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## Natural remedies for hyperlipidemia: A review

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**Abstract**

Hyperlipidemia is a popular disorder and a state of body where there is elevated level of triglyceride above 200mg/dl, LDL above 160mg/dl, Total cholesterol above 200mg/dl and HDL below 40mg/dl. Now it can be found on every other person, when LDL increases it travels through our blood vessels and tends to accumulate in the vessels the accumulation is not for lipids only it consists of calcium and fibrous plaque, and this scenario leads to atherosclerosis. Atherosclerosis causes narrowing of blood vessels, leads to lesser blood flow to the heart results in angina pectoris and gradually heart attack. There are many marketed medicines fighting against this, but they have adverse effects like muscle toxicity. Here, are some natural remedies which we come across everyday are fighting these situations which are very easily available in nature, and we can take it in our regular diet.

**Keywords:** Hyperlipidemia, LDL, cholesterol, natural products, atherosclerosis, metabolism

**Introduction**

On an average about 20% of adult are suffering from hyperlipidemia like diseases. Men are more prone to this disease than women, reason can be assumed due to the presence of estrogen in menstruating women. Secondary form of hyperlipidemia occurs more than familial above the age of 75 years, or we can say elderly people. It is one of the reason for mortality and disability throughout the world <sup>[1]</sup>.

The pathway to a vascular event is a chain of connected events. The ultimate formation of a plaque depends on where it has started forming (some vessels are more prone to obstruct as compared to others) on the basis of what it is made of (amount of lipid, oxidation of low-density lipoprotein [LDL], etc). Hyperlipidemia highlights the development of atherosclerotic plaque by the enhancement of the transport of lipoproteins into the intima of coronary vessels where the macrophages are also migrating forming a fatty streak. Narrows blood vessels. Damage to the endothelial cells overlying a fatty streak helps to transform it to a fibrous plaque.

A quick myocardial infarction (MI) starts with a fissured atheromatous plaque that progresses and forms a rapid thrombosis of a coronary artery. Fissuring occurs in a fragile plaque that contains large deposits of lipid and thinned fibrous cap as a result of macrophages in it <sup>[2]</sup>.

There are some marketed drugs which are fighting against hyperlipidemia the classification

- Antihyperlipidemic Drugs are the drugs which lowers the lipid
  1. Statins (e.g. lovastatin, fluvastatin, pravastatin, simvastatin, atorvastatin, & rosuvastatin), which are HMG-CoA reductase inhibitors decrease cholesterol synthesis.
  2. Ezetimibe, which is cholesterol absorption inhibitor.
  3. Niacin "nicotinic acid", that decreases secretion of lipoproteins.
  4. Fibrates (e.g. clofibrate, fenofibrate, & gemfibrozil), that causes peripheral clearance of lipoproteins.
  5. Resins (e.g. cholestyramine, colestipol, & colestevlam), these are bile acid sequestrants that decreases bile acid absorption

These are quite effective but they have got some severe side effects such as muscle toxicity of statin, but natural drugs or remedies can be used which will have same effects with lesser adverse effects or we can take some dietary approach for hyperlipidemia. More than 50% of garlic, more than 80% of guggul, and 100% of Arjuna in randomized clinical trials have shown effectiveness towards hyperlipidemia <sup>[3]</sup>.

