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Hypocholesterolemic and Antioxidant Potentials of Some Plants and Herbs: A Review.

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Review Article

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ABSTRACT

It is now widely accepted that atherosclerosis is a complex multicellular process involving oxidation of cholesterol and the intracellular accumulation of oxidized cholesterol. This accumulation causes a cascade of inflammatory processes, resulting in an unstable atherosclerotic plaque that ultimately bursts, causing myocardial infarction. From ancient times, botanicals have played a major role in the lifestyle of people. The active phytochemicals derived from these herbs and plants have provided protection against atherosclarosis. The association of hyperlipidemia with the development of atherosclerotic lesion has promoted widespread search for plant based compounds which effectively control the lipid profile in the blood and tissues with least or no toxic effect. Around eighty percent of the global population still relies on botanical drugs and herbal medicines have advanced to clinical use in modern times. Based on these findings, present review is written to identify the "Lipid-Lowering and Antioxidants Properties" of commonly used plants and herbs.

INTRODUCTION

Atherosclerosis is the most frequent cause of morbidity and mortality in the entire world. Atherosclerosis is a multi-factorial disease and about 250 different risk factors have been recognized. It is thought that atherosclerosis is caused by a response to damage to the endothelium from high cholesterol, high blood pressure, and cigarette smoking [1, 2]. There are the several main issues to be addressed in atherosclerosis, viz., hyperlipidemia, clotting factors, oxidation of low-density lipoproteins (LDL) and inflammation [3]. These factors collectively contribute to the development and rupture of atherosclerotic plaque [4]. It can also be related to a hormonal disease such as diabetes mellitus, hypothyroidism and Cushing's syndrome; or to the use of certain medication such as birth control pills, hormone therapy, some diuretics (i.e., water pills), or beta-blockers to treat cardiovascular diseases [5]. In blood plasma, cholesterol is transported by lipoproteins, which can be mainly categorized into five classes, based on the size of cholesterol-lipoprotein complexes: chylomicrons, the very-low-density lipoproteins (VLDL), the intermediate density lipoproteins (IDL), LDL, and the high-density lipoproteins (HDL) [6]. Experimental and clinical studies have shown that the amount of cholesterol transported in the Chylomicrons, VLDL, IDL and LDL classes of lipoproteins, known as pro-atherogenic cholesterol, is a risk factor for the occurrence of cardiovascular disease [7]. Chylomicrons transport exogenous lipids to liver, adipose, cardiac, and skeletal muscle tissue, where their triglyceride (TG) components are unloaded by the activity of lipoprotein lipase (LPL). Epidemiologic studies have reported that Triglyceride-rich particles such as chylomicrons and chylomicron remnants that carry dietary derived fats may play a role in the early stages of developing arteriosclerosis [8]. VLDL is produced by the liver and some VLDL remnants seem to promote atherosclerosis similar to LDL [9]. The underlying mechanism of atherosclerosis involves the deposition and retention of serum lipids consisting of LDL cholesterol in the coronary arteries, resulting in decreased blood flow to heart muscles [10]. The oxidative modification of LDL plays a pivotal role in the progression of atherosclerosis and plaque formation. It is believed that modification of LDL in the arterial wall, particularly by oxidation, is crucial to the cellular uptake of LDL in the first stages of atherosclerotic plaque development [11]. Therefore, by preventing the oxidation of LDL, it may be possible to reduce

the incidence of atherosclerosis. Lowering plasma cholesterol concentrations reduces the availability of atherogenic lipoproteins and also, presumably, the accumulation of cholesterol in the intima of arteries [12]. In contrast, cholesterol transported in HDL particles, known as anti-atherogenic cholesterol, has protective effect on cardiovascular disease [13].

The pharmacological, dietary and herbal treatment of Coronary Heart Disease (CHD) is based on the hypothesis that reduced cholesterol biosynthesis will lead to lower blood levels of cholesterol. Most of the drugs (statins) available today are inhibitors of 3-hydroxy-3-methylgluataryl coenzyme -A reductase, which is involved in cholesterol biosynthesis in the liver [14]. Lowering lipids and cholesterol levels by a drug or dietary interventions could reduce the risk of Coronary Heart Disease. Current interest in natural products has stimulated the search for new cholesterol-lowering agents from these sources. Many herbal medicinal products were reported to have a potential to reduce lipid and cholesterol in body and to enhance the safety profile by elevating HDL levels and inhibiting lipid oxidation [15].

Several synthetic hypocholesteromic agents such as statins, fibrates, resins and nicotinic acid are capable of efficiently reducing plasma total cholesterol (TC) levels, but LDL does not undergo any significant alteration. Also, synthetic hypolipidemic agents have one or more side effects and are unable to increase HDL levels. The major portion of the global population in developing countries still relies on botanical drugs to meet its health needs. The attention paid by health authorities to the use of herbal medicines has increased considerably, both because they are often then only medicine available in less developed areas and because they are becoming a popular alternative treatment in more developed areas. Thus herbal medicines have been given a valuable status and readily available products for primary health care, and WHO has endorsed their safe and effective use. More than 2000 plants have been listed in the Traditional (Herbal/Alternative) systems of medicine and some of these are providing comprehensive relief to the people suffering from cardio-vascular diseases. Botanical dietary supplements (herbs) can ameliorate this process and prevent cardiovascular disease at many steps in the process [16]. Many herbs have antioxidant activity and can reduce low-density lipoprotein oxidation. Some phytosterols found in botanicals can inhibit cholesterol absorption. Recent studies have shown that many compounds of herbal origin are able to reduce plasma TG and TC levels and elevate HDL. These attribute in reducing the risk of CHD [17, 18].

Plants constitute an important source of active natural products which differ widely in terms of structures, biological properties and mechanisms of actions. Various phytochemical components, especially polyphenols (such as flavonoids, phyenyl propanoids, phenolic acids, tannins, etc) are known to be responsible for the free radical scavenging and antioxidant activities of plants [19]. Polyphenols possess many biological effects. These effects are mainly attributed to their antioxidant activities in scavenging free radicals, inhibition of peroxidation and chelating transition metals. In generally, polyphenols all share the same chemical patterns, one or more phenolic groups for which they react as hydrogen donors and in that way neutralize free radicals [20].

