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# AYURVEDIC AND MODERN ASPECTS OF *ARJUNA* (TERMINALIA ARJUNA ROXB): AN OVERVIEW

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## ABSTRACT

To cure human diseases, medicinal plants have been a major source of therapeutic agents since ancient time. *Terminalia arjuna* is one kind of widely used medicinal plant throughout India and used in various indigenous system of medicine like Ayurveda, Siddha and Unani.Arjuna (*Terminalia arjuna* Roxb) tree belonging to family Combretaceae is widely distributed throughout India. In Ayurvedic classics it is regarded as a *hridya* drug (cardiotonic drugs i.e. drugs having beneficial action on the heart). Its stem bark contains glycosides, large quantities of flavonoids, tannins and minerals. *Arjuna* is recorded to possess antioxidant, anti-inflammatory antimicrobial, antibacterial, antifungal, insecticidal, antihelmintic, immunomodulatory, antidiabetic, radioprotective, antimutagenic and lipid lowering effects while glycosides are cardiotonic, thus making Arjuna unique amongst currently used medicinal plants. In this review an attempt has been made to highlight an ayurvedic aspect as well as its phytochemical and pharmacological activities. This article spreads a hopeful array for the researchers to explore it at molecular level and pharmaceutical industries to develop a new product.

**KEYWORDS:** Terminalia arjuna, Arjuna, phytochemical, pharmacological, cardiotonic.

## INTRODUCTION

In India, medicinal plants form the backbone of several indigenous traditional systems of medicine.[1] *Terminalia arjuna* is a miracle herb which was used during ancient times to cure heart problems. *Terminalia arjuna* Wight & Arn. Is popularly known as arjuna.[2]

Terminalia arjuna Roxb effect can prove in number of herat diseases. Mostly found in the Himalayan region, the bark of Arjuna plant is used as traditional Indian medicine for a number of herbal preparations to treat cardiac disorders. *Terminalia arjuna* Roxb is a tree having simple leaf, smooth and thick bark belonging to the Combretaceae family. Flowers are small, regular, sessile, cup-shaped, polygamous, white, creamy or greenish-white and robustly honey-scented and flowering from April to July. The inflorescences are tiny axillary spikes or small terminal panicles, the fruits are obovoid-oblong, dark brown to reddish brown fibrous woody, indehiscent drupe and ripening from February to May.[3] All the parts of the Arjuna have been used for their therapeutic beneficiary effect. *Terminalia arjuna* helpful to maintain healthy heart and reduce the effects of hassle and nervousness.[4] It has antibacterial[5], antimutagenic, hypolipidemic, antioxidant and hypocholesterolaemic and antiinflammatory effects. *Terminalia arjuna* have the ability to protect the liver and kidney tissues against CCl4induced oxidative stress by increasing antioxidative defense activities.[6] Different types of bioactive compound have been isolated from this medicinal plant possesses enormous value in medicine among then arjunolic acid is very well known. The plant parts *T. arjuna* are used in indigenous system of medicine for different ailments. The bark powder has been invent to possess anti-ischemic, antioxidant action, cardioprotective properties[7], hypercholesterolemia effect[8], fungicidal and antibacterial[9], antimicrobial[10], Anti-inflammatory, immunomodulatory and antinociceptive activity[11], *Arjuna* also useful to treat obesity, hypertension and hyperglycemia.[12] The higher antioxidant potential of T. arjuna stem bark is due to the presence of higher amount of phenolic and flavonoids[13]. The *Terminalia arjuna* is one of the best heart tonic[14] therefore, it can be used daily as tonic for healthy cardiovascular system.

**Ayurvedic Aspect**

1. **Charka samhita:** Kashayskandh(bitter taste), *Udardaprashman*, *mahakashya*[15]
2. **Sushrut samhita** :*Nyagrodhadi, Salsaradi*[16]
3. **Ashtang hridaya** :*Nyagrodhadi, Salsaradi*[17]
4. **Bhavprakash nighantu**:*Vatadi varg*[18]
5. **Dhanvantari nighantu :***Amradi varga*[19]
6. **Kaiyedev nighantu:***Aushadadi Nighantu*[20]
7. **Raj nighantu:***Prabhadhadri varga*[21]

**Vernacular Names**[18]

***Hindi***- *Arjun, Arjuna, Koha, Kahu, Arjan.*

***Gujrati***- *Arjun - Sadada, Sadado.*

***Marathi***- *Arjuna, Arjun Sadada, Sadura.*

***Sanskrit***- *Arjuna, Dhanvi, Indradruma, Kakubha, Karvirak..*

***Oriya***- *Arjuna Sahajo.*

***Tamil***- *Vellamatta.*

***Telugu***- *Yerramaddi.*

***Assam***- *Orj un*

*;**Bengali**-Arjhan.*

***Punjabi***- *Arjuna*

**Habitat**[22]

It is found in *Himalay*, *Bangal*, *Bihar*, Mostly found in Madhya Pradesh,

***Raspanchaka of Arjuna***[23]

*Rasa -Kashaya*

*Guna-Laghu, Ruksha*

*Virya-Shita (Cold)*

*Vipaka –Katu*

*Prabhav-Hrudya*

*Doshganata-kaphapittashamaka*

**Morphology**[243,25]

**Bark** -of *Terminalia arjuna* is simple, grey and smooth on external surface and it is thick, soft and of red color from inside.