**Table 1:** Natural Products as potential Therapeutic agents to treat Hyperlipidemia.

Sl. No.	Common Name	Biological Source	Probable Chemical constituent	Probable site or mechanism of action	Clinical Trials
1.	Apple	Scientific name: <i>Malus domestica</i> Family: Rosaceae	Quercetin,	Involve in glycerol phospholipid metabolism. Act through AMPK regulated fatty acid degeneration and cholesterol metabolism [4, 5]	Phase 1 [6]
2.	Rice Water	Water	Allantoin	Allantoin blocks the 3-hydroxymethylglutaryl-coA reductase (HMGCR), mevalonate kinase (MVK) and lanosterol demethylase (LDM) [7]	
3.	Candy Leaves	Scientific Name: <i>Stevia rebaudiana</i> Family: Asteraceae	Aqueous extract of stevia leaves, stevioside	Enhancement of the bile acid excretion by reducing reabsorption from small intestine. The increase in excretion of bile acid and cholesterol activates cholesterol 7 $\alpha$ -hydroxylase that enhances the conversion of liver cholesterol to bile acid thus regulates [8]	
4.	Peas	Scientific name: <i>Pisum sativum</i> Family: Fabaceae	Leutin	Reduction of NF- $\kappa$ B, cyclooxygenase (COX)-2, inducible nitric oxide synthase (iNOS), TNF- $\alpha$ , and IL-1 $\beta$ . Peroxisome proliferator X receptor (PPAR) and retinoic acid X receptor [9, 10].	
5.	Garlic	Scientific name: <i>Allium sativum</i> Family: Amaryllidaceae Part Used: stem	Allicin	decreasing activity HMG-CoA reductase and it is the rate-limiting enzyme of cholesterol biosynthesis so decrease in cholesterol level [11]	Phase2 [12]
6.	Eggplant/ Brinjal	Scientific name: <i>Solanum melongema</i> Family: Solanaceae Part Used: Peels	Anthocyanin	inhibits lipid peroxidation [13]	Phase 3 [14]
7.	Guava	Scientific name: <i>Psidium guajava</i> Family: Myrtaceae Part Used: Leaves	Guava leaf extract	a decrease in HbA1c% [15].	
8.	Mango	Scientific name: <i>Mangifera indica</i> Family: Anacardiaceae Part Used: leaves	Mango leaf extract	Enhancement of the expression of hepatic LDL receptors and protection can enhancement of the removal of LDL-C from the blood and its increases the degradation and catabolism of cholesterol from the body LDL receptors [16].	
9.	Papaya	Scientific name: <i>Carica papaya</i> Family: Caricaceae Part Used: Fruit	Rutin	<ul style="list-style-type: none"> <li>HMG-CoA reductase activity.</li> <li>absorption of dietary cholesterol [17].</li> </ul>	
10.	Pumpkin	Scientific name: <i>Cucurbita pepo</i> Family: Cucurbitaceae Part Used: Seeds	Fiber, PUFA	increasing LDL receptor activity and reduced LDL-C by lowering cholesterol and bile acid absorption [18]	
11.	Pineapple	Scientific name: <i>Ananas comosus</i> Family: Bromeliaceae Part Used: Peels	Bromelain, Saponin, Tannin	Peels reduced oxidative stress [19]	
12.	Cinnamon	Scientific name <i>Cinnamomi Cassiae</i> Family: Lauraceae Part Used: Bark	Cinnamon extract	The PPAR $\gamma$ and mRNA expression was regulated in adipose tissue [20]	
13.	Cardamom	Scientific name <i>Elettaria cardamomum</i> Family: Zingiberaceae Part Used: Seeds	Kaempferol	partial agonist of PPAR $\gamma$ increasing insulin sensitivity and they are involved in the lipid metabolism. In hepatocytes [21].	
14.	Arjuna	Scientific name <i>Terminalia arjuna</i> Family: Combretaceae	ethanolic fraction of T. arjuna-	serum/plasma lecithin cholesterol acyl transferase (LCAT) and accumulation of receptor mediated catabolism of LDL40.	

