PHARMACOLOGICAL SIGNIFICANCE OF TERMINALIA ARJUNA: A REVIEW

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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. The utility of arjuna in various cardiovascular diseases needs to be studied further. Therefore, the present review is an effort on arjuna in cardiovascular disorders, which were particularly performed during the last decade. Most of the studies, have suggested that the crude drug possesses anti-ischemic, antioxidant, hypolipidemic, and antiatherogenic activities. Its useful phytoconstituents are: Triterpenoids, 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.

1. INTRODUCTION

Cardiovascular diseases are the most prevalent noncommunicable diseases worldwide. They are expected to be the second leading cause of disability globally by 2020. In the Indian subcontinent, the high prevalence of cardiovascular disease risk factors against a backdrop of a large population is mainly responsible for its enormous societal and healthcare burden. Moreover, the estimated increase in mortality and morbidity from cardiovascular diseases has been projected to directly follow an explosion in the prevalence of traditional risk factors. Cardiovascular diseases are mostly represented by ischemic heart disease, hypertension, heart failure, rheumatic heart disease, and cardiomyopathies.1 Drugs play an important role both...
in the prevention and treatment of cardiovascular diseases. Various effective pharmacologic agents, like b-adrenoceptor blockers (b-blockers), nitrates, antiplatelet drugs, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II type 1 receptor antagonists (angiotensin receptor blockers [ARBs]), and calcium channel blockers have been available for the last several decades for the treatment of major cardiovascular diseases.\textsuperscript{[2]} Indian patients frequently look for herbal remedies for these conditions for various reasons, such as sociocultural factors, officially recognized Indian systems of medicine, perceived safety of herbal drugs, their easy availability, adverse effects of modern drugs with resultant non-compliance, increasing cost of modern drugs, and suboptimal healthcare facilities.\textsuperscript{[1,2]} The world health organization has estimated that over 75% of the world’s population still relies on plant derived medicines, usually obtained from traditional healers, for its basic health care needs. Several medicinal plants have been described to be beneficial for cardiac ailments in “Atharva Veda” an ancient treatise from which Ayurveda, the Indian system of Medicine owes its origin. Quite a few of them, for example, \textit{Allium sativum} L. (garlic), \textit{Cicer arietinum} L. (bengal gram), \textit{Commiphora mukul} Engl. (guggul), \textit{Curcuma longa} L. (turmeric), \textit{Eugenia jambolana} Willd. (jamun), \textit{Emblica officinalis} Gaertn. (goose berry), \textit{Ocimum sanctum} L. (tulsi), \textit{Terminalia arjuna} Wight & Arn. (arjuna) and \textit{Trigonella foenum-graecum} L. (fenugreek) have been identified and researched for their putative lipid lowering and cardioprotective activities. The plant which has shown most promising and distinct results among these is \textit{Terminalia arjuna}.\textsuperscript{[2]} This tree often grows to a height of about 100 feet or 30 meters and bears yellow blooms and tapering leaves. The bark of the arjuna tree possesses therapeutic properties and has been used by people for centuries to treat different conditions. 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. It was Vagabhatta who, for the first time, advocated the use of stem bark powder in heart ailments.\textsuperscript{[3]}

2. Plant profile

2.1 Habitat

\textit{Terminalia arjuna} is a deciduous and evergreen tree, standing 20–30 m above ground level (Fig. 1). It belongs to Combretaceae family. It is found in abundance throughout Indo-sub-Himalayan tracts of Uttar Pradesh, South Bihar, Madhya Pradesh, Delhi and Deccan region near ponds and rivers. It is also found in forests of Sri Lanka, Burma and Mauritius.\textsuperscript{[4]}
2.2 Scientific classification\footnote{15}

Kingdom- Plantae
Sub kingdom- Tracheobionta
Division- Magnoliophyta
Sub Division- Spermatophyt
Class- Magnoliopsida
Order- Myrtales
Family- Combretaceae
Genus- Terminalia
Species- *arjuna*

2.3 Cultivation

*T. arjuna* grown manually through ripe seeds, coppicing, pollarding, root suckers, stumps and air layering. It grows slowly in the initial phase but later on grows fast. It attains 2-3 meters height in three years.\footnote{5}
2.4 Bark
The outer surface of the bark appeared smooth, pale greenish yellow while the inner surface is finely longitudinally striated and pinkish in color. Bark has pieces that are flat, curved and recurved in shape.\cite{6}

![Fig. 4: Flowers of *terminalia arjuna*.](image)

2.5 Flower
White or Yellowish flowers are found in groups. Flowering occurs in summer and fruit appears in winter or spring season.

