# Egyptian Herbal Monograph

## Volume 1

## Traditional wild medicinal plants

**Egyptian Drug Authority (EDA)**

**2023**

# Egyptian Herbal Monograph

## Medicinal Plants Used Traditionally in Egypt

***Tribulus terrestris* L.** ضريس

### 1. Names & Synonyms (1)

***Tribulus terrestris* L.**

**Family:** Zygophyllaceae.

**Syns.** *Tribulus lanuginosus* L.*, Tribulus robustus* Boiss. & Noê in Boiss.

**Arabic:** Dreiss ضريس, Glaya جلاية

**English:** Caltrops, Land caltrops.

### 2. Geographical distribution (1)

All the phytogeographical regions of the country except that of the oases of the Western Desert.

### 3. Parts used for medicinal purpose

Dried fruits (1-4).

### 4. Major chemical constituents

**Steroidal saponins:** Protodioscin, prototribestin, pseudoprotodioscin, dioscin, tribestin and tribulosin (5,6).
**Flavonoids:** Kaempferol, kaempferol 3-*O*-rutinoside, quercetin, rutin, astragalin, tribuloside (6).
**Phenolic acids and esters:** Ferulic acid, feruloyloctopamine, caffeoyltyramine, coumaroyltyramine, 5-*p-trans*-coumaroylquinic acid and 5-*p-cis*-coumaroylquinic acid (6).
**Others:** Tribulusamides A and B, harmane and norharmane (6).

### 5. Traditional medicinal uses

A. Diuretic and help relieve difficult/painful urination (2,7).

B. Aphrodisiac to increase libido and enhances sexual function (2-4,7).

***T. terrestris* is a traditional medicinal plant for use in the specified indications exclusively based upon long-standing use.**

## 6. Herbal preparations correlated to medicinal use

1. Comminuted dried fruits as herbal tea in the form of decoction (2,3).
2. Powdered fruits (2).
3. Dry extract (ethanol 70-95% or water as solvent) (3,4).

**Herbal preparations (2 and 3) are in a pharmaceutical dosage form. The pharmaceutical form should be described by the pharmacopoeia full standard term.**

## 7. Posology and method of administration correlated to medicinal use

**Preparations 1**
20 – 30 g, daily (2).
3 – 9 g, daily, in divided doses (3).

**Preparations 2**
3 – 6 g, daily (2).

**Preparations 3**
750 – 1200 mg, daily (8).

**Duration of use:**

Occasional use only (2).

**Method of administration**: Oral use (2,3).

## 8. Contraindications

- Hypersensitivity to the active substances and to other plants of the same family.
- In hypotension and liver diseases (2).
- People with androgen-sensitive tumours (4).

## 9. Special warnings and precautions for use

- If the symptoms worsen during the use of the medicinal product, a doctor or a pharmacist should be consulted.

- Patients should avoid excessive exposure to sunlight and use a sunscreen with a high sun protection factor (SPF 30+), due to the possibility of phototoxic reactions (3).

- The use in children under the age of 12 years is not recommended (3).

## 10. Interactions with other medicinal products and other forms of interaction

None reported.

## 11. Fertility, pregnancy and lactation

- Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended (3).
- No fertility data available (3).

## 12. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

## 13. Undesirable effects

- If adverse reactions occur, a doctor or a pharmacist should be consulted.
- Gastrointestinal disturbance may occur in sensitive individuals due to the saponin content (4).
- Except for diuretic effect, increased urination may occur (2).

## 14. Overdose

No case of overdose has been reported.

## 15. Relevant biological activities

- Administration of the aqueous extract of the fruit (at an intragastric dose of 5.0 g/kg b.w. in saline) induced diuresis in rats and was slightly more effective than furosemide. The sodium, potassium and chloride ion concentrations in the urine of treated rats were also increased. Addition of the extract to the bath medium of guinea-pig ileum induced contractile activity (9).
- In the anaesthetized dogs, the ether extract of the fruits of *T. terrestris* produced diuresis and increased the creatinine renal clearance, which suggest increase in the glomerular filtration rate. However, the ether extract did not significantly increase the chloride clearance which excludes inhibition of tubular chloride reabsorption. The aqueous extract of the fruits produced no significant effect on the urine volume or on the creatinine or the chloride renal clearance (10).
- The ethanol extract was tested for activity against artificially induced urolithiasis in albino rats. The extract was administered orally at 25, 50 and 100 mg/kg daily for 4 months. It exhibited dose dependent antiurolithiatic activity and almost completely

inhibited stone formation. Other biochemical parameters in urine and serum which were altered during the process of stone formation were normalized by the plant extract in a dose dependent manner (11).