		Part Used: Bark		Hypolipidemic activity is probably due to its anion exchange property [22].	
15.	Turmeric	Scientific name <i>Curcuma longa</i> Family: Zingiberaceae Part Used: Rhizome	Curcumin	<ul style="list-style-type: none"> <li>Blocking LDL from oxidation prevents atherogenesis.</li> <li>It has been noticed that it lowers lipid peroxidation [23]</li> </ul>	Randomized Controlled Trial [24]
16.	Ginger	Scientific name <i>Zingiber officinale</i> Family Zingiberaceae, PartUsed: Rhizome	gingerols and shogaols	Lowering of cholesterol biosynthesis is associated with increased activity of the LDL receptor, which in turn leads to enhanced removal of LDL from plasma, resulting in reduction plasma cholesterol concentration [25]	double-blinded, placebo-controlled clinical trial [26]
17.	Green Coffee	Green coffee unroasted coffee beans	Chlorogenic acids(CGA)	Increase in the OX-LDL by decreasing homocysteine, because homocysteine induces oxidation by promoting the production of reactive oxygen species . It has seen that CGA has prominent antioxidant, hypolipidemic effects, and is one of the most abundant polyphenol in unroasted green coffee [27]	randomized, placebo-controlled, clinical trial [27]
18.	Chili	Scientific name <i>Capsicum frutescens</i> Family: Solanaceae Part Used: Fruit	Capsaicinoids, Capsaicin	stimulates the conversion of cholesterol to bile acids by regulation of cholesterol 7 $\alpha$ -hydroxylase expression and enhancing the excretions of bile acids in feces [28]	A randomized, double-blind, controlled clinical trial [29]
19.	Neem	Scientific name: <i>Azadirachta indica</i> Family: Meliaceae Part used: Leaves	ethanolic extract of AZI	decreases ROS production and enzymes involve in it include superoxide dismutase (SOD), catalase (CAT) and glutathione Peroxidase (GPX) [30].	
20.	Hibiscus	Scientific name: <i>Hibiscus rosa-sinensis</i> Linn. Family: Malvaceae Part Used: Flowers	ethanolic extract of flower or the lecithin	:Cholesterol acetyltransferase, which combines free cholesterol, free LDL into HDL and transferred back to VLDL and intermediate density lipoprotein. Reduction in triglyceride level was may be due to the effect of inhibition of lipolysis and fatty acid does not get converted to triglyceride [31, 32].	
21.	Aloevera	Scientific name: <i>Aloe barbadensis miller</i> Family: Liliaceae Part Used: Leaves	Aloe-emodin	could mostprobably reduce the production of ROS induced by PA and increase the expression of SOD. Aloe Emodin treatment might has the capability to decreases cardiomyocyte apoptosis [33].	
22.	Strawberry	Scientific name: <i>Fragaria ananassa</i> Family: Rosaceae Part used: fruit	Ellagic acid, fisetin	<ul style="list-style-type: none"> <li>ellagic acid can possibly improve vascular reactivity postprandially,</li> <li>fisetin may normalize lipoproteins through the enhancement of lipoprotein lipase activity and can cause a decrease in glycation of lipoproteins [34, 35]</li> </ul>	
23.	Coconut	Scientific name: <i>Cocos nucifera</i> Family: Arecaceae Part Used: water	water	mature coconut water can reduce hyperlipidemia may be due to the fact that rate of degradation of cholesterol is greater than the synthesis [36]	
24.	Ephedra	Scientific name: <i>Ephedra sinica Stapf.</i> Family: Ephedraceae Part used: whole plant or the branches and tops	ephedraceae	Scavenging of free radicals, includes hydroxyl and superoxide anions, and inhibiting lipid peroxidation and improve lipid profiles [37]	
25.	Black pepper	Scientific name: <i>Piper nigrum Linn.</i> , Family: Piperaceae Part used: pods Part used: pods	piperine	stimulates cholesterol 7 $\alpha$ -hydroxylase activity [38]	Phase 3. A randomized controlled trial and an updated meta-analysis [39]. Crossover, Randomized Controlled Trial [40]

