

## POTENTIALS OF MEDICINAL PLANTS FOR CARDIOVASCULAR DISEASES- AN UPDATE

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### **ABSTRACT**

Since ancient times herbal medicines are used for clinical purposes for the treatment of cardiovascular diseases. Siddhars says that the Siddha system of medicine is a fruitful gift of God. In India, this system is practiced for ages. Sidha system gave us a new way for new drug discovery including CVD. They are a rich source that shows biological and pharmacological properties. As compared to the conventional medications, these medicines don't require any clinical studies prior to their marketing or any approval from regulatory agencies. Their efficacy and safety are rarely proven because of a lack of clinical studies. In this review article, we will collect the available evidence which shows their use as cardiovascular medicines. Most of these herbs usage in CVD is not supported by scientific data. Despite this

fact, herbs show clinical effects on the biological mechanisms of the heart. Their botanical classification, mechanism of action and chemical constituents are discussed.

**KEYWORDS:** Sidha, Life-threatening, alternative medicines, herbs, cardiovascular diseases.

### **INTRODUCTION**

History is proof that herbs are used for medicinal purposes and their usage in daily life as well as in diseased states is still present. Around 25% of commercial medicines are derived from herbs or plants. According to the survey conducted in the U.S showed that one out of every 5 people has taken herbal supplements during their life.<sup>[1-3]</sup> In developing countries numbers are high due to the less accessibility of synthetic medicines. For example, China takes 30% to 50% of herbal medicines.<sup>[1]</sup> Cardiovascular disorders are the leading cause of death worldwide.<sup>[4]</sup> Cardiovascular disease (CVD) causes the death of 1 out of 3 people in

U.S. Pharmacological drugs which targets specific pathway of CVD have seen advancements with new as well as more efficient drug targets emerging. They have limited side effects. Herbal plants have the potential to treat or prevent CVD.<sup>[5]</sup> Herbs containing very effective cardioactive chemical constituents which show positive inotropic actions on the heart. For example, *Digitalis purpurea* or *Digitalis lanata* contains digitoxin and digoxin which is being used for the treatment of congestive heart failure for many decades.<sup>[6]</sup> The main of this review paper is to describe some herbs which can be very useful to eradicate cardiovascular disorders.

## 1. ASIAN GINSENG (PANAX GINSENG)

### Botanical classification<sup>[7]</sup>

Kingdom:	Plantae
Subkingdom:	Viridiplantae
Division:	Tracheophyta
Class:	Magnoliopsida
Order:	Apiales
Family:	Araliaceae
Genus:	<i>Panax</i>
Species:	<i>Panax ginseng</i>

### Plant description

The ginseng plant is a perennial erect herb described in Figure 1 having sturdy taproots. They die back in the fall season and from the roots they reemerge in the spring. They have usually large and palmately compound leaves with 3-5 leaflets. Depending on the species the margin of the leaf may be entire, lobed, or toothed. The fruit is mainly fleshy i.e berries of a drupe. The ginseng plant is a solitary umbel i.e flat-topped flowers cluster with both male flowers and bisexual flowers. To become mature they require 5-7 years of the time period from seed.<sup>[8,9]</sup>



