Medicinal Properties of Terminalia Arjuna: A Review

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ABSTRACT

Terminalia arjuna, also commonly referred to as T. arjuna, is a deciduous tree that belongs to the family Combretaceae. It can be found in many regions of India. T. arjuna is a 60- to 80-foot-tall tree found alongside rivers and streams all over the Indo-sub-Himalayan areas of Delhi, Uttar Pradesh, Chota Nagpur, the southern part of Bihar, Madhya Pradesh and Deccan regions. It has been used to cure several ailments for as far back as the ancient times of India. It is most prevalently consumed to cure and manage several cardiac and vascular diseases, including those like CADs, Angina Pectoris, CHF/Hypertension, and Dyslipidaemia. Its extracts are used to improve cardiac muscles and thus effectively improve heart pumping, heart rate, and blood pressure. The many parts of the tree consist of several phytochemicals, including tannins, flavonoids, glycosides, and triterpenoids like Arjunolic acid, which contribute to its anti-oxidant anti-inflammatory antimicrobial, anticarcinogenic and antimutagenic properties. As of today, there have not been any reports of any harmful side effects regarding its administration. While there are various studies that support its use for a problem of diseases, further research is still required to understand its exact mechanisms. There is also a need for further research on T. arjuna regarding its drug interactions, its specific molecular mechanism of action, and the toxicology involved.
Keywords: Chemical constituents; medicinal properties; cardiovascular; CAD; angina pectoris; CHF; tannins; flavonoids; triterpenoids arjunolic acid.

1. INTRODUCTION

Plants with therapeutic characteristics have long been utilized to heal ailments for thousands of years. [1]. WHO statistics estimate that approximately 80% of the world's population, including 60% of India's rural population, depend on these therapeutic agents [2]. The demand for herbal medicines has only increased in recent years. Due to their easy accessibility, efficiency, and rare side effects. These medicinal plants contain certain bioactive substances such as alkaloids, tannins, carbohydrates, steroids, terpenoids, phenols, and flavonoids, ensuring certain physiological effects on the body [3].

A variety of medicinal plants have been employed in modern-day healthcare, including:

Table 1. Drugs derived from plants [4]

| Natural Plant Source          | Name of the Drug     |
|------------------------------|----------------------|
| Foxglove                     | Digitalis           |
| Willow Bark                  | Salicylates         |
| Cinchona                     | Quinine             |
| Contaminated Rye             | Ergotamine          |

There are a variety of medicinal plants in India which have been extensively employed in Ayurvedic practices. T. arjuna is one of these plants, and it has proven to be one of the most commonly acknowledged herbal medicines for the treatment of a range of disorders [1].

1.1 T. arjuna: Overview

T. arjuna of the family Combretaceae. Long used as a cardioprotective agent, it was first introduced by Vagabhatta, who advocated its stem bark powder’s use for heart diseases and has since been written in various ancient texts like the Sushruta Samhita, Charaka Samhita, and Ashtang Hridayam. [5].

T. arjuna is a 60- to 80-foot-tall tree found alongside rivers and streams all over the Indo-sub-Himalayan areas of Delhi, Uttar Pradesh, Chola Nagpur, the southern part of Bihar, Madhya Pradesh, and Deccan regions. Aside from being found in various regions of India, it has also been seen in many other countries, including Sri Lanka, Burma as well as Mauritius [6,7]. Although this plant grows on all types of soil, it has shown a preference for red lateric, fertile loam and humid soil.

The tree's bark has a smooth outer surface and an inner striated pinkish surface [8]. During April and May, the bark of this tree sheds away [9].

Fig. 1. The bark of the tree Terminalia arjuna

1.2 Chemical Components of Terminalia arjuna

The learoots roots, fruits, ste, as well as ieeds of T.arjuna, have been used in medical practice due to their different phytoconstituents.

2. TERPENOIDS, URSANE TRITERPENOIDS AND GLYCOSIDES

Triterpenoids are structurally diverse organic compounds which include various varieties, due to modifications in its basic backbone, including ursolic and oleanolic acid [39].

The table above lists a number of terpenoids, ursane triterpenoids, and glycosides isolated from a variety of areas of T. arjuna.