Plant sterols and stanols, also called phytosterols and phytostanols, have chemical structures resembling that of cholesterol but are only available to humans through plant foods such as vegetable oils, nuts, seeds, cereals, legumes, fruits, and vegetables or industrial supplements from plant origin [21]. Inclusion of plant sterols/stanols in the diet was known to lower serum cholesterol in man since 1953 [22] and the effects of plant sterols and stanols on cholesterol and bile acid metabolism and their efficacy and safety as serum cholesterol-lowering agents have been reviewed by many researchers [23-25].

Plants and herbs possessing lipid-lowering and antioxidants properties

Medicinal plants play a major role in antiatherosclarotic activity [26]. The herbal hypolipidemics have gained importance to fill the lacunae created by the allopathic drugs. Plants have been the companions of man since time immemorial and formed the basis of useful drugs since they are less toxic than synthetic drugs. Screening of medicinal plants presents an avenue for the discovery of new drugs [27]. A number of plants have been found to be useful in atherosclerosis, hyperlipidemia and diabetes. Some of the plants being used are discussed below:

Guggul (*Commiphora mukul)*

Guggul is an ancient Indian herb that has been shown to lower cholesterol [28] and TG levels [29]. Guggul and gugulipid have a long history in the treatment of cardiovascular diseases including hypercholesterolemia and atherosclerosis [30]. The medicinal activity has been attributed to the oleogum resin (guggul) of the stem bark, which has been in use for thousands of years. Ayurvedic literature is full of praise for guggul and its divine actions, right from healing bone fractures and inflammations to treating cardiovascular disease, obesity and lipid disorders. The cardiovascular therapeutic benefits of guggul and guggulsterone appear to be due to the multiple pharmacological activities, notably the hypolipidemic, antioxidant, and antiinflammatory effects. Guggul works to balance conditions of both low and high cholesterol whether brought on by diet, lack of exercise, chronic stress, or genetic predilection. Gum guggul has been found to act as hypocholesterolemic and hypolipidemic agents in experimental animals like pigs, chicks, rabbits and rats [31]. The first animal study was conducted in rabbits over a period of 2 years [32]. Most

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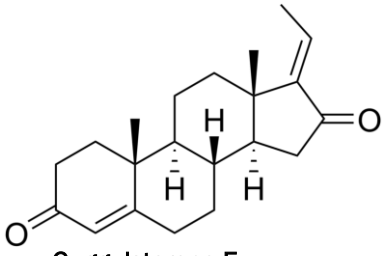
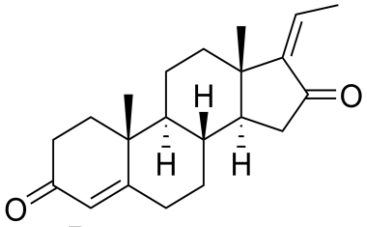
of the subsequent animal studies were conducted in rats. Consistent results were obtained with guggelsterone at doses ranging from 5 to 100 mg/kg of body weight. In one study guggulsterone, 25 mg/kg, lowered serum cholesterol and TG by 27% and 30%, respectively, after a treatment period as short as 10 days [33]. In another study, gugulipid was used as a positive control agent to evaluate the antioxidant, cardioprotective, and hypolipidemic activities of a series of synthetic compounds. Rats received gugulipid orally at a dose of 50 mg/kg for 30 days; gugulipid significantly decreased serum total cholesterol (35%) and lipid peroxide levels (57%). Hepatic microsomal lipid peroxidation was also significantly reduced by gugulipid. In addition, gugulipid significantly reversed the cardiac damage and biochemical changes induced by isoproterenol [34]. The levels of glutathione (GSH) in the brains of gugulipid-treated mice were significantly increased, suggesting inhibition of oxidative stress in the brain by gugulipid [35]. The chemical composition of *C. mukul* is very complex and has not been well defined. It may contain sugars (sucrose, fructose), amino acids, camphorene, cembrene allylcembrol, resin, oils, and several steroids or sterones. Only some steroid components have been purified, including Z and E guggulsterones which have been shown to be responsible for the cholesterol- and lipid-lowering effects of *C. mukul* [36, 37]. Although Wang et al. [38] showed that guggulsterone alone inhibited LDL oxidation; *C. mukul* surely contains other antioxidants because it is more effective in preventing LDL oxidation than guggulsterone [39].



Guggulsterone E

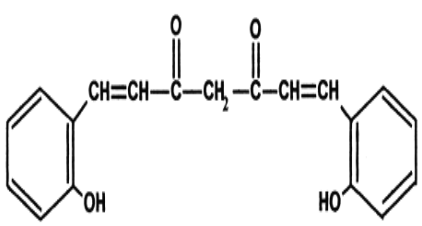


Guggulsterone Z

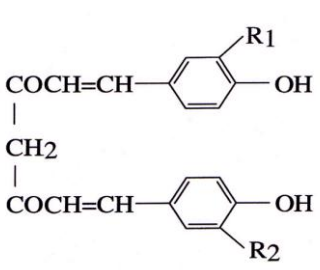
Figure 1: Active compound of *Commiphora mukul*