**Fig 1.**

### **Chemical constituents**

Till now around 200 substances have been isolated from *Panax ginseng*.<sup>[10]</sup> It includes ginsenosides, aminoacids, polyacetylenes, polysaccharides, and volatile oils. In ginseng, the unique component is the presence of total ginsenosides (TGS), which is further classified as dammarane-type, oleanane-type, and ocotillo-type oligoglycosides.<sup>[11]</sup> Saponins in ginseng are dammarane type includes protopanaxatriol- type and protopanaxadiol type, ocotillo type and oleanane type.<sup>[12]</sup> Total ginseng saponin content comprises 4% and it depends on the species, part of the plants, season, and age.<sup>[12,13]</sup> Ginseng polysaccharides (GPS) are divided into two categories, namely starch-like glucans and pectin. Starch-like glucan includes two compounds i.e arabinogalactan (AG) and dextran. Pectin includes galactose (Gal), arabinose (Ara), galacturonic acid (GalA), and rhamnose (Rha).<sup>[14]</sup> Polysaccharide content in ginseng is 28.56%.<sup>[15]</sup> Ginseng contains 18 amino acids. Out of these amino acids fourteen amino acids like arginine, glutamic acid, lysine, serine, threonine, aspartic acid, glycine, leucine, alanine, proline, proline, phenylalanine, isoleucine, and tyrosine.<sup>[16]</sup> In ginseng volatile oils includes heterocycles, sesquiterpenoids, fatty acids, aldehydes, alkane hydrocarbons, and fatty acid ester. Out of them, sesquiterpenoids are highly abundant whereas n- hexadecanoic acid (32.28%) and falcarinol (29.64%) are other major components present in ginseng.<sup>[17]</sup> Depending upon the growth of the plant ginseng volatile oil varies from 0.081% to 0.223%.<sup>[18]</sup> In polyacetylene single bond and triple bond alternate. It is organic in nature. Polyacetylene presence in ginseng accounts for 0.020-0.073%.<sup>[19]</sup> It includes acetic acid, linolenic acid, diacetyl alcohol, and triacetyl alcohol.<sup>[20]</sup> Ginseng contains 12 alkaloids which include adenosine, choline, and spermine. Some trace elements like vitamins and enzymes which are important to the human body are also present.<sup>[12]</sup>

### Activity against CVD

Although ginseng has been considered a very beneficial herb for diseases since ancient times but researchers have confirmed it recently that it has a potent effect against cardiovascular diseases.<sup>[21]</sup> Scientists have been focusing to find a single compound instead of whole ginseng extract which is helpful in showing the effects on cardiac and vascular diseases. In recent studies conducted by the researchers, they have found that in guinea pig ventricular myocytes, ginseng holds the capacity to inhibit the L-type  $\text{Ca}^{2+}$  currents.<sup>[22]</sup> Moreover, ginsenosides like Re, Rh2, and Rg3 also inhibit  $\text{Ca}^{2+}$  channels to a different extent.<sup>[22,23,24,25]</sup> In addition, researchers have observed that administration of ginsenoside Rd has the potential to decrease the hypertensive remodeling by altering the increase in receptor or store-operated  $\text{Ca}^{2+}$  channels.<sup>[26]</sup>

Also, ginseng and ginsenoside Re showed the delay in the  $\text{K}^{+}$  channel in ventricular myocytes of guinea pigs.<sup>[23]</sup> Another study showed that ginsenoside Re protects the heart against the ischemia-reperfusion (IR) injury. It also induces the potassium channel activation through nitric oxide modulation.<sup>[27]</sup> In rats, all ginsenosides inhibit right ventricular hypertrophy<sup>[28]</sup> whereas ginsenoside Rg1 protects against the left ventricular hypertrophy which is induced by abdominal aorta coarctation.<sup>[29,30]</sup>

Electromechanical alterations are suppressed by the ginsenoside Re in cat and human cardiomyocytes<sup>[31]</sup> and ginsenoside Rb1 protects against the MI (Myocardial Infarction) which is induced by the infarction in Sprague-Dawley rats.<sup>[32]</sup> Ginsenoside Re and Rb1 show a potent protective effect against heart failure in animals.

