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Terminalia Arjuna (Roxb. Ex DC.) Wight & Arn.: A Comprehensive Review Of Classical Ayurvedic Documentation, Phytochemistry, Pharmacological Activities, And Clinical Evidence

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Abstract:

Background: *Terminalia arjuna* (Roxb. ex DC.) Wight & Arn. (family Combretaceae), commonly known as Arjuna, has been described as a premier cardiac tonic in Ayurvedic medicine for over three millennia. The bark of this tree has been used extensively in classical texts such as Charaka Samhita and Ashtanga Hridaya for the management of hridroga (cardiac ailments), prameha (metabolic disorders), and vrana (wounds). In recent decades, an expanding body of scientific research has attempted to validate and extend this traditional knowledge through systematic phytochemical, pharmacological, and clinical investigations.

Objective: This review aims to consolidate evidence from classical Ayurvedic literature and contemporary peer-reviewed research to present a critical and comprehensive account of *T. arjuna* across domains of botanical identity, phytochemistry, pharmacological mechanisms, clinical trials, safety profile, and future research directions.

Methods: A systematic search was conducted across PubMed, Scopus, Web of Science, and Google Scholar using relevant MeSH terms and keywords. Classical Ayurvedic texts including Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, Bhavaprakasha Nighantu, and Dravyaguna Vijnana were reviewed alongside contemporary Ayurveda journals.

Results: The bark of *T. arjuna* contains a rich array of phytoconstituents including triterpenoid glycosides (arjunic acid, arjunolic acid, arjunogenin), flavonoids (arjunone, arjunolone, luteolin), tannins (punicalagin, casuarinin), minerals (calcium, magnesium, zinc, copper), and glycosides (arjunetin). Documented pharmacological activities encompass cardioprotective, antihypertensive, antioxidant, anti-inflammatory, antitumour, hepatoprotective, antimicrobial, and anti-diabetic effects, supported by extensive in vitro, in vivo, and clinical data. Clinical studies have shown particular promise in ischaemic heart disease, heart failure, and stable angina.

Conclusion: *Terminalia arjuna* represents a valuable therapeutic agent bridging Ayurvedic tradition and evidence-based medicine. However, standardised clinical trials with larger populations, defined pharmacokinetic profiles, and established drug interaction data remain essential before full integration into mainstream cardiology practice.

Index Terms - Terminalia arjuna; Arjuna bark; cardioprotection; Ayurveda; hridroga; phytochemistry; antioxidant; heart failure; clinical trials.

1. INTRODUCTION

Among the vast pharmacopoeia of Ayurvedic medicine, few plants have commanded as sustained and consistent a therapeutic reputation as *Terminalia arjuna* (Roxb. ex DC.) Wight & Arn. This large, deciduous riparian tree, reaching heights of 20 to 30 metres, is endemic to the Indian subcontinent and is found predominantly along riverbanks and dry watercourses in tropical regions, particularly in the states of Madhya Pradesh, Bihar, Odisha, Uttar Pradesh, and Bengal.1 The dried bark of the tree, the primary medicinal part, has occupied a central position in the management of cardiac disorders in classical Ayurvedic texts for more than three thousand years.

The earliest unambiguous reference to Arjuna as a cardiac remedy is attributed to Vagbhata in the Ashtanga Hridaya (circa 7th century CE), where the bark is specifically prescribed in the management of hridroga (heart disease) with the formulation arjunaksheerapaka — a medicated milk decoction prepared from arjuna bark.2 Charaka, in the Charaka Samhita, lists Arjuna among the prabhavadi group (drugs capable of causing unconsciousness) and in contexts related to raktapitta (bleeding disorders) and kshaya (debilitating conditions).3 Sushruta Samhita mentions the tree within the Nyagrodhadi gana and attributes properties useful in fracture healing and wound management.4 Bhavaprakasha Nighantu, one of the more systematised medieval materia medica texts, records Arjuna as hridroga (cardiac disease), krimi (parasitic infections), kasa (cough), and rakta pitta (bleeding disorders).5

In classical Ayurvedic dravyaguna (pharmacognosy), *T. arjuna* bark is described as having kashaya (astringent) rasa, laghu (light) and ruksha (dry) guna, sheeta virya (cold potency), and katu vipaka. Its primary doshic action is considered to be tridoshahara with a special emphasis on pacifying kapha and pitta doshas.5,6 This classical characterisation aligns interestingly with the contemporary understanding of the drug's anti-inflammatory, antioxidant, and lipid-modulating properties.

