

## CARDIOPROTECTIVE HERBS: AN UPDATED REVIEW

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### ABSTRACT

"All mechanisms and ways that maintain the heart by reducing" comprise cardioprotective measures. Phytochemicals are natural bioactive molecules distinguished from other biochemicals because they exist naturally in fruits, vegetables, and medicinal plants and have an impact on the treatment of numerous diseases. It is imperative to explore the pharmacological and therapeutic potential of biodiversity of plants. Diosgenin, isoflavones, sulforaphane, carotized, catechin, and quercetin are examples of bioactive molecules that can increase the cardioprotective influences of certain cardioprotective plants and decrease the prevalence of cardiac abnormalities.

**Keywords:** Cardioprotective, Medicinal plants, Phytoconstituents, Cardiovascular disease

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### INTRODUCTION

Medicinal plants have the potential to be used as sources of medicine due to their secondary metabolites and therapeutic essential oils. Medicinal plants are used to treat a variety of ailments because they are cheaper, safer, effective, readily available, and accessible. The virtues mentioned have impacted the usage of medicinal plants among various traditional medicine practitioners to the point where herbal usage becomes a daily practice [1-3]. Many people all over the world utilize herbal medicines for their health, and many tribes have incorporated them into their cultural heritage. Polyphenols produce cardio-protective effects primarily by preventing oxidation of low-density lipoprotein. The majority of important pharmacological drugs are derived from plants. Plant-derived drugs are significant within human and animal health care systems around the globe, and are utilized to prevent health issues as well as treat pathology. Medicinal herb treatments for ischemic heart disease-related circumstances have been an established practice for many years. The last decade of the twentieth century has produced an extensive body of phytochemical, biological, and clinical evidence to suggest that plant-based herbal therapies are gaining acceptance for the treatment of numerous diseases [4, 5]. Cardiovascular disease has a significant and growing worldwide burden. In 1990, over 14 million people died from cardiovascular disease; by 2020, that number is expected to increase to about 25 million [6]. Cardiovascular disease is a substantial and growing worldwide burden. In 1990, more than 14 million people died from cardiovascular disease; by 2020, it is expected that that number will increase to nearly 25 million. The occurrences of cardiovascular diseases (CVDs) are increasing around the world, particularly in developing nations that are going through a rapid health transition. Poor dietary and lifestyle behaviors that contribute to diabetes and obesity are amongst the chronic opportunities for increasing CVD occurrences [7, 8].

#### Medicinal plants with cardioprotective potential

*Emblica officinalis* (E. officinalis) or *Phyllanthus emblica* (P. emblica) are small to medium-sized deciduous trees in the family Euphorbiaceae. *Emblica officinalis* (E. officinalis) or *Phyllanthus emblica* (P. emblica) are small to medium-sized deciduous trees in the family Euphorbiaceae [9].

*Tinospora cordifolia* (T. cordifolia) is a deciduous climbing shrub belonging to the Menispermaceae family; and has been shown in research in Wistar rats to effectively prevent cadmium (Cd) poisoning from altering the changes in antioxidants, glycoproteins, and serum marker enzymes (lactate dehydrogenase and creatine

kinase) levels. *T. cordifolia* was indicated to serve as a potent cardioprotective modality for Cd intoxication, toxicity monitoring changes in the enzyme levels. The cardioprotective effects of *T. cordifolia* have also been characterized in rats with myocardial infarction from ischemia-reperfusion [10].

#### *Glycyrrhiza glabra*

The herbaceous perennial *Glycyrrhiza glabra* (G. glabra) is a member of the Fabaceae family. Root is crucial in terms of its therapeutic significance. The primary components are flavonoids such as isoliquiritigenin and liquiritigenin (4',7- dihydroxyflavanone) and saponins such as glycyrrhizin. According to a study done on rats, G. glabra exhibits cardioprotective effects that are followed by ischemia-reperfusion injury. It may also have the ability to prevent myocardial infarction by influencing heart function and having antioxidant benefits. According to a preclinical investigation, therapeutic dosages of G. glabra should not damage the heart because of the normal histoarchitecture of the myocardium [11, 12].

#### *Terminalia arjuna* (T. arjuna)

The large deciduous tree *Terminalia arjuna* (T. arjuna) is part of the Combretaceae family of flowering plants. In the Indian subcontinent, the bark extract is used to treat dyslipidemia, hypertension, congestive heart failure, and anginal pain. The authors Dwivedi *et al.* [20] explain that T. arjuna bark extract had cardioprotective activity to significantly inhibit the rise in oxidative stress due to isoprenaline, and an increase in endogenous antioxidant, as well as coronary vasodilatation [13].