Turmeric *(Curcuma longa)*

Turmeric (*Curcuma longa*), synonymous with curcumin, is a native East Indian and Southeast Asian herb. Turmeric was used by ancient practitioners in India as a stomachic, tonic and carminative. It is used as a household remedy for local application in inflammatory conditions and other painful infections. Studies on the effect of powdered rhizomes of *C. domestica* mixed in the rabbit chow (4% *C. domestica*, w/w, in food pellet) on the cholesterol level in experimental hypercholesterolemic guinea pigs revealed that the dietary intake of *C. domestica* decreased all lipid levels in the aorta and also the serum TG level. In addition, *C. domestica* also reduced cholesterol deposition in the aorta [40] and turmeric rhizome powder (0.0, 0.05, 0.10, 0.15, and 0.20 %) also significantly decreased serum TG, TC and LDL-cholesterol of high cholesterol diet animal [41]. Quiles et al. [42] reported that supplementation with *C. longa* hydroalcoholic extract at dose level of 1.6 mg/kg body wt. reduces oxidative stress and attenuates the development of fatty streaks in rabbits fed a high cholesterol diet. Manjunatha and Srinivasan [43] demonstrated that, individually, both dietary curcumin and capsaicin significantly inhibited the *in vivo* iron-induced LDL oxidation, as well as copper-induced oxidation of LDL *in vitro*. The most active component of turmeric is curcumin, which makes up 2 to 5% of the spice. Curcumin is reported to activate the rate limiting step in cholesterol catabolism, that is, cholesterol 7-α-hydroxylase thereby stimulating the conversion of cholesterol to bile acid, an important pathway in the degradation of cholesterol. Majithiya et al., [44] reported the ability of curcumin at 100, 200 and 400 mg/kg to inhibit LDL oxidation and hypocholesterolemic effect in mice. The active principles in the rhizome of this plant viz; curcuminoids also lower lipid peroxidation by maintaining the activities of antioxidant enzymes like superoxide dismutase, catalase and glutathione peroxidase at higher levels. Antioxidant properties of *C. longa* are due to curcumin and its two derivatives (demethoxy curcumin, and bisdemethoxy curcumin) [45].



Bisdemethoxy curcumin



Curcumin

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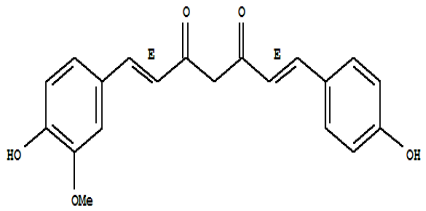
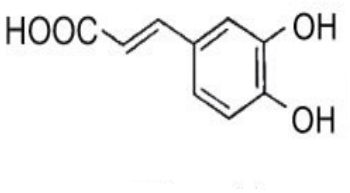


Demethoxy curcumin

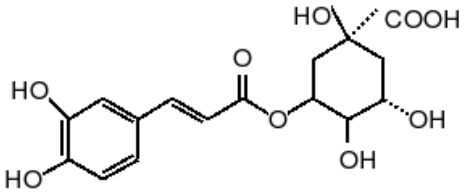
Figure 2: Active compound of *Curcuma longa*

Coriander (*Coriandrum sativum*)

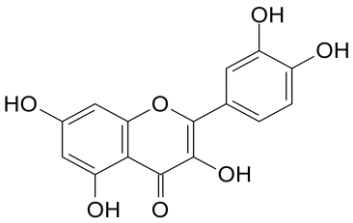
Coraindrum sativum is a very commonly used spice in Indian cuisines. The biochemical effects of this seed on lipid parameters in 1, 2-dimethyl hydrazine (DMH) induced colon cancer in rats has been reported [46]. The cholesterol/phospholipids ratio is closely related to membrane fluidity. The lower ratio of cholesterol/phospholipids in the spice-fed group is closely associated with membrane stability. A change in the concentration of cholesterol will greatly affect the fluidity of the membrane and thereby can bring about abnormal changes in the membrane properties and function. The spice also prevents changes in the ratio of cholesterol/phospholipid, thereby maintaining the membrane fluidity, integrity and function. Coriander works by improving the bile production in the liver and breaking down cholesterol so that it can be flushed out of the system. Dhanapakiam et al. [47] reported that the administration of coriander seeds had a profound influence on the metabolism of lipids in animals fed on cholesterol containing diet. De Almeida et al. [48] concluded that aqueous and etheric coriander extracts contain phenolics and carotenoids which exhibit a considerable antioxidant action. Additionally, coriander has been advocated as an anti-diabetic remedy [49]. *C. sativum* is well known for its antioxidant properties and some of its active components have been identified. Coriander contains active phenolic acid compounds, including caffeic and chlorogenic acid. The flavonoids include quercetin, keampferol, rhamnetin and apigenin. Most of these compounds are known to inhibit free radicals generated in the cellular system, when they are obtained through the diet [50].



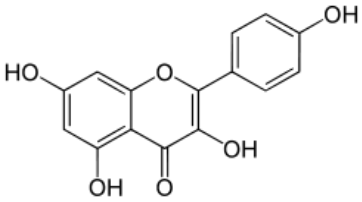
Caffeic acid



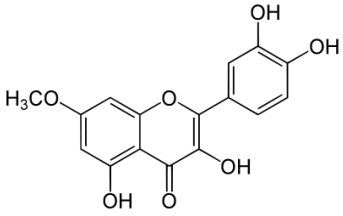
Chlorogenic acid



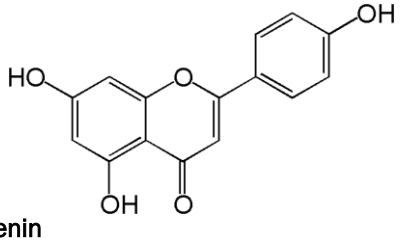
Quercetine



Kaempferol



Rhamnetin



Apigenin

Figure 3: Active compound of *Coriandrum sativum*

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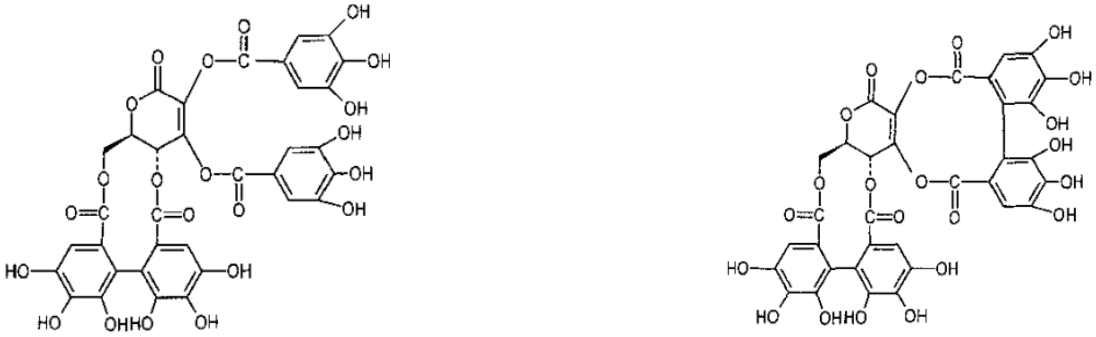
Amla *(Emblica officinalis)*

