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Gafarov Rushen

Assistance

Samarkand State Medical University
Samarkand, Uzbekistan**TRIBULUS TERRESTRIS SUPPLEMENTATIONS IN THE TREATMENT OF ERECTILE DYSFUNCTION: HOW EFFECTIVE ARE THEY?****For citation:** Gafarov Rushen, Tribulus terrestris supplementations in the treatment of erectile dysfunction: how effective are they?, Journal of reproductive health and uro-nephrology research 2025 vol 6 issue 4<http://dx.doi.org/10.5281/zenodo.17895611>**ABSTRACT**

This literature review presents data on the use of the medicinal plant Tribulus terrestris in the pharmacotherapy of erectile dysfunction. Traditionally, Tribulus terrestris has been used in Ayurvedic and Chinese medicine as an aphrodisiac and tonic for the treatment of erectile dysfunction, male infertility, and urinary tract diseases. This review summarizes the results of experimental, clinical, and pharmacological studies describing the mechanisms of action, composition, and range of application of Tribulus terrestris for erectile dysfunction.

Key words: Tribulus terrestris, erectile dysfunction, steroidal saponins.**Gafarov Rushen**

assistant

Samarqand davlat tibbiyot universiteti
Samarqand, O'zbekiston**EREKTEL DISFUNKSIYANI DAVOLASHDA TRIBULUS TERRESTRIS PREPARATLARI: ULAR QANCHALIK SAMARALI?****ANNOTATSIYA**

Ushbu adabiyotlar sharhida Tribulus terrestris dorivor o'simligining erektil disfunktsiya farmakoterapiyasida qo'llanilishi bo'yicha ma'lumotlar keltirilgan. Tribulus terrestris Ayurveda va Xitoy tibbiyotida erektil disfunktsiya, erkaklar bepustligi va siydik yo'llari kasalliklarini davolash uchun afrodisyak va tetiklashtiruvchi sifatida ishlatilgan. Ushbu sharhda Tribulus terrestrisning erektil disfunktsiyada ta'sir mexanizmlarini, tarkibini va qo'llanilish doirasini tavsiflagan eksperimental, klinik va farmakologik tadqiqotlar natijalari umumlashtirilgan.

Kalit so'zlar: Tribulus terrestris, erektil disfunktsiya, steroid saponinlar.**Худоярова Дилдора Рахимовна**

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Самаркандский государственный медицинский университет
Самарканд, Узбекистан**ПРЕПАРАТЫ TRIBULUS TERRESTRIS В ЛЕЧЕНИИ ЭРЕКТИЛЬНОЙ ДИСФУНКЦИИ: НАСКОЛЬКО ОНИ ЭФФЕКТИВНЫ?****АННОТАЦИЯ**

В настоящем обзоре литературы представлены данные по использованию лекарственного растения Якорцы стелющиеся (Tribulus terrestris) в фармакотерапии эректильной дисфункции. Традиционно Якорцы стелющиеся использовались в аюрведической и китайской медицине как афродизиак и тонизирующее средство при лечении эректильной дисфункции, мужского бесплодия и заболеваний мочевыводящих путей. В обзоре обобщены результаты экспериментальных, клинических, а также фармакологических исследований, описывающих механизмы действия, состав и диапазон применения Якорцев стелющихся при эректильной дисфункции.

Ключевые слова: якорцы стелющиеся, Tribulus terrestris, эректильная дисфункция, стероидные сапонины.

Introduction. Erectile dysfunction (ED) is a widely prevalent clinical condition, characterised by the consistent inability to attain or maintain an erection sufficient to permit satisfactory sexual performance. Erection is primarily mediated by parasympathetic nerve

fibres, which release acetylcholine to stimulate nitric oxide (NO) production. NO induces smooth muscle relaxation via the cyclic guanosine monophosphate (cGMP) pathway, allowing the corpora cavernosa to engorge with blood and maintain rigidity. ED can arise

from psychological causes (such as stress and anxiety), vascular conditions (like atherosclerosis and hypertension), endocrine disorders (including hypogonadism), neurological damage (from surgery, trauma, or disease), diabetes mellitus, and certain medications.