**Leaves**-*Terminalia arjuna* Leaves are like *Guava* leaves, they are oblonged, (4-6 inch) long and (2-3 inch) wide, subopposite, glabrous and often inequilateral. There are two glands present near the base of the petiole. The base is rounded or cordate.

**Flowers**- *Terminalia arjuna* flower white or yellowish color flowers are found in groups. Flowering of *Terminalia arjuna* occurs in summer and fruits appear in winter or spring season.

**Fruits-** Fruit is drupe and is often notched near the top, marked with oblique upward curving striations. The fruits are (1-1.5) inch in diameter and with 5-7 longitudinal lobes. These are glabrous with five to seven wings, woody and fibrous.

**Useful parts**[26]

Bark

**Modern aspect**

Taxonomical Classification[27]

Kingdom-Plantae

Division-Magnoliophyta

Class-Magnoliopsida

Order-Myrtales

Family-Combretaceae

Genus-Terminalia

Species-*T. arjuna*

English Name-White Marudah

**Chemical Composition**[28]

*Terminalia arjuna* contains phenols, flavonoids, tannin, saponin, alkaloids, glycosides, phytosterols and carbohydrate, Arjunetin, Fridelin.

**Pharmacognostical studies**[29]

**Macroscopic-***Terminalia arjuna* Bark available in pieces, flat, curved, recurved, channelled to half quilled, 0.2-1.5 cm thick, market samples upto 10 cm in length and upto 7 cm in width. The outer surface of *Terminalia arjuna* is smooth and grey and inner surface is fibrous and pinkish, transversely cut smoothened bark shows pinkish surface, short in inner and laminated in outer part; taste, bitter and astringent.

**Microscopic-**Stem Bark of *Terminalia arjuna* Mature bark shows cork consisting of 9-10 layers of tangentially elongated cells, a few outer layers filled with brown colouring matter; cork cambium and secondary cortex not distinct and medullary rays observed traversing almost upto outer bark; secondary phloem occupies a wide zone, consisting of sieve tubes, companion cells, phloem parenchyma and phloem fibres, traversed by phloem rays, usually uniseriate but biseriate rays also occasionally seen; in the middle and outer phloem region,

sieve tubes get collapsed and form ceratenchyma; phloem fibres distributed in rows and present in groups of 2-10; rosette crystals of calcium oxalate measuring 80-180 17µ in dia., present in most of the phloem parenchyma, alternating with fibres; idioblasts consisting of large cells having aggregates of prismatic and rhomboidal crystals of calcium oxalate in row throughout the zone, measuring 260-600 µ in dia., starch grains, mostly simple, compound of 2-3 components, sometimes upto 5 components, round to oval, elliptical, measuring 5-13 µ in dia., distributed throughout the tissue (absent in T. alata); in a tangential section the uniseriate phloem rays 2-10 cells high and biseriate, 4-12 cells high; in longitudinal section rosette crystals of calcium oxalate found in the form of strands in phloem parenchyma.

**Powder** - Reddish-brown colour; shows fragments of cork cells, uniseriate phloem rays, fibres, a number of rosette crystals of calcium oxalate, a few rhomboidal crystals, starch grains simple and compound, round to oval, elliptic, having 2-3 components with concentric striations and small narrow hilum, measuring 5-13 µ in diameter.

**IDENTITY, PURITY AND STRENGTH**

Foreign matter Not more than 2 per cent, Appendix 2.2.2.

Total Ash Not more than 25 per cent, Appendix 2.2.3.

Acid-insoluble ash Not more than 1per cent, Appendix 2.2.4.

Alcohol-soluble extractive Not less than 20 per cent, Appendix 2.2.6.

Water-soluble extractive Not less than 20 per cent, Appendix 2.2.7.

**Traditional uses**

Following conditions in which Arjuna is extremely beneficial.

Cardio modulator

Blood pressure

Hypo lipedimia

Hyper lipidemia

Hypercholesterolemia.