The modern era of scientific investigation into *T. arjuna* was significantly propelled by the pioneering work of Dwivedi and Agarwal in 1994, which demonstrated marked benefit in patients with refractory heart failure and angina.7 This publication catalysed decades of phytochemical, pharmacological, and clinical research that has substantially elucidated the mechanisms underlying its traditional use. Today, *T. arjuna* bark extract and its derivatives are included in the official Ayurvedic Pharmacopoeia of India and feature in numerous proprietary Ayurvedic preparations for cardiac health, including the widely used Abana and Arjun Tea formulations.

Despite substantial research, a critical and integrated review that bridges classical Ayurvedic scholarship with contemporary biomedical evidence remains relatively sparse in the Indian medical literature. This review seeks to address that gap by providing a thorough synthesis of current knowledge spanning taxonomy, classical documentation, phytochemistry, pharmacological mechanisms, clinical evidence, safety profile, and future research priorities, with particular relevance for practitioners of Ayurveda and integrative medicine.

2. BOTANICAL DESCRIPTION AND TAXONOMY

Terminalia arjuna belongs to the family Combretaceae and the genus *Terminalia*, which comprises approximately 200 species globally. The accepted botanical binomial *Terminalia arjuna* (Roxb. ex DC.) Wight & Arn. was formally established by Wight and Arnott in 1834, based on earlier descriptions by Roxburgh as published by De Candolle in his Prodromus Systematis Naturalis Regni Vegetabilis.1 Synonyms in the botanical literature include *Pentaptera arjuna* Roxb. ex DC., *Pentaptera glabra* Roxb., and *Terminalia berryi* Wight & Arn.

The tree is a large, semi-evergreen to deciduous species. Its trunk is buttressed at the base, and the bark — the therapeutically important part — is smooth, grey to pinkish-grey externally, and pale red to reddish-brown internally. It exfoliates in thin, irregular scales, a feature that facilitates bark collection. The leaves are sub-

opposite, oblong to elliptic-oblong, with a characteristic pair of glands at the base of the lamina near the petiole junction. Flowers are small, white to yellowish-white, borne in slender axillary spikes or terminal panicles, appearing from March to June. The fruit is a five-winged drupe, 2.5 to 5 cm long, with characteristic hard woody wings serving as dispersal structures.8

In Ayurvedic literature, *T. arjuna* is identified by various vernacular designations: Arjuna in Sanskrit, Kahu or Arjun in Hindi, Marudhu in Tamil, Maddi in Telugu, and Neer Maruthu in Malayalam. The Sanskrit name Arjuna translates as 'bright', 'silver-white', or 'clear', most likely referring to the distinctive whitish-grey appearance of the bark.5 The tree is classified under the Priyangvadi gana in Charaka Samhita and within Nyagrodhadi gana in Sushruta Samhita, reflecting its broad applicability across different disease categories in the Ayurvedic classical tradition.3,4

3. Classical Ayurvedic Documentation

3.1 References in Brihat Trayi

The Brihat Trayi (the three major classical texts of Ayurveda) offer varying but complementary accounts of *T. arjuna*. In Charaka Samhita (Chikitsa Sthana, Chapter 26), Arjuna is prescribed in the context of kshataksheena (pulmonary conditions with tissue depletion), hridroga, and rakta pitta. The formulation arjuna ghrita (arjuna bark processed in ghee) is described as beneficial in hridroga characterised by tama (syncope/blackouts) and shoola (chest pain).3 The Charaka Samhita also lists Arjuna in Sandhaniya (fracture healing) gana, highlighting its role in tissue consolidation — a pharmacological property now linked to its tannin and mineral content.3

Sushruta Samhita (Sutrasthana, Dravyasangraha) classifies Arjuna within the Nyagrodhadi gana, recommending the bark for its astringent and haemostatic properties in wounds (vrana), fractures (bhagna), and bleeding disorders. Sushruta's commentary on the bark's propensity to consolidate fractured tissue aligns with modern in vitro evidence of osteogenic activity and calcium-rich composition.4

Ashtanga Hridaya (Uttarasthana, Chapter 12) provides the most explicitly cardiac-focused description among the classical texts. Vagbhata describes the preparation of arjunaksheerapaka — a medicated milk decoction obtained by boiling arjuna bark in milk — and recommends it specifically for hridroga. The text notes its utility in kshaya (wasting) and as a rasayana (rejuvenating therapy). Ashtanga Hridaya's specification of milk as the processing medium (anupana) has modern pharmacological significance, as the lipophilic compounds in ghee/milk may enhance bioavailability of arjuna's active triterpenoids.2

3.2 References in Laghu Trayi and Other Classical Texts

Bhavaprakasha Nighantu (Haritakyadi Varga, verse 67–72) provides one of the most detailed classical pharmacognostic descriptions of Arjuna. The text records the following properties: rasa — kashaya; guna — laghu, ruksha; virya — sheeta; vipaka — katu; karma — hridroga, vrana ropana, kasa, krimi nashana, prameha, rakta pitta. Bhavaprakasha also notes that the bark is vishaghna (anti-toxic), shothahara (anti-inflammatory), and promotes bone healing.5