#### *Withania somnifera* (W. somnifera)

The woody shrub *Withania somnifera* (W. somnifera) is a member of the Zygophyllaceae family. The root is the medicinally helpful part. Pretreatment with W. somnifera extract significantly alleviated the biochemical and histological changes from doxorubicin in Wistar rats. This suggests a possible role for W. somnifera in doxorubicin-induced cardiotoxicity prevention. When given orally to hypercholesteremic rats, the root powder of the plant significantly lowered their triglyceride and total lipid cholesterol levels. A significant increase in liver bile and 3-hydroxy-3-methylglutaryl coenzyme levels as well as high-density lipoprotein cholesterol levels, were also observed. Activity of reductase was also noted [14].

*Terminalia chebula* (T. chebula) is an evergreen flowering tree in the family Combretaceae. Its fruit is a mild laxative, stomachic, tonic. T. chebula extract reduced rise in lactate; decrease in enzyme activities of Tricarboxylic Acid (TCA) cycle, mitochondrial respiration, levels of

Adenosine Triphosphate (ATP) in isoproterenol-induced cardiotoxicity in rats. The results document anti-ischemic property of *T. chebula* [15].

*Sida cordifolia* (*S. cordifolia*) is an upright member of the Malvaceae family. The roots and leaves are the most medicinally important sources. *S. cordifolia* extract pre-treatment showed significant increased levels of catalase activity and Superoxide Dismutase (SOD) as compared to control on the isoproterenol-induced ischaemia study. This activity confirmed its ability to produce cardioprotection [16].

*Tribulus terrestris* (*T. terrestris*) is a small shrub of the Zygophyllaceae family that has hairy or silky hairy properties. ECG and various cardiac biomarkers study showed that *T. terrestris* had protective activity against myocardial ischemia in rats. The anti-ischemic cardioprotective properties of *T. terrestris* can be attributed, at least in part, to its antioxidant, antiapoptotic and anti-inflammatory activities [17].

#### **Trapa Bispinosa (*T. Bispinosa*)**

The aquatic vegetation *Trapa Bispinosa* (*T. Bispinosa*) is part of the family Trapaceae. The fruit is well-known for its medicinal properties. *Trapa bispinosa* demonstrates anti-inflammatory benefits due to its high nutritional (mineral and vitamin) contents. Based on its ability to demonstrate anti-inflammatory and antioxidant properties, it is possible this fruit may also be contributory to the treatment of cardiovascular disease (CVDs). Unfortunately, the potassium content in this fruit has not been published. However, the intake of potassium is suggested to remarkably reduce the risk of high blood pressure and stroke in previous studies. To date, single-dose toxicity studies recommend a 3 g/kg body weight for doses [18].

#### **Serpentina**

Historically, reserpine is an alkaloid derived from the dried root of the plant *R. serpentina*, known as 'snake root' in Hindu medicine using Ayurvedic practices, has been utilized for centuries as an Ayurvedic treatment. The *R. serpentina* root for the treatment of psychoses and high blood pressure was first documented in Indian literature in 1931. However, utilization of Rauwolfia alkaloids in Western medicine began in the mid-1940s following the Second World War. Today, *R. serpentina* in standardized whole root preparations in the United States Pharmacopoeia is monographed, having reserpine alkaloid also monographed. 200-300 mg of powdered whole root, administered orally, is equivalent to 0.5 mg of reserpine [19].

#### **Stephania tetrandra**

The herb *Stephania tetrandra* has been used in Traditional Chinese medicine to treat hypertension. Tetrandrine, an alkaloidal extract from *S. tetrandra*, has been shown to be a calcium ion channel blocker, just like verapamil. Tetrandrine inhibits aldosterone production, blocks T and L calcium channels, and prevents diltiazem and methoxyverapamil from binding to calcium-channel binding sites. In conscious rats, a dose of tetrandrine (15 mg/kg, parenteral) lowered mean, systolic and diastolic blood pressure for approximately 30 min; however, an intravenous dose of tetrandrine (40 mg/kg) resulted in cardiac depression, which resulted in death. An oral dose of tetrandrine (25 and 50 mg/kg) in stroke-prone hypertensive rats resulted in a progressive, long-lasting hypotensive effect after 48 h, without an alteration in plasma renin activity [20, 21].

*U rhynchophylla* extract relaxes norepinephrine precontracted rat aorta via both endothelium-dependent and endothelium-independent mechanisms. *U rhynchophylla* extract likely releases nitric oxide and/or an endothelium-derived relaxing factor for the endothelium-dependent mechanism but does not bind to muscle receptors. Furthermore, research has shown both *in vitro* and *in vivo* that rhynchophylline reduces collagen or adenosine diphosphate plus epinephrine-mediated platelet thromboses and prevents platelet accumulation [22].