Emblica officinalis belonging to the Euphorbiaceae family is popularly known as amlaor, amlaki in India. *E. officinalis* has been reported to exert hypolipidemic activity. *E. officinalis* has been found to reduce serum total cholesterol, aortic cholesterol and hepatic cholesterol significantly [51, 52]. Reversal of dyslipidemia and atheromatous plaques achieved by amla extract seems to be brought about by a number of factors, such as its ability to prevent low-density lipoprotein oxidation, its antioxidant action, besides decreasing synthesis of cholesterol by inhibiting 3-hydroxy-3-methylglutaryl-Coenzyme-A- reductase activity and elevating high-density lipoprotein level to enhance reverse cholesterol transport [53]. The effect of standardized amla extract on atherosclerosis and dyslipidemia on animals is well studied. The tannoid principles of fruits of *E. officinalis* have been traced to its antioxidant activity *in vitro* and *in vivo* [54]. A study conducted in rats found that emblicanin-A and emblicanin-B enriched fractions of fresh juice of emblica fruits showed antioxidant activity in ischemia-reperfusion-induced oxidative stress in rat heart [55].

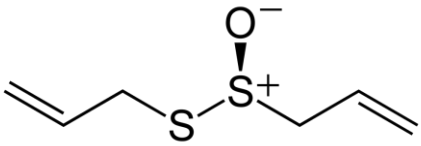


Emblicanin A Emblicanin B

Figure 4: Active compound of *Emblica officinalis*

Garlic (*Allium sativum)*

Garlic is an herb that has a lot of medicinal uses. It can lower the LDL cholesterol levels (by up to 15% provided a person takes a clove of garlic daily) while increasing the good or HDL cholesterol levels [56]. In a study, men with coronary artery disease who were also being treated with statin drugs and low-dose aspirin, two weeks of supplementation with aged garlic extract significantly improved blood flow by improving endothelial function [57]. Aged garlic extract (2.4 gm daily for 7 days) has been shown to prevent oxidation of LDL cholesterol in humans [58]. Garlic indirectly effects atherosclerosis by reduction of hyperlipidaemia, hypertension and probably diabetes mellitus and prevent thrombus formation. In addition, garlic (0.2 and 0.4 g/kg body weight/day, respectively) causes direct antiatherogenic (preventive) and antiatherosclerotic (causing regression) effects by reducing LDL oxidation and oxidative stress in male albino rats fed a high cholesterol diet [59]. Protective effects of organ sulphur compounds from garlic on atherosclerosis have been attributed to its capacity to reduce lipid content in arterial wall [60]. Garlic contains sulphur containing compound allin, which is converted to active ingredient 'allicin' when the garlic bulb is crushed. This compound has an inhibitory effect upon the key enzymes involved in cholesterol biosynthesis, such as HMG-CoA reductase [61].



Allicin

Figure 5: Active compound of *Allium sativum*

Cardamom *(Amomum subulatum)*

Amomum subulatum is one of the world's very ancient spices and has also been universally used for its health benefits. The hepatoprotective effect of cardamom was reflected by the significantly lower level of liver enzymes and serum lipid profile in rats pre-treated with their extract before ethanol. On the other hand, MDA level was significantly reduced as compared to ethanol fed group, whereas, levels of SOD and GSH-Rd activity and trace element level were significantly increased by cardamom pre-treatment [62]. It has been reported that spices may inhibit hepatic HMG-CoA reductase activity, resulting in lowering hepatic and serum cholesterol levels [63].

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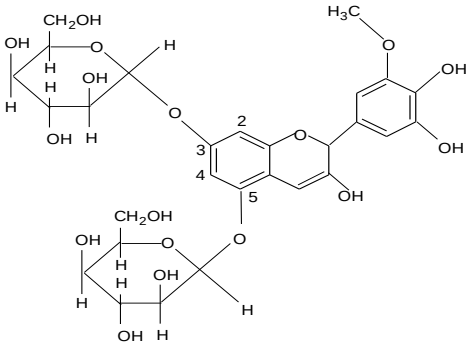
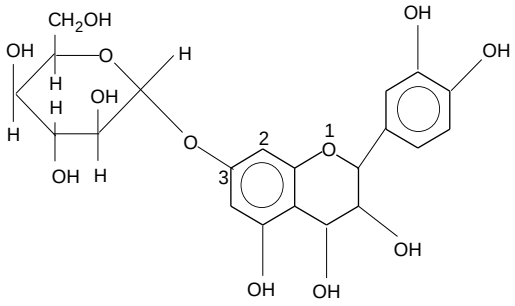
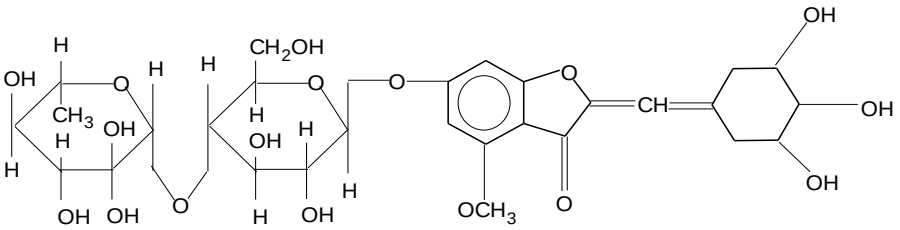
Our laboratory findings show that *A. subulatum* to have the unique ability to lower serum low density cholesterol levels with lowering of serum TG levels and antioxidant effects without causing any side effects and the biochemical tests showed that all the parameters were within normal limits before and after treatment [64, 65]. Previous studies claimed that phenolic compounds could able to reduce the hyperlipidemia. The seeds of *A. subulatum* contains the glycosides, Petunidin-3,5-diglucoside, Leucocyanidin-3-O-ß-D-glucopyranoside, Subulin (New aurone glycoside) and 1-8, Cineole, α-terpinyl Acetate [66].