Raja Nighantu (Prabhadradi Varga) additionally records Arjuna as useful in medoroga (obesity/dyslipidaemia) and kapha disorders, which is consistent with contemporary evidence on its lipid-lowering activity. Dhanvantari Nighantu classifies Arjuna in the Amradi Varga and similarly describes its haemostatic, cardiac, and wound-healing properties.6

Chakradatta, the 11th-century clinical compendium, prescribes specific arjuna formulations such as arjunatvak churna (bark powder) with honey and ghee for heart failure, and arjuna with jaggery and sugarcane juice for haematuria. These formulations reflect a sophisticated understanding of drug-vehicle synergy that contemporary pharmacologists are only beginning to examine systematically.9

3.3 Dravyaguna Properties and Ayurvedic Classification

In the framework of Dravyaguna Vijnana (Ayurvedic pharmacology), *T. arjuna* bark occupies a position of cardinal importance in Hridaya Dravyas (cardioactive drugs) as classified by Priyavrat Sharma in his authoritative textbook.6 The drug is considered a hridya dravya (cardiac tonic), stambhana (astringent/haemostatic), sandhaniya (fracture healing), and kshayahara (anti-wasting). Its sheeta virya (cold potency) helps in conditions associated with pitta aggravation such as burning sensation in the chest, excessive thirst, and haematemesis — symptoms that find modern correlates in ischaemic heart disease with reflux and haemoptysis in pulmonary hypertension.

4. PHYTOCHEMISTRY

4.1 Triterpenoids

The bark of *T. arjuna* is exceptionally rich in pentacyclic triterpenoids, which are widely regarded as the primary active constituents responsible for its cardioprotective and related pharmacological activities.10 The major triterpenoids identified include arjunic acid (2α,3β,19α-trihydroxy-olean-12-en-28-oic acid), arjunolic acid (2α,3β,23-trihydroxy-olean-12-en-28-oic acid), arjunogenin, and arjunolic acid methyl ester. Arjunic acid, also known as terminolic acid, is considered a principal marker compound and has been extensively studied for its vasodilatory, antioxidant, and cardioprotective properties.10,11

Arjunolic acid demonstrates particularly interesting cardiac pharmacology. Studies by Manna et al. demonstrated that arjunolic acid confers significant protection against isoproterenol-induced cardiac injury in rats, reducing indices of lipid peroxidation and myocardial necrosis.12 The compound appears to stabilise mitochondrial membrane potential and upregulate antioxidant enzymes including superoxide dismutase (SOD), catalase, and glutathione peroxidase in cardiomyocytes under oxidative stress.13

4.2 Flavonoids

Several flavonoids have been characterised from the bark, including arjunone, arjunolone (a flavanone), luteolin, quercetin-3-O-glucoside, kaempferol-3-glucoside, and baicalein.14 Arjunone, a specific flavanone unique to this species, has demonstrated significant anti-inflammatory activity through inhibition of cyclooxygenase-2 (COX-2) and lipoxygenase pathways. Luteolin has well-established cardioprotective properties through its ability to reduce NF-κB-mediated inflammatory cytokine production and inhibit platelet aggregation.15

4.3 Tannins and Ellagitannins

The tannin fraction of *T. arjuna* bark is remarkably diverse and constitutes a major portion of the total phenolic content. Ellagitannins identified include punicalagin (both alpha and beta forms), punicalin, casuarinin, castalagin, and granatin B.14,16 Punicalagin, which is also found abundantly in pomegranate, is one of the most potent naturally occurring antioxidants known and has demonstrated significant anti-inflammatory, antiatherosclerotic, and anti-diabetic activities in preclinical models.16 The tannins also contribute to the astringent and wound-healing properties described in classical texts, largely through their ability to cross-link proteins and reduce vascular permeability.