26.	okra	Scientific name: <i>Abelmoschus esculentus</i> Family: Malvaceae. Part Used: fruit and seeds	Extract of okra	The result is due to the rapid catabolism of LDL-C through its hepatic receptors HDL aids the translocation of cholesterol. And it can be assumed that it is a HMG-CoA reductase inhibitor [41]	
27.	Kalmegh	Scientific name: <i>Andrographis paniculata (Burm. f.)</i> Family: Acanthaceae Part Used: Leaves	Andrographolide and Neoandrographolide	. It was seen that And inhibits the LPS/IFNg-induced iNOS and MMP-9 expressions in vascular smooth muscle cell and reduces the neointimal formation in a carotid injury. And increases NF-kB subunit P65 Ser536 dephosphorylation through an activation of protein phosphatase 2A in vascular smooth muscle cell [42]	Randomized Controlled Trial [43]
28.	Red yeast Rice	Scientific name: <i>Monascus purpureus,</i> Family: Monascaceae Monascus	monacolin	It can inhibit HMG-CoA enzyme [44]	A double blind, randomized controlled trial [45]
29	Tulsi	Scientific name: <i>Ocimum tenuiflorum</i> Family: Lamiaceae Part used: whole plant	Rosmarinic acid	It was found to have free radical scavenger activity and lipid peroxidase inhibitor properties [46].	
30	Curry leaves	Scientific name: <i>Murraya koenigii</i> Family: Rutaceae Part Used: leaves	Leaves extract	The antioxidants present in the leaves might be involved in the increase of HDL-C and thus could decrease the LDL-C and TC. The antioxidant might prevent the oxidation of LDL which was considered as the early event in the atheroma [47].	
31.	Sea Cucumber	Scientific name: <i>Apostichopus japonica</i> Family: Stichopodidae		may combine with lipids and act as a carrier to participate in the metabolism of cholesterol, speeding up the transport and excretion of serum lipid [48]	
32	Mint	Scientific name: <i>Mentha piperita</i> Family: Lamiaceae Part Used: leaves	Aqueous extract of the leaves	Decreases lipid peroxidation and increased SOD in liver tissue homogenates. It showed significant decrease in catalase and glutathione levels in liver tissue homogenate [49].	
33.	Sankhpushpi	Scientific name: <i>Convolvulus pluricaulis</i> Family: Convolvulaceae Part Used: whole plant	Methanol extract	Catabolism of LDL-c through its hepatic receptors and effect on HMGCoA reductase action [50].	
34	Guggal	Scientific name: <i>Commiphora mukul</i> Family: Part used: Leaves	E- and Z-guggulsterone Isomers of the guggal	This lipid-lowering activity may be due to the inhibition of hepatic cholesterologenesis and catabolic conversion of cholesterol to bile acids in the liver [51].	Randomiz Controlled Study [52]
35	Sparrow grass/ Satavari	Scientific name: <i>Asparagus racemosus</i> Family: Asparagaceae Part Used: root	digitonin and tomatine	bind to the cholesterol and increase its precipitation <i>in vitro</i> and inhibit the cholesterol absorption without bile acid absorption <i>in vivo</i> [53]	
36	Kantakari	Scientific name: <i>Solanum surattense</i> Family: Solanaceae Part Used: leaves	Leaves extract	decreased in the cholesterologenesis and reduced fatty acid synthesis, and this may be also due to the enhancement of the glucose utilization [54]	
37.	Tamarind	Scientific name: <i>Tamarindus indica</i> Family: Part Used: fruit pulp	limonene	Assuming through an increase in Apo A1, ABCG5, and LDL receptor gene expression in liver and decrease in HMG CoA reductase and stop MTP gene expression [55].	
38.	Drumstick	Scientific name: <i>Moringa oleifera Lam</i> Family: Moringaceae Part Used: fruit	Plant sterols	Partial inhibition of cholesterol synthesis by the de novo or by inhibiting the cholesterol absorption [56].	Randomized controlled trials [57]
39	Amla	Scientific name: <i>Emblia Officinalis</i>	Fruit extract	Found to have action on the lipid metabolism. [58]	A randomized, double blind, placebo