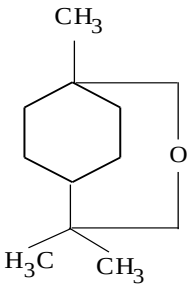
Petunidin-3, 5-diglucoside



Leucocyanidin-3-O-ß-D-glucopyranoside



Subulin

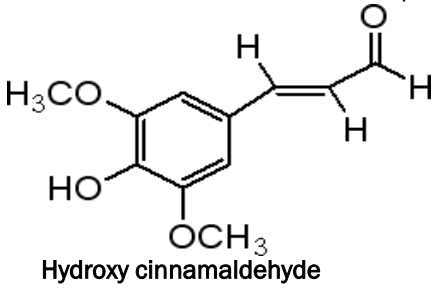


1, 8-Cineole

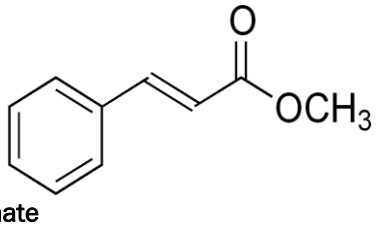
Figure 6: Active compound of *Amomum subulatum*

Cinnamon *(Cinnamomum verum)*

Studies indicated that cinnamon suppresses lipid peroxidation via the enhancement of hepatic antioxidant enzyme activities [67]. Antioxidant activities of volatile extracts isolated from cinnamon were evaluated by various isolated *in vitro* assays [68]. Moselhy and Ali [69] reported that ethanolic extract of cinnamon has more potent antioxidant activity than water extract. The antioxidant properties of cinnamon extracts are attributable to the ability of its phenolic constituents to quench reactive oxygen species. Ciftci et al. [70] showed that supplementing different concentrations of cinnamon oil in diet (especially 1000 ppm) decreased cholesterol levels of serum and chicken meat. Because of the hypolipidemic and antioxidative properties of cinnamon oil in diets, polyunsaturated fatty acid ratios may increase in serum and meat lipids. Cinnamon oil had positive effects on antioxidant metabolism, besides increased the antioxidant enzyme activity and decreased the serum MDA level. Phenolic compounds, such as hydroxy cinnamaldehyde and hydroxycinnamic acid, present in the cinnamon extract, act as scavengers of peroxide radicals and prevent oxidative damages [71]. In addition, the effect of cinnamate, a phenolic compound found in cinnamon bark and other plant materials, on lipid metabolism and antioxidant enzyme activities in rats fed a high cholesterol diet has been studied and indicated that cinnamon suppresses lipid peroxidation via the enhancement of hepatic antioxidant enzyme activities [67].



Hydroxy cinnamaldehyde



Cinnamate

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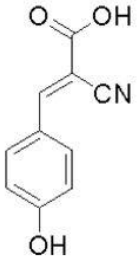
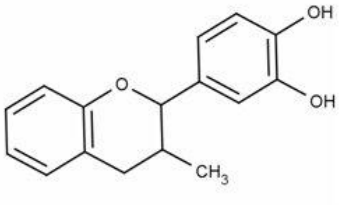


Hydroxycinnamic acid

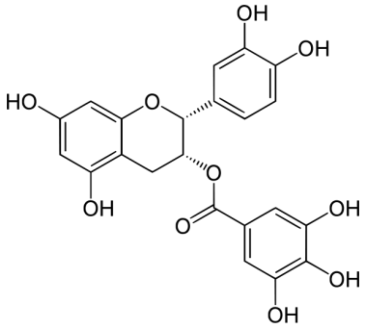
Figure 7: Active compound of *Cinnamomum verum*

Tea (*Camellia sinensis*)

Camellia sinensis (L.) (Theaceae) is commonly known as green tea in the India. Tea supplemented with vitamin E, administered to male hamsters, reduced plasma LDL cholesterol concentrations, LDL oxidation, and early atherosclerosis compared to the consumption of tea alone by the hamsters [72]. It has been reported that lipid lowering effect of black tea administration in hyperlipidaemic rats through reactivation of LPL, increased faecal excretion of cholesterol and bile acids [73]. LPL in the heart is involved in the uptake of TG rich Lipoproteins from circulation. It is shown that high cholesterol diet elevates serum TG levels essentially by preventing its uptake and clearance by inhibiting catabolising enzymes like LPL [74]. Upaganlawar and Balaraman [75] reported that hypertriglyceridemia is due to decrease activity of LPL in the myocardium resulting in decreased uptake of TG from the circulation. Green tea and vitamin E in combination alters the activities of LPL near to the normal by increasing HDL and decreasing TG and cholesterol levels, indicating the potential lipid lowering effects of green tea and vitamin E combination. Yang and Koo [76] also demonstrated that after administration of Chinese green tea for eight weeks significantly lowered the serum cholesterol by increasing faecal bile acids and cholesterol excretions. Increased activity of LPL would promote the metabolism of total cholesterols, including TG. In addition, the excretion of faecal bile acids was observed to be increased significantly in animals simultaneously and sequentially fed with a high-lipid diet and plant product. This increased excretion of bile acid in faeces might be associated with ability of plants activating the important enzyme, 7α-hydroxylase, in the conversion of cholesterol into bile acids [77]. Tea is a rich source of polyphenol called flavonoids, effective antioxidants found throughout the plant kingdom [78]. The slight astringent, bitter taste of green tea is attributed to polyphenol. A group of flavonoids in green tea are known as catechins, which are quickly absorbed into the body and are thought to contribute to some of the potential health benefits of tea. The fresh tea leaves contain four major catechins as colorless water soluble compounds: Epicatechin (EC), epicatechingallate (ECG), epigallocatechin (EGC) and epigallocatechin gallate (EGCG). Epidemiologic observations and laboratory studies have indicated that tea polyphenol act as antioxidants *in vitro* by scavenging reactive oxygen and nitrogen species and chelating redox active transition metal ions and hence tea may reduce the risk of a variety of illnesses, including cancer and coronary heart disease [79]. Inami et al. [80] demonstrated that tea catechin (500 mg: equivalent to 6 or 7 cups of green tea for 4 weeks) decreased the plasma oxidized LDL concentration without significant change in plasma LDL concentration. The mechanism of the beneficial effects of green tea on coronary artery disease might result from a decrease in plasma oxidized LDL.



