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

Farooq Azam¹, Samia Munier¹, Maliha Batool⁵, Bashir Ahmad³, Ghazanfar Abbas*⁴

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

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

³Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan

⁴Institute 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, 2019

**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).

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 1.25 cm 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, cinamnic acid amides and lignanamides (Bourke et al., 1992; Renet 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 and quercetin. 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., 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-transcaffeoyllyramine, N-transcoumaroyllyramine, 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, phycsin, 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, (Chenet et al., 2000) and furfural 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, furostol 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; Obreschkova 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–H2O (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 (CHCl3–MeOH–H2O), MPLC (H2O–MeOH angle) and gel filtration on Sephadex G-25 with H2O (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), antiurithic (Anandet et al., 1994; Shirfuleet 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, progrenolone, 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 (Adimoeljaet 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 (Arwyad 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 (Neychevet 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-cholesterolmic | (Fatima et al., 2014). |
| Leaves | Larvicidal | (Singh et al., 2008; Mitra et al., 2012; Zhu et al., 2017). |
| Leaves | Anti-diabetic | (Amin et al., 2006). |
| Leaves and fruits | Anti-inflammatory | (Baburao et al., 2009; Borran et al., 2017). |
| Fruits | Aphrodisiac | (GamaEl Din et al., 2018, Singh et al., 2012). |
| Fruits | Anti-urothelial | (Anand et al., 1994; Shirifule et al., 2011). |
| Fruits | Anti-cholinergic | (Fatima et al., 2014). |
| Fruits | Hypolipidemic | (Khan et al., 2011; Rahmanulla et al., 2013). |
| Fruits | Analgesic | (Heidari et al., 2007; Borran et al., 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, stems, roots, whole plant | Apoptosis inducer | (Basaiyee et al., 2018) |
| Fruits, roots, stems and leaves | Anti-cancerous | (Kostova et al., 2005; Manish et al., 2009; Kim et al., 2011). |
| Fruits, whole plant | Antimicrobial, Antibiotic | (Arulmozhi et al., 2018, Adaikan et al., 2000, Al-Bayati et al., 2008; Baburao et al., 2009). |
| Whole plant | Neuruphathic 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 | (Najafl et al., 2014). |
| Aerial parts of plant | Erectile dysfunction | (Kalamegam et al., 2008). |
| Whole plant | Immunomodulatory | (Tilvari et al., 2011). |
| Whole plant | Anthelmintic | (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 (Doet 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 corpus 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 of sperm (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 (Gauthamanet 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-picyrilhydrazyl (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 spiroasaponins 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 (Maughanet 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 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 like every 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.

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