## 2. FLAX SEEDS

### Botanical classification<sup>[33]</sup>

Kingdom:	Plantae
Subkingdom:	Viridiplantae
Division:	Tracheophyta
Class:	Magnoliopsida
Order:	Malpighiales
Family:	Linaceae
Genus:	Linum
Species:	Linum usitatissimum

### Plant description

Flax plants have grey-green, lance-shaped alternate leaves and are herbaceous annual. Their height ranges from 1-4 feet (0.9 to 1.2 meters) and have slender stalk 2.5 to 4mm in diameter and have branches. Plants that are cultivated for the seed described in Figure 2 have many branches and are short. The flax plant has many varieties having colors of flowers like white, yellow, red, and blue. Blue is the most common color of flowers. Flowers are self-pollinating with five sepals, five petals, five stamens, and pistil with five styles. The fruit is a small dry capsule with five carpels, each contains two brown, yellow, and shiny seeds. They are usually grown in rotation with other crops to avoid fungal infection which can harm flax plants.<sup>[34,35]</sup>



**Fig 2.**

### Chemical constituents

Flax seeds contain around 40% lipids, 30% dietary fiber, and 20% protein. This composition depends on the variety. In seeds, 76% of protein is found and in cotyledons, 75% of lipids are found whereas endosperm contains 23% of lipids and 16 % of protein.<sup>[36,37]</sup> The composition of lipid flaxseed makes it a potent source of Omega 3 fatty acid, especially  $\alpha$ -linolenic acid (ALA), which contributes up to 52% of total fatty acids. Flax seeds are also a good source of phenolic compounds such as lignans, colloid gum, and high-quality protein.<sup>[37]</sup> Cotyledons contain oils highly sought after  $\alpha$ -linolenic, oleic acids, and linoleic. The oil from the flax seed is especially found as triacylglycerols 98% having a lower content of phospholipids 0.9% and also free-fatty acids 0.1%.<sup>[38]</sup> On average flax seed contains a protein content of about 22 g 100 g<sup>-1</sup>. Flax seeds are a rich source of arginine, glutamic acid, and aspartic acid, and limiting amino acids like lysine and cysteine, and methionine.<sup>[39]</sup> Fiber gives volume to the component and it contains polysaccharides (other than starch) which show activities like anti-hypercholesterolemic, anticarcinogenic, and glucose metabolism controlling

effects.<sup>[40,41]</sup> adding flax mucilage and linolenic acid into the diet can reduce the cholesterol in the plasma and arteriosclerotic lesions.<sup>[42]</sup> Flax seeds contain a complex of phenols like lignans. It contains few derivatives of ferulic acid, secoisolariciresinol, isolariciresinol, and matairesinol.<sup>[36]</sup>

### Activity against CVD

Some major studies<sup>[43]</sup> were conducted to check the action of ALA present in flax seeds, which showed that ALA is inversely correlated with primary cardiovascular events. As the data collected was from a very large population so it was quite persuasive.

1. High intake of ALA gives high protection against fatal myocardial infarction, the study was conducted on 76,283 women for 10 years.<sup>[44]</sup>
2. The ALA content cholesteryl ester fraction tends to reduce the risk of death in patients with coronary artery disease, the study was conducted on 415 people for 5 years.<sup>[43]</sup>
3. There is an inverse relationship between nonfatal acute myocardial infarction and ALA adipose tissue, the study was conducted on 964 people.<sup>[45]</sup>
4. Patients suffering from acute myocardial infarction has low serum levels of ALA, EPA, DHA as compared with the control group, the study was conducted on 157 people.<sup>[46]</sup>
5. High intake of ALA gives 40% less risk of cardiac death, the study was done on 76,763 women.<sup>[47]</sup>
6. Rich diet of ALA shows a low risk of calcified atherosclerotic plaque in the coronary arteries.<sup>[48]</sup>
7. Increase in the 1% of ALA intake (as % of energy) showed a 40% lower risk of nonfatal CAD, the study was conducted on 43,757 men for 6 years.<sup>[49]</sup>

A case-control study was conducted on 96 middle-aged men suffering from incident stroke and they observed that there was a 28% decrease in the risk of stroke by increasing 0.06% phospholipid ALA content.<sup>[50]</sup> After giving dietary supplementation of 600mg/day of secoisolariciresinol for eight weeks, there was a reduction in the blood total cholesterol levels, LDL, and HDL cholesterol.<sup>[51]</sup>

