**ABSTRACT**

*Tribulus terrestris* is an annual plant in the caltrop family (Zygophyllaceae) widely distributed around the world, that is adapted to grow in dry climate locations in which few other plants can survive. While this plant has lots of properties, the aim of this study is to overview its therapeutic effects than its nutritive and industrial effects. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases from 1994 to 2016. totally, of 100 found articles, 47 articles were included. The search terms were “Tribulus terrestris”, “therapeutic”, “pharmacological”. Various studies have shown that *Tribulus terrestris* Possess Anti-infertility, Diabetes Heart disease, Anti-inflammatory effects, Antibacterial activity, Liver disease, Supplementation activity, Kidney disease, Anti-oxidant properties, Anti-cancer, Aphrodisiac activity, Anti-stress Oxidative stress, Liver and kidney, Hyperplasia, Antioxidant and metal chelator activity and Hepatoprotective activity, Anti-Androgenic Activity, Supplemental Sport, Pro-sexual androgen enhancing effects, Aphrodisiac properties. *Tribulus terrestris* not likely to become an important alternative to standard medical therapies unless there are changes to the regulation, standardization, and funding for research of these products.

**Keywords**: *Tribulus terrestris*, “therapeutic”, “pharmacological”.

**INTRODUCTION**

It is proved that herbal medicine is effective in the treatment of many diseases[1-20]. *Tribulus terrestris* is an annual plant in the caltrop family (Zygophyllaceae) widely distributed around the world, that is adapted to grow in dry climate locations in which few other plants can survive. It is an invasive species in North America. Like many weedy species, this plant has many common names, including goat's-head, bindii, bullhead, burra gokharu, Bhakhdi, caltrop, small caltrops, cat's-head, devil's eyelashes, devil's-thorn, devil's-weed, puncture vine, puncturevine, and tackweed[21].

It is native to warm temperate and tropical regions of the Old World in southern Europe, southern Asia, throughout Africa, and Australia. It can thrive even in desert climates and poor soil. A network of fine rootlets arise from the taproot to take advantage of soil moisture, by which the plant can survive in very arid conditions.

The stems radiate from the crown to a diameter of about 10 cm (3.9 in) to over 1 m (3 ft 3 in), often branching. They are usually prostrate, forming flat patches, though they may grow more upwards in shade or among taller plants[22]. Stems branch from the crown and are densely hairy. Leaves are opposite and pinnately compound. Densely hairy leaflets are opposite and up to 3 mm (0.12 in) long. The flowers are 4–10 mm (0.16–0.39 in) wide, with five lemon-
yellow petals, five sepals, and ten stamens. In Southern California, it blooms from April through October, where it is highly invasive in waste places and disturbed sites[23].

A week after reach flower blooms, it is followed by a fruit that easily falls apart into five nutlets or burs. The nutlets are hard and bear two to four sharp spines, 10 mm (0.39 in) long and 4–6 mm (0.16–0.24 in) broad point-to-point. These nutlets strikingly resemble goats' or bulls' heads; the “horns” are sharp enough to puncture bicycle tires and lawn mower tires. They can also cause painful injury to bare feet; however, they are also large enough to pull out as soon as they pierce into the sole, and the resultant hole is only slightly larger than stepping on a push pin if it goes all the way in. Within each nutlet, seeds are stacked on top of each other, separated by a hard membrane. As an adaptation to dry climates, the largest seed germinates first, while the others may wait until more moisture is available before germinating[23, 24].

The spines of the nutlets point upward, where they stick into feet and fur of animals, and are thereby dispersed. This causes damage to domesticated livestock and degrades wool[25].

Anti-infertility
The effects of T. terrestris on semen quality and physiological parameters was evaluated. Result showed significant enhancement in sperm concentration, motility and liquefaction time. Protodioscin, the main phytochemical agent of the Tribulus genus, acts on sertoli cells, germ cell proliferation and growth of seminiferous tubules. This component is known to convert testosterone into dihydrotestosterone, which plays important roles in male attributes [26].

The role of Tribulus terrestris in males with unexplained infertility and its effect on serum testosterone and semen parameters was evaluated. no statistically significant correlations were observed between testosterone (free and total) and LH and semen parameters before and after the treatment. Tribulus terrestris was ineffective in the treatment of idiopathic infertility [27].

Diabetes
the efficacy of the hydroalcoholic extract of T ter restris on the serum glucose and lipid profile of women with non-insulin-dependent diabetes mellitus was evaluated. The study showed preliminary promising hypoglycemic effect of T terrestris in women with diabetes mellitus type 2[28].

Heart disease
The protective effect of partially characterized Tribulus terrestris L. fruit methanol extract against mitochondrial dysfunction in cell based (H9c2) myocardial ischemia model was investigated. Result showed that terres tris L. fruit methanol extract pretreatment was found effective in safeguarding mitochondria via its antioxidant potential, mediated through various bioactives as well as to ameliorate ischemic insult in H9c2 cells. HPLC of T. terrestris L. fruit methanol extract revealed the presence of ferulic acid, phloridzin and diosgenin.T [29].