- The effect of an aqueous extract of *T. terrestris* administered orally at a dose of 5 g/kg body weight was studied in rats with induced hyperoxaluria (intraperitoneal injection of 4 –OH proline at a dose of 2.5 g/kg body weight for three successive days) and maintained by sodium glycolate, twenty-four hours urine was collected and analyzed for creatinine and oxalate. The oxalate excretion reversed to normal from 1.97 + 0.314 to 0.144 + 0.004 mg/mg creatinine ($p<0.01$) within 21 days of administration of *T. terrestris* extract and remained so until 15 days after withdrawal of extract and sodium glycolate (12).

- A study was conducted to investigate the effect of oral treatment of *T. terrestris* extract on the isolated corpus carvenosal tissue of rabbits to determine the mechanism by which protodioscin (PTN) a constituent of *T. terrestris* exerted its pharmacological activity. The animals were treated with extracts at different dose levels that is, 2.5, 5, 10 mg/kg body weight which was administered orally, once daily for a period of 8 weeks. The penile tissue from the sacrificed animals was subjected for responses to both contractions and relaxing pharmacological agents and electrical field stimulation (EFS). The results indicating the relaxant responses to acetylcholine, nitroglycerine and EFS by more than 10, 24 and 10%, respectively compared to their control values and the lack of such effect on the contractile response to noradrenaline and histamine indicated that PTN had a proerectile activity. The enhanced relaxant effect was attributed to the increase of nitric oxide from the endothelium and nitrergic nerve endings, which may account for its claims as an aphrodisiac (13).

- The decoction of root and fruit of Gokshura showed an increased amount of excreted urine volume and root decoction showed more $Na^+$, $K^+$ and $Cl^-$ excretion as compared to fruit decoction. Diuretic action of both root and fruit is similar in terms of urine volume but the root is more effective in the basis of ionic excretion. Hence, while treating patients suffering from ionic imbalance, it is better to use the fruits for protecting the ionic balance during diuresis. In all other conditions, root can be used for diuretic activity (14).

- Comparative diuretic effects of the whole plant and fruits of *Tribulus terrestris* Linn. in Wistar albino rats were investigated. Eight groups of 6 Wistar albino rats in each were used. Watery extract of three different doses (300 mg/kg, 500 mg/kg and 700 mg/kg) for each whole plant and fruits were used to test diuretic effect. Control group was given 0.9% sodium chloride solution and furosemide was used as the standard drug. After fasting, the animals were given watery extract orally and put into metabolic cages. Then urine was collected for 5 hours. Urinary sodium and potassium concentrations were measured by atomic absorption spectrophotometer. When analysing the results, as compared with control, there was no significant diuretic effect in whole plant extract but only fruit extract showed significant diuretic effect (15).

- A comparative study to evaluate and compare the effect of *Tribulus terristris* on urine volume and electrolytes with furosemide was performed. The duration of study was two weeks. 24 rabbits of mixed breed were used. They were fed on grass, grain, seasonal vegetables and water *ad libitum*. Animals were weighed for calculation of dosage of herb. They were divided into three equal groups randomly. Group Tt was given *Tribulus terristris* while Group F was given furosemide, while group C was not given any drug. Tt vs F: the change in 24 hours urine volume was found statistically significant $p<0.05$ on day 01 and day 15. Serum $Na^+$, $K^+$ levels were also found statistically significant $p<0.05$ throughout the study period. The results revealed that the plant has diuretic properties but is less efficacious than furosemide. Keeping in view, the result of our study, we recommend that the use of this herb may be promoted as diuretic agent; it may be helpful in pulmonary oedema and other oedematous conditions (16).

- The preventive and curative urolithiatic efficacy in experimentally induced nephrolithiatic Wistar rats, along with preclinical toxicity was evaluated following oral administration of statistically optimized aqueous extract of *T. terrestris*. Treatment showed augmented renal function, restoration of normal renal architecture and increase in body weight. Microscopic analysis of urine revealed excretion of small sized urinary crystals, demonstrating that treatment potentially modulated the morphology of renal stones. Tissue enzymatic estimation affirmed the antioxidant efficacy of treatment with reduced free radical generation. Significant upregulation of p38MAPK at both the gene and protein level was noted in hyperoxaluric group and interestingly treatment reversed it. Acute oral toxicity study established the Median Lethal Dose (LD50) to be greater than 2000 mg/kg body weight (b.wt.). No observed adverse effect level by repeated oral toxicity for 28 days at 750 mg/kg b.wt. was noted (17).