#### **Veratrum viride**

The perennial herb veratrum, also sometimes called hellebore, is cultivated around the globe. The several varieties include *Veratrum viride*, native to Canada and the eastern United States, *Veratrum californicum*, endemic to the western United States, *Veratrum*

*album*, described from Alaska and Europe, and *Veratrum japonicum*, in Asia. All *Veratrum* plants can produce poisonous alkaloids, causing bradycardia, hypotension, and vomiting. The majority of veratrum poisonings are because of botanical misidentification with other plants. Although veratrum alkaloids were once used to treat hypertension, their usage declined due to their low therapeutic index, unacceptable toxicity, and the replacement of veratrum with safer alternatives for antihypertensive medications [23].

#### **Panax ginseng (*Asian ginseng*)**

*Panax notoginseng* is commonly called pseudoginseng because it is often an adulterant in *P. ginseng* preparations. The root of *P. notoginseng* is traditionally used for hemostasis and analgesia in traditional Chinese medicine, and it is also widely used to treat patients with coronary artery disease and angina [24].

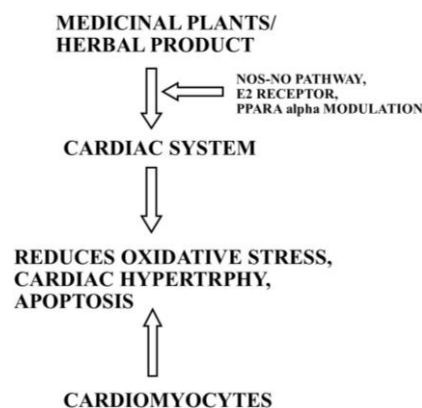
*Salvia miltiorrhiza* (*dan-shen*), native to China, is related to the Western sage *Salvia officinalis*. The root of *S. miltiorrhiza* is traditionally used in Chinese medicine for its cooling, sedative, and circulatory stimulating properties. Like *P. notoginseng*, it has exhibited the ability to dilate coronary arteries at all concentrations, suggesting that it has the potential to be an effective antianginal agent. Furthermore, *salvia miltiorrhiza* may not produce the effects to treat hypertension because its effects on other arteries differ dependent on concentration [25].

*Garlic* (*Allium sativum*) has been used and appreciated by people for the past thousands of years due to its medicinal properties. Garlic is one of the herbal medicines that the scientific community has studied closely. When large amounts of fresh garlic (0.25 to 1.0 g/kg, equivalent to approximately 5-20 average-sized 4-g cloves for a person weighing 78.7 kg) are ingested, the positive benefits mentioned above have been reported. This is further supported by a recent double-blind crossover trial that evaluated the effect of a placebo and 7.2 g of aged garlic extract on blood lipid levels in men with moderate hypercholesterolemia. When compared to placebo, the aged garlic extract produced a reduction in total serum cholesterol by 6.1%, and a reduction in LDL cholesterol by 4.6% [26].

#### **Commiphora mukul (*gugulipid*)**

Ayurveda has long used *Commiphora mukul* (*gugulipid*), a small, thorny tree found in India, to treat lipid disorders. The primary mechanism of action for *gugulipid* is to enhance the liver's uptake and metabolism of LDL cholesterol. 81 In a double-blind, crossover study with 125 patients on *gugulipid* and 108 on clofibrate, median reductions in serum cholesterol and triglyceride concentrations were 11% and 16.8% with *gugulipid* and 10% and 21.6% with clofibrate, respectively. As a rule, patients with high cholesterol did better on *gugulipid* therapy than those with high triglycerides [27, 28].

*Maharishi Amrit Kalash-4* and *Maharishi Amrit Kalash-5* are two complex herbal formulations with significant antioxidant properties shown to inhibit LDL oxidation in hyperlipidemic subjects. They were shown in studies to inhibit platelet aggregation and microsomal lipid peroxidation induced by enzymes and non-enzymatic agents [29].



**Fig. 1: Cardio protective mechanism of medicinal plants/herbal products**

Table 1: Below is a list of various cardioprotective plants' pharmacological status

