

WORLD JOURNAL OF PHARMACEUTICAL RESEARCH

SJIF Impact Factor 8.453

Volume 14, Issue 16, 1250-1258.

Review Article

ISSN 2277-7105

TERMINALIA ARJUNA (ARJUNA): A MULTIFUNCTIONAL ETHNOMEDICINAL TREE WITH CARDIOPROTECTIVE AND THERAPEUTIC PROMISE

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Article Received on 02 July 2025,

Revised on 22 July 2025, Accepted on 12 August 2025 DOI: 10.20959/wjpr202516-38012



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ABSTRACT

A deciduous tree native to India, Terminalia arjuna, also referred to as Arjuna, has been widely employed in Ayurveda for its restorative and cardiotonic qualities. Packed in bioactive substances such as flavonoids, glycosides, tannins, and arjunolic acid, this plant has a variety of pharmacological properties, such as anti-inflammatory, anti-inflammatory, lipid-lowering, antibacterial, wound healing and anticancer activities. It has been shown in clinical and preclinical research to be effective in treating oxidative stress, hypertension, hyperlipidemia, and cardiovascular diseases. A powerful herbal option for the creation of natural therapeutic agents in contemporary healthcare, Terminalia arjuna has a low toxicity level and a long history in traditional medicine.

KEYWORDS: Terminalia arjuna, Cardioprotective, Antioxidant, Arjunolic acid, Traditional medicine, Phytochemicals.

INTRODUCTION



In both traditional and contemporary healthcare systems, medicinal plants are essential. Herbal medicines are preferred by many because of their inherent efficacy, affordability, and lack of negative side effects. Plant-based remedies for a variety of ailments have long been employed in traditional Indian medical systems like Ayurveda and Siddha. In rural regions, these treatments are frequently the main source of medical care. By investigating how plants are used for food, medical, and economic purposes, ethnobotanical studies contribute to the preservation of this important information. A significant percentage of people worldwide still use herbal medicine, which is indicative of its increasing significance in general health. Due to rising demand for plant-based products and increased production, the herbal sector is also growing. One well-known medicinal plant is Terminalia arjuna, also referred to as Arjuna, which is used to treat skin disorders, liver issues, ulcers, and cardiac difficulties. It has natural substances including flavonoids and saponins that decrease cholesterol and act as antioxidants. The purpose of this review is to emphasize the potential of these medicinal plants in contemporary healthcare as well as their health advantages.

BOTANICAL DISTRIBUTION OF TERMINALIA ARJUNA

Taxonomical Classification

Kingdom: Plantae

Order: Myrtales

Family: Combretaceae

Genus: Terminalia

Species: Terminalia arjuna (Roxb.) Wight & Arn.

The huge, deciduous tree Terminalia arjuna, also referred to as Arjuna, is well-known for its cardiovascular advantages and medicinal bark. In traditional Indian medicine, particularly Ayurveda, it has a lengthy history.^[4]

Habitat Characteristics

Attribute	Details
Altitude range	From sea level up to ~1200 meters above mean sea level
Soil preference	Alluvial, loamy, moist, well-drained soil near riverbanks
Climate	Tropical to subtropical, moderate to high humidity
Rainfall tolerance	Moderate to heavy rainfall; drought-resistant once matured

Phytochemical composition

The medicinal potential of Terminalia arjuna is attributed to a range of bioactive substances. Flavonoids, which promote cardiovascular health by decreasing cholesterol and having cardioprotective properties, and tannins, which offer anti-inflammatory and antioxidant properties, are important phytochemicals. Furthermore, T. arjuna contains glycosides that have cardiotonic qualities and triterpenoids with anticancer and antileishmanial actions, like ursolic acid. Its overall health benefits are enhanced by saponins, which also have anti-inflammatory and immune-boosting properties, and important minerals. The potential of T. arjuna for use in a variety of medical applications, such as local medication administration in periodontal therapy, is increased by these substances used together.^[3]

PHARMACOLOGICAL ACTIVITIES:

Cardiovascular effects

Through a variety of molecular processes, Terminalia arjuna provides numerous advantages for heart health. The cardioprotective benefits of the plant are mainly caused by its oleanane triterpenoids, which include arjunic acid, arjunoglycosides, arjunone, and arjunolic acid. Arjuna's bark stem has chronotropic, inotropic, and diuretic properties. Its strong antioxidant properties help prevent the damage linked to heart disorders by lowering oxidative stress in cardiac cells. The herb's anti-apoptotic properties, which are enabled by the control of particular signaling pathways, lessen the amount of cardiac cells that undergo programmed cell death under stressful circumstances like hypoxia. T. arjuna also supports heart health by reducing inflammatory cytokine levels and modulating inflammatory responses. By favorably affecting calcium management and myocardial metabolism, which raises contractility, it improves heart function.