- The influence of hydroalcoholic extract of *T. terrestris* on cisplatin (CIS) induced renal tissue damage in male mice was evaluated. Thirty mice were divided into five groups (n = 6). The first group (control) was treated with normal saline (0.9% NaCl) and experimental groups with CIS (E1), CIS + 100 mg/ kg extract of *T. terrestris* (E2), CIS + 300 mg/kg extract of TT (E3), CIS + 500 mg/kg extract of *T. terrestris* (E4) intraperitoneally. The kidneys were removed after 4 days of injections, and histological evaluations were performed. The data were analysed using one-way analysis of variance followed by Tukey's post-hoc test, paired-sample *t*-test, Kruskal–Wallis and Mann–Whitney tests. In the CIS treated group, the whole kidney tissue showed an increased dilatation of Bowman's capsule, medullar congestion, and dilatation of collecting tubules and a decreased in the body weight and kidney weight. These parameters reached to the normal range after administration of fruit extracts of *T. terrestris* for 4 days. The results suggested that the oral administration of *T. terrestris* fruit extract at dose 100, 300 and 500 mg/kg body weight provided protection against the CIS induced toxicity in the mice (18).

- An extract of the fruit of *Tribulus terrestris* containing protodioscin was investigated in both normal and castrated rats to determine aphrodisiac effects. The treatments

were distilled water, testosterone and extract. Compared to the castrated control animals, treatment of castrated rats with either testosterone or the extract led to a mild to moderate improvement of the sexual behaviour parameters as demonstrated by an increase in mount frequency and intromission frequency and a decrease in mount latency, intromission latency and post-ejaculatory interval (19).

- Rats were fed a standard diet treated with *Mucuna pruriens*, *T. terrestris* (TT), and Ashwagandha (300 mg/kg) for 8 weeks. These herbs are potent of enhancers of sexual function and behaviour by increasing the testosterone levels and regulating the NF-κB and Nrf2/HO–1 pathway in male. The results indicated that the extract of TT was comparatively more potent than the other two. (20).

- The hormonal effects of *T. terrestris* (TT) were evaluated in primates, rabbits and rats to identify its usefulness in the management of erectile dysfunction (ED). Blood samples were analysed for testosterone (T), dihydrotestosterone (DHT) and dehydroepiandrosterone sulphate (DHEAS) levels using a radioimmunoassay. TT increased some of the sex hormones, which is possibly due to the presence of protodioscin in the extract (21).

***Clinical trials:***

- A double-blind clinical trial was done on 45 men with infertility due to oligoasthenoteratozoospermia. Thirty-six men were treated with 500 mg purified extract of the fruits containing protodioscin, orally 3 times daily for 3 months. The nine men in the control group were given a placebo for the same period of time. Spouses of eight of the men in the treated group became pregnant after treatment of their husbands, whereas no pregnancies occurred in the spouses of the men in the control group. An improvement in the sperm morphology, acrosome morphology and reaction seemed to account for the increased fertility after treatment. In addition, the extract was shown to increase the level of dehydroepiandrosterone and might also have contributed to the activation of cell membrane receptors and the production of weak androgens (22).

- A clinical trial involving 30 men with erectile dysfunction, but not diabetes, 30 with neither erectile dysfunction nor diabetes and 15 men with both diabetes and erectile dysfunction was performed to assess the relationship between dehydroepiandrosterone sulfate and erectile dysfunction. The men were given an extract of the *T. terrestris* fruits at a dose of 3 × 250 mg per day for 3 weeks. The results of the study showed a significant increase of dehydroepiandrosterone sulfate levels in subjects with and without diabetes after treatment, and a significant increase in the frequency of successful intercourse of 60% in subjects with or without diabetes and with or without erectile dysfunction (23).

- A clinical trial was conducted on 30 consecutive male patients presenting to Kasr-Al Ainy Andrology outpatient clinic complaining of manifestations of partial androgen deficiency in aging males. In this study, 750 mg/day of *T. terrestris* fruit extract in 3 divided doses, each of 250 mg, as an endogenous testosterone enhancer had been tried for a duration of 3 months and the evaluation of its effect had been monitored

for each patient concerning its effect on serum testosterone (total and free) and luteinizing hormone (LH), as well as its impact on erectile function, which was evaluated by the International Index of Erectile Function-5 (IIEF-5) questionnaire for those patients. Results showed a statistically significant difference in the level of testosterone (total and free) and IIEF-5, but no statistically significant difference in the level of LH before and after treatment. Also, the study showed statistically significant correlation between testosterone (total and free) and IIEF-5, but no statistically significant correlation between the level of LH and the IIEF-5 before and after treatment (24).

