INNSPUB

International Journal of Biosciences | IJB |
ISSN: 2220-6655 (Print), 2222-5234 (Online)
http://www.innspub.net
Vol. 14, No. 1, p. 21-37, 2019

REVIEW PAPER OPEN ACCESS

A review on advancements in ethnomedicine and phytochemistry of *Tribulus terrestris* - a plant with multiple health benefits

Farooq Azam[1], Samia Munier[1], Maliha Batool[2], Bashir Ahmad[3], Ghazanfar Abbas[4*]

[1]*Institute of Pharmacy, Physiology and Pharmacology, University of Agriculture, Faisalabad, Pakistan*

[2]*Department of Veterinary Pathobiology, Texas A&M University, College Station, Texas, United States*

[3]*Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan*

[4]*Institute of Microbiology, University of Agriculture, Faisalabad, Pakistan*

Key words: *Tribulus terrestris,* Ethnomedicine, Traditional uses.

http://dx.doi.org/10.12692/ijb/14.1.21-37 Article published on January 11, 20199

Abstract

Tribulus terrestris (TT) Linn. is an annual medicinal plant that belongs to the Zygophyllaceae family. TT has been mainly planted in the subtropical regions of Pakistan, India, China, Mexico, Spain and South America. It has been extensively used to improve physical performance and sexual functions in men. All parts of the plant have been used as a traditional medicine in various regions of the world. The plant contains phytochemicals like flavonoids and saponins that possess pharmacological activities. As an example, the saponins present in TT possess anti-proliferative and anti-tumor function. The fruit of the plant is used for the treatment of abdominal and urogenital infections. The present study aims to summarize the pharmacological, traditional, medicinal and therapeutic potential of TT.

* **Corresponding Author:** Ghazanfar Abbas ✉ dr.ghazanfaruaf@gmail.com

Introduction

The traditional medicine has been popular among the majority of world, despite of great progress in modern medicine. According to the World Health Organization (WHO), 80% of the world population relies on conventional medications for primary health care and a major portion of the conventional treatments incorporate plant extracts or their dynamic constituents.

Since old times ,the traditional medicinal plants have been used for the common well-being as well as for treatment of infections (Shinwari *et al.,* 2011). Approximately 35,000 of plant breeds has been utilized by humans for therapeutic purposes.

Tribulus terrestris L., member of family Zygophyllaceae, locally named as Bakhra (Hussain *et al.*, 2010), Bhakra Bakhro (Qureshi *et al.*, 2011), konda (in Pashto) in Pakistan and Gokshur or Gokharu (Chhatre *et al.*, 2014) in India, Al-Qutub and Qutiba in Iraq (Al-Yawer*et al.*, 2008), Dagunro, Dareisa (Yoruba), Tisadu, Hanathakama (Hausa), Kaije (Kanuri) in Nigeria (Afolayan *et al.*, 2009), usually familiar as puncture vine, goat head, devil's horn and yellow vine.

Latin title Tribulus initially implied the caltrop (a spiky weapon). The Greek word, τπίβολορ (Angelova *et al.*, 2013), which means 'water-chestnut', in Latin it is interpreted as tribulos(Al-Bayati & Al-Mola, 2008). TT is broadly dispersed in tropical, sub-tropical and mellow calm districts. Tribulus consists of 25 species out of which many are considered harmful weeds.

This is because the sharp edges of tribulus fruits pose a risk, to grazing creatures (Hashim *et al.*, 2014).

Taxonomical classification

TT belongs to kingdom Plantae, division Phanerogams and subdivision Angiospermae. Its class is Dicotyledonae, subclass Polypetalae, series Disciflorae having order Giraniales, family Zygophyllaceae, genus Tribulus and species terrestris Linn. (Chhatre *et al.*, 2014).

Botanical description

TT is a little plush, bushy and flat or horizontal herb. At early stage of development, the root of TT is slim, stringy, round, hollow and light brown in color. The stem length is about 2 meters long, leaves are inverse and brief approximately 1.25cm in length. Fruits contain rough projections and are wooded around 1 cm in breadth which possesses spikes about 6 mm long. It has 2 unequal sets of spines. The wooded star-shaped arrangement known as carpels of about 5-7 mm in length and 5-6 mm in width encased seeds. In every carpel, there are 5 seeds and every seed is 1.5-3 mm long and yellow in color. Cleared upon evaluation that every plant possesses around 2000 seeds. TT is described by small (8-15 mm diameter) yellow petal flowers and thorny fruits. TT is bitter in taste (Perveen*et al.*, 2007; Zadeh*et al.*2013;Hashim *et al.*, 2014).

Habitat

TT is a local plant of tropical locales of Southern, Western and Eastern Asia, Southern Europe, Australia, and Africa (Al-Ali *et al.*, 2003). TT massively develops in moderately hot dry tropical zone everywhere in the world. The plant requires good health and light finished land for development. Broadly it is found in developed crops, gardens, dismissed zone, overgrazed meadows and roadsides (Hashim *et al.*, 2014).

Chemical constituents

TT is a valuable herb frequently used in natural medication and is found in different parts of the world. Furostanol and spirostanol saponins of chlorogenin, diosgenin, gitogenin, hecogenin, tigogenin, neogitogenin, neotigogenin, ruscogenin, and neohecogenin and sarsasapogenin sorts are chiefly found in TT. Four types of sulphated saponins are also isolated from TT (Kostova *et al.*, 2005).

TT consists of alkaloids, saponins, flavonoids, steroids, estradiol, cinammic acid amides and lignanamides (Bourke *et al.*, 1992; Ren*et al.*, 1994; Li *et al.*,1998). The compounds present in the methanolic extracts of TT are inositol, palmitic acid,

estradiol, linoleic acid, stearic acid and beta-sitosterol and these were identified by gas-chromatography and mass spectrometry (GC-MS) analysis (Abirami *et al.*, 2011).

TT flavonoids are chiefly derived from kaempferol, isorhamnetin andquercetin. Quercetin, isoquercitrin, quercetin-3-O-gent, quercetin-3-O-rha-gent, quercetin-3-O-gent-7-O-glu and rutin, are flavonoids having basic parent structure of quercetin(QU *et al.*,, 2007; Alavia *et al.*, 2008). Isorhamnetin, isorhamnetin-3-O-gent, isorhamnetin-3-O-glu, isorhamnetin3, 7-di-O-glu,isorhamnetin-3-O-gent-7-O-glu, isorhamnetin-3-O-p-coumarylglu, isorhamnetin-3-O-gent-7-O-glu, and isorhamnetin-3-O-rutinoside are flavonoids with basic parent structure of isorhamnetin(Kostova*et al.*, 2002; Sun*et al.*, 2002; Zhu *et al.*, 2017). Kaempferol, kaempferol-3-O-gent, kaempferol-3-O-glu, kaempferol-3-O-gent-7-O-glu, kaempferol-3-O-rutinoside and tribuloside contain flavonoids containing basic parent structure of kaempferol (Alavia *et al.*, 2008; Su *et al.*, 2009).

Tribulusin A, tribulusamide C, tribulusterine, terrestriamide, harman, harmine , harmmol, N-trans-caffeoylyramine, N-transcoumaroyltyramine, are the main alkaloids isolated from fruits, leaves and stems of *TT* (Ren *et al.*, 1994; Alavia *et al.*, 2008).

