Evaluation of Pharmacological Potential and Biological Activities of *Tamarix dioica*: A Marvelous Plant

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Abstract

Tamarix dioica commonly known as ghaz or khagal is a native plant of Pakistan present in Sindh, KPK, Punjab, and Baluchistan having great medicinal value as its leaves, stem, and bark is used as herbal medicine. Traditionally it is used to cure diarrhea, dysentery, gastrointestinal disorders, diabetes, dental issues, cold, flu, fever and cough. Extract and paste of its leaves and bark also used to heal and sooth wounds. Leaves, roots and stems of *T. dioica* are rich source of different phytochemicals like tannins, flavonoids, saponins, phenol, steroids and terpenoids thus having great antibacterial, antifungal, anti-inflammatory, antioxidant, and hepato-protective properties. Mast fungal and bacterial infections can be cured using different extract of *T. dioica*. Its essential oil can be effective against different microbial attacks like that of bacteria. Being hepato-protective in nature, its extract can be employed to treat liver disorders. A largest growing issue across the world, diabetes, can also be managed by inhibiting activity of certain metabolic enzymes using *T. dioica* extracts. Besides all these it is stated that *T. dioica* can also have anti-diarrheal, anti-inflammatory and muscle relaxant ability. This review study is aimed to examine the different pharmacological uses of *T. dioica* in different forms and also to evaluate its potential biological activities against various health issues.

Keywords: *Tamarix dioica*, Natural products, Anti-bacterial, Hepato-protective, Anti-fungal, Anti-diarrheal, Anti-diabetic

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Introduction

Natural products continue to promote advancements in biological science, chemistry, and medicine due to their immense structural and chemical diversity, which is matchless to any synthetic library of small molecules (Khan et al., 2018). Since these products have gone through evolutionary optimization to produce drug-like compounds, they continue to be the root of medications and drug leads (Koehn & Carter, 2005; Newman & Cragg, 2012). The history of medicine is overflowing with incredible examples of how the discovery of a natural substance dramatically influenced biological advancements and stimulated medication research and treatment (Shen, 2015). In old times, Man began to differentiate plants with distinct pharmacological actions from those that were useful for medical purposes as he searched for sustenance and learned how to effectively cope with human distress. With the emergence of this association, several plants started to be used as medicines (Shakya, 2016). Plants are one of the most significant and frequent sources of potentially useful new medicinal products. As a result, research into the biological characteristics of medicinal plants is necessary in order to create novel medicines (Khan et al., 2004). For a huge portion of the global community, medicinal plants constitute a highly significant source of medication advancement (Sharma et al., 2012). As specified by the World Health Organization's estimate almost 80% people of the global community depends on medicinal herbs and plants for basic healthcare (Samejo et al., 2011; Devika et al., 2012). According to an estimate of the World Wildlife Fund (WWF) along with IUCN (International Union for Conservation of Nature) there are about 50 thousand to 80 thousand varieties of flowering plants which are used globally in medicine industry (Chen et al., 2016). Through phytochemistry, a number of natural substances have been found, and their extracts are effective in treating a variety of problems without causing any negative effects (Devika et al., 2012). When chemistry, isolation, purification, and characterization of plant active chemicals began, plant medications began to be developed (Shakya, 2016). Many phytochemicals are found in plants, such as amino acids, fatty acids, alkaloids, saponins, tannins, terpenes, glycosides, sterols, and flavonoids which have the ability to prevent diseases (Selvam, 2008).

Deciduous plant or tree in the genus Tamarix, sometimes known as tamarisk, can reach heights of 1 to 18 meters (Samejo et al., 2013). It consists of approximately 50 and 60 different types of flowering plants (Kayden et al., 2010). It bears purple blooms, reddish-colored flowers, and vaginate leaves. Tamarix has a long taproot that can reach 30 m or more into the soil and has the size of a little tree. The tree is found in Pakistan, Iran, Afghanistan, Bhutan, Bangladesh, Nepal, Kashmir, and Myanmar (Bughio et al., 2017).