Reduces stress

Liver tonic

Urinary tract toner

Arjuna is very helpful in treating various health related problems. Below are actions of Arjuna as per the body's organ system.[30-33]

**MEDICINAL USES**[34]

Terminaliaarjuna is a wide spread medicinal plant. The different parts of *Terminalia arjuna* like bark, leaves and fruits etc., Have different medicinal values and are used to cure various diseases. The bark is the main part used in ayurveda as well as in Allopathy for curing various diseases. The bark of arjuna tree contains calcium salts, magnesium salts and glucosides have been used in traditional ayurvedic herbalism According to vagbhata, *Terminalia* bark is cooling, kaphapitta, pacifying, cardiac restorative and help in healing wounds, tuberculosis and poisoning. Chakradatta advised to take it by processing in milk for cardiacdis orders alone or with panchamula.

**Arjun for cardiac support**[35]

In Ayurveda, bark powder is used as cardio protective and it is known as a tonic to heart diseases. Its ksheerpaka is highly effective to normalize high blood pressure and in many rural areas.

Cardiomyopathy like myocardial infraction, Angina, coronaryartery diseases, heart failure, hyper cholesterolemia, and hyper tension are cured by arjuna bark powder.

Used as anischemic and cardio protective agent in hyper tension and ischemic heart diseases.

Arjuna improves pumping capacity of heart by strengthening muscles and vascular system and also be useful in treating excess of cholesterol in blood (Gupta et al., 1). The anticoagulant and antiplatelet aggregation action of arjuna keeps the blood thin and lowers the bad cholesterol while in creasing the good cholesterol.

In high blood pressure it helps to regulate disturbed rhythms and regulate the heart beat rate.

Arjuna reduces the effect of stress and nervousness on the heart. It provides significant cardiac protection in heart attack.

Al though many ayurvedic plants have shown to help coronaryartery diseases, Arjuna by far seems to be the best plant for heart health.

**Other medicinal uses**[36]

It works as a won der fulantioxidant so it helps in stopping earlyaging and help in maintaining youth.

Arjuna is very effective in tubercular cough by stopping blood in cough and healing the ruptured arteries in lungs.

Arjuna maintains normal urine flow and help in suppressing painful maturation.

Bark powder of arjuna has diuretic properties that curecirrhosis 3Bark powder is also used in the treatment of gonorrhea, and spermatorrhoea.

Hot in fusion of powder of bark is used to treat Asthma and also works well in Acne when applied as a paste mixed with honey.

Bark paste is applied for bone bandage in fractures.

Arjuna is effective in tubercular cough by stopping blood in cough and healing the ruptured arteries in lungs.

Arjuna is diuretic taken to flush out the small stones formed in the kidneys. If bark is boiled in water and taken as a drink it is known to break the kidney stones into smaller pieces and expel out of the body.

Terminaliaarjuna reversing the damage by chronic smoking. Smoking causes endo the lialdys function an early event of Antherosclerosis. It is me diated through mainly oxidative stress process. Two weeks of therapy with this medicinal herb leads to reversal of impaired function in endo the lium of smokers.

Juice of leaves is used in earache (otalgia).
Leaves are used to cureulcers and soresexter nally.

**Cardiotonic activities**

In ayurvedic medicine arjunolic acid is used as a cardiac tonic for centuries and it has been first identify from Terminalia Arjuna. The bark extracts have wide component triterpenoid saponin is an arjunolic acid.[37] Physico reported carried on the experimental rabbit and frog heart exposed that Terminalia Arjuna bark had cardiotonic.[38] It was consequently reported that intravenous administration of the glycoside, formation from the bark of Terminalia Arjuna, resulted in rise in blood pressure.[39] It was showed that the bark powder has a cardiotonic property and diuretic. The analytical reported to isolated frog heart exposed that the water base extract of the bark had chronotropic and inotropic activities. The aqueous

extract of the bark is identified from rat atria that resulted positive inotropic.[40] Water base extract of the bark was identify from rat atria that was again resulted in consequent work where produced inotropic action which was showing by propanolol and cocaine[41]. The new element16, 17-Dihydroneridienone, 3-O-β-D-glucopyranosyl-(1-6)-O-β-D-galactopyranoside is identify from arjuna root and applicable as a cardiotonic.[42]

**Coronary flow**

Analysis form bark to inject aqueous extract into isolated rabbit heart to maximum in coronary flow. The dose was 1024 µg/ml that causes highest increase in coronary flow.[43]

**Hypotensive effects**

The analysis of injection of alcoholic and aqueous extract into intravertebral and intracerebro-ventricular extract of bark that was dose-dependent persistent bradycardia and hypoten- sion. Although the alcoholic extract show the hypotensive effect in dogs was obtain by pre-treatment with atropine. In another way tested in dogs where intravenous induce of aqueous extract of Terminalia Arjuna resulted in dose-addict falls in blood pressure.[44]

**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.[45] 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.[46] The cardioprotective effect of the active phytoconstituents of arjuna bark against carbon tetrachloride and sodium fl uoride 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.[47,48]