### 3. GINGER

#### Botanical classification<sup>[52]</sup>

Kingdom: Plantae  
Phylum: Spermatophyta  
Class: Monocotyledonae

Order: Zingiberales  
Family: Zingiberaceae  
Genus: Zingiber  
Species: Zingiber officinale

### Plant description

The rhizomes of ginger are brown in color described in Figure 3. They have a corky outer layer and the center is pale yellow. The leaves are alternatively arranged on the stem and above the ground shoot is erect and they are 6 to 12 inches long. From multiple bases, shoots arise and wrap around one another. The leaves can reach up to 1.9 cm broad and 7 cm in length. They produce cone-shaped pale yellow flowers with a size of 1-inch thickness. It can grow up to 2-4 ft. It is believed to have originated in Southeast Asia.<sup>[53]</sup>



**Fig 3.**

### Chemical constituents

Ginger has many potent chemical constituents like phenolic and terpene compounds.<sup>[54]</sup> Phenolic compounds in ginger basically contain gingerols, paradols, and shogaols. The major polyphenols of gingerols in fresh ginger is 6-gingerol, 8-gingerols and 10-gingerols.<sup>[55]</sup> Some other phenols present in ginger are quercetin, gingerenone-A, zingerone, and 6-dehydrogingerdione.<sup>[56,57]</sup> In ginger terpenes are also present like  $\beta$ -bisabolene,  $\beta$ -sesquiphellandrene,  $\alpha$ -curcumene,  $\alpha$ -farnesene, and zingiberene, they are basically considered as the main compound for essential oil.<sup>[58]</sup> Moreover, it contains polysaccharides, organic acids, lipids, and raw fibers.<sup>[54,58]</sup>



### Activity against CVD

Many studies were conducted and they showed that ginger can decrease the levels of blood pressure and lipids and protects from cardiovascular diseases.<sup>[59,60]</sup> It is also a protective factor against coronary artery disease, a study was conducted by giving a high-fat diet to the rats, it reduced the body weight and increased the serum high-density lipoprotein cholesterol (HDL- C).<sup>[61]</sup> Total cholesterol level and LDL were decreased when rats were fed with the high-fat diet and the levels of HDL were increased when given in combination with aerobic exercise and ginger extract.<sup>[62]</sup> Furthermore when a high-fat diet was given it also reduced the level of TC, triglycerides, very low-density lipoprotein cholesterol (VLDL). It occurred because of the higher liver expression of peroxisome proliferator-activated receptors, which were co-related to atherosclerosis.<sup>[60]</sup> A cross-sectional study suggested that increasing the intake of ginger in a diet can reduce hypertension and coronary heart disease.<sup>[63]</sup>

## 4. GARLIC

### Botanical classification<sup>[64]</sup>

Kingdom: Plantae  
Phylum: Spermatophyta  
Class: Monocotyledonae  
Order: Liliales  
Family: Liliaceae  
Genus: Allium  
Species: Allium sativum

### Plant description

Garlic plants can grow up to 2 feet in height. Long leaves presence is dependent on the variety of plants, they usually arise above the bulb from the short hard stem or may emerge from the softer pseudostem. The garlic plant has cloves described in Figure 4 that are usually covered with the membranous skin into the bulb-like structure. The cluster of flowers is basically enclosed first into tapered bracts; these bracts open when the pinkish or green white flower blooms. Garlic is grown as an annual crop. It can be planted by seeds or by cloves.<sup>[65]</sup>