		Family: Phyllanthaceae Part Used: Fruit			controlled, multicenter clinical trial <sup>[59]</sup>
40	Haritaki	Scientific name: <i>Terminalia chebula</i> Retz. Family: Combretaceae Part used:bark	Bark extract	de novo lipogenesis leading to fatty liver was most probably reduced <sup>[60]</sup>	A Randomized Double-Blind, Placebo Controlled Clinical Trial <sup>[61]</sup>
41	Apamarga	Scientific name: <i>Achyranthes aspera</i> Family- Amaranthaceae Part Used: seed	Aqueous extract	low absorption of cholesterol because rapid excretion of bile acids causing <sup>[62]</sup>	
42.	Barberry	Scientific name: <i>Berberis orthobotrys</i> Family: <i>Berberidaceae</i> Part Used: roots	Extract of root	Extract might change the activity of cholesterol ester transfer protein (CETP), which is a key enzyme in HDL- c LCAT, enzyme which is involved in the trans-esterification of cholesterol and its flux from the cell membrane into HDL,or might have effect on HMG-CoA reductase <sup>[63]</sup> .	
43.	Orchids	Scientific name: <i>Bauhinia purpurea</i> Family: Fabaceae Part Used: leaves and unripe pods	Proanthocyanidines	The cholesterol reducing effect of the extracts most probably due to inhibition of dietary cholesterol esterification <sup>[64]</sup>	
44.	Matura Tree	Scientific name: <i>Cassia auriculata L.</i> Family: Cesalpinaceae Part used: flowers	Ascorbic acid	It might reduce the endogenous cholesterol biosynthesis by decreasing/stopping ir the hepatic HMG-CoA reductase <sup>[65]</sup> .	Radonmized, double-blinded, placebo- controlled trial. <sup>[66]</sup>
45.	Liquorice	Scientific name: <i>Glycyrrhiza glabra</i> Linn, Family: Fabaceae Part Used: roots	glycyrrhizin, glycyrrhizinic acid, glabrin A&B, glycyrrhetol, glabrolide, isoglabrolide,	Free radical scavenging activity <sup>[67]</sup>	
46	Tomato	Scientific name: <i>Solanum lycopersicum</i> Family: Solanaceae Part Used: Fruit	Lycopene	It might act on LDL receptor and prevent the binding of cholesterol <sup>[68]</sup>	
47.	Methi	Scientific name: <i>Trigonella foenum- graecum</i> Family: Fabaceae Part Used: Seeds	Diosgenin	Diosgenin have a protective effect on blood vessels against oxidative stress via developing GSH, and restoring the mRNA expression <sup>[69, 70]</sup>	Randomized Clinical Trials <sup>[70]</sup>
48	Berry	Scientific name: <i>Dioscorea nipponica</i> Family: Dioscoreaceae. Part Used: Rhizome	protodioscin	Most probably it is known to act as a HMG-CoA reductase inhibitor <sup>[71]</sup>	
49.	Vinca	Scientific name: <i>Catharanthus roseus</i> Family: Apocynaceae Part Used: leaves	Vincamine	Reduced the oxidative stress and Reactive oxygen species <sup>[72]</sup> .	
50	Yerba Mate tea	Scientific name: <i>Ilex paraguariensis</i> Family: Aquifoliaceae Part used: Leaves	Mate tea aqueous extract	Activation of PPAR $\alpha$ stops the formation of macrophage foam cells formation of reactive oxygen species (ROS), and associated lipoprotein oxidative modification. <sup>[73]</sup>	

## Discussion

It is found that in USA almost 8% cases occurs due to some drug's adverse reaction, almost 100,000 die each year because of some toxicities shown by some drugs into their body <sup>[74]</sup>, it means a large number of people are dying due to adverse drug reaction. But on the other hand death due to plant product is very rare, National Poison Control Centres of the United States do not have a category in their database for side or adverse reactions to herbs, they do believe that plant remedies are believed to have lesser side effects <sup>[75-77]</sup>.

In hyperlipidemia there is increase in number of lipoproteins, hyperlipidemia, diabetes mellitus, and hypertension. Hypercholesterolemia and hypertriglyceridemia, as vulnerable factors to atherosclerosis, have received the most recent attention <sup>[78]</sup>.

It is seen that some people are intolerant to statin because of myalgia or muscle toxicity, and a randomized, double-blinded, placebo-controlled trial was performed to evaluate red yeast rice in patients with a history of SAM (statin-associated myalgias). Red yeast rice significantly reduced the LDL and total cholesterol levels compared with placebo and did not

increase the incidence of myalgias within a 24-week of period. The process of red yeast rice and therapeutic herbal lifestyle change may offer a lipid lowering option for patients those who are intolerance to statin. Still the occurrence of myalgias after the starting of statin is poorly defined, SAMs are a serious note major clinical concern<sup>[79]</sup>.

So, as of now the phytochemicals identified from plants are introducing an inspiring opportunity for the development of new types of therapeutics. Thus there is a serious need to identify the native natural sources to study in detail their ability on different latest targets in order to develop them as new medicinal agents<sup>[80]</sup>.

In Ayurvedic science the lipids are known as *Medodhatu* the drug which helps in control medodhatu called as *Medoghna*<sup>[81]</sup> which are equally capable of lowering lipids like synthetic drugs, some of them has similar probable mechanism of action of synthetic drugs but benefit is they have lesser or No side effects and they are available abundantly in nature.

### Conclusion

I hereby conclude that all the natural sources which are mentioned above can act as remedies or drug for hyperlipidemia which are easily available and abundantly present in nature with least adverse reaction can be used to treat hyperlipidemia which would be potent like marketed drugs and will be lowered in price

### Conflict of interest statement

We declare that we have no conflict of interest.

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