4.4 Glycosides and Other Constituents

Several glycosides have been isolated from the bark, of which arjunetin (2α,3β,19α,23-tetrahydroxyolean-12-en-28-oic acid 28-O-β-D-glucopyranoside) is among the most studied.17 β-sitosterol glycoside, terminoside A, and several cardenolide-type glycosides with potential cardiac inotropic activity have also been reported, though their concentrations are relatively low compared to the triterpenoid fraction.18

The bark contains significant quantities of calcium (0.5–0.8%), magnesium, aluminium, zinc, and copper as mineral constituents.19 This mineral richness, particularly the calcium content, offers a rational pharmacological basis for the classical Ayurvedic use in bone fracture healing (sandhaniya karma) as

described in both Charaka and Sushruta Samhita. Co-enzyme Q10 has also been reported in bark preparations at trace levels, potentially contributing to mitochondrial bioenergetic support in cardiac muscle.20

4.5 Bark versus Other Plant Parts

While the bark is the therapeutically standardised part in Ayurveda and has been most extensively characterised, other parts of *T. arjuna* have also yielded bioactive compounds. Leaves contain flavonoids such as vitexin, quercetin, and kaempferol, along with phenolic acids. The fruits contain ellagic acid and gallic acid, while the seeds contain fixed oils with palmitic, stearic, and oleic acid fractions.21 However, the comparative clinical significance of these plant parts remains to be established, and current quality control standards in Ayurvedic pharmacopoeia refer specifically to bark.

5. PHARMACOLOGICAL ACTIVITIES

5.1 Cardioprotective Activity

The cardioprotective activity of T. arjuna represents its most extensively studied and best-validated pharmacological property, and constitutes the primary basis for its classical Ayurvedic application as a hridya dravya. Multiple mechanisms have been identified through in vitro and in vivo studies.

In the isoproterenol (ISP)-induced myocardial infarction model in rats, one of the most widely used experimental paradigms for cardiac injury, T. arjuna bark extract significantly reduced elevated serum levels of creatine kinase-MB (CK-MB), lactate dehydrogenase (LDH), and aspartate aminotransferase (AST), which are established biomarkers of myocardial damage.12 Histopathological examination revealed preservation of myocardial architecture and reduced necrotic foci in treated animals. The protective effect was attributed primarily to the antioxidant activity of arjunolic acid and arjunic acid in mitigating reperfusion-induced oxidative stress.

Research by Gauthaman et al. demonstrated that aqueous extract of T. arjuna bark produced significant negative chronotropic and positive inotropic effects in isolated rat heart preparations, consistent with a digitalis-like action.22 Subsequent studies confirmed that these effects were at least partly mediated through modulation of calcium channels and Na+/K+-ATPase activity. The inotropic effect without significant proarrhythmic tendency distinguishes arjuna from cardiac glycosides such as digoxin, suggesting a potentially safer pharmacological profile for the management of heart failure.

Mitochondrial protection is an emerging mechanistic theme in arjuna cardioprotection research. Manna et al. demonstrated that arjunolic acid preserves mitochondrial membrane potential, prevents cytochrome c release, and reduces caspase-3 activation in H2O2-stressed cardiomyocytes, suggesting anti-apoptotic activity through the intrinsic mitochondrial pathway.13 This cellular protection likely underlies the clinical benefit observed in chronic heart failure, where progressive cardiomyocyte apoptosis is a key pathological driver.

5.2 Antihypertensive Activity

Antihypertensive activity has been demonstrated in multiple animal models. In DOCA-salt-induced hypertensive rats, T. arjuna extract significantly reduced systolic blood pressure, improved endothelium-dependent vasorelaxation in isolated aortic rings, and increased serum nitric oxide (NO) levels.23 The vasodilatory effect is at least partially endothelium-dependent, with evidence suggesting upregulation of endothelial nitric oxide synthase (eNOS) activity by arjunic acid and punicalagin.

In another study employing spontaneously hypertensive rats (SHR), chronic administration of T. arjuna bark extract produced dose-dependent blood pressure reduction comparable to a low dose of captopril, with additional benefit in terms of endothelial function improvement.24 The antihypertensive mechanism appears to be multifactorial, involving diuretic activity, ACE inhibition by ellagitannins, and direct vasodilatory effects.

5.3 Antioxidant Activity

The antioxidant capacity of *T. arjuna* bark is among the most potent documented in the Combretaceae family, attributable to its rich polyphenol content. In DPPH, ABTS, and FRAP assays, hydroalcoholic extracts of arjuna bark demonstrate IC50 values in the range of 8–45 µg/mL for free radical scavenging, comparable to ascorbic acid as a reference standard.25 The total phenolic content, measured by the Folin-Ciocalteu method, typically ranges from 90 to 230 mg gallic acid equivalents per gram of dry extract across different extraction methods and geographical origins.26

In vivo, oral administration of T. arjuna extract in aged rats produced significant increases in SOD, catalase, and glutathione reductase activities in cardiac and hepatic tissue, with concomitant reduction in malondialdehyde (MDA) levels, a marker of lipid peroxidation.27 These findings corroborate the classical Ayurvedic concept of rasayana (rejuvenating) activity attributed to Arjuna in Ashtanga Hridaya.

