

Overview of Phytochemical and Pharmacological Aspects of Tribulus Terrestris.

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ABSTRACT :- Tribulus terrestris (TT) is an annual plant of the plant of the (family zygophyllaceae)

Commonly known as Gokshur, Gokhru or puncture vine. It has been used for both the Indian and Chinese system of medicine for treatment of various kind of disease.

The bioactive phytochemicals such as saponins and flavonoid have been isolated and identified from Tribulus terrestris that are responsible for various pharmacological activities.

The aim of the review is to provide a comprehensive overview of the traditional application, phytochemistry and pharmacology and provides evidence for better medicinal usage of Tribulus terrestris.

I. INTRODUCTION :-

TT is an annual plant in the caltrop family (zygophyllaceae) which is commonly known as Tribulus comprises about 20 species in the world of which 3 species, VIZ.

Tribulus cistoides, Tribulus terrestris and Tribulus alatus are commonly occurred in India.

TT plant is used individually as a single therapeutic agent or subordinate component of food supplement. it is mainly planted in the Mediterranean and in subtropical regions such as india , china, south America, Mexico, Spain, Bulgaria and Pakistan .

It has been used for generations to energize, vitalize and improve sexual function of physical performance in men. The fruits and roots of TT have been used as a folk medicine for thousands of year in china, India, Sudan and Pakistan.

PLANT PROFILE :-

TT is commonly known as Gokshur (Sanskrit) and Gokhru (hindi) it is found in all over india up to 11000 Ft in Kashmir, Cylon and all warm regions. It is common weed of pasture lands, road sides and other waste places, chiefly in hot, dry and sandy places including west Rajsthan and Gujrat in India.

TAXONOMICAL CLASSIFICATION-

Kingdom	Plantae
Division	Phanerogams
Subdivision	Angiospermae
Class	Dicotyledonae
Subclass	Polypetalae
Series	Disciflorae
order	Giraniales
Family	Zygophyllaceae
Genus	Tribulus
Species	Terrestris Linn

BOTONICAL DESCRIPTION OF TT :-

It is small, prostrate 10-60 cm height, hirsute or silky hairy shrub. The leaves are opposite, often unequal, pinnate, pinnate from 5-8 pairs and elliptical or oblong lanceolate. They are 5-10 mm long and 2-4 mm wide flower are yellow in colour. The fruits from the five mericarps are ax-shaped, 3-6 mm long and having diameter of 7-12mm and hard texture. The root is slender, fibrous, cylindrical and frequently branched.

Fruits and roots are mainly used as folk medicine for the treatment of various ailments.

Fruits are faint greenish yellow with spines fruits are 5 mericarp of globose, glabrous, mericulate, wedge shaped and woody cocci. The odour of fruit is faintly aromatic and taste is slightly acrid.

CHEMICAL CONSTITUENTS :-

The preliminary phytochemical study of TT revealed the presence of saponins, flavonoids, glycosides, alkaloid and tannins, terpenoids, amide derivatives, amino acid and protein. Furostanol and spirostanol saponins of tigogenin, neotigogenin, gitogenin, neogetogenin, hecogenin, neohecogenin, disogenin, chlorogenin, ruscogenin and sarasapogenin types are frequently found in this plant.

Furostanol glycoside is majorly present in this plant including prostodioscin and prostogracillin. Prostodioscin is the most dominant saponins and spirostanol glycoside are present in small quantities. WU et.al found that the quantity of main flavonoid is about 1.5 times more than main saponins.

The flavonoid content of *Tribulus terrestris* should be studied and isolated kaempferol, kaempferol-3 glucoside, kaempferol-3 rutinoside and tribuloside. Louveaux et.al. detect 18 flavonoid which is caffeoyl derivatives, quercetin isoquercitrin, isorhamnetin, rutin and kaempferol using high performance liquid chromatography (HPLC).

TRADITIONAL USES :-

It is used in folk medicine as a tonic, aphrodisiac, palliative, astringent, stomachic, antihypertensive, diuretic and urinary disinfectant. The fruit of it is very effective in most of the genitourinary tract disorder. TT has been used for centuries in Ayurveda to treat impotence, venereal disease and sexual debility in Bulgaria that plant is used as folk medicine for treating impotence.

The ayurvedic pharmacopoeia of India attributes cardiotoxic properties to the root and fruit in traditional Chinese medicine. The fruits were used for treatment of eye trouble edema abdominal distension and sexual dysfunction. TT is described as a highly valuable drug in the Shennong pharmacopoeia in Unani medicine. TT is used as diuretic, mild laxative and general tonic.