Terminalia arjuna extract provides antioxidant and anti-apoptotic protection against ischemic-reperfusion injury by reducing the phosphorylation of JNK and cjun and controlling the levels of protective proteins such as Bcl2, Bax, caspase 3, heat shock protein-70, and inducible nitric oxide synthase. Additionally, it enhances lipid profiles by reducing cholesterol, which lowers the risk of cardiovascular diseases including atherosclerosis.^[6,7]

Anti-oxidant effect

It has been demonstrated that arjunolic acid, a strong triterpene that was extracted from Terminalia arjuna, provides significant cardioprotective benefits, mainly by reducing myocardial necrosis. Its capacity to stop the depletion of important antioxidant enzymes such as glutathione peroxidase (GPO), catalase, superoxide dismutase, ceruloplasmin, and α-tocopherol is responsible for this protection. By preventing lipid peroxidation and myeloperoxidase activity, arjunolic acid also maintains decreased glutathione and ascorbic acid levels, both of which are essential in the fight against oxidative stress associated with cardiovascular diseases. Furthermore, another molecule from the stem bark of T. arjuna, arjungenin, has shown modest free radical scavenging activity with an IC50 value of 290.6 μg/ml, which is similar to that of vitamin C.^[2] Arjunaphthanoloside, a naphthanol glycoside, and terminoside A, an oleanane triterpene, also prevent lipopolysaccharide-stimulated macrophages from producing nitric oxide (NO), which enhances T. arjuna's therapeutic potential in lowering inflammation and oxidative stress linked to heart disease.^[8]

Anti-platelet effect

The main source of Terminalia arjuna's significant anti-platelet actions is its active ingredient, arjunolic acid. Research demonstrates that arjunolic acid, with an ideal inhibitory concentration (IC50) of 0.048 mM, is more effective than aspirin at inhibiting thrombin-induced platelet aggregation (IC50) of 0.088 mM. Particularly at doses more than 0.16 mM, the rate of platelet inhibition stabilizes as the arjunolic acid concentration rises. Because it can alter the oxidative environment and lower inflammatory mediators two factors that are crucial for platelet activation and aggregation in cardiovascular diseases it probably has antiplatelet properties. By preventing thrombus formation, the decrease in platelet aggregation adds to T. arjuna's cardioprotective qualities.^[9]

Lipid lowering effect

It is known that one of the main risk factors for coronary artery disease is elevated low-density lipoprotein (LDL) and decreased high-density lipoprotein (HDL). According to

research on animals, Terminalia arjuna bark powder and extract dramatically lower triglycerides (TG) and total cholesterol (TC). It is believed that increased hepatic clearance of cholesterol, downregulation of lipogenic enzymes, and inhibition of HMG-CoA reductase are the mechanisms underlying the hypolipidemic effect. In particular, it has been discovered that the ethanol extract of T. arjuna bark can effectively lower LDL cholesterol levels at a dose of 100 mg/kg body weight, while a reduction in total cholesterol is seen at 500 mg/kg body weight. [7]



Anti-hypertensive effect

In particular, Terminalia arjuna's capacity to enhance vascular health has demonstrated notable antihypertensive effects. The bark extract causes vasodilation, which lowers both the systolic and diastolic blood pressure, by relaxing the vascular smooth muscles. It is partially responsible for this impact by improving endothelial function, which is essential for preserving vascular tone. Vasodilatory effects, which relax blood vessels and reduce blood pressure, are mediated by increased nitric oxide synthesis. T. arjuna also aids in the reduction of inflammation and oxidative stress, two components that contribute to the development of hypertension (ISSN 0973-2063 (online) 0973-8894 (print) Bioinformation 20(12): 2080-2085 (2024) Biomedical Informatics (2024) 2083). Its function in controlling blood pressure and lowering cardiovascular risk is further supported by its combination anti-inflammatory and antioxidant qualities. [10]

Anticancer effect

Terminalia arjuna uses a variety of methods to demonstrate strong anti-carcinogenic properties. Flavonoids and triterpenoids, two of its bioactive constituents, have strong antioxidant properties that help lower oxidative stress, a major cause of cancer development. The impact of an aqueous extract of the medicinal plant Terminalia arjuna on the antioxidant

defense system in lymphoma-bearing AKR mice was examined by Verma et al. and demonstrated that arjunolic acid, a crucial component of T. arjuna, decreased oxidative damage by boosting the activity of critical antioxidant enzymes such as glutathione Stransferase, catalase, and superoxide dismutase in cancer-bearing models. Some of the plant's chemicals, especially arjunolic acid, cause cancer cells to undergo apoptosis while leaving healthy cells unaffected. Additionally, T. arjuna's anti-inflammatory qualities lessen the chronic inflammation that aids in the development of cancer by blocking the synthesis of nitric oxide and proinflammatory cytokines. The plant also slows down the growth of cancer cells by inducing cell cycle arrest, which is unique to the G0/G1 phase. It has also demonstrated the ability to prevent angiogenesis, which limits the blood supply required for tumor growth. T. arjuna is a good option for cancer prevention and treatment because of these combined effects.