The primary approach to medical management of erectile dysfunction involves phosphodiesterase type 5 (PDE-5) inhibitors - including sildenafil, tadalafil, vardenafil, and avanafil etc. PDE-5 inhibitors are acting via augmenting nitric oxide (NO) - cGMP signalling, thereby promote smooth muscle relaxation and improve penile blood flow. Other treatment modalities include intracavernosal injections, intraurethral medications, vacuum erection devices, and surgical interventions such as penile prosthesis implantation, testosterone replacement [1,2]. In recent years, attention has turned to alternative therapies, including phytotherapeutic agents like *Tribulus terrestris*, for patients seeking adjunctive or non-pharmacological options.

Tribulus terrestris L. (family Zygophyllaceae), commonly known as puncture vine or Gokshura, is a creeping herbaceous plant widely distributed in tropical and subtropical regions, including India, China, the Mediterranean, and parts of Europe and America. This plant is widely distributed throughout Uzbekistan and possesses substantial natural reserves [3]. Traditionally, it has been used in Ayurvedic and Chinese medicine as an aphrodisiac and tonic for treating ED, male infertility, and urinary tract disorders [4].

Materials and methods. Non-systematic research was performed from the following scientific databases: PubMed, ScienceDirect, Google Scholar. Only articles published in English were included to ensure data reliability.

The following search string was applied across databases: ("*Tribulus terrestris*") AND ("erectile dysfunction" OR "ED"). The search encompassed literature published between 1974 and 2025, and reference lists of retrieved articles were also screened to identify relevant studies.

Results. The majority of assertions regarding the pro-hormonal properties of *Tribulus terrestris* originate from research conducted during the 1970s in Bulgaria. Investigators from Sofia initially isolated and characterized a steroidal saponin mixture from the aerial parts of *T. terrestris* (designated TB-68), primarily for veterinary applications [5,6,7]. Research findings revealed that administration of this saponin

fraction resulted in increased sperm concentration, motility, and viability in rats, as well as improved sexual behavior in boars. These outcomes prompted the hypothesis that the main constituents, protodioscin and protogracillin, may underlie these effects, potentially by being metabolized into dehydroepiandrosterone (DHEA), a precursor of androgenic hormones [5,7].

Consequent to these initial animal investigations, a novel alcohol-based extract of steroidal saponins from *Tribulus terrestris*, standardised to contain at least 45% protodioscin, was formulated and authorised for human use. The introduction of this botanical supplement for human consumption, coupled with promising findings from early studies, prompted the initiation of the first clinical trials; however, the outcomes of these trials were inconsistent [5].

The pharmacological properties of *T. terrestris* are primarily ascribed to its content of steroidal saponins - most notably protodioscin, prototribestin, pseudoprotodioscin, tribestin, dioscin, and tribulosin - as well as its flavonoid, polyphenol, and alkaloid constituents [8,9]. Variations in biological activity are attributable to differences in the concentration and compositional profile of active saponins, which are modulated by the geographical origin of the plant material^[6]. These bioactive constituents are believed to improve sexual function via multiple pathways, such as stimulating the release of luteinizing hormone (LH), enhancing endogenous testosterone synthesis, and increasing the expression of nitric oxide synthase (NOS). This results in elevated nitric oxide (NO) production and cGMP-mediated relaxation of smooth muscle within the corpus cavernosum. Additionally, the antioxidant properties of these compounds may safeguard endothelial function and promote vascular health in penile tissue [9].

Steroidal saponins (SS). These compounds are glycosides composed of a steroidal backbone attached to one or more sugar residues, which confer both hydrophilic and lipophilic characteristics. This amphiphilic nature enables them to interact with cellular membranes and influence the absorption and bioavailability of other active molecules. Listed in Table 1 are some of the steroidal saponins found in drugs used for the treatment of male sexual disorders. Among the various saponins identified in *T. terrestris*, protodioscin is considered the predominant and most biologically active compound, contributing substantially to its androgenic and vasodilatory effects [10].