**Fig 4.**

### Chemical constituents

Cloves of garlic contain many phytochemicals including sulfur-containing compounds such as ajoenes (E-ajoene, Z-ajoene), vinylthiins (2-vinyl-(4H)-1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), thiosulfinates (allicin), diallyl trisulfide (DATS), sulfides (diallyl disulfide (DADS) and some others which total accounts 82% of total garlic sulfur content.<sup>[66]</sup> With the help of the alliinase enzyme alliin (main cysteine sulfoxide) is converted into allicin after chopping off the garlic and breaking down its parenchyma. The main odoriferous constituents in fresh-milled garlic homogenates are S-propyl-cysteine-sulfoxide (PCSO), S-methyl cysteine-sulfoxide (MCSO), allicin.<sup>[67]</sup> Garlic contains several organosulfur compounds like S-allyl-cysteine (SAC), N-acetylcysteine (NAC)<sup>[68]</sup>, and S-ally-mercapto cysteine (SAMC), they are derived from alliin.<sup>[69]</sup>

### Activity against CVD

Many studies have suggested that garlic is very helpful in treating hypercholesterolemia by inhibiting the cholesterol biosynthesis in the liver and by preventing low-density lipoproteins oxidation. It reduces the cholesterol level by stimulating the acidic and neutral steroids excretion or by reducing the lipogenic and cholesterogenic effects of fatty acids synthase, malic, glucose-6 phosphate dehydrogenase, and 3-hydroxy-3-methyl-glutaryl-CoA reductase in hepatocytes.<sup>[70]</sup> It shows a great effect on dyslipidemia by reducing the levels of total cholesterol, TG, and LDL and elevating moderately the levels of HDL.<sup>[71]</sup> In clinical trials in patients, a dose of 300 and 60 mg/day for 12 months and 12 weeks was given, it showed effective results in decreasing TC, TG, and LDL while increasing HDL.<sup>[72,73]</sup> Furthermore a dose of 600mg/day for 12 weeks in diabetic patients suffering from dyslipidemia resulted in high HDL and low LDL and TC levels.<sup>[74]</sup>

Garlic has other significant benefits i.e decreasing systolic and diastolic blood pressure.<sup>[75]</sup> They show effects like inhibiting and reducing cardiovascular diseases like hypertension, thrombosis, hyperlipidemia, arrhythmia, and atherosclerosis.<sup>[76,77]</sup> In in vivo models it showed the antihypertensive effect of aqueous garlic extract in model '2 kidneys 1 clip' of hypertension in rats where thromboxane B2 and prostaglandin E2 levels were reduced.<sup>[78]</sup> Garlic exhibit this activity because of the presence of the active sulfur compounds which stimulate the endothelium-constricting and relaxing factors which cause low blood pressure. They also exhibit the property of vasodilation because they stimulate the production of nitric oxide and hydrogen sulfide.<sup>[79]</sup>

## 5. GINKGO

### Botanical classification<sup>[80]</sup>

Kingdom:     Plantae  
Division:    Ginkgophyta  
Class:       Ginkgoopsida  
Order:       Ginkgoales  
Family:      Ginkgoaceae  
Genus:       Ginkgo  
Species:     Ginkgo biloba

### Plant description

The shape of the ginkgo tree is pyramidal, has erratic branches, and is a deciduous tree up to 30 meters in height and 8 feet in diameter. The bark has a corky texture and is grayish in color. The light-colored wood is very soft and weak. During summer it turns gray-green to yellow-green and in autumn it turns into bright yellow in color. The shape of the leaves is like a fan with radiating veins out into the leaf blade described in Figure 5. The leathery leaves are up to 3 inches long and sometimes they are twice as broad. Leaves look like pinnae of the maidenhair fern. From the central notch, leaves are divided into two lobes.<sup>[81]</sup>



Fig 5.