TT contains some additional ingredients like amino acids, organic acids and many other substances. Amino acids include alanine and threonine (Zhu *et al.*, 2017). TT also contains 4-ketopinoresinol (Lv *et al.*, 2008), coumarin, physcion, emodin and uracil nucleic acid (Liu *et al.*, 2003, Zhu *et al.*, 2017). Organic acids include vanillic acid, benzoic acid, 2-methyl benzoic acid (Zhu *et al.*, 2017), palmitic acid monoglyceride, succinic acid, tribulus acid, docosanoic acid, (Chen*et al.*,2000) andferulic acid (Lv *et al.*, 2008).

Phytochemistry and Pharmacology

Furostanol and spirostanol saponins are studied as most valuable chemicals of TT. Steroidal saponins have been separated from the plant with the assistance of splash reagent are 108, out of which 50 types are furostane saponins and 58 types are spirostane saponins. Due to the presence of anisaldehyde reagent, both furostanol and spirostanol saponins provide yellow stains on thin layer chromatography (TLC). In contrast, with Ehrlich's reagent, furostaol saponins give red color (Cai *et al.*, 2001). The aerial portion of TT contains steroidal saponins, such as protodioscin and protogracilin. These are primary components of the plant with unique biological activities (Gautam *et al.*, 2018; Obreshkova *et al.*, 1998; De-Combarieu *et al.*, 2003). Saponins showed extremely low absorption within the brief wavelength range so high-performance liquid chromatography (HPLC) is preferred over ultraviolet (UV) spectroscopy (Ganzera *et al.*, 2001). Different chromatographic methods utilized for partition of a saponin blend into individual components that includes thin layer chromatography on typical and reversed-phase i.e. HPLC in one or two-dimensional modes (Mutilate *et al.*, 1998). HPLC on reversed-phase columns is the foremost effective and most regularly utilized method. With the advancement of later unused procedure for discovery with evaporative light scattering detector (ELSD) gives an important implies for division and confinement of saponins (Kostova*et al.*,, 2005).

Crude saponin fractions of TT were exposed to column chromatography (CC) by silica gel along with a slope CHCl3–MeOH–H2O. For pure saponins production, a few fractions are at that point chromatographed by column chromatography on gel and medium pressure liquid chromatography (MPLC) pre-packed column with MeOH–H_2O (Wu *et al.*, 1996). Saponin fractions chromatographed by micro porous gum column (eluting with water, 50, 70 and 90% EtOH) and consequent silica gel column chromatography ($CHCl_3$-MeOH-H_2O), MPLC (H_2O–MeOH angle) and gel filtration on Sephadex G-25 with H_2O (Xu *et al.*, 2000).

The crude saponin fractions of TT was isolated by exposure with evaporating light scattering (ELS), HPLC through employing a reversed phase (RP-18)

column and as mobile phase water-acetonitrile gradient. Basic examination and partition of furostanol saponins in extricates was done by employing an acetonitrile and gradient of 0.1% formic corrosive (v/v) in water (De Combarieu *et al.*, 2003).

HPLC-ESI-MS (high-performance liquid chromatography-electrospray ionization-mass spectrometry) strategy for subjective investigation of saponin blends was also utilized (Mulinacci *et al.*, 2003). On thin layer chromatography with Herlich's spray reagent furostanol saponins were effectively found out through color response they showed, reversed-phase and normal-phase silica gel column chromatography were also utilized for unrefined divisions of TT (Wang *et al.*, 2009).

Traditional uses

Uses of this plant are traditionally opted by different nations as TT *is* utilized as a folk medication for diverse purposes and therapies. Previous studies show sundry therapeutic worth of TT as a well-known source to cure an assortment of distinctive infection conditions in Greece, China, and India. TT is either used as herb or as a primary component for the propagation of many medications and for edible supplements such as physical revival, treatment of kidney problems, liver, immune system and cardiovascular system(Tilwari *et al.*, 2011).

Due to diversity of compounds extracted from this plant, its uses are extended from local to systemic illnesses. It is used as a folk medication for an aesthetic stimulant, expanded muscle vigor, sexual strength, aphrodisiac(Zheleva-Dimitrova *et al.*, 2012; Angelova *et al.*, 2013), nutritive and in medications of urinary diseases, cough and heart illnesses(Hashim *et al.*, 2014).In addition, It also has diuretic (Angelova *et al.*, 2013), , antiurolithic (Anand*et al.*, 1994; Shirfule*et al.*, 2011), immunomodulatory (Tilwari *et al.*, 2011), antidiabetic, absorption enhancing, hypolipidemic (Samani *et al.*, 2016), hepatoprotective, analgesic, central nervous system, cardio tonic, anti-inflammatory(Heidari *et al.*, 2007; Borran *et al.*, 2017), antispasmodic, anticancer, antibacterial (Gopinath *et al.*, 2012), anthelmintic, larvicidal, and anticariogenic activities (Chhatre *et al.*, 2014).

It is a magnificent herb demonstrated for its sundry therapeutic activities which can be securely utilized for sundry sicknesses (Fatima *et al.*, 2014). Table 1 shows a vast range of therapeutic activities of different parts of plant and the whole plant extract.

Sexual disorders

Steroidal saponins present in TT *extract* basically include protodioscin, diosgenin, and dioscin altogether enhance the testosterone levels and indeed having an impact on estrogen, pregnenolone, and progesterone to provoke sexual conduct (Adimoelja *et al.*, 1997). Protodioscin (5, 6-dihydroprotodioscin, neoprotodioscin) (Martino-Andrade *et al.*, 2010) is a phytochemical agent categorized into steroidal saponins and present mainly in aerial portion of TT plant in various concentrations (Adimoelja*et al.*, 2000). And clinical studies proved that it enhances sexual desire and upgrade erection by the change of protodioscin into dehydroepiandrosterone (DHEA) (Fatima *et al.*, 2014). Protodioscin also enhance dehydroepiandrosterone, luteinizing hormone and testosterone level. Dehydroepiandrosterone is a potent form attain from testosterone that provokes sexual desire, have a role in muscle expansion and red blood cells manufacturing (Arsyad *et al.*, 1996). To treat infertility in males it increments the caliber of dehydroepiandrosterone. In Europe and USA, various formulations have been retailed that possess TT extricates utilized, to enhance sexual desire, as a food additive (De Combarieu *et al.*, 2003, Mulinacci *et al.*, 2003) and for many other types of diseases (Hashim *et al.*, 2014).For a long period of time,TT is famous as a routine medication deals with male infertility because of the presence of protodioscin, a furostanol saponin. Protodioscin have fortifying impact on spermatogenesis by means of Luteinizing Hormone (LH) invigorating the discharge of male hormone testosterone (Gauthaman *et al.*, 2002, Gauthaman *et al.*, 2008).By the utilization of TT extricates, there was an increment in dihydrotestosterone,

dehydroepiandrosterone and testosterone level that regulate sex drive and play an important role in amount and quality of sperms(Neychev*et al.*,2005).

Effect on erectile dysfunction (ED)

Male weakness or erectile dysfunction (ED) is characterized as the failure of a man to attain and keep up an erection adequate for commonly palatable intimacy with his mate. To defeat the issue of erectile dysfunction different common sexual enhancer possibilities are favored (Xu *et al.*, 2010).

Table 1. Useful activities/effects of different parts of *Tribulus terrestris*.

