Review Article

Medicinal Properties of Terminalia Arjuna: A Review

ABSTRACT

Terminalia arjuna, which is also commonly referred to as *T. arjuna*, is a deciduous tree which 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, southern part of Bihar, Madhya Pradesh and Deccan regions. It is used to cure several ailments for as far back as the ancient times of India. It is most prevalently consumed for the cure and the management of several cardiac and vascular diseases including those like CADs, Angina Pectoris, CHF/Hypertension and Dyslipidaemia. Its extracts are used for the improvement of cardiac muscles and thus it effectively improves heart pumping, heart rate and blood pressure. The many parts of the tree consist of several phytochemicals including tannins, flavonoids, glycosides as well as triterpenoids like Arjunolic acid which contribute to its anti-oxidant, anti-inflammatory, antimicrobial, anticarcinogenic and antimutagenic properties. As of today, there have not been much reports of any harmful side effects with regards to its administration. While there are various studies which support its use for a conundrum of diseases, there is still further research which is still required for the understanding of its exact mechanisms. There is also a need for further research on *T. arjuna* regarding its drug interactions, its specific molecular mechanism of action as well as the toxicology involved.

Keywords: Chemical constituents, Medicinal Properties, Cardiovascular, CAD, Angina Pectoris, CHF, Tannins, Flavonoids, Triterpenoids, Arjunolic Acid

Comment [R11]: Be direct in the summary. Avoid the use of subjective terms such as several, just put the direct idea in the text.

Do not include in the keywords more than six simple or compound words.

INTRODUCTION

Plants with therapeutic characteristics have long been utilised to heal ailments, dating back to thousands of years.. (1) WHO statistics estimate that approximately 80% population of the world, including 60% of the rural population of India, 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 which ensure certain physiological effects on the body.(3)

Comment [R12]: Check punctuation and spaces throughout the text.

Comment [R13]: Avoid using these terms. Write directly.

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

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

Table 1: Drugs derived from plants (4)

Comment [R14]: Put the botanical families to which they belong and some examples of the plants used. Don't just briefly mention this.

Comment [R15]: In a third column, put the bibliographic citation from which the information was extracted.

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)

T. ARJUNA : OVERVIEW

T. arjuna of the family Combretaceae. Long used as an 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, Chota Nagpur, southern part of Bihar, Madhya

Pradesh and Deccan regions. Aside from being found in various regionsof 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 bark of the tree has an outer smooth surface and an inner striated pinkish surface.(8) During the months of April and May, the bark of this tree sheds away. (9)

Comment [R16]: First, describe the botanical characteristics of the species, its geospatial distribution and its edaphoclimatic preferences, then highlight the medicinal benefits of the plant.

Figure 1: The bark of the tree *Terminalia arjuna*

Comment [R17]: Include a photo of the complete tree, leaves, fruits, branches and bark. The idea is that the individual is seen in its entirety and can be identified by the reader.

CHEMICAL COMPONENTS OF *TERMINALIA* ARJUNA

The leaves, root, fruits, stem/bark as well as its seeds of *T.arjuna* have been used in medical practice due to their different phytoconstituents.

Table 2: Phytochemical components of various sections of *T.arjuna*. (1)

Comment [R18]: It is a table that takes up a lot of space in the text, so it is suggested to put the information in paragraphs.

Comment [R19]: The bibliographic citation of each reference from which the information described in this table was obtained must be included.

Parts of the tree which were analysed	**Chemical components which are considered important**
Stem Bark	**Ursane triterpenoids**
	2α,3β-dihydroyurs-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-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) (13) (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)
	Punicallin (33)
	Casuariin
	Casuarinin
	Punicalagin
	Terflavin C
	Terchebulin
	Other compounds
	β-Sitosterol (15)
Roots	**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)
Seeds and Leaves	**Glycosides and Flavonoids**
	Luteolin, 14,16-dianhydrogitoxigenin 3-β-D-xylopyranosyl-(1 > 2)-O-β-D-galactopyranoside (18) (37)
Fruits	**Flavonoids and Triterpenoids**
	Hentriacontane, Arjunic acid, Ellagic acid, Arjunone, Eridelin, Methyl oleaolate, Gallic acid, Cerasidin, Myristyl oleate, β-Sitisterol, Arachidic stearate (38)

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 triterpane, 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)

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) (41) (42) (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)

Comment [R110]: In addition to describing each of them, successful cases should be included of how the aforementioned contributed efficiently to cure or eliminate discomfort. Even not using a general wording, if not when talking about tannins and saying they help coagulation, mention how specifically those of this plant contribute to an improvement.

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)

Comment [R111]: For all this information, it is suggested to use more than two or three citations, since we are talking about an aspect of health and practical applicability in rural areas and it should be justified in a robust and forceful way.

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

Table 3: *Terminalia arjuna* – Pharmacological activities (1)

Pharmacological activity	**Chemical Constituents Responsible**	**Supporting Clinical Trial/Experiment**	**Observation in the concerned clinical trial/experiment**
Antioxidant, anti-inflammatory and immunomodulatory	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 (51)	The process of respiratory oxburst is modestly inhibited by Arjungenin. Its IC50 results to be 60 µg/ml.(1)

Antioxidant activity	Butanolic fraction of *Teminalia 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 antimutagenic 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 antimutagenic 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 mutagen-treated positive control and aberrant cell frequencies were

			reduced in the in vivo trials.
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 scanvenging 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	*Terminalia*	Oberoi et al (60)	*T. arjuna*'s aqueous extracts

potential	*arjuna*'s ethanolic and 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.
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.

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)

Comment [R112]: Be careful in the conclusions of these studies, since if they have not been applied in humans, it is very risky to base a publication of these on the results obtained.

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)

Comment [R113]: Not only can the review be based on a single case study, it is recommended to discuss at least three of each of them and draw conclusions from further research.

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)

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.

Comment [R114]: Excellent

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