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A cardio protective medicinal plant *Terminalia arjuna*: evidence from the traditional medicine and recent research

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Abstract
Terminalia arjuna Roxb. An important medicinal plant of Bangladesh, used in various indigenous system of medicine. This review has been conducted to pile up information that is available in different scientific literatures. It is observed that a large number of phytochemical components have been obtained from the plant e.g. arjunin, arjunetin, gallic acid, terminic acid, pyrocatechols, luteolin, β-sitosterol, calcium, magnesium, zinc, copper and these components exhibit various medicinal and pharmacological activities such as anti-mutagenic, anti-bacterial, anti-viral, anti-oxidant, anti-inflammatory, antiatherosclerotic, anti-diabetic etc. The present comprehensive update review is therefore, an effort to give detailed information on phytochemical and pharmacological studies of *T. arjuna* Roxb. And this information will help the researchers to carry out research on this pharmaceutically important medicinal plant.

Keywords: *Terminalia arjuna*, Ethnomedicinal, cardio protective, systematic study

1. Introduction
After decades of serious obsession with the modern medicinal system, people have started looking at the ancient healing systems like Ayurveda, Siddha and Unnani because of their less adverse effects combined with lower cost that are associated with synthetic drugs [1]. These drugs play an important role in health care programs especially in developing countries. For the treatment of different diseases, about 80% people in the world still rely on conventional medicine [2]. Therefore, the valuation of rich heritage of conventional medicine is essential [3]. The use of therapeutic plant either as a single drug or in combination is increasing in the health care of human being. Phytomedicines or botanical medicines refer to the use of bark, seeds, root, berries, leaves, or flowers of any plant for therapeutic purposes by large number of people. It has now been recognized that the plants which naturally accumulate and synthesis some secondary metabolites like glycosides, alkaloids, tannins, volatiles oils and contain vitamins and minerals, possess medicinal properties [4]. The scientific name of arjun is *Terminalia arjuna* Roxb. It is about 60-80 feet height perennial tree found everywhere in Bangladesh. It is composed of enormous active constituents include glycosides, tannins, flavonoids, triterpenoids, β-sitosterol and minerals [5] which possesses high therapeutic value and traditionally used for the treatment of different ailments for human beings. The bark extract of *T. arjuna* Roxb. Is considerably prevented the isoprenaline-induced increase through oxidative stress, decrease in endogenous antioxidant level and also avoid fibrosis without increasing the heart weight and body weight ratio, as well as it can prevent myocardial changes induced by the action of chronic beta-adrenoceptor stimulation [6]. The bark is anti-dysentric, cardiotonic, lithotriptic, antipyretic, astringent, and tonic while the powder of the bark acts as a diuretic in cirrhosis of liver and gives relief in symptomatic hypertension [7]. In studies in mice, the leaves of *T. arjuna* Roxb. Have been shown to have anti-inflammatory and analgesic properties. It may also be useful in treating hypercholesterolemia by reducing LDL levels [8]. The bark powder has been found to possess cardioprotective properties, anti-ischaemic, antioxidant action [9], hypocholesterolaemic effect, fungicidal [10], antimicrobial, anti-bacterial, anti-fertility, treatment of ulcers, skin disorders and as antidote to poisons. It is also useful to cure obesity, hypertension and hyperglycemia. The bark constituents are promising in anti-mutagenic and anti-carcinogenic potential. The aim of this present study was to deliver valuable information on phytochemical and pharmacological characteristics of *T. arjuna* Roxb.

This compendium review also includes its taxonomy, monograph, morphology, and distribution of this highly significant medicinal plant.

Fig 1: Fruit, leave, flower and bark of *Terminalia arjuna*.

2. Botanical Description

Terminalia arjuna is a deciduous large-sized fluted tree to 30 m tall and 2-2.5 m dbh, with an often buttressed trunk. Its superficial, shallow root system spreads radially along stream banks. The large, spreading crown produces drooping branches. Bark grey or pinkish-green, thick, smooth and exfoliating in thin irregular sheets. Leaves simple, opposite to sub-opposite, 5-25 × 4-9 cm, oblong or elliptic oblong, glabrous, hard, often inequilateral, margin often crenulate, apex obtuse or sub-acute, base rounded or sometimes cordate. The petiole is short (2-4 cm long), sericeous, with 2 (or 1) prominent two glands at petiole apex Inflorescences are short axillary spikes or small terminal panicles, 9-13 cm long with 2.5-6 cm long branches. The rachis short, white and pubescent. Lower receptacle 0.8-1.5 mm long, short sericeous, upper receptacle 1.5- 1.75 mm long, glabrous except at base where slightly pubescent. Flowers are small, cup-shaped, regular, sessile, polygamous, white, creamy or greenish-white and strongly honey-scented. Fruit 2.5-6 x 1.8-2.8 cm long, obovoid-oblong, dark brown to reddishbrown fibrous woody, indehiscent drupe, glabrous with 5-7 equal thick narrow stiff-wings and striated with numerous upwards-curved veins. The generic name Terminalia comes from Latin word 'terminus' or 'terminalis' (ending), and refers to the habit of the leaves being crowded or borne on the tips of the shoots.

