A PHARMACOLOGICAL APPRAISAL ON TRADITIONAL HERBS WITH CARDIOPROTECTIVE POTENTIAL

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ABSTRACT
Cardiovascular disease (CVD) is one of the challenging disease and it is increasing at an alarming rate due to changes in lifestyle and dietary habits, lack of physical exercise, environmental changes, increased physical and mental stress. The main risk factors of cardiac disease include anxiety, hypertension, hypercholesterolemia and atherosclerosis. Siddha system of medicine highly emphasise upon the principle of “Prevention is better than cure”. According to American Heart Association, cardiovascular disease like heart attack and stroke are considered to be no.1 killer diseases of both men and women and death rate is about 36% per year. According to WHO, herbal medicines are safe, effective and possess easily available products for the management of cardiac diseases. More than 2000 plants have been mentioned in traditional system of medicines and providing better results for cardiovascular diseases. Hence, the present review focuses on scientific evaluation of selective herbs that have been mentioned in traditional Siddha literature towards alleviating cardiac disease.

KEYWORDS: Cardiovascular disease, Atherosclerosis, Herbal medicine, Cardioprotective action, Traditional medicine.

INTRODUCTION
Cardiovascular disease (CVD) is complex term for many of the linked pathologies, commonly referred as coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease, rheumatic and congenital heart diseases and venous thromboembolism. An estimated 17.7 million people died from CVDs in 2015, representing 31% of all global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke. It is now increasingly prevalent in developing countries and their origins are well recognized and studied. Currently 80% of CVD mortality occurs in developing nations[1] and CVD is expected to be the major cause of mortality in most developing nations by 2020.[2] The risk factors associated with CVD includes dyslipidaemia, smoking, hypertension, diabetes and abdominal obesity.[3] While other risk factors includes age, autopsy evidence suggests that the process of developing CVD in later years thus risk serve as a crucial factors.[4]

Epidemiologic studies have identified that elevated serum lipids (cholesterol and triglycerides), increased plasma fibrinogen and coagulation factors, increased platelet activation, alterations in glucose metabolism and smoking serves as characteristics of CVD.[5] Normalization of abnormal lipids and lipoproteins, hypertension, inhibition of platelet aggregation and an increase in antioxidant status are believed to improve cardiovascular disease.

Dietary factors play a key role in the development of some human diseases, including cardiovascular disease. Epidemiologic studies indicate that diets rich in fruits, vegetables and spices are associated with lower risk of all-cause, cancer and cardiovascular-disease death.[6,7] These foods contain phytochemicals that have anticancer and anti inflammatory properties, which confer many health benefits.

CVD is a major public health problem in India, often impacting the most productive years of an individual’s life. The epidemiological transition plays out differently in different regions of India because of varied economic development. More than 2000 plants have been listed in the Traditional (Herbal/Alternative) systems of medicine out of these some of the plants provide comprehensive relief to the people from cardio-vascular diseases. WHO reports indicate that about 80% of the global population relies on several herbal medicines that have turned to be more advanced in modern era.[8] The present review focuses on the formulations of herbal plants, which has
cardioprotective effects if given in proper quantity and dose. In this review we have focused mainly on usage of herbal plants and their therapeutic effect for cardiovascular disease.

**SCIENTIFIC VALIDATION OF CARDIOPROTECTIVE HERBS**

**Terminalia arjuna (Tamil Name: Marutha maram)**

*Terminalia arjuna* Wight & Arn. is a deciduous and evergreen tree, standing 20–30m above ground level. It is found in abundance throughout Indo-sub-Himalayan tracts of Uttar Pradesh, South Bihar, Madhya Pradesh, Delhi and Deccan region near ponds and rivers. It is also found in forests of Sri Lanka, Burma and Mauritius. The phytochemical 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. The intravenous administration of the glycoside, obtained from the bark of *Terminalia arjuna*, resulted in rise in blood pressure in frog. The bioflavonoids, by virtue of their free radical scavenging action, prevent oxidation of LDL cholesterol, enhance endothelial derived nitric oxide activity, inhibit endothelial activation and inhibit platelet aggregation. Singh et al. (1982) reported a dose-dependent sustained hypotension and bradycardia after the intracerebro-ventricular and intraventricular injection of aqueous and alcoholic extract of its bark in chloralose anaesthetized dogs in doses as small as 1/100th and 1/20th, respectively to that of intravenous dose. The 70% alcoholic extract of *Terminalia arjuna* on blood pressure of anaesthetized dog was investigated and found that when the drug was administered in doses 5–10 mg/kg. It was observed that the drug produced dose-dependent hypotension which was blocked by propanolol but not by atropine and mepyramine maleate. Recently arjungenin an oleanane terpenoid derived from *Terminalia arjuna* bark and its glucoside, arjun glucoside II, have been demonstrated to exert free radical scavenging activities in human polymorphonuclear cells.