Part(s) of *TT*	Activity	Reference(s)
Plant dry extract	Anticancer	Pavin *et al.*, 2018
Roots	Anti-cholestrolemic	(Fatima *et al.*, 2014).
Leaves	Larvicidal	(Singh *et al.*, 2008; Mitra *et al.*, 2012; Zhu *et al.*, 2017).
Leaves	Antidiabetic	(Amin *et al.*, 2006).
Leaves and fruits	Anti-inflammatory	(Baburao *et al.*, 2009; Borran *et al.*, 2017).
Fruits	Aphrodisiac	(GamalEl Din *et al.*, 2018, Singh *et al.*, 2012).
Fruits	Antiurolithic	(Anand *et al.*, 1994; Shirfule *et al.*, 2011).
Fruits	Anti-cholinergic	(Fatima *et al.*, 2014).
Fruits	Hypolipidemic	(Khan *et al.*, 2011; Rahmathulla *et al.*, 2013).
Fruits	Analgesic	(Heidari *et al.*, 2007; Borran *et al.*, 2017).
Fruits	Antiurolithic	(Anand *et al.*, 1994; D. K. Sharma, 2017).
Fruits	Antioxidant	(Reshma *et al.*, 2016; Borran *et al.*, 2017).
Fruits	Learning and memory	(Prabhu *et al.*, 2014).
Fruits	Against acute pancreatitis	(Borran *et al.*, 2017).
Fruits and seeds	Diuretic	(Al-Ali *et al.*, 2003; Chhatre *et al.*, 2012).
Fruits and roots	Central nervous system	(Adaikan *et al.*, 2000).
Fruits and stems	Cytotoxic	(Sun *et al.*, 2003).
Fruits and leaves	Antifungal	(Al-Bayati & Al-Mola, 2008).
Fruits, stems, roots, whole plant	Apoptosis inducer	(Basaiyye *et al.*, 2018)
Fruits, stems, roots	Anti-cancerous	(Kostova *et al.*, 2005; Manish *et al.*, 2009; Kim *et al.*, 2011).
Fruits, roots, stems and leaves	Antimicrobial, Antibiotic	(Arulmozhi *et al.*, 2018.Adaikan *et al.*, 2000, Al-Bayati *et al.*, 2008; Baburao *et al.*, 2009).
Whole plant	Neuropathic pain relieving	Gautam *et al.*, 2018
Fruits, whole plant	Renoprotective effect	Jiang *et al.*, 2018
Fruits, whole plant	Antihypertensive	(Phillips *et al.*, 2006).
Aerial parts of plant	As food supplements	(De Combarieu *et al.*, 2003).
Aerial parts of plant	Against acute kidney injury	(Najafi *et al.*, 2014).
Aerial parts of plant	Erectile dysfunction	(Kalamegam *et al.*,2008).
Whole plant	Immunomodulatory	(Tilwari *et al.*, 2011).
Whole plant	Anthelminthic	(Deepak *et al.*, 2002).
Whole plant	Estrogenic	(Fatima *et al.*, 2014).
Whole plant	Smooth & skeletal muscle relaxant	(Fatima *et al.*, 2014).
Whole plant	Anti-spasmodic	(Fatima *et al.*, 2014).

The etiologies related with erectile dysfunction are chronic medical conditions, psychosexual components and a few ways of life. Conventional treatment alternatives for erectile dysfunction include the utilize of innate therapeutic plants (phytotherapy), creatures (zootherapy), and other worldliness, whereas nontraditional choices incorporate the routine, standard practice such as drug treatment, behavioral and mental counseling (Afolayan *et al.*, 2009).

In primates, rabbits and rats, hormonal impacts of TT have been studied in order to evaluate its effectiveness within the management of erectile

dysfunction. For this purpose, both acute and chronic administration of TT at various concentrations was given. In primates for acute study, TT extricates were managed intravenously with a dosage of 7.5, 15 & 30 mg/kg. In rabbits and normal rats for chronic study, TT extricates were managed orally with a dosage of 2.5, 5 & 10 mg/kg up to 8 weeks. Blood tests were performed by using radioimmunoassay in order to determine dihydrotestosterone (DHT), dehydroepiandrosterone sulphate (DHEAS), and testosterone (T) levels. It was found that DHT, DHEAS, and T level increased significantly in both acute and chronic administration of TT mainly due to the presence of steroidal saponin protodioscin (Qi *et al.*, 2018, Kalamegam *et al.*, 2008).

In another study, to assess TT impact for the treatment of erectile dysfunction a placebo-controlled study i.e. randomized and two fold blind was performed previously containing thirty healthy men of ≥ 40 years of age, which have been chosen from 100 patients complaining ED. Serum testosterone and International Index of Erectile Function (IIEF-5) was gotten after 30 days of study and before randomization of groups. Two randomized groups of 15 patients each i.e. control group and study group made. For thirty days both groups got 800 mg of TT partitioned into two doses/day. Results showed an advancement within the reaction of both groups before getting the capsules, p-value = 0.0004, compared with amount gotten within the first IIEF-5 (Santos *et al.*, 2014).

TT administered for management of erectile dysfunction as a “prompt therapy” worldwide. For 14 days TT dosage of 2 mg /kg body weight was given daily to adult male mouse. For histochemical, histological and morphometrical studies showed significant increase in the number of spermatids, sperms, spermatocytes, and interstitial cells while thickness of seminiferous tubule was significantly increased. It was concluded that TT extracts given to adult male mouse involved in spermatogenesis (Al-Yawer *et al.*, 2008).

In a study on organ bath, corpus carvenosum muscles showed a concentration-dependent relaxation impact when applied TT extricates on it. When compared with the control group in vivo study revealed that oral administration of the TT extricates for one month appeared a noteworthy concentration-dependent increment in an intracavernous pressure (Do*et al.*,, 2013). Subsequently, TT extracts helpful in treating erectile dysfunction here mechanism of action involved was the response route of nitrous oxide or nitric oxide synthase (NO/NOS) in carpus carvenosum endothelium.

It locally infuses in adjoining smooth muscle cells and ties with intracellular receptor i.e. guanylate cyclase (Burnett*et al.*, 1997).This will leads to the conformational shift in turn enzyme activation occur that convert guanosine triphosphate into cyclic guanosine monophosphate (cGMP) that further functioned by a cGMP-dependent protein kinase, in this way corporal smooth muscle’s contractile condition coordinate (Hedlund *et al.*, 2000).

Spermatogenic effect

Interestingly the plant extract showed positive effect on sperm formation in controlled studies. Effects of TT extracts was examined on the primary spermatocyte in rat. Researchers found that TT can improve male reproductive system and can be used in treatment of male infertility by affecting the testis spermatocyte. Studies show that TT plant due to the presence of saponins increases discharge of luteotropic hormone in distinction to pituitary gland. Luteotropic hormone is also a special stimulant for production of testosterone and hence can improve sexual functions through increased sperm production, improved erectile function and increased libido. Furostanol is one of the saponins in TT that have stimulant effect on spermatogenesis and significantly improves the quality and quantity ofsperm (Karimi *et al.*,2011). TT greatly increases the number of spermatids and sperms as well as increase in number of interstitial (Leyding) cells due to the presence of steroid saponin (Al-Yawer *et al.*, 2008).

Effect on testicular development

The effects of TT extracts was investigated on testicular expansion and body weight of prepubescent rats. In a study conducted on ten rats of two-week-old, divided into 2 groups i.e. control group (A) and experimental group (B). TT extracts were given orally at a dosage of 70 mg/kg every day for twenty days to group B. On 34th day rats were weighed and sacrificed and their testes were removed for further microscopic studies. Then independent-samples t-test statistical analysis was done. Group B that received TT extracts revealed a statistically significant increase in the mean body (p 0.05). After examining the histological slides of testes, it was revealed that by treating with TT extracts seminiferous tubules possess initial spermatids and showed significant increment in it. The conclusion was that TT has a complex provoking impact on germinative and endocrine capacities of testicles(Bashir*et al.*, 2009).