### Chemical constituents

Leaf extract of ginkgo contains flavone glycosides, flavonol, lactone derivatives (ginkgolides A, B, C, J, M), ascorbic acid, catechin, 6-hydroxykinuretic acid, sterols, shikimic acid, iron-based superoxide, bilobalide, and vanillic acid. The major active ingredients are flavanoids and terpenes such as ginkgolides and bilobalide. Seeds of ginkgo contain 4-O-methoxypyridoxine which is a toxic substance and can cause loss of consciousness, convulsions, anti vitamin B6 activity, and also inhibits GABA formation. The roots contain the main active chemical constituent. Commercial manufacturers use leaf extract for the active ingredients. Standardization of leaf extract can be done by evaluating flavones, ginkgolides, and bilobalide.<sup>[82]</sup>

### Activity against CVD

A single dose of 600 mg of ginkgo leaf extract was given to male subjects, they observed inhibition of platelets aggregation which was induced by platelet-activating factor and ADP.<sup>[83]</sup> In another ex vivo study, the standardized leaf extract of ginkgo (SGB) Biloba 87.5 mg was infused intravenously and showed suppressed collagen-induced platelets aggregation.<sup>[84]</sup> Furthermore, on the isolated heart of the guinea pig, SGB 5 to 37 µg/ mL was given and it stimulated the concentration-dependent increase in coronary blood flow. On the isolated heart of rat which was further came in contact with normothermic global ischemia for 40 minutes, then followed by 20 min. Of reperfusion and perfusion with standardized Ginkgo biloba, the concentration of 200 µg/ mL. It increased cardiac recovery and also decreased the leakage of lactate dehydrogenase during the period of reperfusion.<sup>[85,86,87]</sup>

## 6. GREEN TEA

### Botanical classification<sup>[88]</sup>

Kingdom: Plantae

Phylum: Spermatophyta

Class: Dicotyledonae

Order: Theales

Family: Theaceae

Genus: Camellia

Species: Camellia sinensis

### Plant Description

The green tea plant is a variation of the evergreen bush described in Figure 6. It has green leaves (glossy) and flowers are small white to pink in color. The plant has a height up to 9-12 m approximately. They are usually cultivated in warm areas, rainy areas and at high altitude areas, they are grown frequently. When the plant reaches its maturity stage after 3-4 years, young leaves, buds, and other parts are harvested which are high in polyphenols. As soon as leaves are picked, they are steamed or roasted, then they are rolled and dried to remove moisture.<sup>[89]</sup>



**Fig 6.**

### Chemical constituents

Green tea contains proteins up to 15-20% of dry weight, its enzymes are aminoacids 1-4% of dry weight like theanine, tryptophan, glycine, tyrosine, valine, leucine, arginine, glutamic acid, threonine. The concentration of carbohydrates is 5-7% dry weight, it includes cellulose, pectins, fructose, glucose, and sucrose. Minerals and trace elements weigh 5% dry weight such as calcium, chromium, iron, copper, manganese, cobalt, strontium, potassium, aluminum, nickel, sodium, phosphorus, fluorine. In trace amounts, it also contains lipids i.e linolenic and  $\alpha$ -linolenic acids, sterols i.e. stigmasterol, vitamins like B, E, C, xanthines bases like theophylline, caffeine, pigments like carotenoids and chlorophyll, and volatile compounds like alcohols, esters, hydrocarbons, and aldehydes.<sup>[90]</sup> Fresh leaves of green tea contain chemical constituents like theobromine, theophylline, phenolic acids like gallic acids, and amino acids like theanine.<sup>[91]</sup> It also contains flavanols, flavonoids, flavandiols.<sup>[92]</sup> The flavanoids are catechins mainly found in four categories i.e epicatechin, epicatechin-3-gallate, EGCG, and epigallocatechin.<sup>[93]</sup>