**Centella asiatica (Tamil Name: Vallaarai)**

*C. asiatica* has been reported to have a wide range of compounds belonging to different chemical classes. *C. asiatica* is useful in the treatment of vascular diseases such as venous hypertension and atherosclerosis. The major chemical class found in this plant is triterpenesaponosides. The major ones are known as asiatic acid, madecassiacid (6-hydroxy-asiatic acid), asiaticoside, madecassoside and madasagadic acid, betulinic acid, thankunicacid and isothankunic acid. Terpenoids is a heart-friendly phytochemical constituent and is popular among patients with high blood pressure and diabetes. It helps to reduce diastolic blood pressure and lowers the sugar level in blood. The (CAF3) fraction of the ethanol extract (CAE) of *Centella asiatica* had decrease the cholesterol by 79% and a triglyceride decrease by 95% in acute mice model, further investigation of CAF3 in high-fat-fed hamster model. It showed that CAF3 increased SOD and GSH-Px activities and decreased MDA level and it also improved TC, TG, LDL-C, HDL-C, AST and ALT levels. L-CAT and SR-BI gene expression in hamsters were also increased.

**Allium sativum (Tamil Name: Poondu)**

Garlic and its preparations have been widely recognized in the prevention and treatment of cardiovascular and other metabolic diseases, atherosclerosis, hyperlipidemia, thrombosis, hypertension. In modern era scientists have been trying to validate many of these properties of garlic, especially in terms of the identity of the active components, their mechanisms of action and exploring the potential benefits as food supplements. A study was conducted that lasted for 4 weeks. Garlic (1–4% in diet) and garlic protein administration in hypercholesterolemic rats induced by a high-cholesterol diet, significantly reduced serum cholesterol, triglyceride and LDL cholesterol but there was no effect on serum HDL. The chronic effects of garlic on lipid metabolism in rats were encouraging. Abramoviz et al. (1999) investigated the effect of allicin, acriflavine active component of garlic in the formation of fatty streaks in aorta and lipid profile in mice. Aged garlic extract 'Kyolic' also significantly inhibited the development of thickened, lipid-filled lesions in the pre-formed neointimasis produced by balloon-catheter injury of the right carotid artery in cholesterol-fed rabbits. The essential oils of garlic (equivalent to 1 g/kg/day of raw bulbs) proved effective in mediating fibrinolytic activity. Experimental study also revealed that garlic juice (raw garlic; 250 mg/day) had significant effect in enhancing the fibrinolytic activity in rabbit after receiving a cholesterol rich diet for 13 weeks. Ajoene, a constituent of essential oil of garlic, has been shown to inhibit in vitro platelet aggregation in different species of animals i.e., cow, dog, guinea-pig, horse, monkey, pig, rabbit and rat. Chronic oral administration of allicin lowered blood pressure in hypertensive rats.

**Sida cordifolia (Tamil Name: Kurunthotti)**

*Sida cordifolia* (linn) syn belongs to the Malvaceae family is widely distributed along with other species are common in the tropical and sub-tropical plains in India and Sri Lanka. It is useful in the treatment of fever, fits, ophthalmic, rheumatism, colic and nervous disorders. A study was conducted to evaluate the effect of Hydroalcoholic extract of *Sida cordifolia* L. (HESC) *Sidacordifolia* L. (HESC) leaves against myocardial infarction (MI) in rats. Albino rats were administered HESC (100 and 500 mg/kg) and propanolol (10 mg/kg) once daily orally for 30 days. Endogenous biomarkers (LDH and CK-MB) and antioxidants (SOD and catalase) were estimated in serum/perfusate and heart tissue homogenate (HTH).The LDH and CK-MB activities were elevated in HTH and depleted in serum/perfusate of HESC.
Vitis vinifera (Tamil Name: Thiratchai)
The antihypertensive effect of free hydroalcoholic grape skin extract (GSE) obtained from skins of a vinifera grape was investigated in experimental rodent hypertension models. Oral administration of GSE significantly reduced systolic, mean and diastolic arterial pressure in Wistar rats with desoxycorticosterone acetate-salt and N G nitro-L-arginine methyl ester (L-NAME) induced experimental hypertension. Lipid peroxidation of hepatic microsomes estimated as malondialdehyde production was concentration-dependently inhibited by GSE. Similarly, the ethanol-free hydroalcoholic extract obtained from Cabernet sauvignon grape skin has been shown to produce an antihypertensive effect. The red wine has been shown to induce either vasodilatation or no vascular effect in isolated vessels. The Products from red wine, like polyphenol compounds can induce vasodilatation and reduce arterial pressure in normo tensiv rats.

