WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 05, 363-372. Review Article ISSN 2277–7105

ROLE OF TERMINALIA ARJUNA IN CARDIOVASCULAR DISORDERS - A REVIEW ARTICLE

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Article Received on
04 Jan. 2018,
Revised on 25 Jan. 2018,
Accepted on 14 Feb. 2018
DOI: 10.20959/wjpr20185-11206

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ABSTRACT

Terminalia arjuna, commonly known as *arjuna*, belongs to the family of Combretaceae. Its bark decoction is being used in the Indian subcontinent for anginal pain, hypertension, congestive heart failure, and dyslipidemia, based on the observations of ancient physicians for centuries. The utility of *arjuna* in various cardiovascular diseases needs to be studied further. Therefore, the present review is an effort to give a detailed survey of the literature summarizing the experimental and clinical studies pertinent to *arjuna* in cardiovascular disorders, which were particularly performed during the last decade. Most of the studies, both experimental and clinical, have suggested that the crude drug possesses anti-ischemic, antioxidant, hypolipidemic, and antiatherogenic activities. Its useful phytoconstituents are: Triterpenoids, β-sitosterol, flavonoids, and glycosides. Triterpenoids and flavonoids are considered to be responsible for its beneficial antioxidant cardiovascular properties. The drug has shown promising effect on ischemic cardiomyopathy. So far, no serious side effects have been reported with *arjuna* therapy. However, its long-term safety still remains to be elucidated. Though it has been found quite useful in angina pectoris, mild hypertension, and dyslipidemia, its exact role in primary/secondary coronary prevention is yet to be explored.

KEYWORDS: Antioxidant; Cardiovascular disorders; *Terminalia arjuna*.

INTRODUCTION

Arjuna is a potential cardioprotective agent belonging to the Combretaceae family. It is an ayurvedic remedy that has been mentioned since vedic period in many ancient Indian medicinal texts including Charaka Samhita, Sushruta Samhita, and Astang Hridayam. In the Rigveda, the word Arjuna is used (R.V.1/122/5) for the first time.[1] Both Carakacharya and Sushrutacharya have mentioned this plant in their Samhitas, but have not indicated its use for heart diseases. It was Vagbhattacharya who for the first time mentioned the use of Arjuna in the treatment of heart diseases and the same was endorsed by Cakradatta and Bhavamishra. The leaves of kadamba, arjuna, nimbi, patala, pippali and arka are useful for healing of the wounds.[2] A person, who consumes powdered bark of arjuna plant along with ghee or milk or jiggery water will be relieved from Hrdrog, chronic fever and haemorrhages. He lives for longer periods of life.[3] *Terminalia arjuna* is a deciduous and evergreen tree found throughout India. It stands to about 20-30m above ground level, belongs to combretaceae family. Abundantly found throughout Indo-sub Himalayan tracts of Uttar Pradesh, South Bihar, Madhya Pradesh and Deccan regions near ponds and rivers. Also found in forests of Srilanka, Burma and Mauritius.

Ethnomedical uses

The bark has been described as an astringent, demulcent, expectorant, cardiotonic, styptic, antidysenteric, urinary astringent, and has shown to be useful in fracture, ulcers, leukorrhea, diabetes, anemia, cardiopathy, and cirrhosis.[4] According to Chakradatta, powder of bark of arjuna is useful in cardiac disorders with the anupana like ghee, milk or guda and Arjuna ghrit is also useful in cardiac disorders.[5] Decoction of the bark has been used as ulcer wash, while bark ashes have been prescribed for snakebite and scorpion sting.[6] According to Bhavprakash nighantu, property of Arjuna is “Hridhya”.[7] The bark of Terminalia arjuna is useful in cardiovascular diseases. Traditional healers from Kancheepuram district, Tamil Nadu boil the bark powder with water, and inhale it to cure headache and to kill worms in teeth. They also use fruit paste topically on wounds.[8] Fresh leaf juice is used for the treatment of earache and bark powder for treating heart ailments by Malabar tribe, Kerala.[9] Tribals living in Sundargarh District, Orissa use dried bark powder along with rice washed water to treat blood in urine, and tribes living in Malkangiri district chew the fresh bark and swallow the juice as an antacid.[10,11]

HABITAT

Arjuna tree is about 60-80 ft in height, and is seen along rivers, streams, and dry water bodies throughout the Indo-sub-Himalayan tracts of Uttar Pradesh, southern Bihar, Chota Nagpur, Burma, Madhya Pradesh, Delhi, and Deccan region [Figure 1]. It is also found in the forests of Sri Lanka and Mauritius. It grows almost in all types of soils, but prefers humid, fertile loam and red lateritic soils. It can tolerate half submergence for a few weeks. *Arjuna* is propagated by seeds; Germination takes 50-70 days with 50-60% germination.[12]

Figure 1: Terminalia arjuna tree.