### Activity against CVD

On Norwegian 20,000 participants, an epidemiological study by giving five or more cups of green tea per day showed 2.1 and 3.55mmHg Lower systolic blood pressure in men and women.<sup>[94]</sup> In Japanese men and women suffering from abdominal obesity were given green tea extract having 583 mg catechin and observed the effects of EGCG on blood pressure and various other metabolic risk factors involved in obese or overweight men and further observed reduction in 2.7mmHg of diastolic blood pressure.<sup>[95,96]</sup> Another study conducted by Kono and colleagues observed that in 1306 Japanese men who are consuming nine or more cups of green tea per day have total serum cholesterol 8 mg/dl.<sup>[97]</sup> In 240 patients Maron and colleagues observed a reduction in LDL cholesterol while consuming green tea enriched with flavins for 12 weeks.<sup>[98]</sup> Interestingly, there is a lot of evidence that green tea shows an effect on post-prandial lipids<sup>[99]</sup> as well as on HDL cholesterol with diabetes mellitus.<sup>[100]</sup> A study on intake of flavonol and flavone in a Finnish cohort study done on 25,372 male smokers showed that it is inversely proportional to myocardial infarction and also death cases were reduced in coronary heart disease.<sup>[101]</sup>

## 7. HAWTHORN

### Botanical classification<sup>[102]</sup>

Kingdom: Plantae  
Phylum: Spermatophyta  
Class: Dicotyledonae  
Order: Rosales  
Family: Rosaceae  
Genus: Crataegus  
Species: Crataegus pinnatifida

### Plant description

Hawthorn is a shrub that grows 1.5- 4 m tall. It is a dense plant. In the spring season, their flowers bloom and are white in color described in Figure 7 which actually looks like a rose. This plant grows throughout the world. All around the world, there are around 300 species of Hawthorn. Its leaves, fruit, and flowers are used for medical purposes, especially for heart-related diseases. Flowers give an unpleasant smell and they taste slightly bitter. Its fruit is sour.<sup>[103]</sup>

**Fig 7.**

### Chemical constituents

Till now around 150 compounds have been identified. It includes triterpenoids which are further classified into triterpenoids and pentacyclic such as corosolic acid, cuneatanol, crategolic acid, oleanolic acid, etc.<sup>[104-110]</sup> Four steroids are present in Hawthorn i.e stigmasterol,  $\beta$ -sitosterol,  $\beta$ -daucosterol, 24-methylen-24-dihydro lanosterol.<sup>[108-111]</sup> Monoterpenoids and sesquiterpenoids are the chief constituents of volatile oil.<sup>[110]</sup> Lignans are also present which contains two phenylpropane frameworks.<sup>[110]</sup> Hydroxycinnamic acids like caffeic acid, ferulic acid, chlorogenic acid, and  $\beta$ -coumaric are also present.<sup>[113,114]</sup> It includes organic acids which are basically phenolic and other acids. Phenolic acids are benzoic acid, gallic acid, vanillic acid, gentisic acid, anisic acid.<sup>[113,110,112,115]</sup> Other organic compounds are citric acid, malic acid, ascorbic acid, oleic acid, palmitic acid, etc.<sup>[109,111,114,116-119]</sup> Twelve nitrogen-containing compounds are found in Hawthorn.<sup>[120]</sup> recently three new compounds are isolated and identified from this plant i. e and (Z)-3-hexenyl-O- $\beta$ -d-rhamnopyranosyl-(1'' $\rightarrow$ 6')- $\beta$ -D-glucopyranoside, (Z)-3-hexenyl-O- $\beta$ -d-xylopyranosyl-(1'' $\rightarrow$ 6')- $\beta$ -d-glucopyranoside, (Z)-3-hexenyl-O- $\beta$ -d-gluco-pyranosyl-(1'' $\rightarrow$ 6')- $\beta$ -d-glucopyranoside.<sup>[121]</sup> Moreover, plenty of sugar alcohols and sugars have been identified in the Hawthorn plant.<sup>[122]</sup>