PHARMACOLOGICAL ACTION / ACTIVITIES :-

It has diuretic, Aphrodisiac, Antiurrolithic, immuno-modulatory, Antidiabetic, Absorption enhancer, Hypolipidemic, Cardiotoxic, Central nervous system, Hepatoprotective, Anti-inflammatory, Analgesic, Antispasmodic, Anticancer, antibacterial, Anthelmintic, Anticarcinogenic, Larvicidal, Improvement in fertility, Libido enhancing activity, Prevention and treatment of cardiovascular disease, Protective activity in neuronal cells, Improvement of athletic ability activity, Antioxidant activity.

1) DIURETIC ACTIVITY –

The diuretic properties of TT are due to large quantities of nitrates and essential oil present in fruits and seeds. The diuretic activity can also be attributed to the presence of potassium salts in high concentration.

The aqueous extract of TT in oral dose of 5 gm/kg, elicited a positive diuresis which was slightly more than that of furosemide. The concentration of sodium & chloride was increased in urine. The increased tonicity of the smooth muscle which was produced by TT extract. The diuretic action of TT makes it useful as an anti-hypertensive agent.

2) APHRODISIAC ACTIVITY :-

The enhanced relaxant effect observed is due to increase in the release of nitric oxide from the endothelium and nitrergic nerves ending which is claimed as an aphrodisiac. Singh et. al. Evaluated the acute and repeated dose administration of lyophilized aqueous extract of the dried fruits of TT at doses of 50 and 100 mg/kg of body weight as a sexual enhancer. A dose dependant improvement in sexual behaviour was observed with the LAET treatment which was more prominent of chronic administration of LAET. The ethanolic extract of TT fruits was tested in urolithiasis induced by glass bead implantation in albino rats.

3) ANTIUROLITHIC ACTIVITY –

The fruits of TT have long been used in traditional systems of medicine for the treatment of various urinary diseases including urolithiasis calcium oxalate is major types of crystal found in kidney stone.

Calcium oxalate is classified into two types- Calcium oxalate monohydrate stone (COM) and calcium oxalate dehydrate (COD) The inhibitory potency of the plant was tested on the nucleation and growth of most commonly occurring kidney stone and COM.

4) ANTIDIABETIC ACTIVITY :-

Diabetes mellitus is metabolic disorder with chronic Hyperglycemia, which results from a defect in insulin secretion, insulin action the gross saponins of TT showed inhibitory activities against a glucosidase.

Animal experiments indicated that GSTT significantly reduced the postprandial blood glucose levels by intragastric administration of sucrose in normal rats & type-2 diabetic rat. Clinical trials proved that the water extract of TT (WETT) has an antidiabetic activity. The fasting blood glucose 2-h postprandial glucose, glycosylated haemoglobin and lipid profile of diabetic women treated with TT extract (1000 mg day) for 3 months.

5) IMPROVING SEXUAL FUNCTION :-

The active extracts and constituents of TT could improve sexual function through activating aphrodisiac and improving fertility in men. It could also activate sexual desire in postmenopausal women. It is instantly advertised that TT possesses aphrodisiac and pro-sexual activities due to its ability to increase testosterone or testosterone precursor levels.

6) IMMUNOMODULATORY ACTIVITY :-

Saponins isolated from the fruit of *Tribulus terrestris* demonstrated dose-dependent increases in phagocytosis indicating stimulation of non-specific immune response. The alcoholic extract of whole plant of *Tribulus terrestris* exhibit in significant dose-dependent increase in humeral antibody titre and delayed hypersensitivity response.

7) ABSORPTION ENHANCER:-

Ethanol extract of *Tribulus terrestris* enhance the absorption of metformin hydrochloride the biopharmaceutics classification system (BCS)

class -3 drug inverted sac techniques using goat intestine due to presence of saponin in the extract.

8) HYPOLIPIDEMIC ACTIVITY :-

The Aqueous extract of the fruit of *tribulus terrestris* was evaluated for their hyperlipidemic activity in which wistar albino rat hyperlipidemic activity may be due to presence of phenolic compound leading to increase lipoprotein lipase in muscle and decrease activity in the adipose tissue.

Saponins from *Tribulus terrestris* were studied on diet induced hyperlipidemia in mice for its preventive and therapeutic effect was demonstrated by decrease in the level of serum total cholesterol and LDL cholesterol. It also reduced the liver total cholesterol and triglycerides and the increase the activity of superoxide dismutase in the liver.

9) ACTIVITY IN CARDIAC DISORDER :-

Tribulus terrestris showed significant effect in the treatment of various cardiac disease including coronary disease, myocardial infarction, cerebral arteriosclerosis and the sequelae of cerebral thrombosis. Tribulosin protected myocardium against ischemia reperfusion injury through protein kinase epsilon activation.