- The efficacy and safety profiles of *Tribulus terrestris* in aging males with partial androgen deficiency who suffered from erectile dysfunction and lower urinary tract symptoms were evaluated. A total of 70 randomized aging patients with erectile dysfunction and lower urinary tract symptoms were recruited from June 2017 to March 2018 from the andrology outpatient clinic. Thirty-five patients (group A) received *T. terrestris* 3 times daily for 3 months and the other 35 patients (group B) received placebo. The mean of aspartate transaminase was elevated in group A after 3 months of receiving *T. terrestris* (26.5 (before), 27.8 (after), respectively, $p = 0.03$). Moreover, there were significant elevations in the means of both total testosterone together with the score of the validated Arabic index of erectile function (5-item version of the International Index of Erectile Function) (2.2, 10.7 (before), 2.7, 16.1 (after), $p<0.001$, $p<0.001$, respectively). Finally, the mean of the total prostate-specific antigen was elevated in this group (1.4 (before), 1.7 (before), $p = 0.007$, respectively). Interestingly, there were no worsening of the lower urinary tract symptoms in group A as there was no change in the mean score of the international prostate symptom score, which was used to assess these symptoms before and after treatment (mean 14.4 (before), 14.6 (after), $p = 0.67$, respectively). In sum, this study replicates the findings of previous reports about the robust effect of this herbal medicine in elevating the testosterone level and improving the sexual function of patients who suffered from erectile dysfunction with partial androgen deficiency (25).

## 16. Additional information

---

## 17. Date of compilation/last revision

12/07/2023.

## References


| | |
|---|---|
| **1** | Hussein, S. R., Marzouk, M. M. and El Negomy, S. (2020), In: Egyptian Encyclopedia of Wild Medicinal Plants, **10**, 285 - 294. Academy of Scientific Research and Technology, Cairo, Egypt. |
| **2** | Natural Health Product, Tribulus – *Tribulus terrestris* (2019). Health Canada. https://webprod.hc-sc.gc.ca/nhpid-bdipsn/monoReq.do?id=1900 |
| **3** | WHO monographs on selected medicinal plants (2010). Monographs on selected medicinal plants, **4**, 323– 334. |
| **4** | Braun, L. and Cohen, M. (2010). Herbs and Natural Supplements - An evidence-based guide. 3rd edition, Churchill Livingstone. ISBN: 978 0 7295 3910 4. |
| **5** | Dinchev, D., Janda, B., Evstatieva, L., Oleszek, W., Aslani, M. R. and Kostova, I. (2007). Distribution of steroidal saponins in *Tribulus terrestris* from different geographical regions. *Phytochemistry,* **69**(1), 176-186. doi: 10.1016/j.phytochem.2007.07.003. |
| **6** | Ştefănescu, R., Tero-Vescan, A., Negroiu, A., Aurică, E. and Vari, C-E. (2020). A comprehensive review of the phytochemical, pharmacological, and toxicological properties of *Tribulus terrestris* L. *Biomolecules*, **10**(5), 752. https://doi.org/10.3390/biom10050752. |
| **7** | Duke, J. A. (2002). Handbook of Medicinal Herbs. 2nd ed. CRC Press. ISBN 978084931284. |
| **8** | www.webmed.com |
| **9** | Al-Ali, M., Wahbi, S., Twaij, H. and Al-Badr, A. (2003). *Tribulus terrestris*: Preliminary study of its diuretic and contractile effects and comparison with *Zea mays*. *J. Ethnopharmacol*., **85**(2-3), 257-260. doi:10.1016/s0378-8741(03)00014-x. |
| **10** | Singh, R. C. P. and Sisodia, C. S. (1971). Effect of *Tribulus terrestris* fruit extracts on chloride and creatinine renal clearances in dogs. *Ind. J. Physiol. & Pharmac.,* **15**(3), 93-96. |
| **11** | Anand, R., Patnaik, G. K., Kulshreshtha, D. K. and Dhawan, B. N. (1994). Activity of certain fractions of *Tribulus terrestris* fruits against experimentally induced urolithiasis in rats. *Int. J. Exp. Biol*., **32**, 548-552. |
| **12** | Sangeeta, D., Sidhu, H., Thind, S. K., Nath, R. and Vaidyanathan, S. (1993). Therapeutic response of *Tribulus terrestris* (Gokhru) aqueous extract on hyperoxaluria in male adult rats. *Phytother. Res*., **7**, 116-119. |
| **13** | Adaikan, P. G., Gauthaman, K., Prasad, R. N. and Ng, S. C. (2000). Projectile pharmacological effects of *Tribulus terrestris* extract on the rabbits corpus carvenosum. *Ann. Acad. Med. Singapore*, **29**(1), 22-26. |
| **14** | Sudheendran, A., Shajahan, M. A. and Premlal, S. A. (2021). Comparative diuretic evaluation of fruit and root of Gokshura (*Tribulus terrestris* Linn.) in albino rats. *AYU*, **42**, 52 -56. |
| **15** | Maw, A. M., Phyu, K. P., Kyaw, P. P. M., Mar, K. K., San, K.., Thura, A., Aye, N. N., Oo, K. T. and Myint, Y. Y. (2016). Comparative diuretic effects of the whole plant and fruits of *Tribulus terrestris* Linn. in Wistar albino rats. *44th Myanmar Health Research Congress*, Abstract Book, 19-20. |