Tamarix dioica, also known as Ghaz or Khagal, is a member of the Tamaricaceae family and may be found in Pakistan's Sindh province, Balochistan, Khyber Pakhtunkhwa, and Punjab regions (Samejo et al., 2013). *T. dioica* is an annual plant that can adapt to climate changes. It can flourish in both dry and salty soil (Ksouri et al., 2012). Herbal remedies are made from the bark, leaves, and stems of *T. dioica* (Khan et al., 2004). *T. dioica* serves as a diuretic medication, a carminative, and to treat inflammation of the liver and spleen. *T. dioica* tree leaves have antifungal properties in the crude extract. (Khan et al., 2004). Furthermore, this plant is utilized as a constrictor in vaginal discharge symptoms (Khan et al., 2013). *T. dioica* has exhibited antifungal properties against three pathogens, *Aspergillus fumigates*, *Candida glabrata*, and *Trichophyton rubrum*, as well as antimicrobial properties against *Klebsiella pneumonia* and *Pseudomonas aeruginosa* (Bughio et al., 2017). Symptoms like dysentery, inflammation and diarrhea are effectively treated by using *T. dioica*. It is effective against cough, cold, flu and fever, and can be used as astringent, by being leucodermic in nature, against wounds (Zaidi et al., 2012). The dried bark and leaves may be used in a paste that heals wounds (Chaudhary et al., 2015). Additionally, *T. dioica* has a long history of usage in treating a variety of smooth muscle-related diseases of the digestive, respiratory, and cardiovascular systems (Imtiaz et al., 2019).

Natural Occurrence

It is found in Pakistan, Iran, Afghanistan, Bhutan, Bangladesh, Nepal, Kashmir, and Myanmar are all countries where the tamarisk tree naturally occurs (Bughio et al., 2017). In Pakistan, Sindh province, Balochistan, Khyber Pakhtunkhwa, and Punjab regions have *T. dioica*, which is also known as Ghaz, jhau, or khagal, a member of the *Tamaricaceae* family (Samejo et al., 2013). It is a tiny, evergreen tree or shrub with reddish bark that is around 6 meters tall (Iqbal et al., 2019). The diameter of the flowers is around 3 mm. These unisexual, pink, or purple flowers are produced. The spikes are round and placed compactly or tightly together. Fruit is a kind of capsule with three valves that is roughly 5mm long and has a cone-like form (Khan et al., 2013).

Traditional uses

Tamarix species have been proven to exhibit a number of biological properties in clinical pharmacological studies including antidiabetic, hepatoprotective, wound-healing, anti-inflammatory, gastrointestinal disease treatment, or in dental issues (Bahramsoltani et al., 2020). *T. dioica* has long been used to treat inflammation, diarrhea, and dysentery. Being leucodermic in nature, it is employed to treat cough, cold, flu fever, and can also be used as astringent to cure skin wounds caused by heat burn (Figure 1) (Zaidi et al., 2012).

Phytochemicals Analysis of *Tamarix dioica*

T. dioica stems, flowers, leaves, and roots go through phytochemical screening, and the findings confirmed the presence of steroids and phlobatannins in all plant parts as shown in table: 1, flavonoids, phenols, and tannins in the flowers, leaves, and roots, saponins and terpenoids in the stems, flowers, and leaves. However, proteins, amino acids, alkaloids, and glycosides were not found in any section of the plant (Samejo et al., 2013).

Table 1: List of Phytochemicals along with its medicinal Uses

Phytochemicals	Parts of plant	Medicinal uses	References
Steroids	Stems, flowers, leaves and roots	Antibacterial	Yadav et al., 2011; Samejo et al., 2013
Tannins	Flowers, leaves and roots	Anti-hemorrhoidal, hemostatic and anti-diarrheal.	Shahla et al., 2010; Samejo et al., 2013
Flavonoids	flowers, leaves and roots	Anti-allergic, anti-inflammatory, antioxidant, anti-cancer, anti-thrombotic, anti-viral and hepato-protective.	Shahla et al., 2010; Samejo et al., 2013
Saponins	Stems, flowers and leaves	Helpful in lowering cholesterol, antioxidant, anti-inflammatory.	Shahla et al., 2010; Samejo et al., 2013
Phenols	Stems, flowers, leaves and roots	Cardio-protective, anti-apoptosic, anti-inflammatory, anti-aging, anti-atherosclerosis, anticancer, improvement of endothelial function, anti-angiogenesis.	Yadav et al., 2011; Samejo et al., 2013
Terpenoids	Stems, flowers and leaves	Antibacterial, wound healing, increase the antioxidants, and reduce inflammation of tissues by improving blood flow.	Krishnaiah et al., 2009; Selvan et al., 2012; Samejo et al., 2013