Aphrodisiac effect

The plant extracts have strong aphrodisiac effect. To show up the aphrodisiac effect of TT, a study was conducted on mature Sprague-Dawley rats, splitted into five groups each group contain eight rats and these groups were treated with distilled dihydrogen monoxide include castrated and normal rats, treated with TT include castrated rats at a dosage of 5 mg/kg body weight one daily dose given orally, treated with testosterone include castrated and normal rats at a dosage of 10 mg/ kg body weight given subcutaneously for two weeks. Rats include in the castrated group showed a comprehensive decline in sexual behavior parameters that are intromission frequency (IM) and mount frequency (MF) while showed increments in intromission latency (IL), mount latency (ML), ejaculation latency (EL) and post ejaculation interval (PEI). A significant increment in intracavernous pressure (ICP) and prostate weight was concluded (Gauthaman*et al.*,2002).

Antihypertensive effect

The fruit extract of TT is known of have strong antihypertensive effect. In as study 2K1C hypertensive rats were examined through assessment of rotating and local angiotensin-converting enzyme (ACE) action in heart, lung, aorta, and kidney, it showed TT have an antihypertensive mechanism. Rats were divided into four groups; treated with TT, hypertensive, sham and control groups. Firstly, rats got hypertension through incision utilizing silver clip on renal artery. After four weeks of incision TT fruits lyophilized liquid extricates were given orally for four weeks at a dosage of 10 mg/kg of body weight to 2K1C hypertensive rats. Angiotensin-converting enzyme action checked through high-performance liquid chromatography (HPLC) and blood pressure through the tail-cuff method. In 2K1C rats, systolic blood pressure (SBP) was significantly raised in comparison with control rats and angiotensin-converting enzyme and serum action in kidney, lung, heart, and aorta was significantly raised in comparison with normal rats. Hypertensive rats treated with TT when examined their systolic blood pressure was significantly reduced and angiotensin-converting enzyme action was also significantly reduced in comparison with hypertensive rats.

It was concluded that TT showed significantly reduced blood pressure in rats having renovascular hypertension (Sharifi *et al.*, 2003).

Aqueous and methanolic extracts of TT were used to examine perfused mesenteric vascular bed and rat blood pressure.

It was revealed that methanolic extricates are more potent than aqueous extricates, these extricates reduced blood pressure in dosage reliant pattern and have an antihypertensive impact. Mechanism of action involved in it was membrane hyperpolarization and relaxation of arterial smooth muscles via nitric oxide discharge(Phillips *et al.*, 2006).

Antioxidant activity

TT herbaceous preparations showed antioxidant activity that assessed by utilizing 2,2′-azino-bis (3ethylbenzothiazoline-6-sulfonic acid) di-ammonium salt-free radicals, 1,1-diphenyl-2-picrylhydrazyl (DPPH),inhibition of lipid

peroxidation via ferric thiocyanate and ferric reducing antioxidant power (FRAP). Overall quantity of flavonoids and polyphenols were concluded utilizing AlCl3 and Folin Chiocalteu reagent. It was concluded that TT herbaceous preparations showed significant antioxidant potential and restrained lipid peroxidation. The overall tested models exhibited powerful FRAP action and restrained lipid peroxidation organization. The complete amount of flavonoids ranged in between 0.36 % ± 0.004 % to 0.58 % ± 0.01 % while complete quantity of polyphenols ranged in between 2.73 % ± 0.007 % to 3.17 % ± 0.008 %. Hence for that reason the entire analysis helpful to clear the pharmacological potential of TT plant (Zheleva-Dimitrova *et al*., 2012).

Antimicrobial activity

Methanolic extracts of the TT has in vitro antibacterial effect against gram negative bacteria including *Klebsiella, E. coli, Pseudomonas aeruginosa, and Proteus vulgaris* and also against gram positive bacteria i.e. *Staphylococcus aureus*. TT exhibited significant effects across all bacteria (Arulmozhi *et al*., 2018). The detailed action was due to spirosaponins display within the herb(Ajaib*et al.,* 2010). TT fruit bodies were utilized in this think about, to synthesized silver nanoparticles the dried fruit body extricate was blended with silver nitrate. The dynamic phytoconstituents found in TT were responsible for the speedy reduction of silver particle (Ag+) into metallic silver nanoparticles (Ag0). Nuclear constrain magnifying lens, Transmission Electron Magnifying instrument (TEM), UV–visible spectroscopy, Fourier Transform Infrared (FTIR) spectroscopy, X-ray diffraction (XRD) were presently utilized for inspection of silver nanoparticles. The round molded silver nanoparticles diameter was in the range of 16–28 nm. Moreover, the diffraction design affirmed that a higher proportion of silver with fine particles was formed. Kirby–Bauer strategy was used to examine the antibacterial activity of manufactured nanoparticles having clinically restrained multi-drug safe microbes like *Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Staphylococcus aureus and Streptococcus pyogens*. It was concluded that silver nanoparticles of TT plant are less extravagant and fast and have wide utilization in antibacterial therapy in cutting edge medicine (Gopinath *et al*., 2012).

When TT methanolic extricates of various portions including roots, stems, leaves, and fruits were examined across bacteria including *Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Enterococcus faecalis* and *Pseudomonas aeruginosa* showed significant antibacterial action through utilizing agar diffusion test and broth dilution test. It was concluded that 4 mg/mL was the minimum inhibitory concentration (MIC) value of methanolic extricates of roots across *Escherichia coli, Staphylococcus aureus,* and *Enterococcus faecalis* while 2 mg/mL was across *Pseudomonas aeruginosa*. 2 mg/mL was the MIC of stems, leaves, and fruits methanolic extricates of TT across each bacterium. Agar diffusion test revealed that methanolic extricates of all portion of TT showed significant antibacterial action across each bacterium.

It was examined TT clearly showed antibacterial action across extremely pervasive gram-negative bacteria i.e. *Escherichia coli* in urinary tract diseases (Kianbakht *et al*., 2003).

As a supplement used by athlete

Physical action is extensively recommended through world health organization (WHO) for the reluctance of their benefits, well performance and lifestyle diseases; therefore, the nourishing supplements and convenient diet is employed in addition with herbs which can be effectively exhibited. TT as it enhances the testosterone level and is furthermore available to athletes and these are also convenient backups of the banned fascinated drugs which are easily available in retails in an abundant form or an alternate form of supplements (Pokrywka *et al*., 2014).

The primary purpose is to enhance testosterone androgenic and anabolic activity via stimulating internal testosterone propagation. TT in athletes is confidentially used (Maughan*et al*., 2007).

Anti-hyperglycemic and anti-hyperlipidemic effects

Hydro alcoholic extracts of TT showed a significant antidiabetic activity. In a study for three months a thousand mg/day hydro alcoholic extracts of TT evaluated on lipid profile and serum glucose of ninety- eight randomly allocated women with diabetes mellitus.

In diabetic women, TT produced a significant total cholesterol, low-density lipoprotein and blood glucose decreasing impact in comparison to placebo ($p<0.05$).*TT* group became substantially decreased in comparison with placebo, whereas no extensive impact changed was determined inside the high-density lipoprotein levels and triglyceride levels (Samani *et al.*, 2016).