In a recent study, the methanol extract yielded the highest phenolic and fl avonoid 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.[49] In another study, both alcoholic and aqueous extracts of the bark attenuated H2O2-mediated reactive oxygen species generation in human monocytic cells by promoting catalase and glutathione peroxidase (GPO) activities and by sustaining cellular

reducing power. Moreover, the extracts inhibited lipid peroxidation (LPO) and 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase, but had no effect on lipoprotein lipase.[50] In isoprenaline-induced myocardial ischemia (MI), arjuna has been found to possess prostaglandin E2-like activity with coronary vasodilatation and hypotension.[51] The bark extract has shown to signifi cantly prevent isoprenaline-induced increase in oxidative stress and decline in endogenous antioxidant level. Arjunolic acid has been found to prevent the decrease in the levels of superoxide dismutase, catalase, GPO, ceruloplasmin, α-tocopherol, reduced glutathione, ascorbic acid, lipid peroxide, and myeloperoxidase.[52] Further, the bark extract has also shown protective effects against doxorubicin-induced DNA damage and cardiotoxicity.[53,54] Kumar et al. demonstrated that arjuna protects the heart against myocardial changes induced by chronic β-adrenoceptor stimulation.[55] Substantiating this, in a recent experiment, the bark extract signifi cantly attenuated cardiac dysfunction and myocardial injury in rats with congestive heart failure (CHF). Cardioprotective action of arjuna was comparable to fl uvastatin. Arjuna bark extract has a signifi cant prophylactic and therapeutic benefi cial effect in protecting heart against catecholamine-induced CHF, possibly through maintaining endogenous antioxidant enzyme activities and inhibiting LPO and cytokine levels. Recently, Mythili et al. confi rmed the earlier fi ndings that triterpenoids derived from arjuna extract containing arjunolic acid show cardioprotective activity by boosting endogenous antioxidant defense system.[57]

**Antidiabetic activity**

The Terminalia Arjuna extracts have ability to action on diabetic. In the scientifically analysis diabetic rats model treated with Terminalia Arjuna extracts showed two enzymes (glucose-6-phosphatase, fructose-1, 6- diphosphatase) much reduced in liver and kidney. They have an ability to increase insulin secretion which can react on repression of the gluconeogenic key enzymes (glucokinase and phosphofructokinase).[58] Terminalia arjun bark extract exposed antidiabetic activity by value the outermost utilization of glucose which has the ability to kidney glycolysis and repairing the impaired liver and by decreasing its gluconeogenic generation as like as insulin. The tannin, saponin, flavonoids and other constituent's presence in the bark this action may be due to ability of its ingrednts, which could act valuable constitution in enhancing the effect of glycolytic and gluconeogenic enzymes.[59] Have research the prophylactic medium of arjunolic acid against streptozotocin (STZ) treat diabetes in the pancreatic tissue of Swiss albino rats. STZ administration (at a dose of 65mg/kg body wt, injected into the tail vein) causes an increase in the production of both

ROS and reactive nitrogen species (RNS) in the pancreas of labortical animals.[60] Formations of these reactive intermediates minimize the intracellular antioxidant defense, maximize the levels of lipid peroxidation, protein carbonylation, serum glucose and TNF-α.[61]

**Wound healing activity**

Terminalia Arjuna bark extract contain hydroalcoholic, phytoconstituents was reported to be used in topical application on healing rat dermal wounds. In rat wound created on back it have been treated with topical applied as simple ointment. Results prove that fraction III prepared as 1% simple ointment react complete epithelialization on day 20, whereas fraction I react complete epithelialization on day 9, which necessary consists of tannins.[62] The ability shows of Terminalia Arjuna to total epithelisation of excision wounds and maximum tensile strength of incision wounds.[63]

**Antimicrobial activity**

Ear infection is one of the common diseases occurring throughout the world. Different etiological agents are responsible for ear infections. To assess the antimicrobial potential of Terminalia arjuna leaves and bark extracts against Staphylococcus aureus, Acinetobacter sp., Proteus mirabilis, Escherchia coli, Pseudomonas aeruginosa and Candida albicans, pathogens causing ear infections and their comparison with locally available ear drops were studied. Methanol, ethanol, acetone, aqueous (hot and cold) extracts from the leaves and bark of T. arjuna were tested for their antimicrobial activity. Of the three organic solvents evaluated, acetonic leaf extract was found to be best against S. aureus. Organic bark extract showed almost equal inhibition of all tested Gram negative bacteria except P. aeruginosa. However, aqueous extract of T. arjuna bark exhibited good activity against S. aureus. Organic extract obtained from the T. arjuna bark and leaves may be used to treat the bacterial ear pathogens especially S. aureus, which has shown greater inhibition zones than the herbal drops.[64]