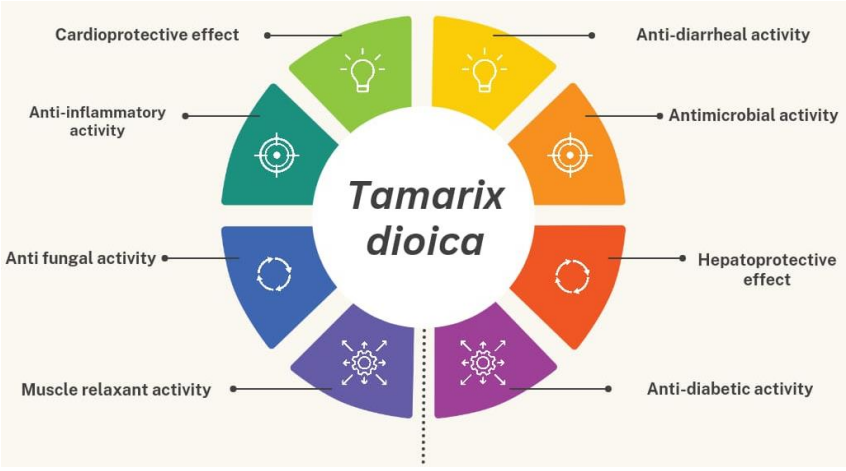

Figure 1: Biological Activities of *T. dioica*

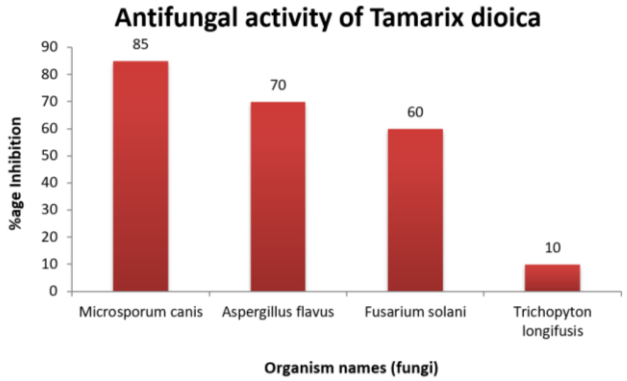

Figure 2: Rate of antifungal activity of *T. dioica*

1. Antifungal activity

Fungi have been identified as a source of severe infection with alarming frequency over the last two decades (Nucci et al., 2005). Fungal infections kill over 1.5 million people and influence over a billion people. As a result of other medical conditions like AIDS, asthma, cancer, organ donation, and corticosteroid treatments, serious fungus diseases can develop (Bongomin et al., 2017) Due to their biocompatibility and minimal toxicity, natural products have a significant potential for the creation of novel medicines with antifungal action. Natural goods have excellent antifungal ability, primarily because they contain quinones, terpenes and flavonoids (Marena et al., 2022). Khan et al. (2004) investigated the antifungal action of the crude preparation of *T. dioica* against six fungi, including *Candida albicans, Fusarium solani, Microsporum canis*, and *Trichophyton longifusis*. Percentage fraction was found to be highest in *Microsporum canisan* and followed by *Aspergillus flavus, Fusarium solani*, and *Trichophyton longifusis* in order of abundance. *T. dioica* tree crude extract is considerably effective against two microorganisms (*M. canis* and *A. flavus*) and relatively effective against one (*F. solani*) (Khan et al., 2004) as shown in figure 2.