Conservational impact of TT against diabetes mellitus (DM) was investigated. Rats were divided into 6 groups of 3 diabetic and 3 non-diabetic categories and separately deal with glibenclamide, normal saline or TT up to thirty days. First diabetic group was treated with saline; second diabetic group was treated with glibenclamide at dosage of 10mg/kg of body weight; third diabetic group was treated with TT extracts at dosage of 2g/kg of body weight, whereas the first, second and third non-diabetic groups were treated with saline solution, glibenclamide and TT extricates all at once.

At the end of experiment for morphological and biochemical investigation liver and serum specimens were composed. Levels of creatinine, alanine aminotransferase (ALT), reduced glutathione and malondialdehyde (MDA) were analyzed in the liver.

It was concluded TT extracts fundamentally reduced the serum creatinine and ALT levels in diabetic groups, the reduced MDA level in liver in both groups i.e. diabetic and non-diabetic (Amin *et al.*, 2006).

In diabetic mice, methanolic extracts of TT showed a fundamental reduction in blood glucose quantity at a dosage of 50 mg/kg of body weight, after 4 and 6 hours of cure in comparison to diabetic mice i.e. untreated. It was concluded that a significant reduction in total cholesterol TC, serum triglycerides TAG and low-density lipoprotein cholesterol LDL revealed in comparison to untreated diabetic mice(Hussain*et al.*, 2009).

TT fruits aqueous extract was investigated as its impact on cholesterol persuaded hyperlipidemia in rats. It was concluded that aqueous extracts at dosage of 580 mg/kg of body weight produced fundamental decrease in different biochemical parameters likevery low density lipoproteins (VLDL), low density lipoproteins (LDL), alanine (AL),triglycerides (TG) and increment in high density lipoproteins(HDL) quantity as compared to aqueous extracts at dosage of 300 mg/kg of body weight (Khan *et al.*, 2011).

Cytological and genetic effects

TT fruits aqueous extrication was utilized and a study was conducted for determination of genetic impacts via cytogenetic approaches and comet test. For twenty-four hours TT extricates at a dosage of 10, 20, 40 and 80 mg/L utilized, a high dosage i.e. 80 mg/L showed significant increment in comet cells. Due to high dosage of TT and micronuclei, chromosomal irregularity in a manner of stickiness, necrotic cells, chromosomal gap, and fragmentation showed and incremented(Qari *et al.*, 2017).

Larvicidal and repellent effect

The larvicidal and repellent effect of the crude ethanol, Crude acetone-petroleum ether and ethanol extricate of TT leaves were used across mature mosquito and third instar larvae to examine repellent and larvicidal impacts. It was determined that *Aedes aegypti* (Diptera: Culicidae) was a vector of dengue fever. Hence concluded that petroleum ether extricate was more competent having LC50 64.6A ppm after that acetone extricates having LC50 173.2A ppm and ethanolic extricates having LC50 376.4A ppm came in a pattern. In comparison with commercially available dosage form i.e. N, N-diethyl-3-methylbenzamide (DEET) that possess 100% repellence action, it was examined that at the same dosage the petroleum ether extracts were the only extracts that showed 100% repellence action or astringent prevention in

comparison to other extracts of TT plant(El-Sheikh*et al.*, 2016).

Anti-urolithiatic potential

To treat urinary ailment containing urolithiasis, aqueous extricates of TT fruits were manufactured by maceration then decoction was done for production of a mother extracts that was ready to utilize for polarity-occupied fractionations.

In kidney stones calcium oxalate can be a main sort of precious stone that has been categorized into two sorts; calcium oxalate dehydrate (COD) and calcium oxalate monohydrate stones (COM). For years, in the treatment of urinary stones plants got preference in use.

The watery extracts of TT fruits considered to assess the antiurolithiatic activity by using peculiar samples. TT kidney stones inhibitory strength has been proved in common initial kidney stones and nucleation. It was concluded that for urolithiasis, an n-butanol fragment in TT possess a higher amount of tannic corrosive, diosgenin and quercetin showed defensive scope instead of curative claim (Sharma*et al.*, 2017).

α-glucosidase inhibitory potential

Different studies were being conducted to illustrate the α-glucosidase inhibitory potential of TT extricates but the main component that is the cause of this inhibition was still unknown but the studies performed showed the inhibition mechanism. When fragmentation of TT was done the idea was drawn from this fragmentation that derivatives of three cinnamic acid amide (1–3) were probably the effective ingredients involved across α-glucosidase inhibition.

There was a leading structure in it that was N-trans-coumaroyltyramine 1, exhibited significant inhibition of α-glucosidase. In addition to it, cinnamic acid amide A-ring possess hydroxyl group and α, β-unsaturation carbonyl group that considered to have discriminating functions in α-glucosidase inhibition. When molecular sampling study did it showed that interaction of hydrogen bond between inhibitors and enzymes and π-π interaction was basically considered for inhibitory activities (Song *et al.*, 2016).

Analgesic effect

An investigation of methanolic extricates showed analgesic activity in an albino mouse that was confirmed through formalin and tail flick assay.

Intraperitoneal injection of percolated extracts was given to mice at a dosage of 50,100 200,400 and 800 mg/kg of body weight.

It was concluded that at a dosage of 100 mg/kg of body weight percolated extracts showed maximum consequential analgesic activity(Heidari *et al.*, 2007).

Urogenital effect

Aqueous extract of TT was found to have positive impact on reproductive system. Aqueous extracts content are phytoestrogen and its metabolites which exert an estrogenic effect (Zadeh*et al.*, 2013; Hajmohamadi*et al.*, 2013).In a study of reproductive system of mature albino mice, It was observed that TT revealed significant increment in diameter of adult follicles, the increment in luteinizing hormone and follicle stimulating hormone levels, number of growing follicles, endometrial glands diameter and endometrial lining cells height increment in luteinizing hormone and follicle stimulating hormone levels, and reduction in estradiol level.

Cardiotonic activity

The saponins contents of TT extracts has been of interest due to their pharmacological behavior for heart diseases. Plant extract was used to treat coronary heart disease (CHD). Saponins have potential to dilate coronary artery and improve coronary circulation. It was concluded in a clinical study of 406 CHD patients that 82.3% was the complete effective rate of remission of angina pectoris (chest pain due to CHD) that was greater in comparison to the control group i.e. 67.2%. Similarly, 52.7% was the efficacious rate of ECG improvement that was also greater in comparison to the control group i.e. 35.8%. It was concluded that it was one the best medicine to treat angina pectoris without any adverse reactions on renal functions, blood system and hepatic functions (Wang *et al.*, 1990).

Conclusion

TT is an acknowledged plant utilized in indigenous medication; in addition, folk medicine also claims uses, especially as an aphrodisiac; analgesic, antibiotic, antifungal, antioxidant, anti-inflammatory activity and effective in urogenital system, nervous, cardiovascular, and musculo-skeletal system. Chemically, TT contains different biologically effective phytochemicals containing alkaloids, flavonoids, linoleic acid, palmitic acid, estradiol, saponins, stearic acid, and Beta-sitosterol etc. TT is very useful in various diseases for which there are significant scientific reports and data available. Thus, it is considered as an important herb with diverse pharmacological activities, which is very beneficial to mankind. Furthermore, Intensive research is required to explore the hidden benefits of plant especially root extracts.

References

Abirami P, Rajendran A. 2011. GC-MS Analysis of Tribulus terrestris. Asian Journal of Plant Science and Research **1,** 13-16.

Adaikan P, Gauthaman K, Prasad R, Ng S. 2000. Proerectile pharmacological effects of Tribulus terrestris extract on the rabbit corpus cavernosum. Annals of the Academy of Medicine, Singapore **29,** 22-26.