3. Distribution of *Terminalia arjuna*

Terminalia arjuna Roxb is a deciduous tree found in dry hill areas by the side of water bodies- ravines, streams and rivers. It is abundance throughout Bangladesh, Madhya Pradesh, Indo-sub-Himalayan tracts of Uttar Pradesh, Delhi, and South Bihar. It is also found in forests of Sri Lanka, Burma and Mauritius [11].

4. Vernacular Names

Assamese: Arjun
Marathi: Arjun, Anjan, Sadura
Bengali: Arjun, Arjhan
Oriya: Hanjal
English: Arjun, White Marudah
Punjabi: Arjon
Gujarati: Sadada, Salado
Sanskrit: Kakubha, Pārtha, Indrādru, Dhavala, Devasāla, Nadisarja,
Hindi: Anjan, Anjani, Arjun,
Tamil: Vella marda, Vella maruthu, Vella matti
Kannada: Holé matti, Maddi, Matti
Telugu: Vella marda, Vella matti, Yer maddi, Erramaddi, Tella madu

5. Taxonomy

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Myrtales
Family: Combretaceae
Genus: *Terminalia*
Species: *Terminalia arjuna* Roxb

6. Unani Description

Unani name: Lesanon insan
Botanical name: *Terminalia arjuna*
Synonyms: Anjan, Anjani, Arjun.
Temperament: 2nd degree hot & dry.
Maza: Slightly bitter in taste.
Muzir: Excessive intake is harmful for person with hot temperament.
Mukhrij: Honey, ghee, oil.
Nafa-e-Khas: Cardio tonic, aphrodisiac.

7. Important Formulations

Important Unani & Ayurvedic formulations containing *Terminalia arjuna are* as follows:

a) Syrup Aswagandharista (Produced by Hamdard Laboratories Waqf: Bangladesh) Indications: Epilepsy, Syncope (Fainting), Arthritis, Insanity, Nervous debility, Memory disorder, Insomnia, Leanness.
b) Arjunarista
c) Arjuna ghreto
d) Arque Arjun
e) Khamira Arjuna

8. Chemical Composition

The chemical constituents of *T. arjuna* Roxb. Are shown in Table 1. The whole plant of *T. arjuna* Roxb contains tannins, triterpenoid, flavonoids, saponins, gallic acid, ellagic acid, OPCs, phytosterols, zinc, copper, calcium, magnesium etc. It also contains oleanolic, arjunic acids, arjunoside I, II, arjunolic acid, 8-hydroxyl hexadecanoic, and β-sitosterol. Major chemical constituents of various parts of *T. arjuna* Roxb are as follows-

a) Stem bark: The stem bark of *Terminalia arjuna* contains following chemical substances-
Triterpenoids: arjunolic acid, arjunic acid, arjunin, arjungenin,terminic acid.
Glycosides: arjunetin, *arjunoside II, *arjunoside I, arjunaphthanoloside, terminoside A. B-Sitosterol
Flavonoids: arjunone, bicalein, arjunolone, luteolin, ethyl gallate, gallic acid, kempferol, pelorgonidin, quercetin, oligomeric proanthocyanidins.
Tanins: terflavin C, castalagin, punicallin, casuarinin, punicalagin, terchebulin, casuariin, pyrocatechols Trace elements/Minerals: zinc, copper calcium, aluminium, silica, magnesium [12, 13, 14, 15].

b) Roots: The roots of *Terminalia arjuna* contains

following chemical substances-β Sitosterol
Triterpenoids: terminic acid, arjunic acid, oleanolic acid, arjunolic acid
Glycosides: arjunoside I, arjunoside II, arjunoside III, arjunoside IV, *2, 19-dihydroxy-3-oxo-olean-12-en28-oic acid 28-O-d glucopyranoside [16, 17].

c) Leaves and fruits
Glycosides
Flavonoids: luteolin [18]

9. Pharmacological Properties
In the traditional system of medicine the physicians are using arjuna in various heart problems, but in the era of evidence based medicine to prove the efficacy of arjuna a series of the clinical trials have been going on since the early 21th century.

