Review Article

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Terminalia arjuna: An Ancient Cardioprotective Herb with Modern Clinical Relevance

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Cardiovascular illnesses continue to be the world's top cause of mortality, hence there is need of safe, reasonably priced and multi-target treatments. Long used as a cardiotonic in Ayurveda, Terminalia arjuna's rich phytochemistry has been associated to anti-inflammatory, lipid-lowering, vasodilatory, antioxidant, and inotropic properties. Small clinical trials indicate benefits in angina and heart failure, whereas preclinical research demonstrate beneficial lipid regulation, reduced infarct size, and enhanced cardiac function. But there aren't many large RCTs and different formulations, which limits the evidence. Its translational potential is highlighted by developments in network pharmacology, nano formulation, and AI-based modeling. The establishment of T. arjuna as an integrated cardioprotective phytopharmaceutical requires standardized extracts, molecular insights, and thorough multicentric studies.

Keywords: Terminalia arjuna, Arjuna (herb), Cardioprotection, Cardioprotective effects, Heart health, Phytochemicals.

Introduction

Cardiovascular diseases (CVDs) accounts for 19.8 million fatalities in 2022 becoming the world's largest cause of death amongst non-communicable diseases, with a disproportionately high burden on low- and middle-income nations. (1) Due to significant part of an aging population, demographic growth, and ongoing exposure to modifiable hazards, the number of deaths has increased even though worldwide age-standardized mortality rates have decreased as a result of advancements in prevention and treatment. The paradox—declining age-standardized rates but rising absolute deaths—reflects demographic transitions, with aging populations identified as the dominant driver of ischemic heart disease mortality worldwide. By 2027, an estimated 7.8 million premature CVD deaths are projected annually, with the steepest rise in low- and middle-income regions. This underscores the urgent need for innovative, affordable, and accessible cardioprotective therapies despite existing treatment advances. (2) Conventional pharmacotherapies (such as antiplatelets, statins, β-blockers, and ACE inhibitors) and surgical interventions have improved outcomes in ischemic heart disease and heart failure, but challenges such as high costs, side effects, poor adherence, and lack of myocardial regeneration still pose as a hindrance. (3) These gaps emphasize the need for sustainable and myocardium-targeted therapies. Plant-based cardioprotective agents have attracted considerable interest for their ability to act on multiple pathways involved in atherothrombosis, oxidative stress, endothelial dysfunction, and adverse cardiac remodelling. *Terminalia arjuna*, a massive evergreen tree, indigenous to Indian subcontinent, long have been used to treat angina, hypertension, and heart failure symptoms. (4) For centuries, *T. arjuna* has been described in Ayurvedic texts as a cardiac tonic, and modern studies attribute its cardioprotective effects to diverse phytochemicals—particularly triterpenoids, flavonoids, glycosides, and polyphenols—with antioxidant, anti-inflammatory, lipid-lowering, vasodilatory, and inotropic activities.

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(5) It is appropriate to connect classical knowledge with contemporary pharmacology. Though translation is hampered by varied preparations, variable dose, and a lack of high-quality randomized studies, T. arjuna provides a polypharmacological profile that is in line with complex CVD pathobiology.

Ethnopharmacological Background

Terminalia arjuna (family Combretaceae), has a well-established role in Indian medicine, particularly Ayurveda, where its preparation from the bark has been regarded as a cardiotonic and remains the most commonly used across the Indian subcontinent. Classical texts such as the Charaka Samhita, Sushruta Samhita, describe it as a remedy that is recommended for conditions resembling angina, heart failure, hypertension, and dyslipidaemia, often in the form of decoctions, powders, or medicated oils. (6) Beyond Ayurveda, T. arjuna is also integrated into Unani and Siddha medicine, valued for its cardioprotective effects. The widespread use of T. arjuna across different traditional systems shows its cross-cultural relevance and similarity to modern cardiovascular disease patterns. This long history of use offers a solid basis for current scientific research to confirm its benefits, standardize formulations, and identify the active compounds and mechanisms behind its cardioprotective effects. (7)

Phytochemistry of Terminalia arjuna

Terminalia arjuna's cardioprotective actions are attributed to multiple classes of secondary metabolites which are concentrated chiefly in the stem bark. The major bioactive groups include triterpenoids, flavonoids, glycosides, tannins and polyphenols.