**Anti-bacterial Activity**

Morbidity and mortality due to diarrhoea continues to be a major problem in many developing countries. Water samples from different areas of Chittagong were collected and 22 Vibrio cholerae were isolated from the samples. In this experiment we found that 85% of the Vibrio cholerae isolated can grow at 6% NaCl whereas none of these can survive at 8% NaCl. Most of the isolates were resistant to at least 2 antibiotics. 95.45% were resistant to ampicillin, 50% to erythromycin, 63.63% to nalidixic acid, 13.63% to cephotaxine, 13.63% to ceftriaxone and 27.27% to cotrimoxazol. Arjun bark extract was used as a biological tool

to resolve the antibiotic resistant V. holerae problem. Arjun extract inhibited the growth of V. cholerae at all concentrations and zone diameter increased with the increase of concentrations. The regression coefficient of the relationship between concentration and zone diameter varies from 0.75 to 0.984 for most of the isolates which indicates that there exists a linear relationship. This revealed that Terminalia arjuna would be a good antibacterial drug in the treatment of Vibrio cholerae infections, provided if found effective and nontoxic through in vivo studies.[65] Morsheed et al[66] evaluated the antibacterial and cytotoxic activity of 50% ethanol extract of bark from Terminalia arjuna on selected four Gram positive and eight Gram negative bacterial strains. The bark extract of Terminalia arjuna showed potential antimicrobial activities against all of the selected strains of microorganisms and the greatest activity was observed against Shigella dysenteriae. For antimicrobial test, Disc diffusion technique was used and the zone of inhibition of microorganisms was measured in mm. In vitro cytotoxicity test was also studied by Brine Shrimp Lethality Bioassay and results illustrated significant ($p<0.05$) cytotoxicity against A. salina, that were expressed as LC50. Terminalia arjuna ethanol extract showed brine shrimp cytotoxicity with lethal concentration 50 (LC50) value of 50.11 µg/ml. To observe antibacterial activity four Gram-negative and two Gram-positive bacteria were tested using agar well diffusion method. The results indicate that antibacterial activity of the extract were concentration dependent ranging from 0.5-10mg/ml. The striking and distinctive feature of observed antibacterial activity of T. arjuna extract is that it exhibited decent activity against the multi-drug resistant Gram- negative bacteria Coliform spp, Klebsiella pneumoniae, Pseudomonas aeruginosa even at low concentrations( 3mg/ml). Minimum Inhibitory Concentration(MIC) was predicted for the extract and it was varied from 3-20mg/ml.[67]

**Antifungal activity**

Aqueous, alcoholic and ethyl acetate extracts of leaves of five Terminalia species (T. alata, T. arjuna, T. bellerica, T. catappa, T. chebula) were tested against five plant pathogenic fungi like Aspergillus flavus, Aspergillus niger, Alternaria brassicicola, Alternaria alternata and Helminthosporium tetramera). The antifungal activities of all these extracts were determined by paper disc method. Nearly all the extracts were found effective against these fungi. It was found that most of.[68]

**Insecticidal Activity**

The toxic effect of some plant extracts on cotton leaf worm, Spodoptera littoralis (Boisd.). Petroleum ether extract of some planta such as Terminalia arjuna, Erythrine caffra, Taxodium distichum and Melaleuca cajuputi. Treatment with each of the four plant extracts caused clear mortality on 4th instar larvae. The reduction in F1 progeny, elongation of the larval duration, and pupal period at any of the tested concentration were noticed. There was moderate gradient reduction in the pupation percentage of the different treatments (71) as compared to the control (93.3). Moderate fluctuation was observed among sex ratio (1:2.3). Percentages of adult emergence and growth were inhibited with increasing the concentrations as observed in four plant extracts (1.7) as compared to control (2.9).[69]

**Anthelmintic activity**

The study was carried out to evaluate the anthelmintic activity of Terminalia arjuna (Roxb.) bark locally used as an anthelmintic. Lethal median concentration (LC50 values) of methanolic extract of T. arjuna bark in egg hatch and larval development tests against Haemonchus contortus ova and larva were found to be 645.65 and 467.74 µg mL-1, respectively. In adult motility assay, efficacy of the extract was evident by the mortality of H. contortus at different hours post exposure. In vivo results revealed maximum (87.3%) egg count percent reduction (ECR) in sheep treated with crude methanolic extract @3g kg-1 body weight on day 11 posttreatment (PT). The data revealed dose-dependent anthelmintic activity both in the in vitro and in vivo studies, thus justifying its use in the traditional medicine.[70]

**Immunomodulatory Efficacy**

A study was made for the evaluation of the immunomodulatory efficacy of Terminalia arjuna bark extract in Aspiculuris tetraptera infected mice. The plant extract were administrated to the infectedmice on 18, 19 and 20 post infection days. The immunomodulatory efficacy due to plant extract was observed th th th on ITH, DTH and Lymphocyte response. PCA, DTH and Lymphocyte response reactions were found to be directly proportional to the dose of drug. PCA response was maximum (8.2 mm) in the group ITTAM and 5 minimum (5.8 mm) in the group ITTAA. DTH response was maximum (7.8 mm) in the group ITTAM and 1 5 minimum (4.9 mm) in the group ITTAA. Lymphocyte count was observed maximum (79%) in the group ITTAM 1 5 and minimum (68.6%) in the group ITTAA. Significant increase in PCA, DTH and lymphocyte responses in 1 the infected and treated mice indicates stimulated cell mediated as well as humoral immunity. Obtained results indicate that studied plant

extract can be good immunnomodulatory agent and may boost the immune response of the host but. methanol extract of Terminalia arjuna is more effective than aqueous extract of Terminalia arjuna plant.[71]