9.1 Angina Pectoris
An open study of *Terminalia arjuna* use in stable and unstable angina demonstrated a 50-percent reduction of angina in the stable angina group after three months (p<0.01). A significant reduction was also found in systolic blood pressure in these patients (p<0.05). During treadmill testing, both the onset of angina and the appearance of ST-T changes on ECG were significantly delayed in the stable angina group (p<0.001), indicating an improvement in exercise tolerance. The unstable angina group did not experience significant reductions in angina or systolic blood pressure. Both groups showed improvements in left ventricular ejection fraction. Evaluation of overall clinical condition, treadmill results, and ejection fraction showed improvement in 66 percent of stable angina patients and 20 percent of unstable angina patients after three months [19].

9.2 Congestive Heart Failure
A double-blind, placebo-controlled, two-phase trial of *Terminalia arjuna* extract treatment in twelve patients with severe refractory heart failure (NYHA Class IV) was conducted. Either 500 mg Terminalia bark extract or placebo was given every 8 hours for two weeks, in addition to the patients' current pharmaceutical medications (digoxin, diuretics, angiotensin-converting-enzyme inhibitors, vasodilators, and potassium supplementation). All patients experienced dyspnea at rest or after minimal activity at the start of the trial. Dyspnea, fatigue, edema, and walking tolerance all improved while patients were on *Terminalia arjuna* therapy. Treatment with *Terminalia arjuna* was also associated with significant improvements in stroke volume and left ventricular ejection fraction, as well as decreases in end-diastolic and end-systolic left ventricular volumes compared to placebo. In the second phase of the study, patients from phase I continued on Terminalia extract for approximately two years. Improvements were noted in the ensuing two to three months, and were maintained through the balance of the study. After four months' treatment, nine patients had improved to NYHA Class II and three improved to Class III [20].

9.3 Hyperlipidemia
Animal studies suggest *Terminalia arjuna* might reduce blood lipids. Rabbits made hyperlipidemic by feeding them an atherogenic diet were given an oral *Terminalia arjuna* extract. Animals given *Terminalia arjuna* had a significant, dose-related decrease in total-and LDL-cholesterol, compared to placebo (p<0.01) [21]. However, the amounts used (100 mg/kg and 500 mg/kg body weight) were very large, and it remains to be seen if these significant changes will be seen in humans taking relatively smaller oral doses.
In a similar study of rats fed cholesterol (25 mg/kg body weight) alone or along with *Terminalia arjuna* bark powder (100 mg/kg) for 30 days, *Terminalia arjuna* feeding caused a smaller increase in blood lipids and an increase in HDL cholesterol compared to the cholesterol-only group. The researchers felt inhibition of hepatic cholesterol biosynthesis, increased fecal bile acid excretion, and stimulation of receptormediated catabolism of LDL cholesterol caused *Terminalia arjuna*'s lipid-lowering effects [22].

9.4 Cardiomyopathy/Post-Myocardial Infarction
A study was conducted on 10 post-myocardial-infarction patients and two ischemic cardiomyopathy patients, utilizing 500 mg bark extract every eight hours for three months, along with conventional treatment. Significant reductions in angina, left ventricular ejection fraction, and left ventricular mass were noted in the *Terminalia arjuna* group, whereas the control group taking only conventional drugs had decreased angina only. The two patients with cardiomyopathy improved from NYHA Class III to Class I during the study [23].

10. Dosage and Toxicity
A typical dose of dried bark is 1-3 g/day, while 500 mg bark extract four times per day has been used in congestive heart failure. No toxicity has been documented.

11. Side effects of *Terminalia arjuna*
Terminalia arjuna Roxb. Has been used in the dose of 1-2 g/day in various clinical studies. At this dosage, it is well tolerated and has fewer side effects like mild gastritis, headache and constipation. No haematological, metabolic, renal and hepatic toxicity has been reported even more than 24 months of its administration [24]. *It* has role in contraindicated obesity. It tends to decrease the amount of fat by eliminating it from the body. For this reason, in the case of an obese person, the risk or benefit ratio of the cardiovascular benefits must be evaluated [57].

11. Botanical-Drug interactions
Terminalia arjuna extracts have been used in clinical studies concomitantly with standard heart medications, including digoxin, diuretics, angiotensin-converting-enzyme inhibitors, and vasodilators, with no reported adverse effects. Simultaneous use of Terminalia with other cardiac medications should be undertaken with caution.

12. Conclusion
The *Terminalia arjuna* has been used in traditional medicine for cardiovascular ailments for a long time. Current scientific literature suggests that the benefit of arjuna could be in patients with ischemic heart disease and heart failure. The mechanisms of action are not very clear but some evidence of antioxidant action, inotropic action and hypolipidemic action has been seen. The preclinical and clinical studies published so far are small and from limited centres. Large clinical studies and more mechanistic pre-clinical studies are needed to establish a firm role for arjuna

in current cardiovascular practice.

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14. Conflicts of Interest

The author declare no conflict of interests.

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