Figure 1:https://greencoverinitiative.com/trees/terminalia-arjuna-arjuna-tree/

These constituents have been repeatedly identified by phytochemical surveys and reviews and form the backbone of mechanistic studies that show antioxidant, anti-inflammatory, lipid-modulating, and vasodilatory. (8) Triterpenoids such as arjunolic acid and arjunic acid, two oleanane-type triterpenoid saponins are frequently isolated from the bark, have been extensively studied for their pharmacological effects. Flavonoids such as arjunone, arjunolone, luteolin, and other related flavones and flavanols are reported to support reactive oxygen species (ROS) scavenging and endothelial protection. In addition, glycosides like arjunetin, together with high-molecular-weight tannins and polyphenols, contribute significantly to the herb's therapeutic potential. Different plant parts and extraction techniques have different phytochemical compositions. Stem bark is the most widely utilized ingredient in both traditional and clinical formulations because it is the richest source of triterpenoids, tannins, and many flavonoids. Although the polyphenols and flavonoids found in leaves and fruits overlap, they are frequently found in varying relative abundances and have fewer triterpenoid saponins. (9) Recent metabolomic investigations of fruit extracts and flowers have identified unique secondary metabolites that may have supplementary bioactivities. When making extracts for study or therapeutic purposes, these variations support part-specific standardization. (10) Comprehensive structure–activity relationship analyses are still scarce, despite the fact that a number of isolated compounds—particularly arjunolic acid—have undergone pharmacological profiling. Although systematic medicinal-chemistry efforts are limited, existing work indicates that the saponin glycosidic moiety and certain oxidation patterns on the oleanane scaffold influence antioxidant and membrane-interacting characteristics. This gap prevents the development of synthetic analogs based on T. arjuna scaffolds or rational optimization. Modern tools like LC–MS/MS and metabolomics, combined with bioinformatics, now allow comprehensive profiling of T. arjuna, linking its metabolites to specific targets and pathways. This integrated approach supports multi-target mechanism discovery and advances standardized, mechanism-driven phytopharmaceutical development. (11)

Mechanisms of Cardioprotective Action of Terminalia arjuna

The diverse range of phytochemicals present in T. arjuna provides cardioprotective activity by acting synergistically on the key pathways implicated in cardiovascular disease. T. arjuna's triterpenoids and

flavonoids have shown to effectively neutralize free radicals and restore glutathione and superoxide dismutase. Hence it results in protection of myocardial membranes from oxidative stress, a central factor in atherosclerosis. (12, 13) Extracts of T. arjuna have also shown to repress pro-inflammatory cytokines (TNF-α, IL-6) and inhibit the activation of the NF-κB pathway. By controlling inflammation, the herb helps to prevent endothelial dysfunction and harmful vascular remodelling, key drivers of heart disease progression. T. arjuna extract reduces atherogenic burden by lowering the levels of LDL and triglycerides and also supports vascular health. Studies suggest that T. arjuna improves heart muscle contraction by supporting calcium balance and stabilizing membranes. Arjunolic acid inhibits apoptosis pathways and protect the cardiomyocytes by stabilizing mitochondrial membranes and enhancing pro-survival signalling. T. arjuna promotes vascular relaxation by influencing nitric oxide pathways and calcium channels, helping regulate blood pressure and enhance coronary blood flow. In-silico studies show that T. arjuna compounds can act on multiple cardiac proteins such as β1-adrenergic receptors, ACE, HMG-CoA reductase, and Na^+/K^+-ATPase, supporting its role as a broad-spectrum cardioprotective herb suited to the complex nature of cardiovascular diseases. (14)