**Radiaprotective and antioxidant properties**

Diffusion controlled rates. The bimolecular rate constants for the reaction of these radicals were in the order of 109 dm3mol-1s-1. The above results indicate that various preparations from T. arjuna and its component baicalein have significant radioprotective and antioxidant activities and the ability to react with radiation-derived or radiationrelated reactive species may be the factor responsible.[72] Sivalokanathan et al[73] investigated to evaluate the antioxidant nature of ethanolic extract of Terminalia arjuna bark on Nnitrosodiethylamine (DEN) induced liver cancer in male Wistar albino rats. The results show an antioxidant activity of Terminalia arjuna bark against DEN-induced liver cancer.

**Antimutagenic activities**

The antimutagenic effect of benzene, chloroform, acetone and methanol fractions from Terminalia arjuna was determined against Acid Black dye, 2aminofluorene (2AF) and 4-nitro-ophenylenediamine (NPD) in TA98 Frameshift mutagen tester strain of Salmonella typhimurium. Among the different fractions, the antimutagenic effect of acetone and methanol fractions was more than that observed with other fractions. Coincubation and pre-incubation modes of experimentation did not show much difference in the antimutagenic activity of the extracts. Moreover, these fractions inhibited the S9dependent mutagens, 2AF and Acid Black dye more effectively than the direct-acting mutagens. Studies are under way to isolate and elucidate the nature of the antimutagenic factor in acetone and methanol fractions.[74]

**Anti-inflammatory, immunomodulatory and antinociceptive activity**

Terminalia arjuna back powder (400 mg/kg, po) significantly reduced formalin-indued paw oedema at 24 h but not carrageenan-induced paw oedema. It significantly increased the anti-SRBC antibody titre in the secondary phase of immune response. The same dose significantly reduced the duration of licks and bites in both phases of formalin-induced pain response and showed significant increase in tail flick latency at higher dose (800 mg/kg, po). These effects of T. arjuna were antagonised by pretreatment with naloxone (1 mg/kg, ip). In another series of experiments, mice pretreated with morphine for three days in increasing doses (10, 15, 20 mg/kg, ip; twice daily) showed a decreased response in antinociceptive activity of morphine

(5 mg/kg, ip). Further, cross tolerance was observed with T. arjuna (800 mg/kg, po) in morphine tolerant animals. These findings support the hypothesis that T. arjuna has anti-inflammatory potential against some phlogistic agents along with some immunomodulatory activity and also has antinococeptive action probably mediated via central opioid receptors.[75]

**Asthma management**

The treatment should be carried on the night of full moon. Prepare a dish from condensed milk sugar a nd rice to make a palatable kheer and put in an open bowl which should be covered with a thin muslin clothand exposed to moonlight, making sure that the moonlight falls directly on the processed dish. Sprinkle1012 gms of powder of the arjuna bark over it and eat early next morning, but the patient must not sleep upto twelve hours afterconsuming the dish. This is said to be an effective and curative device in case of even chronic asthma.[76]

**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.[77] 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.[78] The cardioprotective effect of the active phytoconstituents of arjuna bark against carbon tetrachloride and sodium fl uoride 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.[79,80] In a recent study, the methanol extract yielded the highest phenolic and fl avonoid 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.[81] In another study, both alcoholic and aqueous extracts of the bark attenuated H2O2-mediated reactive oxygen species generation in human monocytic cells by promoting catalase and glutathione peroxidase (GPO) activities and by sustaining cellular reducing power. Moreover, the extracts inhibited lipid peroxidation (LPO) and 3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase, but had no effect on lipoprotein lipase.[82] In isoprenaline-induced myocardial ischemia (MI), arjuna has been found to possess prostaglandin E2-like activity with coronary vasodilatation and hypotension.[83] The