Nelumbo nucifera (Tamil Name: Thamarai)
Nelumbo nucifera, is a renowned herb of Indian systems of medicine has significant protection against myocardial infarction and hypertension. An animal study was aimed to validate the effect of Nelumbo nucifera extracts (NNE) on the cardiac changes associated with isoproterenol (ISO)-induced myocardial infarction (MI). In this study, Male rats were pretreated with Nelumbo nucifera leaf extract (NNE) (400 mg/kg) orally daily for 21 days and were induced myocardial infarction by isoproterenol (100 mg/kg) a synthetic catecholamine and b-adrenergic agonist, used as a model to study several cardiac dysfunctions at an interval of 24 h for 2 days. The study results revealed that Isoproterenol treated rats showed decreased levels of heart creatine kinase and lactate dehydrogenase. The activity of sodium potassium adenosine triphosphatase was decreased and the activities of magnesium adenosine triphosphatase and calcium adenosine triphosphatase were increased in isoproterenol treated rats. Pretreatment with NNE shows the inhibition of necrosis and reduced inflammation in ISO induced rats and normalization of all the biochemical parameters under study. The free radical scavenging, antioxidant, lipid protective and membrane stabilizing properties of NNE could responsible for these effects on histology of the myocardium to isoproterenol treated rats normalized all the biochemical parameters studied. In another study, male albino Wistar rats, were Subcutaneously injected isoproterenol (85 mg/kg) which showed a significant raise in the levels/activities of cardiac marker such as cardiac troponin T, creatine kinase-MB, creatine kinase, lactate dehydrogenase, asparate transaminase, alanine transaminase in serum. Pretreatment with Nelumbo nucfera(100, 200 and 400 mg/kg) daily for a period of 21 days positively altered the activities of cardiac markers and other biochemical parameters to normal.

Punica granatum (Tamil Name: Madhulai)
The pomegranate is native from the Himalayas in northern India to Iran but has been cultivated and naturalized since ancient times over the entire Mediterranean region. It is also found in India and more arid regions of Southeast Asia, the East Indies and tropical Africa. A pilot study in type 2 diabetic patients with hyperlipidemia found concentrated Pomegranate juice (P) decreased cholesterol absorption, increased fecal excretion of cholesterol, had a beneficial effect on enzymes involved in cholesterol metabolism, significantly reduced total and LDL cholesterol and improved total/HDL and LDL/HDL cholesterol ratios. The apolipoprotein-E deficient (E[degrees]) mice showed that pomegranate extracts had the ability to inhibit atherogenesis. Aviram et al also investigated the anti-atherosclerotic effects of a PBP extract after the juice was removed. Four-month-old E[degrees] mice with significant atherosclerosis were given PBP extract (containing 51.5 lag gallic acid equiv/kg/day) with an eight-fold higher polyphenol concentration than PJ for three months. This resulted in a significant reduction in MPM oxidative status as evidenced by a 27-percent decrease in total macrophage peroxide levels, a 42-percent decrease in cellular lipid peroxide levels and a 19-percent decrease in peritoneal macrophage uptake of oxidized LDL. In a double-blind, randomized, placebo-controlled trial, 39 patients were given either 240 mL PJ (polyphenol content not specified) (n=23) or a sports beverage of similar color, flavor, and caloric content daily for three months (n=16). The results demonstrate a reduction in myocardial ischemia and improved myocardial perfusion in patients consuming pomegranate juice.

Crocus sativus (Tamil Name: Kungumapoo)
Crocus sativus L. (Iridaceae), commonly known as saffron, is a perennial stemless herb that is widely cultivated in Iran and other countries such as India and Greece. Saffron contains more than 150 volatile and aroma yielding compounds. It also has many non-volatile active components, many of which are carotenoids including zeaxanthin, lycopene and various α- and β-carotenes. Aqueous and ethanol extracts of C. sativus petals reduced the blood pressure in a dose-dependent manner. Administration of 50 mg/g of aqueous extract changed the blood pressure from 133.5 ± 3.9to 117 ± 2.1 (mmHg). The ethanol extract induced greater changes in electrical field stimulation in the rat isolated vas deferens and guinea-pig ileum than the aqueous extract.