Preclinical and Clinical studies

Across the studies, the crude extract from T. arjuna or it's purified compounds (majorly arjunolic acid) have shown cardioprotective activities like - improved left ventricular function, reduced infract size, attenuation of oxidative stress and inflammation and favourable effects on lipid profiles. (15) For preclinical work animal models of ischemia–reperfusion, experimental myocardial infarction, heart failure, and hypertension have been utilized for testing the herb. Limited comparisons with conventional cardiac medications, inconsistent extract production and dosage guidelines, and the absence of long-term safety or chronic toxicity assessments required for clinical translation continue to limit preclinical research on T. arjuna. (16) Recent work explores nanoparticle-based formulations of T. arjuna, showing better bioavailability, sustained release, and stronger preclinical effects. However, these studies remain preliminary and need standardized comparisons and thorough safety evaluation. (17)

Clinical studies on Terminalia arjuna suggest it may help reduce angina episodes, and offer some benefit in heart failure, but effects on heart function and long-term outcomes remain unclear. Overall, the evidence is weak to moderate because most trials are small, employ various preparations and dosages, and have brief follow-up. There is a paucity of information regarding long-term safety and drug-herb interactions, however the herb seems safe in the short term with just minor adverse effects. Larger, carefully planned multicentre trials using standardized extracts are required to validate T. arjuna's significance in cardiovascular care, even though it may now be helpful as an adjuvant or preventive treatment. (18, 19)

Modern Advances & Translational Potential

Terminalia arjuna can be transformed from a traditional cure into reproducible, mechanism-driven phytopharmaceuticals with translational potential thanks to recent developments in formulation science, systems biology, and computational techniques. By encapsulating T. arjuna's extracts or isolated molecules like arjunolic acid in nano-formulations like lipid nanoparticles, PLGA carriers, and metal nanoparticles has shown to improve bioavailability, control release, and enhance cardioprotective effects in preclinical ischemia models. (20) Studies suggest that T. arjuna may work synergistically with standard drugs like statins, β-blockers, and ACE inhibitors, with early trials showing improved lipid profiles and angina relief when used in combination. (21) Systems biology analyses reveal its compounds act on multiple heart-related targets (AKT1, TNF, IL-6, MAPK14), supporting a multi-target mechanism. Additionally, in-silico and machine-learning studies predict that key compounds such as arjunolic acid and arjunone strongly bind to β1-adrenergic receptors and ACE, indicating potential benefits in heart failure and hypertension. (22) T. arjuna has promise for regenerative medicine because of its anti-inflammatory and antioxidant properties, which may increase stem-cell survival following cardiac damage. Ex-vivo research has demonstrated that preconditioned stem cells are more resilient. It is becoming a contemporary integrative cardioprotective drug in conjunction with developments in nanotechnology, adjunctive therapy, systems pharmacology, and AI-driven predictions; nonetheless, the majority of the evidence is still preclinical, necessitating standardized formulations and carefully planned clinical trials. (23, 24)

Future Perspectives

Future research should adopt a multi-omics strategy to map the pathways influenced by T. arjuna and

identify reliable biomarkers. Majorly priority should be given to develop standardized phytopharmaceutical formulations to ensure reproducibility. Instead of depending solely on symptomatic outcomes, clinical translation needs large, multicentric randomized controlled trials (RCTs) engineered to detect hard endpoints like hospitalization and mortality. To ensure safety in actual polypharmacy situations, it is equally crucial to systematically investigate drug–herb interactions, especially those involving statins, anticoagulants, antiplatelets, and ACE inhibitors. T. arjuna may reach its full potential and bridge the gap between traditional knowledge and current cardiovascular medicine if it were positioned as an evidence-based preventive therapy in addition to contemporary medicines. (25)

Conclusion

Terminalia arjuna is a potential ancient cardiotonic that is becoming more and more relevant in modern medicine. A wide range of cardioprotective properties, including as lipid-lowering, anti-inflammatory, antioxidant, and vasodilatory activities, are supported by its rich phytochemical profile. However, thoroughly planned randomized controlled trials, greater molecular insights, and standardized formulations are necessary for effective clinical translation. The potential for T. arjuna to transform from a traditional herbal remedy into a validated, widely used cardioprotective phytopharmaceutical lies in the integration of emerging technologies, such as network pharmacology for multi-target mapping, omics-based approaches for pathway discovery, and nanoformulation for enhanced bioavailability.

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