Each type has its own pharmacodynamic effect on the body. Ali et al [24] discovered Terminoside A, an oleanane-type triterpan, from T. arjuna stem bark in a research. The Terminoside A thus extracted exhibited characteristics that prevented the synthesis of nitric oxide. In macrophages stimulated by lipopolysaccharides, it also decreased the quantity of inducible nitric oxide synthase (iNOS or simply iNOS [20,21].
Table 2. Phytochemical components of various sections of *T. arjuna* [1]

| Parts of the tree that were analyzed | Chemical components which are considered important |
|-------------------------------------|--------------------------------------------------|
| Stem Bark                           | **Ursane triterpenoids**                         |
|                                     | 2α,3β-dihydroxyurs-12,18-oic acid 28-O-β-D-glucopyranosyl ester [10] |
|                                     | Kajiichigoside F1                                |
|                                     | 2α,3β,23-trihydroxyurs-12,18-dien-28-oic acid 28-O-β-D-glucopyranosyl ester Qudranoside VIII |
|                                     | 2α,3β,23-trihydroxyurs-23-trihydroxyurs-12,19-dien-28-oic acid 28-O-β-D-glucopyranosyl ester  |
|                                     | **Triterpenoids**                                |
|                                     | Arjunin [11]                                    |
|                                     | Arjunic acid                                    |
|                                     | Arjungenin [12-14]                              |
|                                     | Terminic acid [15]                              |
|                                     | Arjunolic acid [13,14]                           |
|                                     | Terminoltin [16]                                |
|                                     | **Flavonoids and Phenolics**                    |
|                                     | Arjunone [17]                                   |
|                                     | Luteolin [18]                                   |
|                                     | Baicalein [19]                                  |
|                                     | Ethyl gallate                                   |
|                                     | Kempferol                                       |
|                                     | Gallic acid                                     |
|                                     | Pelargonidin                                    |
|                                     | Oligomeric proanthocyanidins                    |
|                                     | Quercetin                                       |
|                                     | Gallic acid, ellagic acid and its derivatives such as 3-O-methyl-ellagic acid 4-O-β-D-xylopyranoside, 3-O-methyl ellagic acid 3-O-rhamnoside  |
|                                     | (+)-catechin, (+)-gallocatechin and (−)-epigallocatechin [20]  |
|                                     | 3-O-methyl ellagic acid 4′-O-α-L-rhamnophranoside |
|                                     | (−)-epicatechin [10]                             |
|                                     | **Glycosides**                                  |
|                                     | Arjunetin [11,21,13,14]                         |
|                                     | Arjunolone [17]                                 |
|                                     | Arjunoside I, II [12,22]                        |
|                                     | Arjunaphthanoloside [23,24]                     |
|                                     | Arjunolitin [25]                                |
|                                     | Arjunasides A-E, Arjunglucoside IV and V [25,26]|
|                                     | Terminarjunoside I and II [27]                  |
|                                     | Olean-3β, 22β-diol-12-en-28 β-D-glucopyranosie-oic acid [28] |
|                                     | Terminoside A [29]                              |
|                                     | Termionic acid                                  |
|                                     | **Trace elements along with Minerals**          |
|                                     | Magnesium, Calcium, aluminium, silica, zinc, copper [30] |
|                                     | **Tannins**                                     |
|                                     | Pyrocatechols [31]                              |
|                                     | Castalagin [32]                                 |
|                                     | Punicalin [33]                                  |
|                                     | Casuarin                                        |
|                                     | Casuarinin                                     |
|                                     | Punicalagin                                    |
|                                     | Terflavin C                                    |

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### Parts of the tree that were analyzed

| Chemical components which are considered important |
|---------------------------------------------------|
| Terchebulin                                        |
| **Other compounds**                                |
| β-Sitosterol [15]                                  |
| **Glycosides**                                     |
| Arjunetosie (3-O-β-D-glucopyranosyl-2α, 3β, 19α-trihydroxyolean-12-en-28-oic acid 28-O-β-D-glucopyranoside) [34] |
| **Triterpenoids**                                  |
| Arjunoside I-IV [35]                               |
| Oleanolic acid                                    |
| Arjunolic acid [15]                                |
| 2α,19α-Dihydroxy-3Oxo-Olean-12-En28-Olic acid 28-O-β-D-glucopyranoside [36] |
| Terminic acid                                     |
| Arjunic acid [13,14]                               |
| **Glycosides and Flavonoids**                     |
| Luteolin, 14,16-dianhydrogitoxigenin 3-β-D-xylpyranosyl- (1 > 2)-O-β-D-galactopyranoside [18,37] |
| **Flavonoids and Triterpenoids**                   |
| Hentriacontane, Arjunic acid, Ellagic acid, Arjunone, Eridelin, Methyl oleaolate, Gallic acid, Cerasidin, Myristyl oleate, β-Sitisterol, Arachidic stearate [38] |