Table 1. Phytochemicals of *Tribulus terrestris* with implications in erectile function.

Compound	Chemical type	Principal pharmacological/ biological action
<i>Protodioscin</i>	Furostanol type SS	Considered the principal active saponin; implicated in androgen stimulation (via LH), increased NO signaling in penile tissues, and erectile enhancement ^[11,12]
<i>Prototribestin</i>	Furostanol type SS	Shares structural similarity with protodioscin; may influence androgenic activity and support NO-mediated vasodilation within the corpus cavernosum, contributing to erectile enhancement. ^[8,11]
<i>Pseudoprotodi-oscin</i>	Furostanol type SS	It is proposed to modulate libido and erectile response through mechanisms involving nitric oxide and dehydroepiandrosterone (DHEA), as well as through neurosteroid-mediated pathways ^[4,11]
<i>Tribestin</i>	Spirostanol type SS	Exhibits adaptogenic and aphrodisiac effects, playing a contributory role in the overall saponin-mediated augmentation of sexual function and the maintenance of vascular tone. ^[11,12]
<i>Disocin</i>	Spirostanol type SS	Reported to facilitate hormonal homeostasis and to confer protective effects on reproductive tissues by mitigating oxidative damage ^[8,11]
<i>Tribulosin</i>	Glycosidic saponin	Associated with enhanced vasodilation, increased stress resilience, and endothelial protection, thereby indirectly supporting the restoration of erectile function ^[11,12]

<i>Flavonoids</i>	Polyphenolic compounds	Demonstrate potent antioxidant and anti-inflammatory effects, supporting endothelial function and promoting increased nitric oxide availability in the penile microcirculation ^[9,11]
<i>Polyphenols</i>	Phenolic acids	Offer antioxidant protection to endothelial cells, reduce oxidative stress, and contribute to the maintenance of vascular homeostasis essential for normal erectile function. ^[8,11]
<i>Alkaloids</i>	Nitrogen-containing compounds	Relatively less well-characterised; may play a role in neuromodulation and circulatory support, potentially complementing the activity of saponins ^[11,12]

The efficacy of *Tribulus terrestris* L. (TT) supplementation on erectile dysfunction (ED), androgen profile, and sexual function was assessed in several clinical and preclinical studies included in this review. The principal bioactive agents underlying these effects are steroidal saponins, with protodioscin representing the most prominent component; this saponin comprises up to 90% of the total saponin fraction in extracts obtained from the aerial parts of *Tribulus terrestris* [9]. Studies indicate that the aerial parts of *Tribulus terrestris* contain higher concentrations of protodioscin, making them a more favourable and recommended choice for supplementation. These saponins were shown to elevate not only testosterone, but also luteinizing hormone (LH), dehydroepiandrosterone, and its sulphated derivative^[9]. Although protodioscin is recognized as the principal saponin underlying the biological effects of *Tribulus terrestris*, Zhang et al. [13] demonstrated that its oral bioavailability is limited in vivo. Notably, co-administration with other saponin-rich extracts - such as those from *Dioscorea* - has been shown to enhance protodioscin absorption and improve its pharmacokinetic properties. These observations underscore the importance of formulation strategies to optimise the clinical efficacy of *Tribulus terrestris* supplementation.

Beyond their potential endocrine actions, saponins from *Tribulus terrestris* are also thought to function as neurosteroids, possibly increasing dehydroepiandrosterone (DHEA) levels and exhibiting antagonistic effects on GABA. Through these mechanisms, they may enhance sexual function independently of testosterone^[10]. Although some studies observed increases in serum testosterone, the evidence remains inconclusive regarding TT as a reliable testosterone booster in humans. Animal studies in rabbits and rats indicated that TT supplementation could elevate sex hormone levels, possibly due to protodioscin content, further supporting its potential role in male sexual health [16].

