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Aphrodisiac & Tonic Activity of Tribulus Leaf

Botanical Name:	*Tribulus terrestris*
Family:	Zygophyllaceae
Part Used:	Aerial parts

Tribulus terrestris is a prostrate spreading herb, the fruit of which contains sharp, rigid spines and for this reason it is known as puncture vine. It is native to many geographical zones, including the Mediterranean regions, India, China, Africa and Australia. In the 1990s attention focused on the Bulgarian research of a standardised extract of Tribulus leaf (TLSE, standardised to not less than 45% furostanol saponins calculated as protodioscin), used as a male tonic and for the treatment of infertility and menopause. Research undertaken by MediHerb has shown that the phytochemical profile of the herb varies depending upon the geographical origin and the plant part utilised. Only herb sourced from the Central European regions of Bulgaria and Slovakia have been found to contain protodioscin, which is an important indicator of quality and efficacy. Additionally only the leaves and stem of the plant contain protodioscin, the fruit do not contain this phytochemical.

Traditional Uses

There is little information available on the traditional use of Tribulus leaf. In Ayurveda the plant and fruit have been used to treat spermatorrhoea, gonorrhoea, impotence, uterine disorders after parturition, cystitis, painful urination, kidney stones and gout.[1] Tribulus is consumed as a green leafy vegetable by the Batemi of East Africa.[2]

Scientific Studies

Constituents

The active constituents of Tribulus leaf include the steroidal saponins, mainly furostanol glycosides (including protodioscin and protogracillin) and small quantities of spirostanol glycosides.[3-5] Tribulus leaf contains a higher concentration of steroidal saponins than the fruit, and there is a higher protodioscin content in leaf of Eastern European origin than in leaf of other geographical locations – *see Analytical Studies below*).

The furostanol glycosides are a subclass of steroidal saponins. They have a sugar group at the carbon-3 (C-3) position and a second sugar group at position C-26. Furostanol glycosides readily convert into spirostanol saponins (with one sugar group at C-3) in the presence of plant enzymes.[6] Such degradation, resulting in loss of sugars, may occur postharvest, in manufacturing or during experimental analysis.

Analytical Studies

An analytical investigation in 1998 of twenty Tribulus preparations, most available for sale in the USA, found insufficient levels of furostanol saponins in the majority of products except TLSE.[7] Many Tribulus products on the market are quite different in phytochemical profile from the Bulgarian extract. A study conducted in the US in late 2001 found that the level of protodioscin varied substantially with the plant part (leaf, stem or fruit) and the origin of the Tribulus (Bulgaria, India or China). Only leaf from Bulgaria was high in protodioscin. An analysis of three products selected from the US market found substantial levels of protodioscin only in the product manufactured in Bulgaria. The other two samples (one of which contained Tribulus fruit) were deficient in protodioscin.[8] An Australian study investigating plant material produced similar results. An Eastern European variety of Tribulus (from Slovakia) contained high levels of protodioscin in the leaf but none in the fruit. Leaf from Australia and India did not contain protodioscin.[9]

So if a Tribulus product is made from the root or fruit of the plant, or is sourced from anywhere else other than Eastern Europe, it will probably contain low levels of protodioscin and therefore will be quite different to the Bulgarian standardised extract. This is despite what might be claimed on the label for such products, because often inferior methods of analysis have been used to measure the furostanol saponins, such as gravimetric or colorimetric techniques. The quality of Tribulus products is best assessed by high performance liquid chromatography as used in the two studies cited above.

Pharmacodynamics

TLSE is a product obtained from the aerial parts of Eastern European *Tribulus terrestris*, which contains mainly saponins of the furostanol type (not less than 45%, calculated as protodioscin). Another trade preparation, VT,

has also been studied and contains TLSE, vitamins, folic acid and potassium orotate.

Hormonal & Sexual Activity

Oral doses of TLSE have demonstrated the following effects *in vivo*.