### 3. FLAVONOIDS ALONG WITH PHENOLICS

From a medicinal point of view, *T. arjuna*’s bark is perhaps the most significant portion of *T. arjuna*’s bark is regarded the most important part of the plant. The bark contains a variety of flavonoids such as flavones, arjunolones, kempferol, baicalein, pelargonidin and quercetin. Because of an inverse link between high dietary flavonoid consumption and the development of ischemic heart diseases (CADs), these flavonoids are particularly useful for treating cardiovascular disorders [1].

Luteolin, a molecule isolated from the butanolic fraction, exhibits antimutagenic properties [1]. It also has a very efficient antibacterial property as it inhibits gram negative pathogenic growth with the minimum inhibitory concentration of 12.5μg/disc.

Other actions of these bioflavonoids include inhibition of oxidation of LDL molecules, activation of endothelium and aggregation of platelets [1,40-43].

The phenolic content contributes to a free radical scavenging action which makes *T. arjuna* a strong agent against proliferation and oxidation [1,44].

### Tannins: Tannins are polyphenols that are water soluble and may be found in a range of plant components. Tannins possess a variety of properties. One such property is that it is an anticarcinogen along with tea polyphenols. It also has an anti-mutagenic property as well as an anti-oxidant property. There three properties are interrelated as oxygen-free radicals are produced by a variety of carcinogens and mutagens. which these tannins ultimately decrease for protecting cellular oxidative cellular damage.

Another important property of tannins is its antimicrobial activity. Studies have shown that Yeasts, fungi, bacteria, and viruses have all been found to be inhibited by tannins.

Tannins also aid in the clotting of blood, the reduction of blood pressure, the reduction of serum cholesterol levels, the production of liver necrosis, and the modulation of immune responses [45].

### 4. PHARMACOLOGICAL ACTIVITIES OF *Terminalia arjuna*

Even though each part of *T. arjuna* has its own pharmacological effects on the body due to their varying composition, the bark of the tree is regarded to the most clinically relevant.
The bark has been shown to have astringent, expectorant, demulcent, cardiotonic, anti-
dysenteric, styptic and urinary astringent effects, as well as being beneficial in the management of
cirrhosis, anaemia, leukorrhea, fractures, cardiomyopathy, diabetes and ulcers [8,46].

Chakradatta introduced an ulcer wash made from an infusion of the bark prepared using milk
and perhaps even ghee/butter in Ancient India. The ashes of the bark was employed for the
management of snakebites and scorpion stings [47].

It has been used in many forms throughout India for a variety of conditions. *T. arjuna*'s bark is
boiled in water and breathed in which then alleviates headaches and eliminate worms in the
teeth in the Kancheepuram District of Kerala. They also use its fruit's paste as a topical agent
on wounds [48]. The bark powder is mixed with rice water by tribals in the Sundargarh District of
Odisha to treat haematuria (there is blood in the urine [49].

A more detailed analysis of the same on the basis of clinical trials and experiments has been
tabulated below.