Anti-inflammatory effect

Terminalia arjuna's varied phytochemical makeup is largely responsible for its well-known anti-inflammatory qualities. Important substances that mediate inflammation include triterpenoids, flavonoids, tannins, and glycosides. Research has shown that T. arjuna bark extracts can effectively reduce inflammatory responses by preventing lipopolysaccharide (LPS)-stimulated macrophages from producing nitric oxide (NO). Additionally, certain formulations that incorporate T. arjuna have shown improved analgesic and antiinflammatory properties, most likely as a result of the phytoconstituents and other herbal ingredients working in concert. The anti-inflammatory properties of Arjuna Kaseera Paka (AKP), an ayurvedic formulation of T. arjuna made from cow milk, were evaluated and contrasted with a hydroalcoholic extract. According to the study, AKP is more effective, possibly as a result of the milk solids. Even at lower drug concentrations, milk solids improved the absorption of T. arjuna phytoconstituents, leading to improved efficacy. This combined effect supports the plant's traditional usage in Ayurvedic medicine by highlighting its potential as a natural anti-inflammatory agent.



Anti-bacterial effect

Many pathogens have been shown to be significantly inhibited by Terminalia arjuna's antibacterial properties. Extractions from its bark, leaves, roots, and fruits were found to have antibacterial properties against both Gram-positive and Gram-negative bacteria. Although the sensitivity varied depending on the plant part and the bacterial species involved, investigations specifically indicated that the aqueous extracts were efficient in reducing the growth of tested microbial strains. Terminalia arjuna has been shown to have a variety of phytochemicals that enhance its effectiveness in addition to its well-known antibacterial qualities. The primary bioactive components were phenolic compounds, flavonoids, and tannins, all of which have antibacterial qualities. These substances successfully fought infections by interfering with the bacterial cell walls, which caused cell lysis and death. The results supported the traditional use of T. arjuna in medicine by indicating that its phytochemical components may have antibacterial properties.

Wound healing effect

Terminalia arjuna's rich phytochemical composition, especially its tannin content, shown notable wound healing efficacy. Bark tannins can improve tissue tensile strength and drastically reduce wound size. By encouraging collagen turnover, which is necessary for skin regeneration, the herb sped up wound healing. The pulverized bark has historically been administered topically to promote healing results. To investigate the potential for wound healing, an alcoholic extract from T. arjuna bark was given to rat cutaneous wounds utilizing in vivo techniques. The study discovered that the content of tannin was associated with favorable effects. The ability of Himax ointment and lotion containing T. arjuna extract to heal wounds was comparable to that of the traditional drug nitrofurazone. All things considered, these results demonstrate Terminalia arjuna's therapeutic potential as a successful natural wound-healing substitute, emphasizing how well it works to promote quicker recovery and improve healing results when compared to traditional therapies.^[5]

TOXICITY AND SIDE EFFECTS

In many clinical research, T. arjuna has been utilized at a dose of 1 to 2 g daily, and it has been discovered that this is the ideal dosage for patients, especially those with CAD. Constipation, headaches, and moderate gastritis are less common adverse effects of these dosages. After taking it for more than two years, no reports of hematological, hepatic, metabolic, or renal damage were found. After 28 days of treatment with T. arjuna capsules (500 mg at 8 hours), Bhawani et al. [82] recently reported that there was no discernible difference in the body and organ weights of the 93 patients with dilated cardiomyopathy (DCMP) of idiopathic and ischemic cause between the control and treated groups. Biochemical indices and hematological studies showed that the extract had no harmful effects. Histopathological alterations and gross abnormalities were not seen, and no mortality was noted during the 28-day period. Because arjunolic acid has antioxidant properties, Yaidikar et al.90 found that pretreatment with the bark of T. arjuna effectively reduced cerebral I/R-induced oxidative damage. As a result, supplementing with arjunolic acid may be helpful in stroke-prone populations. Rats' heart damage from sodium nitrite was lessened by arjunolic acid from T. arjuna, which also helped to restore the proper ratio of pro- to antiinflammatory cytokines. Furthermore, cardiac tissues were shielded by arjunolic acid against intrinsic and extrinsic cell death pathways. 91 Higher doses of T. arjuna were found to raise the hepatic LPO and lower the serum concentration of thyroid 76 A. Amalraj, S. Gopi Journal of Traditional and Complementary Medicine 7 (2017) 65e78 hormones (Parmar et al92). To fully explore T. arjuna's medicinal potential, well-controlled multicentric clinical trials involving a bigger sample size and a standardized product are essential. [5]

CONCLUSIONS

One particularly promising medicinal plant with a long history in conventional systems like Ayurveda is Terminalia arjuna. Numerous pharmacological effects, including as cardioprotective, antioxidant, antihypertensive, anti-inflammatory, and anticancer characteristics, are supported by its abundant phytoconstituents, particularly arjunolic acid and flavonoids. Its effectiveness and safety at therapeutic levels are supported by scientific data from numerous in vivo and in vitro investigations. The plant has enormous medicinal potential, but in order to confirm its place in evidence-based medicine, further standardized

clinical studies and formulation development are required. Including T. arjuna in contemporary medication regimens may offer a safer, all-natural substitute for treating systemic and cardiovascular conditions.

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