2. Antibacterial activity

Bacterial infections are a significant danger to human health, and they are being worsened by drug resistance. These illnesses can cause significant death and disability, stressing the importance of rapidly identifying and treating pathogenic microbes (Deusenbery et al., 2021). Bacterial infections are among the most prevalent ailments in humans. Furthermore, when host immunity is concerned with underlying conditions, inflammation, or other illness, vulnerability to bacterial infections increases (Angus et al., 2013). Natural compounds with anti-infective characteristics account for approximately 80% of pharmaceutical agents and are direct employed for therapy of human illnesses along with being used as the main constituents in many drug formulations. Natural plant chemicals inhibit many virulent factors of bacteria like: sensing of quorum, biofilms of bacteria, movement, colors, enzymes, surfactants as well as poisons of bacteria (Liu et al., 2019).

According to a research published by Bughio et al. (2017) found that action of volatile oils extracted from leaves and flower of *T. dioica* is much greater in case of *Escherichia coli*, which is MIC at 10 µg/ml, than in case of *Staphylococcus aureus* ,which is MIC at 100 µg/ml. Volatile oils extracted from flowers exhibited a maximum zone of inhibition in diameter(mm) / concentration (µg/ml) levels as 16/1000, 11/500, 8/100, and 3/10, while in case of *S. aureus* volatile oils extracted from flower exhibited a zone of inhibition in diameter(mm) / concentration (µg/ml) levels as 12/1000, 7/500, and 3/100. However, no suppression zone is shown at concentration of 10 µg/ml. The anti-bacterial activity of volatile oils extracted from leaves of *T. dioica* in case of *E. coli* had a zone of inhibition at concentration levels of 10, 100, 500 and 1000 µg/ml as 2, 6, 11 and 14 mm in diameter, accordingly, while in case of *S. aureus* volatile oils of leaves had zone of inhibition as 0, 2, 5 and 10 mm in diameter, accordingly at same concentrations levels as in case of *E. coli*. Similarly, no suppression zone is shown at concentration 10 µg/ml in case of *S. aureus* as in *E. coli* (Bughio et al., 2017).

According to another research published by Bughio et al. (2021) *T. dioica* has less antibacterial effects in extract form. *T. dioica* methanol and ethyl acetate extracts show no antibacterial action against bacterium species such as *E. coli* and *S. aureus*. The extract of *T. dioica* containing methanol has some antimicrobial potential while the extract having ethyl acetate has none, which could be attributed to the reduced extraction power of antibiotic compound as well shown in table 2 (Bughio, 2021) .

Table 2: Exploring the Protective Potential in CCL_4 induced hepatotoxicity in mice.

Assay	Organism used	Treatment groups	Percentage protection	Reference
T. dioica (Ghaz) Protective Potential in the CCl_4 Induced Hepatotoxicity Animal Model	Mice	Silymarin 100 + CCl_4, ME 200 + CCl_4, ME 300+ CCl_4 AE 200 + CCl_4 and AE 300mg/kg + CCl_4	78.75%, 77.2%, 71.65%, 76.34% and 91.97% respectively.	Komal et al., 2021

3. Hepatoprotective effect:

The liver is a crucial organ for filtering. However, some pathogens, including the viruses, hepatitis B and C and malaria-causing Plasmodium species effectively target the liver and can cause chronic illnesses in human liver cells (Protzer et al., 2012). Natural remedies for liver illnesses have long been found in foods like fruits, veggies, plant extracts, plants, insects, and mammals. Numerous herbal remedies have been tested in clinical settings as effective hepatoprotective drugs against frequently occurring liver illnesses (Zhang et al., 2013).

The aim of the research by Komal et al. (2021) was to investigate the hepatoprotective activity of *T. dioica* in rats against acute liver injury caused by CCl4. *T. dioica* products improved the histopathological and biochemical markers in rats and decreased acute CCl4-mediated liver injury in vivo. The *T. dioica* may lessen the degree of the liver injury brought on by carbon tetrachloride. Six days of pretreatment with various *T. dioica* formulations before administering CCl4 resulted in variable degrees of hepatoprotection. When compared to the positive control group (silymarin 100mg/kg) and the methanolic extracts (ME200 and ME-300), respectively, *T. dioica* water extract (300mg/kg) showed the greatest overall protection to liver cells (91.97%) (Komal et al., 2021).