Afolayan AJ, Yakubu MT. 2009. Erectile dysfunction management options in Nigeria.The journal of sexual medicine **6,** 1090-1102. http://dx.doi.org/10.1111/j.1743-6109.2008.01064.x

Ajaib M, Khan Z, Khan N, Wahab M. 2010. Ethnobotanical studies on useful shrubs of district Kotli.Azad Jammu & Kashmir, Pakistan, Pakistan Journal of Botany **42,** 1407-1415.

Al-Ali M, Wahbi S, Twaij H, Al-Badr A. 2003. Tribulus terrestris: preliminary study of its diuretic and contractile effects and comparison with Zea mays. Journal of Ethnopharmacology **85,** 257-260. http://dx.doi.org/10.1016/S0378-8741(03)00014-X

Al-Bayati FA, Al-Mola HF. 2008. Antibacterial and antifungal activities of different parts of Tribulus terrestris L. growing in Iraq. Journal of Zhejiang University Science **B9,** 154-159. http://dx.doi.org/10.1631/jzus.B0720251

Al-Yawer M, Hassan A, Haddad F, Al-Anee H, Al-Khateeb E. 2008. Effects of AL-Qutub (Tribulus terrestris) on the Spermatogenesis of the Mouse Testis: Histological, Histochemical and Morphometrical Studies. Journal of the Faculty of Medicine Baghdad **50,** 246-254.

Alavia SHR, Matin YM, Hadjiaghaee R, Ajani Y. 2008. Flavonoid Glycosides from Tribulus terrestris L. orientalis. Iranian Journal of Pharmaceutical Sciences **4,** 231-236.

Amin A, LotfyM, Shafiullah M, Adeghate E. 2006. The protective effect of Tribulus terrestris in diabetes. Annals of the New York Academy of Sciences **1084,** 391-401. http://dx.doi.org/10.1196/annals.1372.005

Anand R, Patnaik G, Kulshreshtha D, Dhawan B. 1994. Activity of certain fractions of Tribulus terrestris fruits against experimentally induced urolithiasis in rats. Indian journal of experimental biology **32,** 548-552.

Angelova S, Gospodinova Z, Krasteva M, Antov G, Lozanov V, Markov T, Bozhanov S, Georgieva E, Mitev V. 2013. Antitumor activity of Bulgarian herb Tribulus terrestris L. on human breast cancer cells. Journal of BioScience & Biotechnology **2,** 25-32.

Arulmozhi P, Vijayakumar S, Kumar T. 2018. Phytochemical analysis and antimicrobial activity of some medicinal plants against selected pathogenic microorganisms. Microbial pathogenesis **123,** 219-226. http://dx.doi.org/10.1016/j.micpath.2018.07.009

Baburao B, Rajyalakshmi G, Venkatesham A, Kiran G, Shyamsunder A, Gangarao B. 2009. Anti-inflammatory and antimicrobial activities of methanolic extract of Tribulus terrestris Linn plant.International Journal of Chemical Sciences **7,** 1867-1872.
http://dx.doi.org/10.1080/01443615.2018.1445706

Basaiyye SS, Naoghare PK, Kanojiya S, Bafana A, Arrigo P, Krishnamurthi K, Sivanesan S. 2018. Molecular mechanism of apoptosis induction in Jurkat E6-1 cells by Tribulus terrestris alkaloids extract. Journal of traditional and complementary medicine **8,** 410-419.
http://dx.doi.org/10.1016/j.jtcme.2017.08.014

Bashir A, Tahir M, Samee W, Munir B. 2009. Effects of Tribulus terrestris on testicular development of immature albino rats.Biomedica **25,** 63-68.

Bayati Zadeh J. 2013. Physiological and pharmaceutical effects of Tribulus terrestris as a multipurpose and valuable medicinal plant. International Journal of Advanced Biological and Biomedical Research **1,** 556-562.

Borran M, Minaiyan M, Zolfaghari B, Mahzouni P. 2017. Protective effect of Tribulus terrestris fruit extract on cerulein-induced acute pancreatitis in mice. Avicenna journal of phytomedicine **7,** 250.

Bourke C, Stevens G, CARRIGAN MJ. 1992. Locomotor effects in sheep of alkaloids identified in Australian Tribulus terrestris.Australian veterinary journal **69,** 163-165.
http://dx.doi.org/10.1111/j.1751-0813.1992.tb07502.x

Burnett AL. 1997. Nitric oxide in the penis: physiology and pathology.The Journal of urology **157,** 320-324.
http://dx.doi.org/10.1016/S0022-5347(01)65369-2

Cai L, Wu Y, Zhang J, Pei F, Xu Y, Xie S, Xu D. 2001. Steroidal saponins from Tribulus terrestri.Planta medica **67,** 196-198.
http://dx.doi.org/10.1055/s-2001-11650

Chen H, Chen Q, Xuan W. 2000. A new organic acid from Tribulus terrestris. Academic Journal of Second Military Medical University **11**.

Chhatre S, Nesari T, Somani G, Kanchan D, Sathaye S. 2014. Phytopharmacological overview of Tribulus terrestris.Pharmacognosy reviews **8,** 45-51.
http://dx.doi.org/10.4103/0973-7847.125530

Chhatre S, Nesari T, Somani G, Kenjale R, Sathaye S. 2012. Comparative evaluation of diuretic activity of different extracts of Tribulus terrestris fruits in experimental animals. International Journal of Research in Phytochemistry and Pharmacology **3,** 129-133.

DeCombarieu E, Fuzzati N, Lovati M, Mercalli E. 2003. Furostanol saponins from Tribulus terrestris.Fitoterapia **74,** 583-591.
http://dx.doi.org/10.1016/S0367-326X(03)00152-7

Deepak M, Dipankar G, Prashanth D, Asha M, Amit A, Venkataraman B. 2002. Tribulosin and β-sitosterol-D-glucoside, the anthelmintic principles of Tribulus terrestris.Phytomedicine **9,** 753-756.
http://dx.doi.org/10.1078/094471102321621395

Do J, Choi S, Choi J, Hyun JS. 2013. Effects and mechanism of action of a Tribulus terrestris extract on penile erection. Korean journal of urology **54,** 183-188.
http://dx.doi.org/10.4111/kju.2013.54.3.183

El-Sheikh TM, Al-Fifi ZI, Alabboud MA. 2016. Larvicidal and repellent effect of some Tribulus terrestris L.,(Zygophyllaceae) extracts against the dengue fever mosquito, Aedes aegypti (Diptera: Culicidae). Journal of Saudi Chemical Society **20,** 13-19.
http://dx.doi.org/10.1016/j.jscs.2012.05.009

Ganzera M, Bedir E, Khan I. 2001. Determination of steroidal saponins in Tribulus terrestris by reversed-phase high-performance liquid chromatography and evaporative light scattering detection. Journal of Pharmaceutical Sciences **90,** 1752-1758.
http://dx.doi.org/10.1002/jps.1124

Gautam M, Ramanathan M. 2018. Saponins of Tribulus terrestris attenuated neuropathic pain induced with vincristine through central and peripheral mechanism. Inflammopharmacology 1-12.
http://dx.doi.org/10.1007/s10787-018-0502-0

Gauthaman K, Adaikan P, Prasad R. 2002. Aphrodisiac properties of Tribulus Terrestris extract (Protodioscin) in normal and castrated rats.Life sciences **71,** 1385-1396.
http://dx.doi.org/10.1016/S0024-3205(02)01858-1

Gauthaman K, Ganesan AP. 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,** 44-54.
http://dx.doi.org/10.1016/j.phymed.2007.11.011

Gopinath V, MubarakAli D, Priyadarshini S, Priyadharsshini NM, Thajuddin N, Velusamy P. 2012. Biosynthesis of silver nanoparticles from Tribulus terrestris and its antimicrobial activity: a novel biological approach,Colloids and Surfaces B. Biointerfaces **96,** 69-74.
http://dx.doi.org/10.1016/j.colsurfb.2012.03.023

Hajmohamadi S. 2013. Physiological and pharmaceutical effects of tribulus terrestris as a multipurpose and valuable medicinal plant. International Journal of Advanced Biological and Biomedical Research **1,** 1289-1295.