![Fig. 5: Fruits of *terminalia arjuna*.](image)

2.6 Fruit
Fruits are 1-1.5 inch in diameter and 5-7 longitudinal lobes. These are glabrous with 5-7 wings, woody and fibrous. Fruit is drupe and is often notched.
2.7 Leaves
Terminalia Arjuna contain simple and smooth leaf\(^7\) Leaves are like that of Guava leaves - oblong, 4-6 inch long and 2-3 inch wide, subopposite, glabrous and often inequilateral. There are two glands near the base of the petiole. The margin is crenulate with apex at obtuse or subacute angle. The base is rounded or cordate. Petioles run for 0.5 to 1.3 cm\(^3,4\).

2.8 Inflorescence
Terminalia Arjuna the inflorescences are short axillaries spikes or small terminal panicles.\(^7\)

3. Phytochemical constituents\(^{2,13}\)

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<tr>
<th>Sr. No.</th>
<th>Part used</th>
<th>Major chemical constituents</th>
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| 1       | Stem bark | **Triterpenoids and tannins**  
Arjunic acid, Arjunin  
Arjyunetin, Lactone  
Arjunanin, Arjunolic acid  
Casuarinian  
**Flavonoids and phenolics**  
Arjunolone, Baicalein  
Catechin, Gallocatechin, Epicatechin  
**Ursane triterpenoids**  
2α, 3β- dihydroxy urs-12,18 dien-28 oic acid 28-O-β-D-glucopyranosyl eater  
2α, 3β, 23-trihydroxyurs-12,18 oic acid 28-O-β-D-glucopyranosyl eater  
Oqudranoside VIII, Kajichigoside F1  
**Glycosides**  
Arjunogluicoside I and II  
Terminovic acid  
Arjunogluicoside IV, V  
Terminoside A  
Terminogluicoside I, II |
The active constituents of Terminalia arjuna in stem bark, fruits, root bark and seeds are well characterized. The active constituents of Terminalia arjuna include various polyphenols (60–70%) such as Flavonoids (gallic acid, arjunone, arjunolone, luteolin, ellagic acid, oligomeric proanthocyanidins, etc.), Triterpenoids, saponins (arjun glycosides, arjunolic acid, arjunic acid, arjungenin) tannins (20–24%), phytosterols and minerals such as calcium, magnesium, zinc and copper. Terminalia arjuna is also rich in amino acids such as tryptophan, tyrosine, histidine, and cysteine (13). Various chemical constituents present in Arjuna is given in table.

### 3.1 Terpenoids and Glycoside

Initially an oleanane triterpenoid termed, arjunin, arjunolic acid and a lactone, arjunetin was isolated from the benzene and alcoholic extracts of its bark.

Presence of arjunic acid and arjungenin in the bark stem was subsequently confirmed and two more glucosides namely arjun glucoside I and arjun glucoside II were reported. Later on a triterpene carboxylic acid, terminic acid, and arjunoside III and and arjunoside IV were isolated from the ethyl acetate extract of its root. Terminic acid was also isolated from the n-hexane extract of Terminalia arjuna heartwood along with β-sitosterol. Another oleanane type triterpane, terminoside A has been isolated, purified from the acetone fraction of the ethanolic(alcoholic) extract of its stem bark. A-naphthanol glycoside termed, arjuna-naphthanoloside possessing antioxidant activity has also been isolated from its bark.
3.2 Flavonoids and Flavones

*Terminalia arjuna* bark contains a very high level of Flavonoids detected from its bark are namely, arjunolone, flavones, bicalein, quercetin, kempferol and pelargonidin. Recently a new flavonoid named luteolin has been isolated from butanol extract of *Terminalia arjuna*. *Terminalia arjuna* possessed a high phenolic content to the tune of 72.0–167.2 mg/kg.

3.3 Tannins

Some of the well known hydrolysable tannins from the bark are pyrocatechols, punicallin, punicalagin, terchebulin, terflavin C, castalagin, casuariin and casuarinin. Some 15 types of tannins and related type of compounds have been isolated from its bark so far Tannins are known to enhance synthesis of nitric oxide and relax vascular segments precontracted with norepinephrine.

3.4 Minerals

The bark also contains large amounts of magnesium, Calcium, copper.
4. Pharmacological significance\(^{[5,21]}\)

Initially T. arjuna was mentioned as ‘Hirdya’ the drug which strengthens the heart, but further studies and clinical evidences show that it also possesses good anticancer and antiviral activities.\(^{[10]}\)

4.1 Antioxidant effect

T. arjuna bark extract have shown antioxidant effect on N-nitroso-diethylamine (DEN) induced hepatocellular carcinoma in rats induced by a single intraperitoneal injection of DEN (200 mg/kg). Significant increases in lipid peroxidases were observed while the levels of enzymatic and non-enzymatic antioxidants were decreased when subjected to DEN induction. The enzyme levels were ameliorated significantly by administration of ethanolic extract of T. arjuna bark at a concentration of 400 mg/kg in drug treated animals. The protective effect of the extract is against DEN induced liver cancer.