5.4 Hypolipidaemic Activity

Dyslipidaemia is a major risk factor for cardiovascular disease, and its pharmacological modification represents an important clinical goal. T. arjuna bark extract has demonstrated significant lipid-lowering activity in several experimental models. In high-fat-diet-induced hyperlipidaemic rats, oral supplementation with T. arjuna extract produced significant reductions in total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), with significant elevation of high-density lipoprotein cholesterol (HDL-C).28

The mechanisms proposed include inhibition of hepatic HMG-CoA reductase (analogous to statin mechanism), upregulation of LDL receptor expression, and increased activity of lipoprotein lipase. Punicalagin and ellagic acid have been specifically implicated in the LDL-lowering effect through their ability to reduce LDL oxidation and inhibit macrophage uptake of oxidised LDL, which is a critical early step in atherogenesis.16,28

5.5 Anti-Inflammatory Activity

Chronic low-grade inflammation is now recognised as a central pathophysiological mechanism in cardiovascular disease, metabolic syndrome, and numerous other chronic conditions. T. arjuna bark extract has demonstrated significant anti-inflammatory activity in carrageenan-induced paw oedema, cotton pellet granuloma, and acetic acid-induced peritonitis models.29 The anti-inflammatory effect involves inhibition of pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6, which has been demonstrated through NF-κB pathway inhibition.

Arjunone, the flavanone specific to this species, has been identified as a potent dual inhibitor of COX-2 and 5-lipoxygenase, suggesting potential application in arthritis and pain management beyond its cardiac applications.30 Anti-inflammatory activity may also contribute to the anti-atherogenic effects of arjuna, since vascular inflammation is a key driver of plaque formation and instability.

5.6 Antidiabetic Activity

Several studies have examined the antidiabetic potential of T. arjuna, motivated by its classical use in prameha (urinary disorders including diabetes mellitus equivalents). In streptozotocin-induced diabetic rats, T. arjuna bark extract significantly reduced fasting blood glucose, improved glucose tolerance, and restored near-normal pancreatic histology, suggesting both insulin secretagogue and insulin sensitising mechanisms.31

Inhibition of alpha-glucosidase and alpha-amylase activities by T. arjuna extract has been demonstrated in vitro, indicating an additional mechanism of post-prandial glucose regulation.32 This finding is particularly relevant given contemporary interest in multi-target natural product therapy for type 2 diabetes, where arjuna could potentially address coexisting cardiovascular and metabolic risk simultaneously.

5.7 Hepatoprotective Activity

Hepatoprotective activity has been demonstrated against paracetamol, carbon tetrachloride (CCl4), and alcohol-induced hepatotoxicity in rodent models. T. arjuna extract significantly reduced elevated serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels and normalised hepatic glutathione content in CCl4-treated rats.33 The mechanism involves both antioxidant protection and stabilisation of hepatocyte membrane integrity by tannin fractions.

5.8 Antimicrobial Activity

Methanol and ethanol extracts of *T. arjuna* bark have demonstrated moderate to good antimicrobial activity against a range of pathogenic bacteria including *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella typhi*, with minimum inhibitory concentrations (MIC) ranging from 250 to 1000 µg/mL.34 Antifungal activity against *Candida albicans* and dermatophytes has also been reported. The tannin fraction, particularly punicalagin, appears primarily responsible for antimicrobial activity, possibly through disruption of bacterial cell membrane integrity and inhibition of microbial enzymes.

5.9 Antitumour Activity

In vitro antiproliferative activity has been demonstrated against several human cancer cell lines including MCF-7 (breast), HeLa (cervical), A549 (lung), and HT-29 (colon) by various T. arjuna extracts and isolated compounds.35 Arjunic acid and luteolin have shown selective cytotoxicity against cancer cells with relative sparing of normal cell lines, suggesting potential therapeutic indices. Proposed mechanisms include induction of apoptosis via caspase-3 activation, inhibition of angiogenesis, and cell cycle arrest at the G2/M phase.35 It must be noted, however, that antiproliferative activity demonstrated in cell culture does not necessarily translate to clinical anti-cancer efficacy, and these findings should be interpreted with appropriate caution.

5.10 Other Activities

Additional pharmacological activities reported for T. arjuna include thyroid-modulating activity (reduction of elevated thyroxine in hyperthyroid models), anti-platelet aggregation effects, wound healing acceleration, diuretic activity, anti-ulcer activity, and immunomodulatory effects.36,37 These activities, while preliminary, collectively reinforce the holistic therapeutic profile described in classical Ayurvedic texts and suggest potential applications extending well beyond cardiac disease.

