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TERMINALIA ARJUNA: A TRADITIONAL CARDIO-PROTECTIVE

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ABSTRACT

Terminalia arjuna, commonly known as *arjuna*, belongs to the family of Combretaceae. Its bark decoction is being used in the Indian subcontinent for anginal pain, hypertension, congestive heart failure, and dyslipidemia, based on the observations of ancient physicians for centuries. The utility of *arjuna* in various cardiovascular diseases needs to be studied further. Therefore, the present review is an effort to give a detailed survey of the literature summarizing that *arjuna* is used in cardiovascular disorders, which were particularly performed during the last decade. Systematic reviews, meta-analyses, and clinical studies of *arjuna* were retrieved through the use of es. Most of the studies, both experimental and clinical, have suggested that the crude drug possesses anti-ischemic, antioxidant, hypolipidemic, and antiatherogenic activities. Its useful phytoconstituents are: Triterpenoids, β-sitosterol, flavonoids, and glycosides. Triterpenoids and flavonoids are considered to be responsible for its beneficial antioxidant cardiovascular properties. The drug has shown promising effect on ischemic cardiomyopathy. So far, no serious side effects have been reported with *arjuna* therapy. However, its long-term safety still remains to be elucidated. Though it has been found quite useful in angina pectoris, mild hypertension, and dyslipidemia, its exact role in primary/secondary coronary prevention is yet to be explored.

KEYWORDS: Antioxidants, Cardiotonic drugs, Flavonoids, Myocardial ischemia, *Terminalia arjuna.*

INTRODUCTION

Morphological characters

Arjuna is a potential cardioprotective agent belonging to the Combretaceae family. It is an ayurvedic remedy that has been mentioned since vedic period in many ancient Indian medicinal texts including Charaka Samhita, Sushruta Samhita, and Astang Hridayam. It was Vagabhatta who, for the first time, advocated the use of stem bark powder in heart ailments. The bark has been described as an astringent, demulcent, expectorant, cardiotonic, styptic, antidysenteric, urinary astringent, and has shown to be useful in fracture, ulcers, leukorrhea, diabetes, anemia, cardiopathy, and cirrhosis.[1] Chakradatta, the great ancient physician, recommended it to be given as a decoction of bark with milk or as a ghrita (a preparation with ghee or butter).[2] Decoction of the bark has been used as ulcer wash, while bark ashes have been prescribed for snakebite and scorpion sting. Traditional healers from Kancheepuram district, Tamil Nadu boil the bark powder with water, and inhale it to cure headache and to kill worms in teeth. They also use fruit paste topically on wounds. Fresh leaf juice is used for the treatment of earache and bark powder for treating heart ailments by Malabar tribe, Kerala. Tribals living in Sundargarh District, Orissa use dried bark powder along with rice washed water to treat blood in urine, and tribes living in Malkangiri district chew the fresh bark and swallow the juice as an antacid.[3]

Arjuna tree is about 60-80 ft in height, and is seen along rivers, streams, and dry water bodies throughout the Indo-sub-Himalayan tracts of Uttar Pradesh, southern Bihar, Chota Nagpur, Burma, Madhya Pradesh, Delhi, and Deccan region. It is also found in the forests of Sri Lanka and Mauritius.It grows almost in all types of soils, but prefers humid, fertile loam and red lateritic soils. It can tolerate half submergence for a few weeks. *Arjuna* is propagated by seeds; Germination takes 50-70 days with 50-60% germination.

Figure 1: Leaves and Fruits.

Figure 2: Bark.

The outer surface of the bark is smooth, while the inner surface has longitudinal striation and is pinkish in color. The bark gets flaked off itself in the month of April–May. On microscopic examination of the mature bark, a cork consisting of 9-10 layers of tangentially elongated cells, 2-4 cells thick phellogen, and phelloderm consisting of tangentially elongated cells are seen. The phloem is broad, consisting of ceratenchyma, phloem parenchyma, phloem fibers, and crystal fibers with rosette crystals of calcium oxalate. Periderm and secondary phloem are present in the old bark.[4]

Leaves are sub-opposite, coriaceous, oblong/elliptic, dull green from the upper side and pale brown on the lower side, often unequal sided with 10-15 pairs of nerves. Flowers are white in color and bisexual, arranged in spikes with linear bracteoles. Fruits are ovoid/oblong with 5-7 hard angles or wings. The lines on wings are oblique and curving upward.

Various extracts of the stem bark of *arjuna* have shown to possess many pharmacological properties including inotropic, anti-ischemic, antioxidant, blood pressure lowering, antiplatelet, hypolipidemic, antiatherogenic, and antihypertrophic. Thus, in the present article, we have made an attempt to review and give up-to-date information pertinent to the usage of *arjuna* as a potential cardioprotective agent.[5]

Chemical constituents[6,7]

From medicinal point of view bark of T. arjuna was considered to be the most important constituent. Hence most of the early studies were limited to bark stem of the plant. Chemical analysis of the bark showed evidence of sugar, tannins (12%), colouring matter, a glycoside, and carbonates of calcium, sodium and traces of chloride of alkali metals. Subsequently presence of an alkaloid as well as a glycoside was confirmed. The major chemical constituents of various parts of T. arjuna are shown below. The glycoside was capable of increasing the force of contraction of the frog heart. Attempt to isolate the glycoside resulted into finding of an organic acid with a high melting point, a phytosterol, an organic ester easily hydrolysed by mineral acids, 12% tannins consisting largely of pyrocatechol tannins, large quantities of calcium and smaller amounts of aluminium and magnesium salts, colouring matter and sugar.