4.2 Anti ischemic effect

Ischemic mitral regurgitation (IMR) is a frequent complication of acute myocardial infraction and a progress factor for morbidity and mortality. In vivo ischemic reperfusion injury induced oxidative stress, tissue injury of heart and haemodynamic effects were prevented in T. arjuna treated rabbit hearts. arjuna bark extract at the dose of 500 mg, given 8 h to patients with stable angina with approvocable ischemia on tread mill exercise, led to improvement in clinical and treadmill exercise parameters as compared to placebo therapy. These benefits were comparable to isosorbidate mononitrate (40 mg/day) therapy and the extract was well tolerated.

4.3 Antibacterial effect

T. arjuna bark extract exhibited antibacterial activity against Escherichia coli, Plasmodium vulgaris and Plasmodium aerogenes. The bark of T. arjuna shows activity in dichloromethane and aqueous fraction against the bacteria tested at 1,000–5,000 ppm dosage. High activity was observed at 4,000 and 5,000 ppm against Plasmodium aerogenes.

4.4 Anticancer effect

There are some chemical substances present in plants that may act as anticarcinogens or antimutagens by blocking or trapping ultimate carcinogen electrophile in a nucleophilic chemical reaction to form innocuous products. The bark of T. arjuna is rich in polyphenols (60–70%) including flavones, flavanols and tannins. The high content of tannins and...
polyphenols are mainly responsible for anticancer activity. The antimutagenic effect of benzene, chloroform, acetone and methanol fractions were studied. Among the different fractions the antimutagenic effect was more in the methanol and acetone fractions. The acetone fraction was more effective in reducing DNA damage by nitroquinoline-N-oxide. The tannin fraction isolated from T. arjuna has antimutagenic effect against NPD in TA98, Sodium azide in TA100 and 2AF (S-9 dependent) a promutagen in both TA98 and TA100 tester strains of Salmonella typhimurium tested on Ames assay.

5. Cardiovascular effects\textsuperscript{[11,12]}

The body needs constant nourishment to ensure that the cardiovascular system operates efficiently. However, 60 millions Americans suffer from cardiovascular disorders which include a wide range of diseases of heart and blood vessels such as chronic venous insufficiency and high blood pressure. These can lead to events such as heart attack and stroke. Many herbal drugs are used to cure cardiovascular disorders the most common one of which is T. arjuna. The oleanane triterpenoids (arjunic acid, arjunoglycosides, arjunone, arjunolic acid etc.) present in this plant are mainly responsible for the cardio protective effect. This plant is effective in many cardiac disorders like angina, myocardial infraction, hypertension, hypercholesteremia, cardiac arrest etc. Experimental studies have revealed that its bark possesses significant inotropic and hypotensive effect, increasing coronary artery flow and protecting myocardium against ischemic damage. It has also been detected to have mild diuretic, antithrombotic, prostaglandin E enhancing and hypolipidemic activity. There is simple clinical evidence of its beneficial effect in coronary artery disease alone and along with statin’s.

5.1 Anti ischemic effect

Ischemic mitral regurgitation (IMR) is a frequent complication of acute myocardial infraction and a progress factor for morbidity and mortality. The powder of the bark given to healthy volunteers less than 70 years old have shown to reduce IMR and there was improvement in E/A ratio (E: Early Echocardiographic phases and A: Late Atrial Phase of ventricular filling) and reduction in anginal frequency. Oral administration of T. arjuna for 12 weeks in rabbits have shown to cause augmentation of myocardial antioxidants, superoxide dismutases, catalyze and glutathione along with induction of heat shock protein 72. In vivo ischemic reperfusion injury induced oxidative stress, tissue injury of heart and haemodynamic effects were prevented in T. arjuna treated rabbit hearts. In T. arjuna treated rabbits the
normalization of left ventricular end diastolic pressure occurred in 10 min of reperfusion and the extent of myocardial lipid peroxidation was also found to be less in T. arjuna treated rabbits. T. arjuna bark extract at the dose of 500 mg, given 8 h to patients with stable angina with approvable ischemia on treadmill exercise, led to improvement in clinical and treadmill exercise parameters as compared to placebo therapy. These benefits were comparable to isosorbidate mononitrate (40 mg/day) therapy and the extract was well tolerated.

5.2 Lipid lowering effect
High level of low density lipoproteins (LDL) and low levels of high density lipoproteins (HDL) cholesterol are important coronary risk factors. The ethanol extract of the bark was found to be very effective in lowering LDL cholesterol levels at the dose of 100 mg/kg body weight. The total cholesterol level was also reduced at the dose of 500 mg/kg body weight.

5.3 Antihypertensive effect
The hypotensive effect was observed with the aqueous extract of T. arjuna fraction containing tannin related compounds in rats. The hypotensive effect of this fraction was not affected by pretreatment of rats with propranolol but was attenuated by pretreatment with atropine. Thus, cholinergic mechanism may be involved in a decrease of blood pressure.

REFERENCES