Crude saponin fraction of this plant has shown significant effect in treatment of various cardiac disease including hypertension, coronary heart disease, myocardial infarction, cerebral arteriosclerosis and thrombosis. The aqueous extract of *tribulus terrestris* fruit has significant acetylcholinesterase (ACE) inhibitory effect in vitro methanol and aqueous extract of *Tribulus terrestris* are shown to possess significant antihypertensive activity by direct arterial smooth muscle relaxation and membrane hyperpolarization in spontaneously hypertensive rats.

10) CENTRAL NERVOUS SYSTEM (CNS) 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), *Embllica officinalis* (fruit), and TT (fruit and root), present in equal quantities in the tablet.

Harmine, a β -carboline alkaloid present in *Tribulus terrestris* 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.

11) HEPATOPROTECTIVE ACTIVITY :-

The Tribulus terrestris 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 TT extract (250 mg/kg) for acetaminophen-induced toxicity in freshwater fish.

12) ANTIINFLAMMATORY ACTIVITY :-

The ethanolic extract of TT inhibited the expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in lipopolysaccharide stimulated cells.

The ethanolic extract of TT inhibits the expression of mediators related to inflammation and expression of inflammatory cytokines, which has a beneficial effect on various inflammatory conditions. It also suppressed the expression of proinflammatory cytokines such as tumour necrosis factor-alpha (TNF- α) and interleukin (IL)-4 in macrophage cell line.

13) ANALGESIC ACTIVITY :-

Analgesic activities of TT were studied in male mice using formalin and tail flick test. The study indicated that the methanolic extract of TT at a dose of 100 mg/kg produced analgesic effect. This analgesic effect of the TT extract may be mediated centrally and peripherally.

Effect of the extract was lower than morphine and higher than acetylsalicylic acid (aspirin) in both tests. The analgesic effect of the extract in both tests therefore the involvement of opioid receptors in the analgesic effect of TT is excluded. However the other mechanisms responsible for the analgesic effect of TT remain to be investigated. The results of ulcerogenic studies indicate that the gastric ulcerogenicity of TT is lower than indomethacin in the rat's stomach.

14) 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.

15) ANTICANCER ACTIVITY :-

Chemopreventive potential of the aqueous extract of the root and fruit of TT at 800 mg/kg on 7, 12-dimethylbenz anthracene (DMBA) and croton oil induced papillomagenesis in Swiss albino male mice depicted significant reduction in tumour incidence, tumour burden, and cumulative number of papillomas, along with a significant increase in the average latent period in mice treated orally with TT suspension.

The aqueous extract of TT 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- κ B) signaling. Thus TT has clinical therapeutic effects against liver cancer cells.

TT extract pre-treatment protected against radiation damage by inhibiting radiation-induced glutathione depletion and decreasing lipoperoxidation level in the liver of mice. The mechanism of action involves up- and down regulation of polyamines' homeostasis, suppression of proliferation, and induction of apoptosis.

16) ANTHELMINTIC ACTIVITY :-

The methanolic extract of Tribulus terrestris was found to be more effective than the petroleum ether, chloroform and water extract for in vitro anthelmintic activity on the nematode *Caenorhabditis elegans*.

17) ANTIBACTERIAL ACTIVITY :-

All parts of TT plant like fruits, stem, leaves and roots shows antibacterial activity against *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*.

The methanolic extract of fruit of TT 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.

18) LARVICIDAL ACTIVITY :-

The petroleum ether extract of the leaves of TT exhibited better larvicidal activity against the third instar larvae and adults of the mosquito, *Aedes aegypti*, which is the vector of dengue fever.

19) ANTICARIOGENIC ACTIVITY :-

The ethanolic extract of fruits of TT possesses significant anticariogenic activity against *Streptococcus mutans*, the pathogen responsible for dental caries. The growth, acid production,

adhesion and water insoluble glucan synthesis of *S. mutans* were significantly inhibited in the presence of the ethanol extract of TT.

20) IMPROVEMENT IN FERTILITY :-

The ethanolic extract of TT influences spermatogenesis. The hexanic and aqueous soluble fraction in the methanol fraction promoted changes in the intertubular compartment because they increased the nuclear volume, cytoplasmic volume and individual volume of leydig cells in male wistar rats.

The in vitro addition of TT extract to human sperm could affect male fertility capacity. The incubation of human semen with 40 and 50 of TT extract significantly enhanced the total sperm motility, number of progressive motile spermatozoa and curvilinear velocity over 60-120 min of holding time. Overall the sperm viability significantly improved.