According to the systematic analysis conducted by Vilar N. et al. [10], four studies - two from Egypt, one from Bulgaria, and one from India - reported positive outcomes associated with *Tribulus terrestris* supplementation. Across these studies, improvements were observed in at least one of the following parameters: serum testosterone levels, International Index of Erectile Function (IIEF) scores, overall erectile function, sperm motility, penile strength, and management of premature

ejaculation. In each of the four studies reviewed, participants received a daily dose of at least 750 mg of *Tribulus terrestris*, administered in divided doses with a minimum frequency of twice per day. This dosing regimen was consistently maintained throughout the intervention periods, ensuring regular exposure to the supplement and allowing for the assessment of its effects on various reproductive and sexual health parameters.

In a placebo-controlled clinical study by Gamal El Din SF et al. [15], thirty-five patients received TT (750 mg/day in three divided 250 mg doses) for 3 months. Evaluation of serum testosterone (total and free), LH, and erectile function (by IIEF-5) revealed statistically significant improvements in both hormone levels and erectile function scores post-intervention. A minor but statistically significant increase in aspartate transaminase was observed (p=0.03), portraying a potential effect on the liver, but no other adverse effects were observed. Another placebo-controlled study by Kamenov et al. ^[16] allocated ninety participants to each study cohort, with one receiving three tablets of *Tribulus terrestris* extract daily and the other receiving a placebo over 12 weeks. At the conclusion of the intervention, the cohort supplemented with *Tribulus terrestris* extract showed significant improvements in International Index of Erectile Function (IIEF) scores - particularly in erection quality, libido, and orgasmic function - while the placebo cohort did not demonstrate comparable benefits.

In the investigation by Do et al. (2013) [4], the impact of *Tribulus terrestris* extract on erectile function was examined through intracavernous pressure (ICP) assessments following a month-long oral supplementation regimen in an animal model. The study reported a marked, dose-dependent rise in ICP, with the most pronounced effect at a dosage of 100 mg/kg-day when compared to controls. Evaluation of the corpus cavernosum (CC) further indicated a significant increase in cyclic adenosine monophosphate (cAMP) concentrations after administration of the extract. However, this effect did not follow a strictly linear dose-response, as the highest cAMP levels were detected at the 0.5 mg dose, with diminished values at both smaller and larger doses. Although the cAMP response lacked linearity, the overall findings indicate that *T. terrestris* enhances penile smooth muscle relaxation and erectile function, supporting its potential utility as a botanical therapy for erectile dysfunction.

Table 2. Experimental and clinical findings on the effects of tribulus terrestris in erectile dysfunction.

Study/Author (year)	Model / Population	Dose and Duration	Key Findings	Outcomes
Do et al. ^[4]	Experimental animal study (male rats)	25-100 mg/kg/day, 1 month	Dose-dependent increase in ICP; highest at 100 mg/kg. Non-linear rise in cAMP (peak at 0.5 mg).	↑ Intracavernous pressure; ↑ cAMP levels; enhanced corpus cavernosum smooth-muscle relaxation
GamalEl Din SF et al. and Roaiiah MF et al. ^[15,17]	35 male patients with ED	750 mg/day (3 × 250 mg) for 3 months	↑ Total & free testosterone, ↑ LH, ↑ IIEF-5; minor AST elevation (p=0.03)	IIEF-5 ↑, Serum T↑, after administering drug for 3 months.
Kamenov et al. ^[16]	180 men (90 per group)	3 tablets/day	↑ IIEF (erection,	IIEF-5↑, GEQ (positive

	with mild-moderate ED	(Tribestan®; 250 mg each) for 12 weeks	libido, orgasm), ↑ satisfaction vs. placebo	response)
<i>Santos et al.</i> [18]	60 men with mild ED	400 mg/day for 4 weeks	↑ IIEF-5, ↑ sexual desire	IIEF-5↑, variable testosterone outcomes