| Pharmacological activity | Chemical Constituents Responsible | Supporting Clinical Trial/Experiment | Observation in the concerned clinical trial/experiment |
|--------------------------|-----------------------------------|-------------------------------------|--------------------------------------------------------|
| Antioxidant, anti-
inflammatory and
immunomodulator | Arjunic acid, arjunetin and arjungenin | Varghese et al. [50] | The enzymes were shown to have strong non-competitive inhibitory and reversible action in both of *T. arjuna*'s aqueous and alcoholic extracts. The enzymes concerned are CYP344, CYP2D6 and CYP2C9 present in the human liver microsomes [1]. |
| Antioxidant | Oleanane triterpenoids | Pawar and Bhutani [54] | The process of respiratory oxburst is modestly inhibited by Arjungenin. Its IC50 results to be 60 μg/ml [1] |
| Antioxidant activity | Butanolic fraction of *Terminalia arjuna* bark [52] | Singh et al [52] | The butanolic component of *T. arjuna*’s bark’s alcoholic extract shows cardioprotective activity in a patient with Doxorubicin-induced cardiotoxicity. |
| Antioxidant and antimitogenic activity | Alcoholic extract of *Terminalia arjuna* stem bark (ALTA) | Viswanatha et al [53] | In the DPPH assay, liquid peroxidation assay and superoxide radical scavenging activity, the alcoholic extract of *T. arjuna* showed significant antioxidant activity with EC50 values of 2.491 ± 0.160, 71.000 ± 0.025, and 50.110 ± 0.150 respectively. In the micronucleus test, EC50 values of 2.410 ± 0.140, 40.500 ± 0.390, and 63.000 ± 0.360 in percentage of micronucleus in *T. arjuna*’s alcoholic extract (100 and 200 mg/kg p.o) resulted in significant reductions in both the normochromatic and polychromatic erythrocytes, as well as quite a decrease in the P/N ratio [1] |
| Potential to be antimitogenic and anticarcinogenic | *Terminalia arjuna* bark has substantial flavonoids and tannins. | Ahmad et al [54] | *T. arjuna* extracts were shown to be effective in reducing metaphase abnormalities. In vitro, the frequency of sister chromatid exchanges was decreased, but the replication index rose. Clastogeny was reduced in the |
| Pharmacological activity                  | Chemical Constituents Responsible | Supporting Clinical Trial/Experiment | Observation in the concerned clinical trial/experiment |
|------------------------------------------|----------------------------------|-------------------------------------|--------------------------------------------------------|
| Anti-oxidant and antimicrobial activity  | Terminalia arjuna bark’s Methanolic extract | Mandal et al. [55]                  | T. arjuna's methanolic extracts have potent antibacterial activity as well as scavenging of free radicals. It is a potent antibacterial agent against K. pneumonia and E. coli (gram-negative bacteria). These properties are because of the flavonoid compounds in T. arjuna [56]. |
| Antimicrobial activity                   | Terminalia arjuna leaf extract (acetonic) and bark extract (aqueous [7]) | Aneja et al. [57]                   | The aqueous extract resulted in being an efficient antimicrobial against S. aureus bacteria [58] However, the acetone extract of the leaf extract of T. arjuna was seen to have the most potent antimicrobial agent against S. aureus [1]. The organic extracts were shown to be highly efficient against the proliferation of gram-negative bacteria, with the exception of P. aeruginosa. |
| Cardio-protective potential             | Terminalia arjuna bark powder which was used for 12 weeks before ischemic-reperfusion injury [1] | Gauthaman et al [59].              | Myocardial endogenous antioxidants were boosted following chronic oral treatment of T. arjuna bark in rabbits. It also induces HSP-72 (Inducible Heat Shock Protein 72). The prevents myocardial ischemic reperfusion injuries due to protection against oxidative stress. |
| Anticarcinogenic potential              | Terminalia arjuna’s ethanolic and aqueous extracts | Oberoi et al. [60]                 | T. arjuna’s aqueous extracts enhances sarcoplasmic reticular function and thus induces cardiotonic action. Arrhythmias are less likely to arise as a result of this. As a result, T. arjuna’s aqueous extract is seems as a safe cardiotonic that is good to heart health and may be used in conjunction with chronic health-care treatment programmes [1] |
| Free radical scavenging and DNA damage protection | Terminalia arjuna bark’s ethanolic extract along with its fractions | Phani Kumar et al. [61]           | T. arjuna bark’s ethanolic extract (together with its components) protect against hydrogen peroxide-induced DNA damage [62] The ethyl acetate fraction has especially been effective in maximally inhibiting DPPH, ABTS, metal chelation, hydroxyl and nitric oxide radicals. T. arjuna extracts have also been demonstrated to ameliorate a variety of impairments related to free radical production and DNA damage. |
Pharmacological activity | Chemical Constituents Responsible | Supporting Clinical Trial/Experiment | Observation in the concerned clinical trial/experiment
--- | --- | --- | ---
Gastro-productive effect | Methanolic extract of *Terminalia arjuna* | Devi et al. [63] | Two groups of ulcer-induced animals were studied. One group received Diclofenac Sodium (DIC) and *T. arjuna*, whereas the other received simply Diclofenac Sodium. In comparison to merely providing DIC, the DIC + *T. arjuna* treatment plan demonstrated a considerable reduction in the lesion index [64]. *T. arjuna*'s gastroprotective effect was validated by other histological research.

5. CARDIOVASCULAR ROLE OF *T. arjuna*

The bark stem of *T. arjuna* has inotropic, chronotopic and diuretic properties [7]. Experiments on animals revealed an augmentation in coronary blood flow, which increased the force of cardiac muscle contraction, resulting in a drop in blood pressure along with heart rate as well as bradycardia with accordance with the dose administered [65,66,67,7].