6. CLINICAL STUDIES

6.1 Ischaemic Heart Disease and Stable Angina

The landmark clinical study by Dwivedi and Agarwal (1994), published in the Journal of the Association of Physicians of India, remains perhaps the most cited clinical investigation of T. arjuna. In this controlled study, 58 patients with refractory chronic stable angina were administered arjunaksheerapaka (bark powder boiled in milk, 500 mg twice daily) for three months alongside conventional therapy, with a control group receiving conventional treatment alone. The arjuna group showed significant reduction in anginal frequency (by approximately 50%), improvement in treadmill exercise tolerance, and reduction in ischaemic ST changes on ECG. Systolic blood pressure was also significantly reduced in the treatment group.7

A subsequent randomised, double-blind, placebo-controlled crossover trial by the same group in 58 men with stable angina confirmed these findings. Patients crossed from the arjuna arm to placebo showed deterioration in exercise tolerance and increase in anginal episodes, while those crossing from placebo to arjuna showed corresponding improvements, providing stronger causal evidence.38 The beneficial effects were maintained during a long-term follow-up of 2 years in a subset of patients.

A more recent double-blind randomised controlled trial by Bharani et al. evaluated T. arjuna bark extract (500 mg TDS) against isosorbide mononitrate (40 mg OD) in 58 patients with stable angina. Both groups showed comparable reduction in anginal frequency and improvement in exercise tolerance as assessed by treadmill

test, suggesting that arjuna may possess clinically relevant anti-anginal efficacy comparable to standard nitrate therapy, with potentially fewer side effects such as headache.39

6.2 Heart Failure

Chronic heart failure (CHF) is an area where T. arjuna has generated significant clinical interest, given the need for safe adjuvant therapies and the proven inotropic activity in preclinical models. In a prospective, open-label study by Bharani et al. involving 12 patients with New York Heart Association (NYHA) class IV heart failure on maximal standard medical therapy, the addition of arjuna bark extract (500 mg TDS in milk) for two weeks produced significant improvements in dyspnoea, fatigue, and exercise tolerance, along with reductions in echocardiographic left ventricular end-diastolic volume.40

A study by Kumar et al. (2012) evaluated the effect of T. arjuna bark extract on cardiac function in 30 patients with dilated cardiomyopathy using two-dimensional echocardiography as the primary outcome measure. After three months of arjuna supplementation added to standard therapy, left ventricular ejection fraction (LVEF) improved significantly from a mean of 38.2% to 46.5%, and left ventricular end-systolic diameter decreased.41 These echocardiographic improvements, if reproducible in larger trials, would represent a clinically meaningful outcome.

6.3 Dyslipidaemia

An open-label clinical study by Gupta et al. examined the effect of T. arjuna bark extract (500 mg BD) for 12 weeks in 105 patients with hypercholesterolaemia. Significant reductions were observed in total cholesterol (mean reduction 9.7%), LDL-C (mean reduction 15.8%), and triglycerides (mean reduction 12.7%), with a significant increase in HDL-C (mean increase 12.7%). These effects were more pronounced in patients with higher baseline lipid levels and in those with concomitant hypertension.42

6.4 Hypertension

A randomised open-label comparative study evaluated T. arjuna extract against enalapril in mild to moderate hypertension. After 12 weeks, both groups showed significant reduction in systolic and diastolic blood pressure, though the enalapril group demonstrated a somewhat greater reduction. The arjuna group showed additional benefits in terms of improvement of quality-of-life scores and reduction in serum triglycerides, suggesting a broader cardiovascular benefit.43 Importantly, the tolerability profile was superior in the arjuna group, with fewer adverse effects.

6.5 Limitations of Existing Clinical Studies

While the clinical evidence for T. arjuna is encouraging and consistent in direction, it is important to acknowledge substantial methodological limitations in the existing literature. Most studies suffer from small sample sizes (typically 12 to 60 participants), short durations (2 weeks to 6 months), inadequate randomisation or concealment procedures, lack of blinding or allocation concealment, and absence of validated primary endpoints. Many studies have been conducted at single centres in India without adequate external validation. The specific pharmacokinetics, optimal dosing regimens, and long-term cardiovascular outcome data (mortality, major adverse cardiac events) are largely absent. Future research must address these limitations through well-designed, multicentre, adequately powered randomised controlled trials with standardised drug preparations and internationally accepted outcome measures.

7. SAFETY AND TOXICOLOGY

7.1 Preclinical Safety Studies

Acute oral toxicity studies of T. arjuna bark extract in rodents have consistently demonstrated a wide safety margin. The LD50 for aqueous extract administered orally in rats and mice has been reported at values exceeding 3,000 mg/kg body weight, which is approximately 300 to 600 times the proposed therapeutic dose.44 Sub-acute and subchronic toxicity studies (28-day and 90-day duration) at doses up to 1,000 mg/kg

in rats have shown no significant adverse effects on haematological parameters, serum biochemistry, organ weights, or histopathological findings in liver, kidney, heart, and spleen.44,45

Genotoxicity evaluation using Ames test (Salmonella microsome assay) and chromosomal aberration assay has shown T. arjuna bark extract to be non-mutagenic and non-genotoxic at therapeutic concentrations.46 Reproductive toxicity studies in female rats revealed no significant teratogenic effects at doses up to 300 mg/kg, though these data are limited and caution should be exercised in the first trimester of pregnancy.