Discussion. *Tribulus terrestris*, a phytotherapeutic agent traditionally used as an aphrodisiac, has garnered attention as a potential adjunct or alternative therapy for ED^[4]. Multiple randomised controlled trials indicate that supplementation with *Tribulus terrestris* (400-1500 mg daily for 1-3 months) may improve erectile function, as assessed by the International Index of Erectile Function (IIEF) scores, particularly in men with mild-to-moderate ED [10]. The proposed mechanisms include upregulation of nitric oxide synthase activity, leading to enhanced nitric oxide-mediated vasodilation, and the possible modulation of androgenic hormones by steroidal saponins such as protodioscin. However, evidence for a consistent increase in serum testosterone remains inconclusive. Safety analyses reveal a favourable adverse event profile, though potential drug interactions, notably via CYP3A4 inhibition, warrant caution [19].

The findings across the reviewed studies suggest that *Tribulus terrestris* (TT) exerts diverse physiological effects on male sexual function, though these effects are not uniformly observed across all patient populations or study designs. Notably, while some studies report significant increases in serum testosterone following TT supplementation [15,17], others demonstrate improvements in sexual desire [10,16,18] and erectile function independent of changes in androgen levels [16,18]. Additionally, several investigations have documented enhancements in sperm parameters [17,18], suggesting that TT may exert broad benefits on male reproductive health beyond its role in androgen modulation.

A consistent observation among studies reporting positive outcomes is the duration and frequency of intervention. Trials with longer supplementation periods - typically spanning three to four months, with administration at least twice daily - tended to yield more pronounced improvements in erectile function and related parameters [4,10,15,16,17,18]. In contrast, studies employing shorter intervention periods, such as four weeks, often failed to distinguish TT from placebo, highlighting the importance of sustained supplementation for achieving therapeutic efficacy. These findings underscore the need for future research to prioritize longer intervention durations and to systematically assess optimal dosing regimens.

Bioavailability remains a critical factor influencing TT's clinical effectiveness. Evidence suggests that co-administration with other

botanicals, such as *Dioscorea* species, can enhance the absorption and pharmacokinetic profile of key active constituents like protodioscin [13]. This raises the possibility that combination therapies or novel formulations may further potentiate the therapeutic potential of TT, warranting further exploration in well-designed clinical trials.

Phytochemical analysis also reveals that the aerial parts of TT, particularly those harvested during pre-flowering and flowering stages, contain the highest concentrations of protodioscin. This supports the preferential use of aerial plant parts in supplement formulations to maximize efficacy. Furthermore, geographic origin appears to affect the phytochemical profile and potency of TT extracts, suggesting that source standardization could be critical for consistent clinical outcomes. Geographical variation further contributes to differences in pharmacological potency, as saponin content and composition are known to fluctuate with environmental conditions and cultivation practices [8,9,11,12]. Consequently, future research should aim to identify and standardize extracts derived from regions with the highest bioactive concentrations.

To date, there is no solid evidence that TT supplementation is a testosterone booster. Importantly, studies that reported null effects of TT supplementation on testosterone levels did not focus on patients with low testosterone. Overall, *Tribulus terrestris* appears to offer a safe and moderately effective phytotherapeutic option for improving erectile function, with its greatest benefit observed in select patient populations. Further large-scale, rigorously-controlled studies and meta-analyses are warranted to clarify optimal dosing strategies, standardise extract composition, and confirm long-term safety and clinical effectiveness.

Conclusions. *Tribulus terrestris* demonstrates moderate efficacy as a phytotherapeutic agent in the management of erectile dysfunction, with the strongest evidence supporting its use in men with mild-to-moderate forms of the condition. While the safety profile is generally favourable, the evidence for a consistent testosterone-boosting effect remains inconclusive, and the long-term safety and efficacy require further elucidation. Standardisation of extract composition, optimal dosing strategies, and large-scale, well-controlled clinical trials are needed to fully define the therapeutic role of *Tribulus terrestris* in ED and to guide evidence-based clinical recommendations.

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