Research done on rats found that pretreatment with atropine reduced the hypotensive effect of *T. arjuna* with a fraction containing tannin-related chemicals isolated from the aqueous extract. Pretreatment of the rats with propranolol had no impact, suggesting that the hypotensive effect was related to cholinergic processes [31].

In myocardial infarction which is induced by isoprenaline, *T. arjuna* exhibited PGE2 like activity in the heart by producing vasodilatation and hypotension [5]. *T. arjuna*'s bark extract reduced the oxidative stress which upsurged on induction by isoprenaline and reduced the amount of natural antioxidants in the body [5].

One of the triterpenoids found in *T. arjuna*, Arjunolic acid, prevents the decline of superoxide dismutase, glutathione peroxidase, catalase, alpha-tocopherol, ceruloplasmin, ascorbic acid, reduced glutathione (GSH), MPO (myeloperoxidase) and lipid peroxide levels, implying that Arjunolic acid's cardioprotection by Arjunolic acid is most likely due to protection against damage to heart via myocardial necrosis [68]. Another study found that arjunolic acid had cardioprotective properties through boosting the body's natural antioxidant defences [69].

Animal experiments showed that the *T. arjuna* bark, when administered in various forms, was capable of reducing total cholesterol (TC) and triglyceride (TG) levels [5,70,71,72,73].

When compared to the other fractions of *T. arjuna* bark, the ethanolic fraction has powerful antioxidant and hypolipidemic effects [74,75]. The down regulation of lipogenic enzymes, the enhances hepatic clearance of cholesterol and inhibition of HMG-CoA reductase are likely to be responsible for the hypolipidemic effect [76].

Angina Pectoris: A study was undertaken where the sample size of 30 patients suffering from stable angina were administered with 500 mg of *T. arjuna* bark extract three times a day. The bark's anti-ischemic activity was proven by a considerable reduction in the serum cholesterol levels, systolic blood pressure, plasma cortisol and the mean anginal frequency. There was also an improvement in the ECG changes [5,77].

Chf/ Hypertension: A study was undertaken where the sample size of 10 patients suffering from Congestive Heart Failure (CHF) were given 4g of *T. arjuna* bark powder twice a day for a month as part of a research. With considerable diuresis, there was enhancement seen with dyspnea, functional class, and general well-being. Both the systolic as well as the diastolic blood pressures dropped significantly [78].

6. TOXICITY AND SIDE EFFECTS OF *Terminalia arjuna*

Most traditional and herbal medicines like *T. arjuna* are known for producing the least amount of side effects, hence their popularity. No cases of *T. arjuna* toxicity have been documented [19].
*T. arjuna* is most widely used for the cure and control of coronary artery disorders (CAD), with an ideal dose of 1-2 g per day, and 500 mg of the bark extract three times per day for congestive heart failure. The side effects reported in this treatment are rather minor like headaches, mild gastritis and constipation. After more than 2 years of this drug administration, there were no signs of haematological, hepatic, metabolic and renal toxicity [77,79].

A study reported that there was a reduction in thyroid hormone concentration in euthyroid animals and an increase in hepatic LPO (Lipid Peroxidation) upon the administration of *T. arjuna*. Therefore, care must be taken when consuming this plant extract as it carrier a risk of development of hypothyroidism and hepatotoxicity [80-85].

7. CONCLUSION

*T. arjuna*, a tree seen all around India, is being utilised for hundreds of years for curing a conundrum of ailments, but more importantly for cardiac health. Its active constituents include tannins, triterpenoids, flavonoids and certain minerals like calcium, magnesium, zinc and copper.

Its extracts are used for the improvement of cardiac muscles, effectively improving heart pumping, heart rate and blood pressure.

*Terminalia arjuna* can be administered in a variety of conditions such as Angina Pectoris, Congestive Heart Failure, Cardiomyopathy or Post Myocardial Infarction and Hyperlipidemia.

While there are various studies which support their application in clinical practice, such studies lack the standardisation of extract to be used, well conducted studies for long term effects and the bioavailability of the drug.

There is also a need for further research on *T. arjuna* regarding its drug interactions, its specific molecular mechanism of action as well as toxicology.

NOTE

The study highlights the efficacy of "herbal, ayurvedic,traditional" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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