Cinnamomum zeylanicum (Tamil Name: Lavangapattai)
Cinnamon is a very popular culinary spice and is also used in candy, incense, toothpaste and perfumes. In traditional medicine cinnamon has been used as antitussive, antiarthritic, antimicrobial, antifungal, anti-oxidant, anti-inflammatory agent and used in treatment of sore pain and dental problems. Cinnamaldehyde has
potential activity against the production of nitric oxide and it can inhibit the expression of inducible nitric oxide as an enzyme that has a role in oxidative stress. Short term use of cinnamon can significantly reduce blood pressure especially among prediabetic or type 2 diabetic cases. In a meta-analyzed performed in three clinical trials studies showed that average drop in systolic blood pressure was 5.39 mmHg, while average drop in diastolic blood was 2.6 mmHg. Cinnamon with dose of 50 mg/kg for 2 weeks was given to dogs. During this period systolic blood pressure and heart rate in treated dogs was lower significantly than normal group. The decrease in blood pressure was hypothesized as decrease in vascular resistance and decrease in cardiac stroke volume. In a study, hemodynamic parameters like left ventricular systolic and diastolic pressures, ventricular contraction and relaxation, left ventricular developed pressure, work index of the heart and coronary flow in animals receiving cinnamon were measured during the 8 weeks period of training. The results revealed that treated group had enhanced cardiac force and contractility, positive inotropic effect, improved heart performance, increased coronary flow, better myocardial contractility and cardiac work.

The idea of Suvai as an attribute representing the pharmacological properties of a substance has recently been brought under scientific scrutiny. Medicinal herbs have been identified by ancient sages called Siddhars to possess the above tastes in combination or in single. Each taste is a combination of two elements among the panchaboothas (earth, water, fire, air and space).

<table>
<thead>
<tr>
<th>Humors</th>
<th>Pacifying tastes</th>
<th>Promoting tastes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vatham</td>
<td>Sweet, Sour, Salt</td>
<td>Pungent, Bitter, Astringent</td>
</tr>
<tr>
<td>Pitham</td>
<td>Sweet, Bitter, Astringent</td>
<td>Sour, Salt, Pungent</td>
</tr>
<tr>
<td>Kabam</td>
<td>Pungent, Bitter, Astringent</td>
<td>Sweet, Sour, Salt</td>
</tr>
</tbody>
</table>

The Siddha system is a traditional system of medicine practice in South India and is one of the oldest traditional systems of the world. It has in store a lot of herbs with potent Cardioprotective action. This sytem of medicine mentions cardiac diseases in its texts as Ratha rogam and the cardiac pain as due to Ratha vayu. The perspective of pathogenesis of cardiac diseases in Siddha medicine is due to the derangement of three humours vatham, pitham and kabam.

The cardiac disorders such as atrial and ventricular fibrillations, valvular dysfunctions, bundle branch block, bradycardia and tachycardia can be correlated due to alterations in vatham which is concerned with the myocardial contractility, Valvular function, Conduction of impulses. Hypertension, Coronary arterial disease, High output failure, Ischemia and Myocardial infarction can be due to altered pitha humour which is the predominant constituent of blood and metabolic activities. Also altered Kapha humour which is considered to be a constituent of fluid and fat is said to cause Atherosclerosis, stenosis and congestive cardiac failure due to accumulated Kapham. Hence according to Siddha philosophy, medicinal herbs are chosen on the basis of six taste theory according to their nature to pacify the deranged humours thereby favouring cardio protection.

The Siddhars Theory, “Elements of Macrocosm exists in microcosm”, whenever an imbalance is founding the human body (Microcosm), herbs with corresponding taste and elements (Macrocosm) can be chosen to exert its pharmacological action and pacify the altered humours.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Botanical Name</th>
<th>Tamil Name</th>
<th>Suvi (Taste)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Terminalia arjuna</td>
<td>Marutha maram</td>
<td>Astringent</td>
</tr>
<tr>
<td>2</td>
<td>Centella asiatica</td>
<td>Vallaarai</td>
<td>Astringent, sweet, bitter</td>
</tr>
<tr>
<td>3</td>
<td>Allium satiium</td>
<td>Poondu</td>
<td>Pungent</td>
</tr>
<tr>
<td>4</td>
<td>Sida cordifolia</td>
<td>Kurunthotti</td>
<td>Astringent</td>
</tr>
<tr>
<td>5</td>
<td>Vitis vinifera</td>
<td>Thiratchai</td>
<td>Sweet</td>
</tr>
<tr>
<td>6</td>
<td>Nelumbo nucifera</td>
<td>Thamarai</td>
<td>Sweet, Astringent</td>
</tr>
<tr>
<td>7</td>
<td>Punica granatum</td>
<td>Madhulai</td>
<td>Sweet</td>
</tr>
<tr>
<td>8</td>
<td>Crocus sativus</td>
<td>Kungunapoo</td>
<td>Bitter</td>
</tr>
<tr>
<td>9</td>
<td>Cinnamomum zeylanicum</td>
<td>Lavangapattai</td>
<td>Pungent, Sweet</td>
</tr>
</tbody>
</table>

CONCLUSION
It is a well known fact that medicinal plants are a boon to the mankind as they provide us with phyto compounds with wide range of medicinal values. In this review we have shed light to the few plants with cardiovascular effect along with Siddha perception of Cardioprotective action through Suvai (tastes). Through this review, we have highlighted the beneficial effects of these plants behind the traditional claims with special reference to cardiovascular diseases.
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