| | |
|---|---|
| **16** | Jabbar, A., Nazir, A., Khalil, J., Ansari, N. I., Qureshi, K. M. and Javed, F. (2012). To compare the Effects of *Tribulus terristris* with Furosemide on urine volume and electrolytes. *Annals*., **18**(2), 196-200. |
| **17** | Kaushik, J., Tandon, S., Bhardwaj, R., Kaur, T., Singla, S. K., Kumar, J. and Tendon, C. (2019). Delving into the antiurolithiatic potential of *Tribulus terrestris* extract through *in vivo* efficacy and preclinical safety investigations in Wistar rats. *Scientific Reports*, **9**, 15969. https://doi.org/10.1038/s41598-019-52398-w. |
| **18** | Raoofi, A., Khazaei, M. and Ghanbari, A. (2015). Protective effect of hydroalcoholic extract of *Tribulus terrestris* on Cisplatin induced renal tissue damage in male mice. *International Journal of Preventive Medicine*, **6**, 11, DOI: 10.4103/2008-7802.151817. |
| **19** | Gauthaman, K., Adaikan, P. G. and Prasad, R. N. (2002). Aphrodisiac properties of *Tribulus terrestris* extract (Protodioscin) in normal and castrated rats. *Life Sci.*, **71**(12), 1385-1396. doi: 10.1016/s0024-3205(02)01858-1. |
| **20** | Sahin, K., Orhan, C., Akdemir, F., Tuzcu, M., Gencoglu, H., Sahin, N., Turk, G., Yilmaz, I., Ozercan, I. H. and Juturu, V. (2016). Comparative evaluation of the sexual functions and NF-κB and Nrf2 pathways of some aphrodisiac herbal extracts in male rats. *BMC Complement. Altern. Med*., **16**(1), 318. doi: 10.1186/s12906-016-1303-x. |
| **21** | Gauthaman, K. and Ganesan, A. P. (2008). The hormonal effects of *Tribulus terrestris* and its role in the management of male erectile dysfunction- an evaluation using primates, rabbit and rat. *Phytomedicine*, **15**(1-2), 44-54. doi: 10.1016/j.phymed.2007.11.011. |
| **22** | Adimoelja, A., Setiawan, L. and Djojotananjo, T. (1995). *Tribulus terrestris* (protodioscin) in the treatment of male infertility with idiopathic oligoasthenoteratozoospermia. In*: Proceedings of the First International Conference of Medical Plants for Reproductive Medicine*. Taipei, Taiwan, Province of China. |
| **23** | Adimoelja, A. and Adaikan, P. G. (1997). Protodioscin from herbal plant *Tribulus terrestris* L. improves the male sexual functions, probably via DHEA. In: Proceedings of the 6th Biennial Asian-Pacific Meeting on Impotence in Kuala Lumpur, Malaysia. *International Journal of Impotence Research*, **9**(Suppl 1), 20. |
| **24** | Roaiah, M. F., El Khayat, Y. I., GamalEl Din, S. F. and Abd El Salam, M. A. (2016). Pilot study on the effect of botanical medicine (*Tribulus terrestris*) on serum testosterone level and erectile function in aging males with partial androgen deficiency (PADAM). *J. Sex Marital Ther*., **42**(4), 297-301. doi: 10.1080/0092623X.2015.1033579. |
| **25** | GamalEl Din, S. F., Abdel Salam, M. A., Mohamed, M. S., Ahmed, A. R., Motawaa, A. T., Saadeldin, O. A. and Elnabarway, R. R. (2018). *Tribulus terrestris* versus placebo in the treatment of erectile dysfunction and lower urinary tract symptoms in patients with late-onset hypogonadism: A placebo-controlled study. *Urologia Journal*, **86**(2), 74-78. doi: 10.1177/0391560318802160. |