### Activity against CVD

Through gavage in high cholesterol and fat models of rabbit total flavonoids present in the leaves of *C.pinnatifida* helped in the reduction of the serum levels of total cholesterol (TC) and triglyceride (TG).<sup>[123]</sup> The presence of total flavanoids also inhibits the mature adipocyte secretion of leptin as well as of PAI-1 in a dose-dependent manner.<sup>[124]</sup> The main active chemical constituents are hyperoside and ursolic acid and they were administered to animals in two doses. Levels of Total cholesterol were decreased whereas HDL and superoxide dismutase were increased as compared to the control group. The damage caused by oxygen-

free radicals to the vascular endothelium is also reduced, ultimately helps in preventing atherosclerosis.<sup>[125,126]</sup> It is a good source to ameliorate cardiovascular system effects. It increases myocardial contractility and also expands the coronary artery. *C.pinnatifida* decreases the heart rhythm, peripheral consumption, and myocardial oxygen consumption.<sup>[127]</sup> Flavanol dimers and multimers reduced blood pressure slowly in mice, cats, and rabbits, which was co-related to the expanded peripheral vessels.<sup>[128,129]</sup> Total flavonoids reduce the arrhythmia and burst size of LDH after a deterioration in cardiocytes due to hypoxia and ischemia.<sup>[130]</sup>

## 8. MILK THISTLE

### Botanical classification<sup>[131]</sup>

Kingdom: Plantae  
Phylum: Spermatophyta  
Class: Dicotyledonae  
Order: Asterales  
Family: Asteraceae  
Genus: *Silybum*  
Species: *Silybum marianum*

### Plant description

It is a toxic plant, branched annual or biennial. It can grow up to 2-6 feet in height described in Figure 8. Branches of the stem are above and rigid. Its ingestion in cattle and sheep can cause nitrate poisoning. Leaves are green in color, elliptic-lanceolate having a distinct pattern like white marble, with scattered short hair on the lamina and long tangled hair on the midrib. I reproduce via seeds. Corolla is reddish-purple in color 20-28mm long having an unequal lobe 4-6mm long. Albino forms white flowers. From April to October color of the flowers' heads is pink to purple having spiny bracts at bases.<sup>[131,132]</sup>



Fig 8.



### Chemical constituents

The main constituent of *Silybum marianum* is silybin. It contributes about 50% to 70% of the total composition. In this plant, flavonolignans are also present like silydianin, isosilybin, silychristin, and some other unidentified organic polymers. Flavonols like quercetin, kaemferol, and taxifolin are present in minor quantities. The composition of the compounds varied depending on the conditions in which it grows and upon the species or variety. Variation of silymarin composition influences its biological activity.<sup>[133]</sup> Plant tissue culture is the alternative method to get more concentration of silymarin and the standardized content of silymarin is only 80%. Enhanced content of silymarin is obtained by changing the growth regulators like chitosan, salicylic acid, and methyl jasmonate which further increases the activity of chalcone synthase. Chalcone synthase is the main enzyme that is responsible for the synthesis of silymarin, more the quantity of this enzyme more will be the production of silymarin.<sup>[134]</sup>

### Activity against CVD

Silymarin was given orally to Wistar albino rats weighing around 200 to 250gm at three different dose levels i.e 100 mg/kg, 250 mg/kg, and 500 mg/kg through gastric lavage for one week. It was observed that endogenous antioxidant enzymes were protected by the silymarin, during ischemia-reperfusion it suppressed the neutrophil infiltration and also limited the infarct size, by reducing the serum MDA, tissue MDA as well as serum marker enzymes in rats who were subjected to coronary artery occlusion for 30 min. followed by 4 hrs of reperfusion. It also restored the heart rate at the end of the reperfusion process.<sup>[135]</sup>

### CONCLUSION

This review explored and collected very informative data of 8 traditional medicinal plants along with their active components which are very useful for the treatment of CVD. These herbs are involved in treating CVD as well as reducing the side effects due to the natural presence of treating disorders. In this review paper, the authors made an effort to gather valid information of medicinal plants used for CVD from various research articles using search engines such as Scopus, Medline, Pubmed, Google scholar, and websites. This review will provide very informative data about the herbs in the field of CVD and also for those who are seeking medicine with fewer side effects and more therapeutic effects.

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