4. Anti-diabetic activity

The biochemical condition known as diabetes mellitus (DM) is the one that is spreading the fastest. It is mainly defined by hyperglycemia, which is linked to abnormal protein, fat, and carbohydrate metabolism (Kameswararao et al., 2003). For the control of elevated blood sugar level after a meal, α-glucosidase inhibition was designated as a primary goal, and the anti-diabetic potential of extracts of plant parts was mainly due to the poly-phenols found in plant extracts (Raza et al., 2018). Although *T. dioica* is traditionally employed in medicine to treat diabetes, there is much less empirical support for this use of the plant. In a research by Niaz et al. (2021), α-glucosidase suppression was used to measure the in vitro anti-diabetic potential. The outcomes showed that the portion which had the highest level of inhibition for α-glucosidase is of ethyl acetate, having a 122.81±2.05 µg/ml value of IC_{50}. The chloroform portion demonstrated the second-highest enzyme suppression. According to the statistical study, the ethyl acetate fraction substantially inhibited α-glucosidase more than any other extract (p 0.05). When compared to other fractions, the n-hexane fraction responded to enzyme suppression the least. The results showed that *T. dioica's* ethyl acetate extract had the highest potency in terms of scavenging free radicals and inhibiting α-glucosidase, indicating a modest anti-diabetic potential (Figure 3) (Niaz et al., 2021).

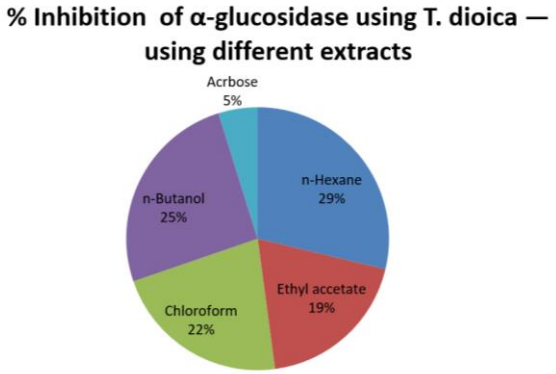

Figure 3: The %age inhibition of alpha-glucosidase using *T. diocia* & different extracts

5. Anti-diarrheal activity

Osmotic gradients in feces cause diarrhea, which is simply a changed flow of ions and water. In many instances, the illness is deadly. Around the globe, enteric infections that induce diarrhea play a significant role in morbidity and death. Each year, there are between 2 and 4 billion cases of infectious diarrhea, with babies being the most common victims (Hodges et al., 2010). Due to their typically low cost and possibility for quick translation to the field, natural goods represent a possibly alluring source of anti-diarrheal therapeutics. In many regions of the globe, there is also an extensive history of oral proof supporting the effectiveness of different anti-diarrheal medications. In models of gastroenteritis, several natural product extracts with Cl- channel inhibition action have demonstrated effectiveness (Thiagarajah et al., 2014). Imtiaz et al. evaluated a hydro-methanolic raw *T. dioica* extract (TdCr) in vivo using diarrheal paradigm induced by oil (castor oil) in mouse to ascertain the anti-diarrheal impact of *T. dioica*. The significant anti-diarrheal impact was demonstrated by TdCr in values 100, 200, and 400 mg/kg in the model having diarrhea caused by castor oil during in-vivo studies. When given orally in dosages of 100, 200, and 400 mg per kilogram, the methanolic preparation of this plant significantly reduced the incidence of diarrhea. It showed 29% n-Hexane. In comparison to the control group, there was a significant reduction of loose feces as 13.62%, 45.0%, and 60.62% at ($p< 0.05$), ($p < 0.01$) and ($p < 0.005$) respectively, as shown in table 3 (Imtiaz et al., 2019).

Table 3: Exploring the smooth muscle relaxant properties of *T. dioica* on albino rats

Assay	Organism used	Concentration of *T. dioica*	% inhibition	Reference
T. dioica Roxb's Smooth Muscle Relaxant (Anti-diarrheal) Properties.	Albino rats	*T. dioica* given as 100, 200 and 400 mg/kg.	13.62%, 45.0% and 60.62% respectively	Imtiaz et al., 2019