Hashim S, Bakht T, Marwat KB, Jan A. 2014. Medicinal properties, phyto-chemistry and pharmacology of tribulus terrestris L. (Zygophyllaceae). Pakistan Journal of Botany **46,** 399-404.

Hedlund P, Aszódi A, Pfeifer A, Alm P, Hofmann F, Ahmad M, Fässler R, Andersson KE. 2000. Erectile dysfunction in cyclic GMP-dependent kinase I-deficient mice. Proceedings of the National Academy of Sciences **97,** 2349-2354.
http://dx.doi.org/10.1073/pnas.030419997

Heidari M, Mehrabani M, Pardakhty A, Khazaeli P, Zahedi M, Yakhchali M, Vahedian M. 2007. The analgesic effect of Tribulus terrestris extract and comparison of gastric ulcerogenicity of the extract with indomethacine in animal experiments. Annals of the New York Academy of Sciences **1095,** 418-427.
http://dx.doi.org/10.1196/annals.1397.045

Hussain AA, Mohammed AA, Ibrahim HH, Abbas AH. 2009. Study the biological activities of Tribulus terrestris extracts. World Acadamy of Science Engineering and Technology **57,** 433-435.

Hussain K, Nisar MF, Majeed A, Nawaz K, Bhatti KH. 2010. Ethnomedicinal survey for important plants of Jalalpur Jattan, district Gujrat, Punjab, Pakistan.Ethnobotanical Leaflets **2010,** 11.

Jiang YH, Jiang LY, Wu S, Jiang WJ, Xie L, Li W, Yang CH. 2018. Proteomic analysis reveals the renoprotective effect of Tribulus terrestris against obesity-related glomerulopathy in rats. Biological and Pharmaceutical Bulletin b18-00304.
http://dx.doi.org/10.1248/bpb.b18-00304

Karimi JH, Malekzadeh SS, Hoshmand F. 2011. The effect of the Tribulus terrestris extract on spermatogenesis in the rat. Journal of Jahrom University of Medical Sciences **9,** 8-13.
http://dx.doi.org/10.29252/jmj.9.4.8

Khan S, Kabir H, Jalees F, Asif M, Naquvi K. 2011. Antihyperlipidemic potential of fruits of

Tribulus terrestris linn. Internnational Journal of Biomedical Research **2,** 98-101.

Kianbakht S, Jahaniani F. 2003. Evaluation of antibacterial activity of Tribulus terrestris L. growing in Iran.Iranian Journal of Pharmacology and Therapeutics **2,** 22-20.

Kim HJ, Kim JC, Min JS, Kim M-j, Kim JA, Kor MH, Yoo HS, Ahn JK. 2011. Aqueous extract of Tribulus terrestris Linn induces cell growth arrest and apoptosis by down-regulating NF-κB signaling in liver cancer cells.Journal of ethnopharmacology **136,** 197-203.
http://dx.doi.org/10.1016/j.jep.2011.04.060

Kostova I, Dinchev D. 2005. Saponins in Tribulus terrestris–chemistry and bioactivity.Phytochemistry reviews **4,** 111-137.
http://dx.doi.org/10.1007/s11101-005-2833-x

Kostov I, Dinchev D, Rentsch GH, Dimitrov V, Ivanova A. 2002. Two new sulfated furostanol saponins from Tribulus terrestris. Zeitschrift für Naturforschung C **57,** 33-38.
http://dx.doi.org/10.1515/znc-2002-1-206

Li JX, Shi Q, Xiong Q-B, Prasain JK, Tezuka Y, Hareyama T, Tanaka K, Namba T, Kadota S. 1998. Tribulusamide A and B, new hepatoprotective lignanamides from the fruits of Tribulus terrestris: indications of cytoprotective activity in murine hepatocyte culture.Planta medica **64,** 628-631.
http://dx.doi.org/10.1055/s-2006-957535

Lubna FM, Arshiya SM, Saad AM, Shabiya SM. 2014. Pharmacological activities of Tribulus terrestris. World Journal of Pharmacy and Pharmaceutical Sciences **4,** 136-150.

Manish K, Meenaksh P, Ravindra S, Ashok K. 2009. Evaluation of radiomodulatory influence of Tribulus terrestris root extract against gamma radiation: hematological, biochemical and cytogenetic alterations in Swiss albino mice.Pharmacologyonline **1**, 1214-1228.

Maughan RJ, Depiesse F, Geyer H. 2007. The use of dietary supplements by athletes.Journal of sports sciences **22,** 95-113.
http://dx.doi.org/10.1080/02640410310001405 81

Mitra N, Mohammad-Mehdi D, Reza ZM. 2012. Tribulus Terrestris L.(Zygophyllaceae) Flavonoid Compounds. International Journal of Modern Botany **2,** 35-39.
http://dx.doi.org/10.5923/j.ijmb.20120203.01

Najafi H, Firouzifar MR, Shafaat O, Ashtiyani SC, Hosseini N. 2014. Protective effects of Tribulus terrestris L extract against acute kidney injury induced by reperfusion injury in rats. Iranian journal of kidney diseases **8,** 292.

Neychev VK, Mitev VI. 2015.Pro-sexual and androgen enhancing effects of Tribulus terrestris L.:Fact or fiction. Journal of ethnopharmacology **179,** 345-355.
http://dx.doi.org/10.1016/j.jep.2015.12.055

Obreshkova D, Pangarova T, Mitkov S, Dinchev D. 1998. Comparative analytical investigation of Tribulus terrestris preparations.Farmacija **45,** 10-12.

Pavin NF, Izaguirry AP, Soares MB, Spiazzi CC, Mendez ASL, Leivas FG, Cibin FWS. 2018. Tribulus terrestris Protects against Male Reproductive Damage Induced by Cyclophosphamide in Mice. Oxidative medicine and cellular longevity 2018.
http://dx.doi.org/10.1155/2018/5758191

Perveen A, Abid R, Fatima R. 2007. Stomatal types of some dicots within flora of Karachi, Pakistan.Pakistan Journal of Botany **39,** 1017.

Phillips OA, Mathew KT, Oriowo MA. 2006. Antihypertensive and vasodilator effects of

methanolic and aqueous extracts of Tribulus terrestris in rats.Journal of ethnopharmacology **104,** 351-355.
http://dx.doi.org/10.1016/j.jep.2005.09.027

Pokrywka A, Obmiński Z, Malczewska-Lenczowska J, Fijatek Z, Turek-Lepa E, Grucza R. 2014. Insights into supplements with Tribulus terrestris used by athletes.Journal of human kinetics **41,** 99-105.
http://dx.doi.org/10.2478/hukin-2014-0037.

Prabhu N, Hadigal S. 2014. Effect of Tribulus terrestris on learning and memory in wistar rats.journal of Pharmacognosy and Phytochemistry **6**, 68-71.
http://dx.doi.org/10.5530/pj.2014.4.10

Qari SH, El-Assouli S. 2017. Evaluation of cytological and genetic effects of Tribulus terrestris fruit aqueous extract on cultured human lymphocytes. Saudi Journal of Biological Sciences. http://dx.doi.org/0.1016/j.sjbs.2017.01.012.