Anti-inflammatory effects
anti-inflammatory active extract fractions of Tribulus terrestris (family Zygophyllaceae) was evaluate d. The different chloroform fractions F1, F2, F4, F5, F7, F9, F11 and F14 revealed 4, 7, 7, 8, 9, 7, 7 and 6 major spots, respectively. The results obtained in this experiment strongly support and validate the traditional uses of this Sudanese medicinal plant[30].

the effects of N-trans-p-cafeeyl tyramine (CT) isolated from T. terrestris on the production of nitric oxide (NO), was investigated .it was found that the ethanolic extract of T. terrestris (EETT) and CT inhibited the production of NO, tumor necrosis factor-a (TNF-a), interleukin (IL)-6 and IL-10 in the LPS-stimulat ed RAW 264.7 cells in a dose-dependent manner. these findings indicate that CT isolated from T. terrestris is a novel and potent modulator of inflammatory responses. Thus, it may prove beneficial to further evaluate CT as a possible treatment for chronic inflammatory diseases [31].

Antibacterial activity
Antimicrobial activities of an ethanol extract of Tribulus terrestris alone and in combination with Capsella bursa-pastoris and Glycyrrhiza glabra were examined in vitro against six pathogens. It provided scientific evidence to support uses of T. terrestris and its mixture with C. bursa-pastoris and G. glabra for the treatment of oral infections[32].
Liver disease
the influence of hydroalcoholic extract of TT plant on cisplatin (CIS) (EBEWE Pharma, Unterach, Austria) induced renal tissue damage in male mice was investigated. The results suggested that the oral administration of TT fruit extract at dose 100, 300 and 500 mg/kg body weight provided protection against the CIS induced toxicity in the mice[33]. The anticalapetic effect of Tribulus terrestris on haloperidol-induced catalepsy in albino mice was evaluated. The result demonstrates Tribulus terrestris has a protective effect against haloperidol-induced catalepsy, which is comparable to the standard drug used for the same purpose. Our study indicates Tribulus terrestris can be used to prevent haloperidol-induced extrapyramidal side effects[34].

Supplemental activity
One anti-doping study reported an incident with a TT supplement contaminated by a banned steroid. Toxicological studies regarding TT have been carried out on animals only, however, one accidental poisoning of a man was described. The Australian Institute of Sport does not recommend athletes' usage of TT. So far, the published data concerning TT do not provide strong evidence for either usefulness or safe usage in sport [35].

Kidney disease
The protective effect of aerial parts of the Tribulus terrestris L extract on acute kidney injury (AKI) was investigate. Result found that Oral administration of Tribulus terrestris extract for 2 weeks can decrease kidney functional disturbance, oxidative stress, and cellular damages following reperfusion injury in rats [37].

Anti-oxidant properties
The protective and anti-oxidant activities of the methanolic extract of Tribulus terrestris fruits (METT) against sodium valproate (SVP)-induced testicular toxicity in rats was assessed. These results affirm the traditional use of T. terrestris fruits as an aphrodisiac for treating male sexual impotency and erectile dysfunction in patients. The study recommends that T. terrestris fruits may be beneficial for male patients suffering from infertility [38].

Anti-cancer
Inhibitory effect of TT against the progression of castration-resistant prostate cancer was investigated. Cell cycle arrest and induction of apoptosis in cancer cells and endothelial cells might be plausible mechanisms of actions for the observed antitumor and antiangiogenic activities of TED [39].

The antitumoral properties of TT was evaluated. The study shows experimental evidence that TT has a preventive efficacy against UVB-induced carcinogenesis and the molecular knowledge on the mechanisms through which TT saponins regulate cell death suggests great potential for TT to be developed into a new medicine for cancer patients [40].

Aphrodisiac activity
the influence of Tribulus terrestris extract on androgen metabolism in young males was investigated. The findings anticipate that Tribulus terrestris steroid saponins possess neither direct nor indirect androgen-increasing properties. The study will be extended in the clarifying the probable mode of action of Tribulus terrestris steroid saponins [42]. Sexual behaviour and intracavernous pressure (ICP) were studied in both normal and castrated rats to further understand the role of TT containing protodioscin (PTN) as an aphrodisiac. There was also a mild to moderate improvement of the sexual behaviour parameters as evidenced by increase in MF and IF; decrease in ML, IL and PEI. These results were statistically significant. It is concluded that TT extract appears to possess aphrodisiac activity probably due to androgen increasing property of TT (observed in our earlier study on primates) [43].

The effect of acute and repeated dose administration of lyophilized aqueous extract of the dried fruits of Tribulus terrestris (LAET) on sexual function in sexually sluggish male albino rats. Findings of the present study validate the traditional use of T. terrestris as a sexual enhancer in the management of sexual dysfunction in males [44].

Anti-stress
The effect of tribulus terrestris saponins (TTS) on behavior and neuroendocrine of chronic mild stress (CMS) depression rats was observed. Result CMS can affect rat behavior and neuroendocrine and cause depression. TTS has the antagonism on CMS and produce antidepressive effects[45].