bark extract has shown to signifi cantly prevent isoprenaline-induced increase in oxidative stress and decline in endogenous antioxidant level. Arjunolic acid has been found to prevent the decrease in the levels of superoxide dismutase, catalase, GPO, ceruloplasmin, α-tocopherol, reduced glutathione, ascorbic acid, lipid peroxide, and myeloperoxidase.[84] Further, the bark extract has also shown protective effects against doxorubicin-induced DNA damage and cardiotoxicity.[52,53] Kumar et al. demonstrated that arjuna protects the heart against myocardial changes induced by chronic β-adrenoceptor stimulation.[85] Substantiating this, in a recent experiment, the bark extract signifi cantly attenuated cardiac dysfunction and myocardial injury in rats with congestive heart failure (CHF). Cardioprotective action of arjuna was comparable to fluvastatin. Arjuna bark extract has a signifi cant prophylactic and therapeutic benefi cial effect in protecting heart against catecholamine-induced CHF, possibly through maintaining endogenous antioxidant enzyme activities and inhibiting LPO and cytokine levels.[86] Recently, Mythili et al. confi rmed the earlier fi ndings that triterpenoids derived from arjuna extract containing arjunolic acid show cardioprotective activity by boosting endogenous antioxidant defense system.[87]

**Hypolipidemic and antiatherogenic activity**

Earlier animal experiments have demonstrated that arjuna bark powder/extract reduces the total cholesterol (TC) and triglyceride (TG) levels.[88-91] 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 signifi cant 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 effi cacy of arjuna fractions was found to be in the order: Ethanol fraction > solvent ether fraction > petroleum ether fraction.[92] The ethanolic fraction possesses potent antioxidant and hypolipidemic properties compared to other fractions, and this has been substantiated by other studies also.[93,94] Subsequent work done by Sharma et al. also substantiated the hypolipidemic and antioxidant effect of arjuna. In addition to this, they also found that recipes (Arjuna Omelette and Arjuna En Upma) incorporating arjuna bark showed good

acceptability, meriting their inclusion in the daily diet of the people needing long-term intervention for elevated lipids and oxidative stress levels.[95] The hypolipidemic action is thought to be mediated through increased hepatic clearance of cholesterol, down-regulation of lipogenic enzymes, and inhibition of HMG-CoA reductase.[96] Further, Parmar et al. showed that there is a possibility of involvement of thyroid hormones (suppression of thyroid function) in the amelioration of cardiac and hepatic LPO by the bark extract in albino rats.[97]

## CLINICAL RESEARCH ON ARJUNA

### 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 signifi cantly, along with a signifi cant decrease in systolic blood pressure (SBP), improvement in ECG changes, and reduction in plasma cortisol and serum cholesterol levels.[98] Later, in a study, 500 mg of bark powder was administered twice daily to 25 coronary artery disease (CAD) patients for 3 months. A reduction in the grade of positivity of treadmill test (TMT) response was observed in six patients, in addition to improvement in exercise tolerance and a reduction in the frequency of anginal attacks and use of sublingual nitrates.[99] Subsequently, in an open-label trial, it was demonstrated that there was a 50% reduction in angina episodes along with a signifi cant delay in the time to the onset of angina on TMT and appearance of ST–T changes in ECG after arjuna therapy was administered in stable angina patients. Signifi cant lowering of SBP and body mass index, with a marginal improvement in left ventricular ejection fraction (LVEF) and a slight increase in high density lipoprotein (HDL) levels were also observed. In unstable angina patients, there was an insignifi cant reduction in anginal frequency. These results suggest that monotherapy with arjuna is fairly effective in patients with stable angina, but has a limited role in unstable angina.[100] In yet another study, 500 mg of bark powder was administered 8 hourly to 10 patients of post-myocardial infarction angina and 2 patients of ischemic cardiomyopathy for a period of 3 months. These patients were compared with matched patients of post-myocardial infarction angina receiving only conventional treatment. Signifi cant reduction in anginal frequency, improvement in LVEF (from 42.25 ± 9.96% to 52.57 ± 12.32%), and reduction in left ventricular mass (LVM; from 159.18 ± 51.11 g/m2 to 140.62 ± 55.65 g/m2) was noted.[101] The effi cacy of Hartone (an herbal product containing arjuna) was studied in 10 stable angina patients. The results were compared with those of 10 patients of stable angina on 20 mg of isosorbide mononitrate (ISMN) administered twice daily. It was observed that

Hartone gave symptomatic relief in 80% of patients as compared to 70% in ISMN alone group. In addition, arjuna was better tolerated than ISMN.[102] In a randomized, double-blind, cross-over study, 58 male patients with chronic stable angina (class II–III) with evidence of provocable ische mia on TMT received 500 mg of 90% alcohol extract 8 hourly, ISMN (40 mg/day), or a matching placebo for 1 week each after a washout period of at least 3 days. It was found that arjuna therapy was associated with a signifi cant decrease in the frequency of angina and the need for isosorbide dinitrate. Improvements in clinical and TMT parameters were observed with both arjuna and ISMN as compared to placebo. No signifi cant differences were observed in the above parameters when arjuna and ISMN therapies were compared.[103]