21) LIBIDO ENHANCING ACTIVITY :-

TT was considered to be a safe alternative for the treatment of HSSD in postmenopausal women because it was effective in reducing symptom with few side effects through a randomized, double blinded, placebo controlled trial. Its probable mechanism of action involves an increase in the serum levels of free and bioavailable testosterone.

Other clinical research established that regarding the treatment in the domains of desire and sexual interest of 74 postmenopausal women with sexual dysfunction. The TT treatment (250 mg, orally three times a day for 90 days) was considered to be effective in treating sexual problems among menopausal women.

22) PREVENTION AND TREATMENT OF CARDIOVASCULAR DISEASE :-

The clinical treatments are thrombolysis and nerve protection. Thrombolysis has a significant effect. However, it is limited by a narrow therapeutic time window. Therefore the development of neuroprotective agents is of great significance. Studies have shown that GSTT has a neuroprotective effect on cerebral ischaemia injury, and these saponins have been commercially available as active compounds in traditional Chinese medicine formulations, such as "Xin-nao-shutong", which has been used for the treatment of cardiovascular disease.

TT plays an important role in the treatment of cardiovascular disease with anti-

myocardial ischaemia and myocardial ischaemia-reperfusion injury.

The methanol extract of *T. terrestris* (METT) fruits, which mainly contains ferulic acid, phloridzin and diosgenin, had an effect on mitochondrial dysfunction in a cell-based (H9c2) myocardial ischaemia model. TT significantly suppressed the proliferation of ox-LDL-induced human umbilical vein endothelial cells (HUVECs) and the apoptosis rate. It also prolonged the HUVEC survival time and postponed the cells' decaying stage (from the 69 h to over 100 h).

23) PROTECTIVE ACTIVITY IN NEURONAL CELLS :-

TT has a protective effect for neuron injury mainly via its anti-inflammatory and antioxidant effects. It plays a neuroprotective role in rat cerebral ischaemia reperfusion injury by inhibiting the inflammatory response and PPAR γ protein expression. GSTT decreased the damage to PC12 cells induced by H₂O₂.

The apoptosis of retinal ganglion cells (RGCs) is an important cause of glaucoma. TT can block the optic nerve injury pathway and enhance the survival of the optic nerve to protect the optic nerve. It was reported that TT could reduce the degeneration of RGCs and the retinal nerve fibre layer in hyper-intraocular pressure rabbits by intravenous administration with TT sterilization powder.

24) IMPROVEMENT OF ATHLETIC ABILITY ACTIVITY :-

Athletic fatigue is generally measured by the levels of testosterone and corticosterone. Herbs and herbal combinations have been used to improve athletic ability through several ways that mimic epinephrine effects, mimic testosterone effects, and increase the productions of corticotropin and cortisol.

TT contains gitonin, protodioscin, and tribulosaponins A and B, which are believed to mimic testosterone-like effects in humans because of the similarities of their chemical structures. The main effect is an increase of testosterone anabolic and androgenic action via the activation of endogenous testosterone production.

25) ANTIOXIDANT ACTIVITY :-

TT exhibited effective antioxidant activity in a concentration-dependent manner by 2,2-di-(4-tert-octylphenol)-1-picrylhydrazyl (DPPH), H₂O₂,

and superoxide scavenging activity, as well as the FRAP (Ferric reducing antioxidant power) assay. Diosgenin from the callus of *T. terrestris* was found to have great antioxidant activity.

26) ABSORPTION ENHANCER :-

TT promotes absorption. The biopharmaceutics classification system (BCS) is a scientific classification method based on solubility in vitro and permeability of drugs in the intestine. Metformin hydrochloride (HCl) is a BCS class III drug with a high solubility and poor absorption characteristics. Therefore, it is necessary to increase the intestinal permeability of drugs to improve their bioavailability. The experiment indicated that TT can enhance the absorption of Metformin HCl in a goat intestine [109]. The absorption enhancement effect of TT was concluded by the presence of saponin.

II. CONCLUSION :-

TT is commonly available weed of significant value in the traditional systems of medicine, viz. Ayurveda, Chinese, Siddha and Unani. The whole plant of TT has been explored exhaustively for its phytochemical and pharmacological activities such as diuretic, aphrodisiac, antiurolithic, antihyperlipidemic, antibacterial, analgesic and anti-inflammatory.

The pharmacological experiment performed on the plant must be extended to the next level of clinical trials to generate novel drug. This will help TT in achieving a status of medicine or to be prescribed as a dietary supplement in various disease conditions.

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