7.2 Clinical Safety Data

In reported clinical studies, T. arjuna bark extract at doses of 500 mg two to three times daily has been generally well tolerated for durations up to 12 months. The most commonly reported adverse effects in clinical studies include mild gastrointestinal disturbances (nausea, constipation) in a small percentage of patients (approximately 5–10%), which tend to be transient and resolve without dose modification.7,39 These effects are consistent with the astringent (kashaya) properties of the bark.

Rare cases of hepatotoxicity have been reported in post-marketing surveillance, though causality is difficult to establish given the frequent co-administration of multiple herbal preparations in Ayurvedic practice.47 Clinicians should exercise caution in patients with pre-existing hepatic impairment and monitor liver function tests in patients on long-term therapy.

7.3 Herb-Drug Interactions

Potential herb-drug interactions are a critical consideration for arjuna use in cardiac patients who are typically on multiple pharmacological agents. In vitro studies suggest that T. arjuna extract may inhibit CYP3A4 and CYP2D6 enzymes at high concentrations, potentially affecting the metabolism of co-administered drugs including beta-blockers, antiarrhythmics, and statins.48 In a pharmacokinetic interaction study in healthy volunteers, co-administration of arjuna extract with amlodipine resulted in a modest increase in amlodipine plasma AUC, suggesting potential pharmacokinetic enhancement.49

Additive hypotensive effects with antihypertensive agents and potential augmentation of antiplatelet activity with aspirin and clopidogrel should be monitored clinically. Patients on warfarin should be carefully observed, as the tannin-rich extract may theoretically interfere with vitamin K metabolism, though specific data are lacking. The clinical significance of these interactions at therapeutic doses remains to be systematically established and represents an important area for future investigation.

7.4 Contraindications and Special Populations

Based on available data, T. arjuna should be used cautiously in pregnancy (particularly first trimester), during lactation, and in patients with severe hepatic or renal impairment. Patients with known allergies to Combretaceae family plants should be screened. Classical Ayurvedic literature does not explicitly enumerate contraindications in terms equivalent to biomedical pharmacovigilance, but the sheeta virya (cold potency) of the drug suggests caution in conditions associated with ama (undigested metabolites), mandagni (poor digestive fire), and kapha-predominant disorders according to Ayurvedic diagnostic principles.

8. QUALITY CONTROL AND STANDARDISATION

The Ayurvedic Pharmacopoeia of India (API) has established monographic standards for T. arjuna bark, specifying macroscopic and microscopic descriptors, physicochemical constants (loss on drying, total ash, acid-insoluble ash, water-soluble extractive, alcohol-soluble extractive), thin layer chromatographic (TLC) profile, and limits for heavy metal contamination.50 The API specifies not less than 1.0% of arjunic acid as the quantitative chemical marker for bark quality assessment by HPLC.

Despite this official standardisation, significant variability in marker compound content across different geographical sources, harvest seasons, bark ages, and processing methods has been documented in independent quality surveys of commercially available products.51 A study evaluating 12 commercial arjuna bark formulations found arjunic acid content ranging from 0.4% to 3.8%, suggesting that a substantial

proportion of marketed products may not meet pharmacopoeial standards. This variability directly impacts clinical reproducibility and should be addressed through strengthened regulatory enforcement and improved good agricultural and collection practices (GACP).

9. Limitations and Gaps in Current Knowledge

Despite the considerable body of research accumulated over the past three decades, several critical gaps remain in the current understanding of T. arjuna that limit its full clinical integration.

The most significant limitation is the absence of large-scale, rigorously conducted randomised controlled trials (RCTs) with hard cardiovascular endpoints. Almost all existing clinical data derive from small, single-centre, short-duration trials with surrogate endpoints and methodological limitations that compromise their evidentiary weight by contemporary standards of evidence-based medicine. No trial has yet examined the effect of T. arjuna on cardiovascular mortality, myocardial infarction, stroke, or hospitalisation for heart failure — the endpoints that drive clinical cardiology practice.

Pharmacokinetic data for the key active constituents are critically insufficient. The absorption, distribution, metabolism, excretion (ADME) profile of arjunic acid, arjunolic acid, and the principal flavonoids has not been fully characterised in humans. Bioavailability studies, tissue distribution data, and identification of active metabolites are essentially absent from the published literature for most compounds, making rational dose optimisation and drug interaction prediction impossible.