RASPANCHAK OF TERMINALIA ARJUNA (Acc. to Ayurved)

Rasa – Kashya	**Virya- Sheeta**	**Prabhava- Hridhya**
Guna- Laghu, Rooksha		**Vipaka- Katu**

PHARMACOGNOSTIC FEATURES

The outer surface of the bark is smooth, while the inner surface has longitudinal striation and is pinkish in color.[4] The bark gets flaked off itself in the month of April–May [Figure 2].[11]

Figure 2: Bark stem of Terminalia arjuna.

On microscopic examination of the mature bark, a cork consisting of 9-10 layers of tangentially elongated cells, 2-4 cells thick phellogen, and phelloderm consisting of tangentially elongated cells are seen. The phloem is broad, consisting of ceratenchyma, phloem parenchyma, phloem fibers, and crystal fibers with rosette crystals of calcium oxalate. Periderm and secondary phloem are present in the old bark.[13 and14]

Leaves are sub-opposite, coriaceous, oblong/elliptic, dull green from the upper side and pale brown on the lower side, often unequal sided with 10-15 pairs of nerves [Figure 3]. Flowers are white in color and bisexual, arranged in spikes with linear bracteoles [Figure 4]. Fruits are ovoid/oblong with 5-7 hard angles or wings. The lines on wings are oblique and curving upward [Figure 5].[4]

Figure 3: Leaves of *Terminalia arjuna.*

Figure 4: Flower of *Terminalia arjuna.*

Figure 5: Fruits of *Terminalia arjuna* (ripe, fresh).

Major chemical constituents of *arjuna* have been shown in Table 1.,[15.,16.,17.,18.] and [19.]

Table 1: Major chemical constituents of arjuna.

Part of plant	Major chemical constituents	Major chemical constituents
Stem bark	Triterpenoids	Arjunin, arjunic acid, arjunolic acid, arjungenin, terminic acid, ajunglucosides IV and V, arjunasides A-E, 2-alpha, 3-beta-dihydroxyurs-12,18-dien-28-oic acid 28-O-beta-d-glucopyranosyl ester
	Glycosides	Arjunetin, arjunoside I, arjunoside II, arjunaphthanoloside, terminoside A
	Flavonoids	Arjunolone, arjunone, baicalein, luteolin, gallic acid, ethyl gallate, quercetin, kempferol, pelargonidin, oligomeric proanthocyanidins
	Tannins	Pyrocatechols, punicallin, punicalagin, terchebulin, terflavin C, castalagin, casuariin, casuarinin
	β-sitosterol	
	Minerals/trace elements	Calcium, aluminum, magnesium, silica, zinc, copper
Roots	Triterpenoids	Arjunic acid, arjunolic acid, oleanolic acid, terminic acid
	Glycosides	Arjunoside I, arjunoside II, arjunoside III, arjunoside IV, 2α, 19α-dihydroxy-3-oxo-olean-12-en 28-oic acid 28-O-β-d-glucopyranoside
	β-sitosterol	
Leaves	Flavonoids	
	Alkaloids	
	Tannins	
	Steroids	
	Phenolic compounds	
	Oxalic acid	
	Inorganic acid	
Fruits	Glycosides	
	Flavonoids	Luteolin
Seeds	Cardenolide	14,16-dianhydrogitoxigenin-3-beta-d-xylopyranosyl (1-- > 2)-O-beta-d-galactopyranoside

EXPERIMENTAL STUDIES

Various extracts of the stem bark of *arjuna* have shown to possess many pharmacological properties including inotropic, anti-ischemic, antioxidant, blood pressure lowering, antiplatelet, hypolipidemic, antiatherogenic, and antihypertrophic.[20] Thus, in the present article, we have made an attempt to review and give up-to-date information pertinent to the usage of *arjuna* as a potential cardioprotective agent.