**Oxidative stress**
the effect of Tribulus terrestris on different parameters of oxidative stress and gene expression profiles of antioxidant enzymes was examined. T. terrestris also reduced hyperoxaluria- caused oxidative stress, and restored antioxidant enzyme activity and their expression profile in kidney tissue. Histological analysis depicted that T. terrestris treatment decreased renal epithelial damage, inflammation, and restored normal glomerular morphology [46].

the possible protective effects of Tribulus terrestris fruit aqueous extract (TTFAEt) on lipid profile and oxidative stress in isoproterenol (ISO) was evaluated .Pretreatment with extract significantly showed a protective effect against ISO altered lipid profile, lipid peroxidation and antioxidant enzyme levels. The present study showed therapeutic effect of TTFAEt on lipid profile and oxidative stress in isoproterenol (ISO) induced myocardial necrosis in experimental rats[47].

**Liver and kidney**
Prominent pathological changes observed in liver were severe vascular and sinusoidal congestion with diffuse degenerative changes and mononuclear infiltration into peripheral areas, while the kidney showed vascular and glomerular congestion, cloudy swelling of tubular epithelium. Coadministration of ethanolic extract of T. terrestris or vitamin E along with Cd significantly reversed the Cd induced changes along with significant reduction in Cd load[48].

**Hyperplasia**
the effectiveness and tolerability of an oral formulation, comprising standardized extracts of Murraya koenigii and Tribulus terrestris leaves, versus tamsulosin in the treatment of symptomatic BPH was examined. The findings suggest that the M koenigii- and T terrestris-based formulation significantly lowered IPSS scores in the initial treatment of symptomatic BPH. Further trials are needed to determine if the beneficial effect is sustained beyond the 12-week observation period of this trial[49].

**Antioxidant and metal chelator activity**
testicular tissue peroxidation of Tribulus terrestris Linn was investigate (TT) . eTT exhibited protective effect against Cd-induced testicular damage. The protective effect appears to be mediated through inhibition of testicular tissue peroxidation by antioxidant and metal chelator activity and also, may be indirectly by stimulating the testosterone production from Leydig cells[50].

**Hepatoprotective activity**
The potential protective role of Tribulus terrestris in acetaminophen-induced hepatotoxicity in Oreochromis mossambicus was investigated. Histopathological changes of liver, gill and muscle samples were compared with respective controls. The results of the present study specify the hepatoprotective and antioxidant properties of T. terrestris against acetaminophen-induced toxicity in freshwater fish, O. mossambicus[51].

**Anti-Androgenic Activity**
The in vitro antiandrogenic activity of plant extracts and their positive effects on different parameters of PCOS were proved in vivo and its effect was confirmed [52].

**Supplemental Sport**
The influence of the Tribulus terrestris extract on the parameters of the functional preparadness and athletes' organism homeostase was investigated. The declining tendency of urea, cholesterol and bilirubin concentrations has appeared. The concentration of blood testosterone increased statistically reliable during the first half (10 days) of the experiment; it did not grow during the next 10 days while consuming Tribulus still [53].

The effect of T. terrestris on strength, fat free masswas determined. No between-group differences were noted in the urinary T/E ratio. It was concluded that T. terrestris did not produce the large gains in strength or lean muscle mass that many manufacturers claim can be experienced within 5-28 days. Furthermore, T. terrestris did not alter the
urinary T/E ratio and would not place an athlete at risk of testing positive based on the World Anti-Doping Agency's urinary T/E ratio limit of 4:1[54].

**Pro-sexual and androgen enhancing effects**

Aphrodisiac effect of TT as an androgen enhancing botanical supplement was evaluated. It is becoming increasingly clear that the deep-seated traditional view of TT bioactivity focused exclusively on its androgen enhancing properties is outdated and incapable for accommodating the emerging evidence from recent clinical and experimental studies pointing toward new and, perhaps, more plausible modes of action. Novel paradigms guiding the development of new testable hypotheses for TT aphrodisiac properties are needed to stimulate further investigations into potential biological mechanisms in which many apparently conflicting observations can be reconciled[55].

**Aphrodisiac properties**

Synergism and antagonism impact of different plant metabolites present in crude fruit extract of Tribulus terrestris 'the herbal Viagra' have been studied. Variability in plant composition, biomass and metabolites concentration in different modules was significantly contributed by spatial factor. However the edaphic parameters also changes with both spatial and temporal factors significantly. Fruit is the officinal part and the fruit production significantly related with soil nitrogen (P<0.01), whereas the soil nitrogen and pH also influenced the alkaloid content in fruit (P<0.05). The linear relation between fruit protein and fruit alkaloid (P<0.01) also observed and the relationshp in between different soil parameters were established. Bioassay work confirmed its aphrodisiac properties, and site III is suggested for maximum biomass and high concentration of different metabolites[56].

**CONCLUSION**

Tribulus terrestris not likely to become an important alternative to standard medical therapies unless there are changes to the regulation, standardization, and funding for research of these products.

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