gokshur suspension continuously at pre-, peri-, and post-initiation stages of papillomagenesis, as compared to the control group treated with DMBA and croton oil alone. The root extract of Gokshur exhibited be Gokshurer chemopreventive potential than the fruit extract at the same concentration (800 mg/kg body weight) in skin papillomagenesis in mice.^[72] The aqueous extract of Gokshur blocked proliferation in HepG2 cells and could also induce apoptosis through the inhibition of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling. Thus, Gokshur has clinical therapeutic effects against liver cancer cells.^[73] The aqueous root extract of Gokshur produced significant radioprotection when given orally (800mg/kg) for seven consecutive days prior to gamma irradiation. gokshur extract pre-treatment protected against

radiation damage by inhibiting radiation-induced glutathione depletion and decreasing lipoperoxidation level in the liver of mice.^[74] Saponins isolated from the aerial parts of Gokshur were studied for their cytostatic/ cytotoxic activity on human fibroblasts. The effects were determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide analysis and ³Hthymidine incorporation to assess cell viability and proliferation, respectively. Saponins showed a dose-dependent decrease in ³Hthymidine incorporation into the DNA, indicating decreased proliferation. Similarly, they were found to be less toxic for normal human skin fibroblasts. The mechanism of action involves up- and down regulation of polyamines' homeostasis, suppression of proliferation, and induction of apoptosis.^[75]

Anti-arthritis activity

In the present study, methanolic extract of *Tribulus terrestris* fruit was reviewed for anti-arthritis activity in rat. The anti-arthritis activity of *Tribulus terrestris* (200mg/kg and 300 mg/kg p.o) was assessed using Freund's complete adjuvant (FCA) induced arthritis in rats. The herbal extracts at dose 200mg/kg and 300 mg/kg p.o was administered for 21 days after the injection of FCA in the rats paws. Mishra et al. (2013) suggested that an important mechanism of anti-arthritis activity is the membrane stability modulating effect. The activity is probable due to presence of flavonoids. These flavonoids are having the surface charge neutralizing effects. It was found that the administration of *T. terrestris* (200 and 300 mg/kg bodyweight) leads to inhibition of leukocyte migration which may have beneficial effect for joint preservation. The activity may be due to presence of steroidal glycoside.^[76] The researchers have shown that dry extract of *T. terrestris* increases calcium level in the blood serum in broilers parent.^[77]

Skeletal muscle relaxant activity

Ethanol (95%) extract of the dried entire plant, administered intraperitoneally to mice showed skeletal muscle relaxant activity.^[61]

Smooth muscle relaxant activity

Ethanol (95%) extract of the dried aerial plant, showed smooth muscle relaxant activity on rabbit duodenum.^[61]

Antioxidant property

Tribulus terrestris also has antioxidant properties.^[78] In another study, the researchers found that the extract from *Tribulus terrestris* significantly reduce the formation of hydroperoxide, thus implying that this species is powerful natural antioxidants.^[79]

Anti-cholestrolemic effect

Saponin fraction of dried root, administered by gastric intubation to rabbits decreased the development of protein, carbohydrate, lipid dystrophy of the liver vs cholesterol loaded animals.^[61]

Hypoglycemic and hypolipidemic effects

The extract of both *T. alatus* and *T. terrestris* significantly decreased the blood glucose levels in diabetic rats.^[80]

Analgesic activity

Chloroform extract of the dried entire plant, administered intra peritoneally to mice showed analgesic effect. The dried fruit, administered by gastric intubation to mice in a preparation containing *Bombyx mori*, *Aconitum sinense*, *Alpinia species*, *Mentha arvensis*, and *Sophora flavescens*, was active vs acetic acid induced writhing.^[61]

Antibacterial activity

All parts (fruits, stems, leaves, and roots) of Turkish and Iranian *Gokshur* showed antibacterial activity against *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, in contrast to the aerial parts of Yemeni *Gokshur* which had no detectable antibacterial activity against these bacteria, while only the fruits and leaves of Indian *Gokshur* were active exclusively against *E. coli* and *S. aureus*. These different results relating to the antibacterial activity of *Gokshur* may be due to using different geographic sources of the plant, types of strains, and assay methods. The methanolic extract of fruits of *Gokshur* was found to be most active against gram-positive and gram-negative bacteria, while moderate activity was observed in its petroleum ether extract and chloroform extract.^[81,82]

Anthelmintic activity

The methanolic extract of GOKSHUR was found to be more effective than the petroleum ether, chloroform, and water extracts for in vitro anthelmintic activity on the nematode

Caenorhabditis elegans. Further bioactivity-guided fractionation confirmed tribulosin and β -sitosterol-d-glucoside to be the active components with ED50 of 76.25 and 82.50 $\mu\text{g/ml}$, respectively.^[83,84]

Substitute and Adulterants^[85]

The fruits of *Pedaliium murex* Linn are occasionally substituted to *Tribulus terrestris* Linn, being considered as large Gokhru. The fruits of *Acanthospermum hispidum* DC are frequently found mixed with the later.

Cultivation^[86]

The herb is a common weed, springs up soon after first showers. It prefers medium and sandy soil. The plant can be propagated by seeds. It bears flowers and fruits almost throughout the year.

Contraindications^[85]

Tribulus terrestris Linn is very safe and no contraindications are noted with *Tribulus terrestris* Linn.

Recommended Dose of Gokshur In Ayurveda^[87]

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.

Thus the fruit of the plant *Tribulus terrestris* has been shown to exhibit diuretic, anti-urolithiatic, CNS (Central nervous system) stimulant, antimicrobial, antifungal activities in rats, antioxidant and antihypertensive activity in rat heart. *Tribulus terrestris* contains biologically – rich compounds as steroids, saponins, flavonoids, alkaloids and unsaturated acids, which are involved in promoting numerous physiological responses. The leaves increase the menstrual flow, cure gonorrhoea. The fruits are useful in urinary complaints, painful micturition and impotence. The fruits are also used to treat coughs, scabies and anaemia. The roots are said to be stomachic, appetizer, diuretic and carminative. It has also been used as medicine in India, South Africa, and Japan. Some steroidal saponins have previously been isolated from this plant as the active components.

CONCLUSION

Gokshur, a commonly available weed, is of significant value in the traditional systems of medicine, viz. *Ayurveda*, Chinese, Siddha, and Unani. *Gokshur* is also a reputed herb in the

folk medicine of many countries for a number of diseases. The whole plant of *Gokshur* has been explored exhaustively for its phytochemical and pharmacological activities such as diuretic, aphrodisiac, antiurolithic, immunomodulatory, antihypertensive, antihyperlipidemic, antidiabetic, hepatoprotective, anticancer, anthelmintic, antibacterial, analgesic, and anti-inflammatory. Considering the available literature on *Gokshur*, the plant could have a potential as a herbal medicine for effective blood pressure control due to its diuretic activity (potassium sparing), anti-hyperlipidemic activity and cardioprotective activity. Though *Gokshur* 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.

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