Epicatechin



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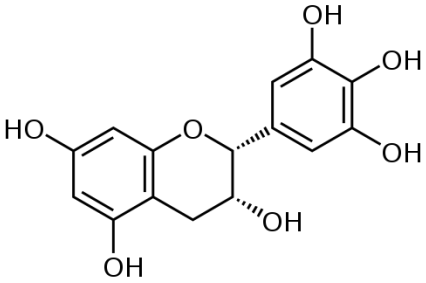
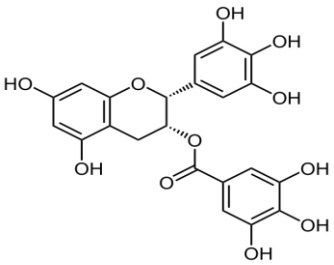


Epigallocatechin

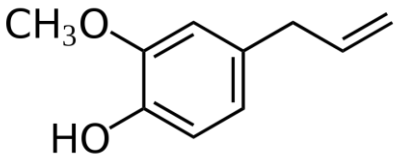


Epigallocatechin gallate

Figure 8: Active compound of *Camellia sinensis*

Tulsi (*Ocimum sanctum*)

Ocimum sanctum Linn, (Labiatae) commonly known as "Tulsi" in Hindi is a medicinal plant commonly grown in India. It has been observed that tulsi leaves exert hypocholesterolemic, hypotriglyceridemic and hypophospholipidemic effects in the rabbits and rats [81, 82]. Some scientists also reported significantly increased activity of two antioxidant enzymes in liver i.e. SOD and catalase following treatment with aqueous extract of *O. sanctum* [83, 84]. Recent chromatographic studies have showed that *O. sanctum* contain various active constituents viz. eugenol, luteolin, ursolic acid, and oleanolic acid among which eugenol content ranged from 0.175 to 0.362% (w/w). Eugenol (1-hydroxy-2-methoxy-4- allylbenzene) the active constituent present in *O. sanctum* has been found to be largely responsible for the therapeutic potentials of Tulsi [85].

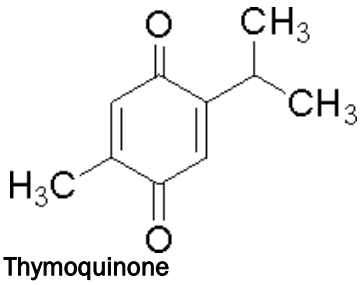


Eugenol

Figure 9: Active compound of *Ocimum sanctum*

Kalonji *(Nigella sativa)*

Nigella sativa belongs to family Ranunculaceae. It is an annual, erect herb, 30-40 cm high. Seeds of *N. sativa* are commonly known as kalonji has a long history of use in folk medicine as a diuretic and hypotensive agent. The essential oil of *N. sativa* seed has an antioxidant property that makes it useful in treating cardiovascular disorders [86]. The powder of seeds of *N. sativa* were orally administrated to hypercholesterolaemic patients (n=10) at the dose of 1 gm before breakfast for 2 months and was found to reduce cholesterol, LDL, TG to a highly significant extant [87]. Tasawar et al. [88] reported that there was significant ($P<0.05$) decrease in cholesterol, LDL, VLDL and triglycerides, and significant increase of HDL in interventional group (*N. sativa* seed powder 500 mg/daily along with statin 10-20 mg for 180 days) as compared to non interventional group (statin 10-20 mg/daily). Nader et al. [89] suggested the potential beneficial effects of thymoquinone (TQ, active constituent of *N. Sativa* seeds oil) in diminishing the risk of atherosclerosis via antioxidant mechanism.



Thymoquinone

Figure 10: Active compound of *Nigella sativa*

Some plants and herbs possessing lipid-lowering and antioxidants properties have been listed in the table (Table-1).

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Table-1: Plants and herbs used as Hypolipidaemic/ antiatherosclarotic agents

Name of Plants/Herbs	Activity	Dose and Duration	Model	References
Achillea wilhelmsii	Hypolipidaemic/hypotensive	Hydroalcoholic extract in the form of 15-20 drops twice daily for more than 6 months	Human beings	[90]
	Lipid lowering	Alcohol extract of Achillea at a dose of 15-20 drops twice daily for six months	Human beings	[86]
Aegle marmelos (Bael)	Antioxidant	Aqueous extract at 125 and 250 mg kg−1 twice a day for 4 weeks	Rats	[91]
	Lipid lowering	Ethanolic extract at 125 &250 mg/kg dose levels for one week	Rats	[92]
Allium cepa (onion)	Inhibits platelet aggregation	Onion slices (67.6-93.6 mg/day) with meals for 1 week	Human beings	[93]
	Hypoglycaemic, hypolipidaemic and antioxidant	1 ml *A. cepa* solution (0.4 g *A. cepa*/rat)	Rats	[94]
	Hypolipidaemic and antiatherosclerotic	200, 250 and 300mg/kg) of *A. cepa* aqueous extracts for six weeks	Rats	[95]
*Allium sativum (*Garlic*)*	Hypolipidaemic	Garlic powder tablets with 9.6 mg allicin-releasing potential for 12 weeks	Human beings	[96]
	Inhibits lipid peroxidation, increase GSH and SOD in liver and kidney	Fresh garlic homogenate daily in three different doses (250, 500 and 1000 mg/kg/day) for 30 days	Rats	[97]
	Suppressed LDL oxidation and antioxidant	1.2 gm 3 times a day for 2 weeks	Human beings	[14]
	Hypocholesteromic and antioxidant effects	Ethanolic extract at 0.2 and 0.4g/kg body weight/day for 60 days	Rats	[59]
Amomum subulatum	Lowering serum lipid profile and antioxidant	2 % cardamom flour for five weeks	Rats	[64]
	Antiatherosclarotic and antioxidant	Methanolic extract of *A. subulatum* seeds at the doses 150 and 250 mg/kg b.wt. for 90 days	Rabbts	[63]
Argania spinosa	Hypolipidaemic and cholesterol lowering	Argan oil (1ml/100 g weight) daily during 7 weeks	Rats	[98]
	Decreased oxidative stress	7 weeks of treatment with argan oil (10 ml/kg)	Rats	[99]
Avena sativa (oat)	Hypocholesterolaemic	20 gm oat bran for 8 weeks	Human beings	[100]
	Cholesterol lowering effect	Oat supplemented diet (20% w/w) for 4 weeks	Rats	[101]
Bacopa monniera (Brahmi)	Antioxidant action	Extract administered in doses of 5 and 10 mg/kg, orally for 7, 14 or 21 days	Rats	[102]
	Antioxidant	Ethanolic extract of *Bacopa monnieri* 300 mg/kg, for 10 days	Rats	[103]
Camellia sinensis (Green tea)	Cholesterol lowering effect	Daily capsule containing theaflavin-enriched green tea extract (375 mg) for 12 weeks	Human beings	[104]
	Hypocholesterolaemic and antioxidant effect	3 gm of green tea in 500 mL of water per day for 45 and 90 days	Human beings	[105]
Capparis decidua (ker)	Hypolipidaemic/ Antiatherosclarotic effect	Alcohol extract of *C. decidua* at 500 mg/kg body weight for 60 days	Rabbits	[106]
		Ethanolic extract of *C. decidua* at 500 mg/ kg body weight for 30 days	Rats	[107]
Cinnamomum verum (Cinnamon)	Inhibit lipid peroxidation and elevating antioxidants enzymes levels	Aqueous and ethanolic extracts of cinnamon 200 mg/kg for 7 days	Rats	[69]
	Hypolipidaemic action	200 mg/kg. of cinnamon extract for period of 12 weeks,	mice	[108]