Mechanistic research, while extensive in aggregate, tends to be fragmented across multiple pharmacological targets without integration into a coherent mechanistic framework that could guide drug development. The relative contribution of individual phytoconstituents versus synergistic multi-component activity to the overall pharmacological effects has not been adequately resolved through fractional activity studies.

The classical Ayurvedic formulations — particularly arjunaksheerapaka and arjuna ghrita — have been inadequately studied in comparison to simple bark powder or hydroalcoholic extract. The possibility that traditional processing methods enhance bioavailability, modify pharmacokinetics, or produce synergistic effects with milk lipids or ghee deserves systematic investigation rather than assumption.

10. Future Scope and Research Directions

The research landscape for T. arjuna in the coming decade holds considerable promise, provided the field can overcome the limitations outlined above. Several specific research directions merit priority consideration.

From a clinical research perspective, the most urgent need is for multicentre, double-blind, placebo-controlled RCTs with adequate sample sizes ($n > 200$) and follow-up duration of at least 12 to 24 months, examining hard cardiovascular endpoints in well-defined patient populations. The growing infrastructure of Ayurveda clinical research under the Central Council for Research in Ayurvedic Sciences (CCRAS) and the establishment of Ayurvedic hospital research networks provide an institutional framework for such ambitious trials. Integration with national heart failure registries and cardiac outcome study infrastructure could facilitate data collection and validation.

Nanotechnology-based drug delivery systems offer exciting possibilities for improving the bioavailability of arjuna's lipophilic triterpenoids, which may have poor oral absorption in conventional formulations. Nanoparticle formulations of arjunolic acid and arjunic acid have demonstrated improved bioavailability and enhanced cardiac targeting in preclinical studies, and merit systematic development.52

The concept of reverse pharmacology — taking well-validated traditional knowledge and building modern evidence systematically — is ideally suited to T. arjuna research. The TKDL (Traditional Knowledge Digital Library) documentation of classical formulations could guide clinical protocol design, ensuring that research designs honour the classical intent while meeting contemporary scientific standards.

Metabolomic and proteomic approaches to characterise the totality of biochemical changes induced by T. arjuna treatment in cardiac patients could provide new insights into mechanisms and identify novel biomarkers of response. Systems biology approaches integrating network pharmacology analysis have already generated testable hypotheses about multi-target activity of arjuna phytoconstituents that could guide mechanistic studies.53

Gender-specific pharmacology deserves attention, as most preclinical and clinical studies have either used predominantly male subjects or have not stratified analyses by sex, despite well-recognised sex differences in cardiovascular disease presentation and drug response. The interaction between the phytoestrogenic activity of certain arjuna flavonoids and cardiovascular outcomes in post-menopausal women is a particularly intriguing and understudied area.

11. Conclusion

Terminalia arjuna stands as a remarkable example of the convergence of ancient empirical wisdom and modern scientific evidence. Its over 3,000-year history of use as a cardiac tonic in Ayurvedic medicine, codified in canonical texts from Charaka Samhita to Bhavaprakasha Nighantu, reflects an accumulated clinical observation that has been substantially — though not yet completely — validated by contemporary biomedical research. The rich phytochemical constitution of its bark, encompassing bioactive triterpenoids, ellagitannins, flavonoids, and minerals, provides multiple pharmacological mechanisms that collectively account for its cardioprotective, antihypertensive, antioxidant, anti-inflammatory, and hypolipidaemic activities.

The clinical evidence, while predominantly derived from small single-centre trials with methodological limitations, consistently supports the beneficial effects of T. arjuna in ischaemic heart disease, stable angina, and chronic heart failure. The safety profile established across preclinical and clinical studies is reassuring, with the drug demonstrating a wide therapeutic index and minimal serious adverse effects at therapeutic doses. However, the same evidence base, assessed critically, makes clear that T. arjuna has not yet met the evidentiary standards required for mainstream cardiology integration — large-scale RCTs with hard cardiovascular endpoints are conspicuously absent.

The path forward lies in a research agenda that maintains fidelity to classical Ayurvedic formulation principles while embracing rigorous contemporary scientific methodology. Investment in pharmacokinetic characterisation, standardised product development, adequately powered clinical trials, and mechanistic integration through systems biology approaches will be essential to fully realise the therapeutic potential of this ancient cardiac remedy. For practitioners of Ayurveda and integrative medicine in India, T. arjuna represents both a jewel of their pharmacopoeial heritage and an ongoing scientific responsibility — to generate the quality of evidence that this venerable plant deserves

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