Terminalia arjuna — Indena photo

Terminalia arjuna

Description

Terminalia arjuna is a deciduous tree found throughout India growing to a height of 60-90 feet. The thick, white-to-pinkish-gray bark has been used in India's native Ayurvedic medicine for over three centuries, primarily as a cardiac tonic. Clinical evaluation of this botanical medicine indicates it can be of benefit in the treatment of coronary artery disease, heart failure, and possibly hypercholesterolemia. It has also been found to be antiviral and antimutagenic.

Active Constituents

Terminalia's active constituents include tannins, cardenolide, triterpenoid saponins (arjunic acid, arjunolic acid, arjungenin, arjunglycosides), flavonoids (arjunone, arjunolone, luteolin), gallic acid, ellagic acid, oligomeric proanthocyanidins (OPCs), phytosterols, calcium, magnesium, zinc, and copper.[1,2]

Mechanisms of Action

Improvement of cardiac muscle function and subsequent improved pumping activity of the heart seems to be the primary benefit of Terminalia. It is thought the saponin glycosides might be responsible for the inotropic effect of Terminalia, while the flavonoids and OPCs provide free radical antioxidant activity and vascular strengthening.[3] A dose-dependent decrease in heart rate and blood pressure was noted in dogs given Terminalia intravenously.[4] Recently, two new cardenolide cardiac glycosides were isolated from the root and seed of Terminalia.[5,6] The main action of these cardenolides is to increase the force of cardiac contraction by means of a rise in both intracellular sodium and calcium.

Clinical Indications

Angina Pectoris

An open study of Terminalia use in stable and unstable angina demonstrated a 50-percent reduction of angina in the stable angina group after three months ($p<0.01$). A significant reduction was also found in systolic blood pressure in these patients ($p<0.05$). During treadmill

testing, both the onset of angina and the appearance of ST-T changes on ECG were significantly delayed in the stable angina group ($p<0.001$), indicating an improvement in exercise tolerance. The unstable angina group did not experience significant reductions in angina or systolic blood pressure. Both groups showed improvements in left ventricular ejection fraction. Evaluation of overall clinical condition, treadmill results, and ejection fraction showed improvement in 66 percent of stable angina patients and 20 percent of unstable angina patients after three months.[7] In this study Terminalia was also associated with a lowering of systolic blood pressure.

Two clinical studies found similar results when *Terminalia arjuna* was compared to isosorbide mononitrate in stable angina patients.[8,9] Both studies showed a similar reduction in the number of anginal episodes, as well as improvements in stress tests. In one study 58 males with chronic stable angina with evidence of ischemia on treadmill testing received *Terminalia arjuna* (500 mg every eight hours), isosorbide mononitrate (40 mg daily), or a matching placebo for one week each, separated by a wash-out period of at least three days in a randomized, double-blind, crossover design. Terminalia therapy was associated with a significant decrease in the frequency of angina and need for isosorbide dinitrate. Treadmill parameters improved significantly during therapy with Terminalia compared to those with placebo. Similar improvement in clinical and treadmill parameters were observed with isosorbide mononitrate compared to placebo therapy. No significant differences were observed in clinical or treadmill parameters when *Terminalia arjuna* and isosorbide mononitrate therapies were compared.[8]

Congestive Heart Failure

A double-blind, placebo-controlled, two-phase trial of Terminalia extract in 12 patients with severe refractory heart failure (NYHA Class IV) was conducted, in which either 500 mg Terminalia bark extract or placebo was given every eight hours for two weeks, in addition to the patients' current pharmaceutical medications (digoxin, diuretics, angiotensin-converting-enzyme inhibitors, vasodilators, and potassium supplementation). All patients experienced dyspnea at rest or after minimal activity at the start of the trial. Dyspnea, fatigue, edema, and walking tolerance all improved while patients were on Terminalia therapy. Treatment with Terminalia was also associated with significant improvements in stroke volume and left ventricular ejection fraction, as well as decreases in end-diastolic and end-systolic left ventricular volumes compared to placebo. In the second phase of the study, patients from phase I continued on Terminalia extract for two years. Improvements were noted in the ensuing 2-3 months, and were maintained through the balance of the study. After four months' treatment, nine patients improved to NYHA Class II and three improved to NYHA Class III.[10]

Cardiomyopathy/Post-Myocardial Infarction

A study was conducted on 10 post-myocardial-infarction patients and two ischemic cardiomyopathy patients, utilizing 500 mg Terminalia extract every eight hours for three months, along with conventional treatment. Significant reductions in angina and left ventricular mass, in addition to improved left ventricular ejection fraction, were noted in the Terminalia group; whereas, the control group taking only conventional drugs experienced decreased angina only. The two patients with cardiomyopathy improved from NYHA Class III to NYHA Class I during the study.[11]

Hyperlipidemia

Animal studies suggest Terminalia might reduce blood lipids. Rabbits made hyperlipidemic on an atherogenic diet were given an oral Terminalia extract, and had a significant, dose-related decrease in total- and LDL-cholesterol, compared to placebo ($p<0.01$)[12] However, the amounts used (100 mg/kg and 500 mg/kg body weight) were very large, and it remains to be seen if similar changes will be observed in humans taking relatively smaller oral doses. In a similar study of rats fed cholesterol (25 mg/kg body weight) alone or along with Terminalia bark powder (100 mg/kg) for 30 days, Terminalia feeding caused a smaller increase in blood lipids and an increase in HDL cholesterol, compared to the cholesterol-only group. The researchers concluded that inhibition of hepatic cholesterol biosynthesis, increased fecal bile acid excretion, and stimulation of receptor-mediated catabolism of LDL cholesterol were responsible for Terminalia's lipid-lowering effects.[13]

In another study, rabbits were fed a cholesterol-rich diet in combination with three indigenous Terminalia species; *Terminalia arjuna*, *T. belerica*, and *T. chebula*. Upon histological examination, the rabbits fed the diet and *T. arjuna* exhibited the most potent hypolipidemic effect, with partial inhibition of atheroma.[14]

In a randomized, controlled trial, Terminalia bark was compared to vitamin E. One-hundred-and-five patients with coronary heart disease (CHD) were matched for age, lifestyle, and diet variables, as well as drug treatment status. None of the patients were previously on lipid-lowering medications. Placebo, vitamin E (400 IU), and Terminalia (500 mg) were administered. Results showed no significant changes in the placebo group or the vitamin E group. The Terminalia group had a significant decrease in total cholesterol and LDL cholesterol. Lipid peroxidase levels decreased significantly in both vitamin E and Terminalia groups; however, there was a greater decrease in the vitamin E group.[15]

Other Clinical Indications

Terminalia bark harbors constituents with promising antimutagenic and anticarcinogenic potential that should be investigated further.[16-19] *In vitro* studies have also shown Terminalia to possess anti-herpes virus activity.[20]

Botanical-Drug Interactions

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

Dosage and Toxicity

A typical dose of dried bark is 1-3 grams daily, while 500 mg bark extract four times per day has been used in congestive heart failure. No toxicity has been documented.

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