Commiphora mukul (Guggul)	Inhibit platelet aggregation and maintain antioxidant status	Alcoholic extract of *C. mukul* at dose of 100, 200, 400mg/kg/day for 31 days	Rats	[37]
	Hypolipedaemic and antioxidant potential	Methanolic extract of *C. mukul* at a dose of 100mg/kg/day for 6 weeks	Rabbits	[85]
Coriandrum sativum (Coriander)	Reduce plasma lipids profile	4% *C. sativum* fruits powder for one month	Rats	[109]
	Cholesterol lowering property	Dried coriander seeds 10% for 75 days	Rat	[47]
Crataegus pinnatifida (Hawthorn)	Hypocholesterolemic effect	Diet supplemented with 0.5% hawthorn fruit aqueous ethanolic extract for 4 weeks	Hamsters	[110]
	Lower Plasma cholesterol	0.37% hawthorn dichloromethane extract for 4 weeks	Hamsters	[111]
Croton cajucara	Hypolipidaemic effect	Clerodane diterpene trans-dehydrocrotonin extracted from the stem bark of Croton cajucara at a dose of 25 or 50 mg kg−1 daily for 2 weeks	Mice	[112]
	Antioxidant and free radical scavenging	1.5 ml of the *Croton cajucara* BENTH. Extract for 5 days	Rats	[113]
Curcuma longa (Turmeric)	Hypocholesterolemic action	0.2 g curcuminoids/100 g diet and 1.0 g curcuminoids/100 g diet for 2 wk.	Rats	[114]
	Reduction of atherosclerosis and oxidative stress	Hydroalcoholic extract of *C. longa* at a dosage o1.66 mg/kg body wt for 10, 20, and 30 days	Rabbits	[42]
Cyamopsis tetragonolobus (Guar gum)	Cholesterol-lowering effects	5% guar gum (GG) diets	Rats	[115]
	Hypocholesterolemic effects	Control diet supplemented with 10% GG	Hamsters	[116]
Emblica officinalis (Amla)	Antioxidant action	10 and 20 mg of *E. officinalis* for 21 days	Rats	[117]
	Reduce dyslipidaemia and plaque formation	Amla extract was given in two doses (10 mg and 20 mg/kg/d orally) for 4 months	Rabbits	[53]
Ginkgo biloba	Inhibit lipid peroxidation	8.75, 17.5, 26.25 mg/kg intravenously to the experimental groups respectively 30 min prior to the ulcerative challenge	Rats	[118]
	Prevent oxidative modification of atherogenic lipoproteins (LDL)	Ginkgo biloba extract (2× 120mg daily) for 2 months	Human beings	[119]
Hordeum vulgare (Barley)	Antioxidative effect	Same diet as the group control but containing 1% (w/w) Barley Leaf Essence for 12 weeks	Rabbits Hamsters	[120] [121]
	Cholesterol-lowering potency	Beta-glucan (2, 4, or 8 g/100 g) from barley for 3, 6 and 9 weeks		
	Lowering total and LDL cholesterol	Whole-grain foods containing 0, 3, or 6 g ß-glucan/d from barley for 15 weeks	Human beings	[122]
Medicago sativa (Alfalfa)	Hypocholesterolaemic and antiatherosclarotic properties	1 & 2% o f 3 0% alcoholic and 1 & 2% of aqueous extract of alfalfa for 28 days	Rabbits Rabbits	[123]
	Preventive effects on the progression of fatty streak formation	Basic diet supplemented with alfalfa t for a period of 12 weeks		[124]
*Myristica fragrans (*Nutmeg)	Antioxidant potential	100-500 mg/kg body weight of the aqueous extract for a period of 28 days	Rats	[125]
	Hypolipidaemic effects	Hydroalcoholic extract of fruits of *M. fragrans* at doses of 150 and 450 mg/kg for 7 days	Mice	[126]