- Improved libido, sexual activity and intracavernous pressure in rats (2.5–10 mg/kg/day), and a proerectile effect on corpus cavernosum smooth muscle of rabbits (tissue isolated after treatment, 2.5–10 mg/kg/day).[10]
- Aphrodisiac activity demonstrated in castrated rats (5 mg/kg/day) may be due to the androgenic activity of TLSE.[11] The results of an *in vivo* study investigating the effect of TLSE on the brain tissue of normal rats (5 mg/kg/day) add further evidence of this, indicating that TLSE may have a central effect. The authors suggested that an aphrodisiac activity of TLSE may be mediated by increase in both androgen receptor and nitric oxide synthase (NOS) containing neurons. (NOS is present in the regions of the brain that regulate sexual functions).[12]
- Marked stimulation of spermatogenesis, increased density of Sertoli cells, increased tenacity and viability of spermatozoa, and accelerated and emphasised sexual activity in rats (70 mg/kg/day).[13] Female rats treated with the saponin fraction produced more offspring.[4]
- Increased plasma testosterone concentrations compared to controls in male lambs and rams (250 mg/day); acceleration of sexual development, activation of spermatogenesis and stimulation of seminiferous tubule growth in immature sheep.[14]
- Increased testosterone levels, improved semen production and normalised sexual activity in rams with sexual impotence; no morphologic changes in the structure of either testes or epididymides were observed during the treatment period.[15]
- Restored libido and sexual reflexes in 71% of boars with absence of libido. Five animals with prolonged poor libido also improved (70 mg/kg/day).[16]

TLSE (750 mg/day for 5 days) increased serum FSH and oestradiol compared to baseline values in human female volunteers and increased the level of LH and testosterone in male volunteers,[17] thus demonstrating increased sex hormone production in both men and women.

Mechanism of Action

Saponins from Tribulus appear to increase FSH in women, which in turn increases levels of oestradiol. They may do this by binding with, but only weakly stimulating, hypothalamic oestrogen receptors, which are part of the negative feedback mechanism of oestrogen control. The weak stimulus (as opposed to oestrogen) leads the body to interpret that oestrogen levels are lower than they really are and it subsequently increases production. In the postmenopausal woman Tribulus might alleviate symptoms of oestrogen withdrawal by the binding of its steroids to vacant receptors in the hypothalamus (in this low oestrogen situation). This could be sufficient to convince the body that more oestrogen is present in the bloodstream than actually is. A similar mechanism via the hypothalamus could apply for men.

Tonic Activity

TLSE increased the nonspecific resistance in mice with experimental lung infection, possibly due to the activation of alveolar macrophages.[18] TLSE has been shown to intensify protein synthesis and enhance the activity of some enzymes connected with energy metabolism. VT increased the absorption of iron from the small intestine and inhibited lipid peroxidation during stress.[19]

TLSE (oral; 100 mg/kg/day for 5 days) increased static physical endurance in rats. Treatment with VT (oral; 300 mg/kg/day for 1 month) markedly increased endurance. VT (by injection) accelerated the restoration process after heavy exercise, had a slight protective action on capillary and peritoneal lesions and decreased capillary permeability.[20] The mechanism of improved endurance was probably not directly connected with the adrenergic system. VT does not stimulate the CNS and its mechanism of action is different from that of psychostimulants.[19,20] VT improved resistance to stress and endurance *in vivo* compared to controls. It increased the concentration of dopamine and serotonin metabolites and the levels of noradrenaline in the hypothalamus.[21]

VT given for 5 days (equivalent to 270 mg/day TLSE) increased serum concentrations of growth hormone, insulin and aldosterone in human volunteers without exceeding normal values and with no clinical suggestion of hyperfunction of the respective endocrine glands. Greater increases were seen in the group actively engaged in sports compared to the untrained group. There were no effects on cortisol, testosterone or prolactin levels.[22]

Pharmacokinetics

Pharmacokinetic studies of TLSE in rats indicated that 12–14% of protodioscin is excreted in the bile and 6–7% in the urine (at 24 hours) when administered intravenously (50 and 200 mg/kg). After oral administration of the same individual doses, 2–4% of protodioscin was excreted in the bile, but protodioscin was not detected in the urine.[23]

Toxicology

LD_{50} values for oral administration of TLSE in both mice and rats were greater than 10 g/kg, indicating very low toxicity. No lethality, change in behaviour or changes in biochemical indices were observed in rats given oral doses ranging from 75–300 mg/kg for 30 and 90 days, or dogs receiving 75 mg/kg for 180 days.[24] There was no evidence

of induced carcinogenicity after oral administration of TLSE at 50 or 150 mg/kg/day for 93 weeks in rats.[25]

Tribulus staggers, a unique neuromuscular disorder in sheep, is believed to be due to the accumulation of the harmala alkaloids in the blood over a period of time.[26] A photosensitization reaction known as geeldikkop has been reported in livestock after excessive consumption of Tribulus.[27-29] These reactions have not been observed in humans and are highly unlikely at the recommended dosage.