Qi P, Zheng Y, Shen Y, Wang J, Bi Q, Feng R, Wu W. 2018. Characterization and discrimination of steroidal saponins in Tribulus terrestris L. and its three different aerial parts by Cheimical profiling with chemometrics analysis. Journal of separation science. http://dx.doi.org/10.1002/jssc.201800513

QU NN, YANG SS. 2007. Extraction and Determination of Chemical Constituents of Flavonides in Tribulus terrestris L.Journal of Liaoning University of Traditional Chinese Medicine **3,** 122.

Qureshi R, Maqsood M, Arshad M, Chaudhry AK. 2011. Ethnomedicinal uses of plants by the people of Kadhi areas of Khushab, Punjab, Pakistan. Pakistan Journal of Botany **43,** 121-133.

Rahmathulla S. 2013. Effect of Tribulus terrestris fruit aqueous extract on hyperlipidaemia and maintenance of liver architecture in isoproterenol-induced myocardial infarction in rats. International Journal of Pharma and Bio Sciences **4,** 983-992.
http://dx.doi.org/10.1.1.432.3509

Ren Y, Chen H, Yang G, Zhu H. 1994. Isolation and identification of a new derivative of cinnamic amide from Tribulus terrestris.Acta Pharmaceutica Sinica **29,** 206.

Reshma P, Sainu NS, Mathew AK, Raghu K. 2016. Mitochondrial dysfunction in H9c2 cells during ischemia and amelioration with Tribulus terrestris L. Life sciences **152,** 220-230.
http://dx.doi.org/10.1016/j.lfs.2016.03.055

Samani NB, Jokar A, Soveid M, HeydariM, Mosavat SH. 2016. Efficacy of Tribulus terrestris extract on the serum glucose and lipids of women with diabetes mellitus. Iranian journal of medical sciences **41,** S5.

Santos JC, Reis L, Destro-Saade R, Luiza-Reis A, Fregonesi A. 2014. Tribulus terrestris versus placebo in the treatment of erectile dysfunction: a prospective, randomized, double-blind study. Actas Urológicas Españolas (English Edition) **38,** 244-248.
http://dx.doi.org/10.1016/j.acuroe.2014.03.009

Sharifi AM, Darabi R, Akbarloo N. 2003. Study of antihypertensive mechanism of Tribulus terrestris in 2K1C hypertensive rat.Journal of Life Sciences **73,** 2963-2971.
http://dx.doi.org/10.1016/j.lfs.2003.04.002

Sharma DK. 2017. Enumerations on phytochemical and pharmacological properties of tribulus terrestris LINN: Indian Viagra. Asian Journal of Science and Technology **8,** 6462-6267.

Sharma I, Khan W, Ahmad S. 2017. In vitro and ex vivo approach for anti-urolithiatic potential of bioactive fractions of gokhru with simultaneous HPLC analysis of six major metabolites and their exploration in rat plasma.Pharmaceutical biology **55,** 701-711.

http://dx.doi.org/10.1080/13880209.2016.1266671

Shinwari ZK, Qaiser M. 2011. Efforts on conservation and sustainable use of medicinal plants of Pakistan.Pakistan Journal of botany **43,** 5-10.

Shirfule A, Sangamwar A, Khobragade C. 2011. Exploring glycolate oxidase (GOX) as an antiurolithic drug target: Molecular modeling and in vitro inhibitor study. International journal of biological macromolecules **49,** 62-70.
http://dx.doi.org/10.1016/j.ijbiomac.2011.03.016

Singh S, Nair V, Gupta YK. 2012. Evaluation of the aphrodisiac activity of Tribulus terrestris Linn. in sexually sluggish male albino rats. Journal of pharmacology & pharmacotherapeutics **3,** 43.
http://dx.doi.org/10.4103/0976-500X.92512

Singh S, Raghavendra K, Singh R, Mohanty S, Dash A. 2008. Evaluation of Tribulus terrestris Linn (Zygophyllaceae) acetone extract for larvicidal and repellence activity against mosquito vectors. The Journal of communicable diseases **40,** 255-261.

Song YH, Kim DW, Curtis-Long MJ, Park C, Son M, Kim JY, Yuk HJ, Lee KW, Park KH. 2016. Cinnamic acid amides from Tribulus terrestris displaying uncompetitive α-glucosidase inhibition. European journal of medicinal chemistry **114,** 201-208.
http://dx.doi.org/10.1016/j.ejmech.2016.02.044

Su L, Feng SG, Qiao L, Zhou YZ, Yang RP, Pei YH. 2009. Two new steroidal saponins from Tribulus terrestris.Journal of Asian natural products research **11,** 38-43.
http://dx.doi.org/10.1016/j.steroids.2008.12.008

Sun B, Qu W, Bai Z. 2003. The inhibitory effect of saponins from Tribulus terrestris on Bcap-37 breast cancer cell line in vitro.Zhong yao cai Zhongyaocai Journal of Chinese medicinal materials **26,** 104-106.

Sun W, Gao J, Tu G, Guo Z, Zhang Y. 2002. A new steroidal saponin from Tribulus terrestris Linn.Natural Product Letters **16,** 243-247.
http://dx.doi.org/10.1080/10575630290020541

Tharakan B, Manyam BV. 2005. Botanical therapies in sexual dysfunction.Phytotherapy Research **19,** 457-463.
http://dx.doi.org/10.1002/ptr.1634

Tilwari A, Shukla N, Devi PU. 2011. Effect of five medicinal plants used in Indian system of medicines on immune function in Wistar rats. African Journal of Biotechnology **10,** 16637-16645.
http://dx.doi.org/10.5897/AJB10.2168

Wang B, Ma L, Liu T. 1990. 406 cases of angina pectoris in coronary heart disease treated with saponin of Tribulus terrestris. Zhong xi yi jie he za zhi Chinese journal of modern developments in traditional medicine **10,** 85-87, 68.

Wang J, Zu X, Jiang Y. 2009. Five furostanol saponins from fruits of Tribulus terrestris and their cytotoxic activities. Natural product research **23,** 1436-1444.
http://dx.doi.org/10.1080/14786410902940990

Xu YX, Chen H-S, Liang H-Q, Gu ZB, Liu WY, Leung WN, Li TJ. 2000. Three new saponins from Tribulus terrestris.Planta medic **66,** 545-550.
http://dx.doi.org/10.1055/s-2000-8609

Xu Y, Liu Y, Xu T, Xie S, Si Y, Liu Y, Zhou H, Liu T, Xu D. 2010. A new furostanol glycoside from Tribulus terrestris.Molecules **15,** 613-618.
http://dx.doi.org/10.3390/molecules15020613

Yang Q, Yang C. 2000. A New Steroidal saponin from Chlorophytum malayense.Acta Botanica Yunnanica **22,** 191-196.

Zheleva-Dimitrova D, Obreshkova D, Nedialkov P. 2012. Antioxidant activity of tribulus terrestris a natural product in infertility

therapy.Internatinal Journal of Pharmacy and Pharmaceutical Sciences **4,** 508-511.

Zhu W, Du Y, Meng H, Dong Y, Li L. 2017. A review of traditional pharmacological uses, phytochemistry, and pharmacological activities of Tribulus terrestris.Chemistry Central Journal **11,** 60. http://dx.doi.org/10.1186/s13065-017-0289-x