Momordica charantia (Karela)	Hypolipidaemic action	Diets for 14 days containing *M. charantia* freeze-dried powder at the level of 0.5, 1 and 3%	Rats	[127]
	Antioxidant effect	Seed extracts at concentration of 150 mg/kg b.w for 30 days	Rats	[128]
Moringa oleifera	Hypocholesterolaemic action	Leaves extract at concentration of 200 mg/ml for 30 days	Rats	[129]
	Hypolipidemic	Methanolic extract of *M. oleifera* at 150, 300 and 600 mg/kg along with hyperlipidemic diet for 30 days	Rats	[130]
Nigella sativa	Modify the plasma lipid profile	Powder of seeds of *N. Sativa* at the dose of 1 gm before breakfast for 2 months	Human beings	[87]
	Hypocholesterolemic and antiatherogenic cardioprotective properties	Diet supplemented with 1000 mg /kg b. wt. of *N. sativa* powder (NSP) and 500 mg/kg body *N. sativa* oil (NSO) for 8 weeks	Rabbits	[131]
	Lipid lowering action	*N. sativa* seed powder 500 mg/daily along with statin 10-20 mg for 180 days	Human beings	[88]
Ocimum sanctum (Tulsi)	Hypocholesterolaemic and antioxidant potential	Administration of *O. sanctum* seed oil (0.8g/kg b.w./day) for 4 weeks	Rabbits	[81]
	Lipid-lowering and antioxidative effects against hypercholesterolemia	During the last 3 weeks, out of 7 weeks of experiment rats were daily fed with essential oil of *O. Sanctum* leaves (80 µl/kgbw/day)	Rats	[82]
	Hypolipedaemic and antioxidant potential	Aqueous extract of *O. sanctum* at a dose of 100mg/kg/day for 6 weeks	Rabbits	[85]
Panax ginseng (Ginseng)	Reduction of bile flow and in bile secretion of total lipids and cholesterol	Single intraperitoneal injection of ginseng at 25, 50 or 100 mg kg^{-1} (1 ml $^{-1}$) 30 min before bile collection	Rats	[132]
	Antioxidant potential and hypolipidemic effect	Administration of *P. ginseng* extract for 8 weeks (6 g / day)	Human beings	[133]
Plantago ovata (Psyllium)	Hypolipidemic effect	Diets containing 7.5 or 10 g/100 g *P. ovata* for 4 weeks	Guinea Pigs	[134]
	LDL-Cholesterol lowering action	15 gm of Psyllium /day for 30 days	Human beings	[135]
Paeonia lactiflora	Lowering effect on LDL cholesterol and triglyceride level	Methanol extract of *P. lactiflora* at the dose of 200 and 400 mg/kg once a day for 4 weeks	Rats	[136]
Phyllanthus niruri	Lipid lowering effect	*P. niruri* extract orally fed at 100 mg/kg b.w. for 30 days	Rats	[137]
	In vivo antioxidant action	Methanol extract of *P. niruri* at the dose of 125 and 250 mg/kg body for 14 days	Rats	[138]
Sesamum indicum	Anti-atherogenic effects	Atherogenic diet reformulated with sesame oil 17% (contain 170g/ kg sesame oil) for 12 weeks	Mice	[139]
	Hypolipidemic and decreases plasma membrane lipid peroxidation	8% sesame protein isolate with or without 2% cholesterol in comparison with casein to rats for 28 days	Rats	[140]
Solanum melongena	Modest hypocholesterolemic effect	*S. melongena* 2% (w/v) infusion for five weeks	Human beings	[141]
	Hypolipidaemic action	Diet supplemented with 10% of *S. melongena* fruit for 6 weeks	Rabbits	[142]
Terminalia arjuna	Reduce dyslipidaemia and act as antioxidant agent	Ethanolic extract of *T. arjuna* at the dose of 250 mg/kg per oral for once a day from day 4 to 10 day	Rats and hamsters	[143]
Terminalia chebula	Antioxidant activity and cardioprotective effects	Ethanolic extract of Terminalia at the dose of 500 mg/kg orally for 30 days	Rats	[144]

Trigonella foenumgraecum (Fenugreek)	Hypolipidemic and hypocholesterolaemic effect Reduces LDL oxidation, serum total cholesterol and triacylglyceride levels	Hexane and ethyl alcohol extract of fenugreek at 25 and 50 gm for 20 days Fenugreek seed powder of 25 gm orally twice daily for 3 weeks and 6 weeks	Human beings Human beings	[145] [146]
Withania somnifera (Ashwagandha)	Cardioprotective effects Hypolipidaemic effects	100 mg/kg for 180 days Ethanolic extract of 100 and 200 mg/kg bw dissolved in distilled water	Rats and Frogs Rats	[147] [148]
Zingiber officinale	Antiatherosclerotic, triglycerides, cholesterol, VLDL, LDL and Inhibit lipid peroxidation Hypoliidaemic and antiatherosclerotic effect	Ethanolic extract of 25, 250 microg of ginger /day in 1.1% alcohol and water for 10 weeks 200, 250 and 300mg/kg of *Z. officinale* aqueous extract for 6 weeks	Mice Rats	[149] [95]

CONCLUSIONS

Atherosclerosis is a condition in which patchy deposits of fatty material (atheromas or atherosclerotic plaques) develop in the walls of medium sized and large arteries, leading to reduced or blocked blood flow to the heart or the brain. Hyperlipidemia constitutes a major etiopathological factor for atherosclerosis. Most recent findings indicate a multi-faceted cause to the problem of cardiovascular disease, including excessive intake of saturated fats, carbohydrate metabolic dysfunction, nutritional deficiencies, hormonal imbalance, and a high-stress lifestyle. Nature has provided specific compounds capable of augmenting dietary and lifestyle changes for improved cardiovascular health and may afford a way to lower cholesterol without resorting to synthetic drug preparations and their potential side effects. Herbs have been used as medical treatments since the beginning of civilization and some herbal derivatives (e.g., aspirin, reserpine, and digitalis) have become a mainstay of human pharmacotherapy. From the reports on their potential effectiveness against hypercholesterolemia, it is assumed that the botanicals have a major role to play in the management of hyperlipidemia, which need further exploration for necessary development of drugs and nutraceuticals from natural resources. However, many herbal remedies used today have not undergone careful scientific assessment. Continuing research is necessary to elucidate the pharmacological activities of the many herbal remedies now being used to treat atherosclerosis, hyperlipidemia and other cardiovascular diseases. Currently used hypolipidaemic synthetic drugs are effective but they lag behind the desired properties since they frequently produced side effects, have poor patient compliance and are expensive. In contrast, plant – derived drugs are effective hypolipidaemic agent in terms of efficacy, safety on long term use, cost and simplicity of administration in prevention of atherosclerosis. However, for the foreseeable future, long term tolerance studies are needed before being recommended for human use.

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