Clinical Studies

Male Infertility and Impotence

In a 5-year study of 100 Bulgarian couples in which the men were immunologically infertile, pregnancy was achieved in 44% of couples after the men were treated with TLSE. Treatment with TLSE correlated with a drop in antisperm antibody titre, improvement of sperm motility and increased penetration of the cervical mucus by sperm.[30]

The results of open clinical trials conducted by four Bulgarian research teams, including a total of 363 men, indicated that TLSE had a stimulating effect on sexual function.[31-35]

- Treatment with 750 mg for 60 days significantly increased motility and rate of movement of spermatozoa from 38 men with idiopathic oligospermia. In some cases, after repeated treatment at a dosage of 1500 mg/day, a normalisation of the sperm profile was observed, accompanied by an increased serum level of LH and testosterone and decreased oestradiol.
- Two groups of men with oligospermia after varicocele operation were treated with either 750 mg for 60 days or 1500 mg for 90 days. Significant improvement in sperm motility was observed in both groups. Treatment with 1500 mg also resulted in an increase in ejaculate quantity in all patients.
- Patients with unilateral or bilateral hypotrophy of the testes and oligospermia demonstrated improvement in ejaculate volume, spermatozoal concentration and motility after treatment (1500 mg/day, 60 days). Testosterone levels were also increased. A light palpable pain in the testicular region with slight oedema was reported by patients during the treatment, which abated 2–3 months after treatment.
- Treatment of 51 infertile males with 750 mg/day TLSE for 3 months significantly increased ejaculate volume, spermatozoa concentration, motility and velocity. Spermatozoa morphology normalised and ejaculate liquefaction time decreased. Semen immune parameters decreased: leukocyte counts, α-amylase values (an enzyme involved in ejaculate liquefaction), and secretion of local immunoglobulins. Cholesterol, LDL, triglycerides and VLDL decreased and HDL increased. Libido was normalised or enhanced in those reporting poor libido.
- Thirty-one pregnancies were recorded for 100 couples with infertility involving an immunological cause within 12 months of initiating TLSE treatment. The average time taken to conceive was 5.2 months. Prior to treatment spermatozoa number and quality varied between males, but all males and 74% of females had abnormal results for sperm-agglutinating antibody tests. The dosage used was 750 mg/day for males and 750 mg/day from days 21 to 27 of the menstrual cycle for females until conception.
- Improvement in sperm profile was not observed in patients with chronic prostatitis (750–1500 mg/day).
- Of 14 patients suffering reduced libido, 12 showed considerable improvement after 30 days (1500 mg/day) and one patient was slightly improved after 60 days' treatment. Libido was improved in 27 of 36 patients with chronic prostatitis. The other 9 patients, with chronic prostatitis for over 5 years, demonstrated no improvement. Libido was incidentally improved in patients with hypotrophy of the testes and idiopathic oligospermia.
- Libido and sexual activity were improved in some patients with Klinefelter's syndrome (genetic hypogonadism), Noonan syndrome (a multifaceted disorder which includes cryptorchidism) and simple cryptorchidism.
- TLSE was well-tolerated in all of the above studies.

Tribulus has been part of a number of herbal formulations successfully used in uncontrolled clinical trials in India and Russia to treat sexual dysfunction or sexual inadequacy in men. The main formulations contained 7–12.5% of Tribulus by weight. Improvement in sexual function was observed in convalescing postmyocardial infarction male patients,[36] and in leprosy patients experiencing testicular and epididymal changes. Patients with oligospermia showed objective improvement.[37] Impotence and loss of libido improved in male diabetics.[38] Improvement was observed in men with impotence.[39,40] Sperm count and motility improved in approximately 60–70% of subfertile and oligospermic men.[41,42]