6. Anti-inflammatory activity

Inflammation results by the invasion of microbes like viruses, fungi or bacteria in body cells, tissues or in blood circulatory system (Artis et al., 2015). Responses to certain conditions like tissue death, cell injury, degradation or cancer can also results in inflammation (Rock et al., 2011; Waisman et al., 2015). Inflammation of gastric cells is mostly caused by *Helicobacter pylori* (*H. pylori*) which affect almost 50% population of the world. This *H. pylori* damages gastric mucosa, gastric hormonal release and thus affecting different cellular protein targets thus inducing inflammatory responses in host (Wang et al., 2014). Natural products have magnificent ability for the cure and prevention of inflammation and thus benefit human health (Yuan et al., 2006). Since ancient times extracts and parts of plants are used as great anti-inflammatory agents (Khalifa et al., 2004). Great anti-inflammatory properties are displayed by *T. dioica*. *T. dioica* preparations strongly inhibited IL-8 release at a concentration of 100 g/ml. Secretions of IL-8 in cells of gastric epithelia infected by *H. pylori* are inhibited by using this plant. Data were divided into three categories based on IL-8 secretions inhibition potential as: mild inhibition, moderate inhibition and strong inhibition. Mild inhibition occurs when IL-8 secretion are greater than 2000 pg/ml. moderate inhibition occurs when IL-8 secretion range between 1000 and 2000 pg/ml. And strong inhibition occurs when IL-8 secretions are less than 1000 pg/ml. The inflammatory reaction brought on by *H. pylori* depends on both IL-8. *T. dioica* demonstrated potent inhibition of IL- 8 release in cells contaminated with Helicobacter pylori at 100 g/ml (Zaidi et al., 2012).

7. Muscle Relaxant

Smooth muscles influence the contraction of vascular walls directly and control blood flow in vessels (Brozovich et al., 2016). Major regulator of respiratory, vascular, digestive and urinary system are smooth muscles because of their contractile activity. Many clinical disorders results due to the inappropriate contraction of these muscles (Kim et al., 2008). It is typically used to treat a variety of diseases

linked with smooth muscle present in the cardio-vascular, digestive and respiratory systems according to a research by Imtiaz et al. (2019) In order to ascertain the impacts on smooth processes, ex vivo studies were carried out using isolated tissues. The pharmacological foundation for its conventional usage is provided by ex vivo studies, which show the existence of substantial vaso-dilatory, broncho-dilatory, spasmolytic, and a few cardio depressant actions. This may be due to the ATP dependent K^+ gates opening characteristic (Imtiaz et al., 2019).

8. Cardio-protective effects

Cardio-protection is a wide term that refers to any measures intended for reducing the harmful effect of myocardial ischemia and perfusion. Heart attacks, impaired heart contractile functioning, impaired coronary blood flow, and myocardial infarction are some consequences of damage (Heusch, 2013). A 4/, 5, 7-trihydroxy flavone, apigenin is present in *T. dioica* which has proven beneficial for bone development and has anti-inflammatory, antioxidant, depressive, and cardiovascular protective effects. It is a powerful tumor cell inhibitor (Agrawal et al., 2011; Montano et al., 2011; Kumar et al., 2013) In examinations by Imtiaz et al. (2019) to assess the therapeutic potential in diseases affecting the cardiovascular system, TdCr demonstrated a cardio-depressant activity in a rabbit paired with atrial preparation, altering both the rate and force of cardiac contraction. Its cardio-depressant impact was comparable to cromakalim, a KATP channel opener, which possess a cardio-depressant effect by reducing the duration of the cardiac action potential and promoting hyper-polarization.

Conclusion

This book chapter reveals that *T. dioica* is a valuable plant having potential antifungal, hepatoprotective, anti-inflammatory, antibacterial, anti-diarrheal, anti-diabetic and muscle relaxant properties. The results of various experiments and in vivo studies have demonstrated its pharmacological applications in different living systems. The leaves, stem, bark, flower and root of this plant being rich in many phytochemicals have been used in traditional folk medicines in ancient times. Due to presence of many biologically active compounds, *T. dioica* has great potential for future drug discoveries. It can be used to make many effective drugs to treat different diseases and infection. Besides its vast number of biological applications due to different properties, the research and knowledge about its anti-cancer, anti-oxidant and cytoprotective properties is scarce. So, more research work is needed to be carried out for better understanding of these properties which is required to estimate the correct doses and usage in pharmaceutical industry and to treat various diseases.

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