**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 signifi cant diuresis, and a fall in both systolic and diastolic blood pressure.[104] Subsequently, the effect of bark extract (500 mg 8 hourly) was studied in a double-blind placebo-controlled two-phase trial comprising 12 patients with refractory CHF. In the fi rst phase, arjuna was administered for a period of 2 weeks. A decrease in echo-left ventricular end-diastolic and end-systolic volume indices, an increase in left ventricular stroke volume index, and an increase in LVEF were recorded suggesting improvement. On long-term evaluation (20-28 months), in addition to continued improvement in symptoms and signs, they also reported an improvement in quality of life.[105] A study done with abana (herbal formulation containing arjuna) in hypertensive individuals revealed an improvement in cardiac function as indicated by an increase in ejection fraction and a signifi cant reduction of the SBP, echocardiographic left ventricular internal diameter, posterior wall thickness, and interventricular septal thickness.[106] Recently, arjuna has also been shown useful in improving cardiovascular endurance and in lowering SBP in normal healthy subjects.[107]

**Rheumatic heart disease**

Effi cacy 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 signifi cant improvement in LVEF, exercise duration, and signifi cant reduction in heart size.[108]

**Ischemic mitral regurgitation**

In a randomized, double-blind, placebo-controlled study done in patients with ischemic mitral regurgitation (IMR) following acute myocardial infarction, arjuna was found to signifi cantly decrease IMR and anginal frequency. In addition, there was also signifi cant improvement in diastolic dysfunction (E/A ratio; from 0.93 ± 0.31 to 1.38 ± 0.40 at 12 weeks.[109]

**Cardiomyopathy**

In addition to its anti-ischemic property, arjuna was found to reduce LVM and improve LVEF.[78] A recent observational study revealed that when patients of dilated cardiomyopathy with reduced LVEF received arjuna in addition to their standard therapy, there was a signifi cant improvement in left ventricular parameters as well as functional capacity.[110]

**Platelet aggregation**

The bark extract has been found to decrease platelet activation and possess antithrombotic properties in vitro in 20 patients of angiographically proven CAD and 20 age- and sex-matched controls. The possible mechanism could be by desensitizing platelets by competing with platelet receptor or by interfering with signal transduction.[111] In another recent randomized, double-blind, parallel-group, placebo-controlled study in patients with type 2 diabetes mellitus, 500 mg of arjuna administered thrice daily resulted in a signifi cant increase in mean cardiac output from 4.34 ± 0.38 to 4.86 ± 0.20 (l/min). In addition to this, there was a reduction in mean systemic vascular resistance from 1729 ± 93.52 to 1484 ± 115.5 (dyne sec/cm5). Arjuna also caused signifi cant inhibition of platelet aggregation.[112]

**Oxidative stress/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 profi le. In addition to this, patients got symptomatic relief after 1 month of treatment.[113] Antioxidant effect of bark powder (500 mg) has been demonstrated to be comparable to vitamin E (400 IU) in a randomized, controlled, open trial done in 105 patients with coronary heart disease. The authors also observed a signifi cant decrease in TC, LDL, and lipid peroxide levels. The hypocholesterolemic effect was attributed to the soluble fi bers and sitostanol content, while the antioxidant effect was attributed to the fl avonoids.[114] Further, it was observed in a study that when the bark powder was given along with statin for 3 months, it resulted in 15% reduction in TC, 11% reduction in TG, and 16% reduction in LDL, while there was minimal decline in lipoprotein (a) and nitrite levels.[115] In a prospective cohort study, dyslipidemic

patients received arjuna powder (5 g, BD) for 3 weeks followed by Arogyavardhini Vati (500 mg, BD) for 4 weeks. A signifi cant reduction in TC, LDL, TG, serum C-reactive protein, blood glucose, and an increase in HDL level were found, which supported the role of arjuna in dyslipidemic patients.[116]

**Lipoprotein(a)**

A signifi cant reduction in lipoprotein(a) levels amounting to 24.71% following the administration of arjuna in a patient of β-thalassemia associated with hyperlipoproteinemia and metabolic syndrome has been reported.[117]

**Endothelial dysfunction**

In a double-blind, placebo-controlled, cross-over study involving 18 healthy male smokers and an equal number of age-matched non-smoker controls, it was observed that the hydroalcoholic extract of bark when given for 2 weeks led to signifi cant regression of the endothelial abnormality amongst smokers.[118] Thrombotic condition In a recent study done to investigate the in vitro thrombolytic and membrane-stabilizing action of four Bangladeshi medicinal plants including arjuna, the methanol extract was found to possess signifi cant thrombolytic activity (30.57%). It also signifi cantly inhibited the hemolysis of RBCs in both hypotonic solution and heat-induced conditions. This showed that it has moderate thrombolytic activity; however, more research is needed to isolate the secondary metabolites responsible for the activity.Not much data is available to comment on the effect of arjuna on cytochrome P450 (CYP450) enzyme. Results from a recent in vitro study indicate that arjuna extracts contain constituents that can potently inhibit the activity of CYP1A.[119]

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