(A) Stem bark

1. **Triterpenoids:** Arjunin, arjunic acid, arjunolic acid, arjungenin, terminic acid.

2. **Glycosides:** Arjunetin, arjunoside I, arjunoside II, arjunaphthanoloside, terminoside A Sitosterol.
3. **Flavonoids:** Arjunolone, arjunone, bicalein, luteolin, gallic acid, ethyl gallate, quercetin, kempferol, pelorgonidin, oligomeric proanthocyanidins.
4. **Tanins:** Pyrocatechols, punicallin, punicalagin, terchebulin, terflavin C, castalagin, casuariin, casuarinin.
5. **Minerals/trace elements:** Calcium, aluminium, magnesium, silica, zinc, copper.

(B) Roots

1. **Sitosterol**
2. **Triterpenoids:** Arjunic acid, arjunolic acid, oleanolic acid, terminic acid
3. **Glycosides:** Arjunoside I, arjunoside II, arjunoside III, arjunoside IV, 2,19-dihydroxy-3-oxo-olean-12-en28-oic acid28-O-_-dglucopyranoside

(C) Leaves and Fruits

1. **Glycosides**
2. **Flavonoids:** Luteolin

Literature studies based on autonomic control of cardiovascular functions[8-14]

The cardiovascular system is subject to precise reflex regulation so that an appropriate supply of oxygenated blood can be reliably provided to different body tissues under a wide range of circumstances. The sensory monitoring for this critical homeostatic process entails primarily mechanical (barosensory) information about pressure in the arterial system and, secondarily, chemical (chemosensory) information about the level of oxygen and carbon dioxide in the blood. The parasympathetic and sympathetic activity relevant to cardiovascular control is determined by the information supplied by these sensors. The autonomic nervous system modulates beat-to beat fluctuations in heart rate (HR).

It modulates the electrical and contractile activity of the myocardium via the interplay of sympathetic and parasympathetic activity. Cardiovascular autonomic neuropathy, a common form of autonomic dysfunction, causes abnormalities in heart rate control, as well as defects in central and peripheral vascular dynamics. Methods to quantify HR and blood pressure variability have been evaluated as indicators of sympathetic and parasympathetic modulation of the cardiovascular system in humans and in experimental models. These methods seemed to detect early autonomic dysfunction at a time when other metabolic dysfunctional changes

were not clearly observed. Baroreflex sensitivity and Heart rate variability are the two frequently used parameters to assess autonomic control of cardiovascular functions.

Baroreflex sensitivity

The evaluation of baroreflex sensitivity (BRS) is an established tool for the assessment of autonomic control of the cardiovascular system. Arterial baroreceptors provide the central nervous system with a continuous stream of information on changes in blood pressure (which are sensed by the stretch receptors in the wall of the carotid sinuses and aortic arch), on the basis of which efferent autonomic neural activity is dynamically modulated. Activation of arterial baroreceptors by a rise in systemic arterial pressure leads to an increase of the discharge of vagal cardio inhibitory neurons and a decrease in the discharge of sympathetic neurons both to the heart and peripheral blood vessels. This result in bradycardia decreased cardiac contractility and decreased peripheral vascular resistance. Heart rate variability Heart rate variability (HRV) can detect cardiac autonomic impairment in individuals before traditional cardiovascular autonomic function tests. HRV analysis is the ability to assess over all cardiac health and the state of the autonomic nervous system (ANS) responsible for regulating cardiac activity.

Cardiovascular functions

Cardiomyopathy refers to a disease process which affects the myocardium in patients causing a wide range of structural abnormalities eventually leading to LVH (left ventricular (LV) hypertrophy) diastolic and systolic dysfunction or a combination of these. The systolic dysfunction is impairment in the ability of the heart to eject blood. The principle hallmark of systolic dysfunction is a depressed LV ejection fraction dysfunction. Diastole is the time period where the myocardium is no longer generating force and subsequently returns to an unstressed length and force. Diastolic dysfunction occurs when there is prolongation and slowing of this process.

Histopathological examination of normal cardiac tissue demonstrates normal myofibrillar structure with striations, branched appearance and continuity with adjacent myofibrils. Cardiac tissues having cardiomyopathy shows widespread alterations in myocardial structure with subendocardial necrosis and myovacuolations. Treatment with T. arjuna, is seen to preserve myocardium.

From the Literature studies it has been revealed that T. arjuna bark exerting significant inotropic and hypotensive effect, increasing myocardial contractility, coronary artery flow and protecting myocardium against ischemic damage.

CONCLUSION

The efficacy of Terminalia arjuna as a cardioprotective agent, a potent anti inflammatory and antioxidant preventing LDL cholesterol oxidation and its potential to reduce atherogenic lipid levels in various diseases. Its molecular actions in different cells of the cardiovascular system are also reported. Its role in improving the autonomic control plays an important part in improving cardiovascular functions. This herbal drug with multiple beneficial effects without causing side effects can modulate the existing treatment strategies. However, there are some identified lacunae, like standardization of the 'drug', toxicity studies along with pharmacological interactions with other drugs and large multicentre randomized clinical trials, before its use by modern medicine is acceptable.

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