Plants name	Family	Chemical constituents	Medicinal use	Dosage form
<i>Allium sativum</i> (Bulb) [30]	Liliaceae	Lavonoids, tannins, saponins, and cardiac glycosides	Antihyperlipidemic, and cardioprotective	Garlic oil
<i>Ficus hispida</i> (Leaves) [31]	Moraceae	Mucilage, gums, flavonoids, phenols, sterols, amino acids, $\beta$ -amyrine acetate, protein, carbohydrates, n-triacontanol, lupeol acetate, $\beta$ -sitosterol, Glycosides, flavonoids, steroids, tannins,	Cardioprotective, antipyretic, hepatoprotective	Methanol
<i>Trichopus zeylanicus</i> (leaves) [32]	<i>Trichopus zeylanicus</i>		Cardioprotective, adoptogenic	Ethanol
<i>Tribulus terrestris</i> (fruit) [33]	Zygophyllaceae	Alkaloids, glycosides, and steroidal saponins	Cardioprotective, antilithiatic,	Aqueous
<i>Semecarpus anacardium</i> (dried nuts) [34]	Anacardiaceae	Phenolic compounds, biflavonoids, sterols, glycosides, ursuhenol,	Cardioprotective, antioxidant	Ethanol
<i>Crocus sativus</i> (flowers) [35]	Iridaceae	Carotenoid compounds, crocetin, crocin, safranal	Cardioprotective, hypnotic,	Aqueous
<i>Ocimum sanctum</i> (leaves) [36]	Lamiaceae	Saponins, tannin, steroid, flavonoids	Cardioprotective, antioxidant	Hydroalcohol
<i>Moringa oleifera</i> (leaves) [37]	Moringaceae	Tannins, saponins, alkaloids, terpenes	Antipyretic, and cardioprotective	Hydroalcohol
<i>Lagenaria siceraria</i> [38]	Cucurbitaceae	Flavonoids, terpenoids	Antihyperlipidemic, and cardioprotective	Juice
<i>Picrorhiza kurroa</i> (Rhizome) [39]	Scrofulariaceae	Glycosides, phenolic compounds	Anti-inflammatory, and cardioprotective	Ethanol
<i>Croton sparsiflorus</i> (leaves) [40]	Euphorbiaceae	Saponins, tannins, phenols, flavonoids,	Anti-inflammatory, and cardioprotective	Methanol
<i>Azadirachta indica</i> (leaves) [41]	Meliaceae	Tannins, flavonoids, steroids,	Cardioprotective, chemopreventive,	Aqueous
<i>Coleus forskohlii</i> (Roots) [42]	Lamiaceae	Forskolin hydrochloride, demethylcryptojaponol,	Antiobesity, and cardioprotective	Ethanol
<i>Psidium guajava</i> (leaves) [43]	Myrtaceae	Carotenoid, flavonoid,	Cardioprotective,	Aqueous
<i>Hydrocotyle asiatica</i> (whole plant) [44]	Umbelliferae	Flavonoids, and glycosides	Cardioprotective, antipsoriatic,	Alcohol
<i>Terminalia arjuna</i> (Bark) [45]	Combretaceae	Lactones, phytosterol, flavonoids,	Antihyperlipidemic, and cardioprotective	Alcohol
<i>Callistemon lanceolatus</i> (leaves) [46]	Myrtaceae	Phenolic compounds, carbohydrates,	Antioxidant, and cardioprotective	Ethanol
<i>Phyllanthus niruri</i> (whole plant) [47]	Phyllanthaceae	Flavonoids, terpenoids, alkaloids,	Cardioprotective, anticancer,	Aqueous
<i>Curcuma longa</i> (Rhizome) [48]	Zingiberaceae	Curcumin, ar-turmerone, $\beta$ -sesquiphellandrene,	Cardioprotective, anti-inflammatory	Ethanol
<i>Tribulus macropterus</i> (Aerial parts) [49]	Zygophyllaceae	Flavonoids, saponins, alkaloids	Cardioprotective	Methanol
<i>Cordia myxa</i> (fruit) [49]	Boraginaceae	Saponins, and tannin	Cardioprotective	Methanol
<i>Hibiscus sabdariffa</i> (petals) [50]	Malvaceae	Tannins, saponins, phenols, glycosides	Antioxidant, and cardioprotective	Aqueous
<i>Camellia sinensis</i> (leaves) [51]	Theaceae	Tannins, flavonoids, steroids	Cardioprotective	Aqueous

### Mechanism of medicinal plants/herbal products

Medicinal/herbal plants have demonstrated anti-inflammatory, anti-oxidative, and anti-apoptotic effect, activation of the signaling pathway of endothelial nitric oxide synthase-nitric oxide (NOS-NO) and stimulation of angiogenesis, decreased endothelial permeability, regulation of the K-ATP channel to prevent free radical-mediated oxidative actions, and anti-apoptotic effects, improved mitochondrial functioning, as well as inhibition of various protein expressions (contractile) and control of calcium levels [52].

### CONCLUSION

Herbal medications are widely prevalent in the world so medical providers should remember to inquire about these health behaviors while performing clinical histories, and stay informed on the potential benefits or harm of these treatments. Although the specific molecular mechanisms are still not resolved, many researchers have looked at the therapeutic and preventive benefits of plant phytoconstituents for the treatment of cardiac disorders using chemoprevention. Phytoconstituents may offer cardioprotective benefits by scavenging oxygen free radicals, inhibiting important enzymes, and modulating certain factors. In addition to allopathic treatment regimens, screening of the native medicinal plants of the surrounding landscape, in order to identify specific plant phytoconstituents with therapeutic action against cardiovascular disease, is justified.

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All authors have contributed equally

### CONFLICT OF INTERESTS

Declared none

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