Antioxidant and cardioprotective effect

Dried, pulverized bark has been shown to augment endogenous antioxidant compounds of rat heart and prevent oxidative stress associated with ischemic–reperfusion injury of the heart.[21]

It was suggested that the alcoholic extract of *arjuna* in rabbit induces myocardial heat shock protein 72 and augments myocardial endogenous antioxidants which offer cardioprotection against oxidative stress associated with myocardial ischemic–reperfusion injury.[22] The cardioprotective effect of the active phytoconstituents of *arjuna* bark against carbon tetrachloride and sodium fluoride induced oxidative stress, probably via its antioxidant properties, has also been documented. In the above models, ferric reducing/antioxidant power assay revealed that ethanol extract enhanced the cardiac intracellular antioxidant activity.[23,24] In a recent study, the methanol extract yielded the highest phenolic and flavonoid content and was found to possess the highest total antioxidant capacity. Thus, it can be inferred that there exists a linear correlation between the antioxidant capacity and the total phenolic content of the extracts.[25]

Hypolipidemic and antiatherogenic activity

Earlier animal experiments have demonstrated that *arjuna* bark powder/extract reduces the total cholesterol (TC) and triglyceride (TG) levels.[26,27,28and29] On comparing the hypolipidemic property of the bark in different solvent fractions (petroleum ether, solvent ether, ethanol, and water) in hyperlipidemic rats, it was observed that only the ethanolic fraction exerted significant lipid-lowering effect. Solvent ether and ethanolic fractions caused a decrease in the plasma levels of lipids in triton as well as in high fat diet (HFD) fed models of hyperlipidemia in hamsters. In an *in vitro* experiment with *arjuna* fractions at concentrations of 50-500 μg/ml, they were found to inhibit the oxidative degradation of lipids induced by metal ions in human low density lipoprotein (LDL) and rat liver microsomes. When these fractions were tested against the generation of oxygen free radicals, they counteracted the formation of superoxide anions and hydroxyl radicals in nonenzymic test

systems. The efficacy of *arjuna* fractions was found to be in the order: Ethanol fraction > solvent ether fraction > petroleum ether fraction.[30]

CLINICAL USES

Angina/myocardial infarction

The anti-ischemic effect of bark powder was evaluated in 30 patients of stable angina/post-infarct angina (500 mg tds). The authors observed that the mean anginal frequency decreased significantly, along with a significant decrease in systolic blood pressure (SBP), improvement in ECG changes, and reduction in plasma cortisol and serum cholesterol levels.[31]

CHF/hypertension

In one of the earliest studies, 10 patients with CHF received 4 g of *arjuna* bark powder twice daily for 1 month. The researchers observed improvement in the functional class, breathlessness, and overall well-being with significant diuresis, and a fall in both systolic and diastolic blood pressure.[32]

Rheumatic heart disease

Efficacy of *arjuna* in decompensated rheumatic heart disease was studied in a double-blind study in which 30 patients of rheumatic valvular heart disease with CHF were administered 200 mg *arjuna* thrice daily. The results revealed a significant improvement in LVEF, exercise duration, and significant reduction in heart size.[33]

Dyslipidemia

In a study on 21 patients with coronary heart disease administered 1 g of bark powder twice daily with milk for 4 months, the patients showed improvement in lipid profile. In addition to this, patients got symptomatic relief after 1 month of treatment.[34]

CONCLUSION

The eternal interest in medicinal plants has led to the discovery of new chemical constituents and pharmacological actions of *arjuna*. Its efficacy as an anti-ischemic agent, a potent antioxidant, and an antiatherogenic agent has been amply demonstrated in various experimental and clinical studies. However, major lacunae of these studies include the lack of phytochemical standardization of the extract, bioavailability studies, and well-designed studies to evaluate its long-term toxicity effects. Its exact role in primary/secondary coronary prevention needs to be investigated. In addition to this, studies to look for the effect

of *arjuna* on CYP450 enzymes and its interactions with other drugs like statin, aspirin, angiotensin-converting enzyme (ACE) inhibitors, and β-blocker need to be designed. Increasing the awareness regarding its medicinal usage can give a direction to the physicians to respond to the challenges in treating cardiovascular diseases.

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