Androgen Production in Healthy Men

No significant difference in serum testosterone, androstenedione or luteinizing hormone was apparent for healthy men (20–36 y.o.) administered TLSE compared to controls. Volunteers were randomly assigned to receive one of two doses of Tribulus extract of Bulgarian origin (corresponding to 6 mg/kg/day or 12 mg/kg/day of saponins) or placebo.[43]

Female Infertility

In an open study involving infertile women, TLSE (750–1500 mg) was administered every day for 2–3 months (Group 1), only on days 5 to 14 of the menstrual cycle for 2–3 months (Group 2), or used in the preovulatory phase in combination with an ovulation stimulant for 3 months (Group 3).[16] Group 1 did not show improvement in the ovulation parameters measured and side effects were observed, especially when the treatment was abruptly terminated. Of the 36 women in Group 2, 6% of women experienced normalised ovulation with resultant pregnancy, 61% demonstrated normalised ovulation without pregnancy and 33% demonstrated no effect from treatment. Parallel control studies on a comparable cohort were carried out utilising three ovulation stimulants. The best results were obtained with 62 women treated using epimestrol: 39% had normalised ovulation with pregnancy, 35% had normalised ovulation without pregnancy and 26% demonstrated no effect from treatment. No side effects were recorded for the TLSE group, compared with an incident rate of 6.5%, 10.6% and 38% in women treated with ovulation stimulants. For the 20 women treated with TLSE and an ovulation stimulant (Group 3), the effect from their combined use was better than treatment with either single agent.

Menopause

In an open study, 98% of 50 menopausal women experienced symptom improvement after TLSE treatment, but not after placebo. Fifty-two percent of patients were experiencing natural menopause and 48% had postoperative symptoms after removal of their ovaries. Predominant symptoms included hot flushes, sweating, insomnia and depression. The dosage prescribed varied, but generally a maintenance dose of 500–750 mg/day of TLSE was reached after higher initial doses. Treatment did not result in significant changes in FSH, LH, prolactin, oestradiol, progesterone and testosterone, although FSH tended to be lower.[16]

Body Composition & Exercise Performance

TLSE given for 8 weeks at a daily dose of 3.2 mg/kg did not enhance body composition or exercise performance in 8 resistance-trained males when coupled with a resistance-training program in a randomised, double-blind, placebo-controlled trial. The authors concede that the lack of improvement in body composition in both groups may be attributed to the fact that these subjects were already lean and may not have consumed enough protein or calories to gain lean body mass. In addition the method chosen to assess exercise performance was not the most objective measure available.[44] The dose of TLSE used was low (240–260 mg/day).

Clinical Summary

Actions

Tonic, aphrodisiac, oestrogenic in females (indirectly), androgenic in males (indirectly), fertility agent.

Therapeutic Indications

- Male and female infertility, impotence, decreased libido, menopause.
- To restore or build vitality (especially during convalescence or after surgery) and to assist in responding to stress; to improve physical performance.

Dosage & Administration

The recommended adult dosage for the hormonal effects is one tablet containing 100 mg of furostanol saponins (calculated as protodioscin), 3 times per day. Health care professionals need to be wary of Tribulus products made using different plant parts and/or quantified with nonspecific test methods (ie other than spectrophotometric).[3] The beneficial therapeutic effects of TLSE must not be attributed to all Tribulus products, due to the low level of furostanol saponins measured in many products.

Suggested Combinations

Tribulus combines well with damiana, Korean ginseng, Rhodiola, saw palmetto or Withania in male sexual inadequacy and infertility; black cohosh, shatavari or wild yam in low libido in women and menopause; and Withania, Siberian ginseng, Rhodiola or Korean ginseng for tonic use.

Adverse Reactions

As with all saponin-containing herbs, oral intake may cause reflux and irritation of the gastric mucous membranes.

Contraindications & Cautions

According to traditional Chinese medicine Tribulus should be used with caution in pregnancy.[45] If Tribulus is being used to promote fertility in women, its use should be ceased immediately after pregnancy is established. While it is unlikely that normal human doses of Tribulus would cause cholestasis, this should be considered in unexplained cases of cholestasis in patients taking Tribulus. Steroidal saponin-containing herbs such as Tribulus are best kept to a minimum in patients with pre-existing cholestasis.

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