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 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 prone to this disease than women, reason can be assumed due to the presence of estrogen in menstruating women. 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). Hyperlipidemias 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 [2].

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, & colesevelam), 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 [3].

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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: *Malus domestica* Family: Rosaceae | Quercetin, | Involve in glycerol phospholipid metabolism. Act through AMPK regulated fatty acid degeneration and cholesterol metabolism | Phase 1 [8] |
| 2.      | Rice Water  | Water             | Allantoin | Allantoin blocks the 3-hydroxy-3-methylglutaryl-coA reductase (HMGR), mevalonate kinase (MVK) and lanosterol demethylase (LDM) [7] |                |
| 3.      | Candy Leaves| Scientific Name: *Stevia rebaudiana* 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 7α-hydroxylase that enhances the conversion of liver cholesterol to bile acid thus regulates [9] |                |
| 4.      | Peas        | Scientific name: *Pisum sativum* Family: Fabaceae | Leutin | Reduction of NF-κB, cyclooxygenase (COX)-2, inducible nitric oxide synthase (iNOS), TNF-α, and IL-1β. Peroxisome proliferator X receptor (PPAR) and retinoic acid X receptor [9, 10]. |                |
| 5.      | Garlic      | Scientific name: *Allium sativum* 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] | Phase 2 [12] |
| 6.      | Eggplant/Brinjal | Scientific name: *Solanum melongena* Family: Solanaceae Part Used: Peels | Anthocyanin | inhibits lipid peroxidation [13] | Phase 3 [14] |
| 7.      | Guava       | Scientific name: *Psidium guajava* Family: Myrtaceae Part Used: Leaves | Guava leaf extract | a decrease in HbA1c% [15]. |                |
| 8.      | Mango       | Scientific name: *Mangifera indica* 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: *Carica papaya* Family: Caricaceae Part Used: Fruit | Rutin | • HMG-CoA reductase activity. • absorption of dietary cholesterol [17]. |                |
| 10.     | Pumpkin     | Scientific name: *Cucurbita pepo* 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: *Ananas comosus* Family: Bromeliaceae Part Used: Peels | Bromelain, Saponin, Tannin | Peels reduced oxidative stress [19] |                |
| 12.     | Cinnamon    | Scientific name: *Cinnamomi Cassiae* Family: Lauraceae Part Used: Bark | Cinnamon extract | The PPARγ and mRNA expression was regulated in adipose tissue [20] |                |
| 13.     | Cardamom    | Scientific name: *Elettaria cardamomum* Family: Zingiberaceae Part Used: Seeds | Kaempferol | partial agonist of PPARγ increasing insulin sensitivity and they are involved in the lipid metabolism. In hepatocytes [21]. |                |
| 14.     | Arjuna      | Scientific name: *Terminalia arjuna* Family: Combretaceae | Ethanolic fraction of T. arjuna | Ethanolic fraction of T. arjuna- serum/plasma lecithin cholesterol acyl transferase (LCAT) and accumulation of receptor mediated catabolism of LDL40. |                |
| 15. | Turmeric | Scientific name: Curcuma longa | Curcumin | Hypolipidemic activity is probably due to its anion exchange property [22]. Randomized Controlled Trial [24] |
| 16. | Ginger | Scientific name: Zingiber officinale | 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 | Scientific name: Zingiber officinale | 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 been noticed 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: Capsicum frutescens | Capsaicinoids, Capsaicin | stimulates the conversion of cholesterol to bile acids by regulation of cholesterol 7α-hydroxylase expression and enhancing the excretions of bile acids in feces [28]. A randomized, double-blind, controlled clinical trial [28] |
| 19. | Neem | Scientific name: Azadirachta indica | ethanolic extract of AZI | decreases ROS production and enzymes involve in it include superoxide dismutase (SOD), catalase (CAT) and glutathione Peroxidase (GPX). A randomized, double-blind, placebo-controlled trial [27]. |
| 20. | Hibiscus | Scientific name: Hibiscus rosa-sinensis | 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]. A randomized, placebo-controlled, clinical trial [27] |
| 21. | Aloevera | Scientific name: Aloe barbadensis | Aloe-emodin | could mostprobably reduce the production of ROS induced by PA and increase the expression of SOD. Aloe Emolin treatment might has the capability to decreases cardiomycyte apoptosis [33]. A randomized, placebo-controlled, clinical trial [27] |
| 22. | Strawberry | Scientific name: Fragaria ananassa | Ellagic acid, fisetin | Ellagic acid can possibly improve vascular reactivity postprandially, fisetin may normalize lipoproteins through the enhancement of lipoprotein lipase activity and can cause a decrease in glycation of lipoproteins [34, 35]. A randomized, placebo-controlled, clinical trial [27] |
| 23. | Coconut | Scientific name: Cocos nucifera | 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]. A randomized, placebo-controlled, clinical trial [27] |
| 24. | Ephedra | Scientific name: Ephedra sinica | ephedractae | scavenging of free radicals, includes hydroxyl and superoxide anions, and inhibiting lipid peroxidation and improve lipid profiles [37]. Phase 3. A randomized controlled trial and an updated meta-analysis [39]. Crossover, Randomized Controlled Trial [40] |
| 25. | Black pepper | Scientific name: Piper nigrum | piperine | stimulates cholesterol 7a-hydroxylase activity [38]. A randomized, placebo-controlled, clinical trial [27] |
|   |   | Scientific name: | Part Used | Extract/Component | Result/Effect | Randomized Controlled Trial |
|---|---|-----------------|-----------|------------------|---------------|-----------------------------|
| 26. | okra | Abelmoschus esculentus 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. | Randomized Controlled Trial |
| 27. | Kalmegh | Andrographis paniculata (Burm. f) Family: Acanthaceae Part Used: leaves | Andrographolide and Neoandrographolide | It was seen that And inhibits the LPS/IFNγ-induced iNOS and MMP-9 expressions in vascular smooth muscle cell and reduces the neointimal formation in a carotid injury. And increases NF-κb subunit P65 Ser536 dephosphorylation through an activation of protein phosphatase 2A in vascular smooth muscle cell. | A double blind, randomized controlled trial |
| 28. | Red yeast Rice | Monascus purpureus, Family: Monascaceae Monascus | monacolin | It can inhibit HMG-COA enzyme. | A double blind, randomized controlled trial |
| 29. | Tulsi | Ocimum tenuiflorum Family: Lamiaceae Part used: whole plant | Rosmarinic acid | It was found to have free radical scavenger activity and lipid peroxidase inhibitor properties. | A double blind, randomized controlled trial |
| 30. | Curry leaves | Murraya koenigii 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. | A double blind, randomized controlled trial |
| 31. | Sea Cucumber | Apostichopus japonica Family: Stichopodidae | Aqueous extract of the leaves | 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. | A double blind, randomized controlled trial |
| 32. | Mint | Mentha piperita 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. | A double blind, randomized controlled trial |
| 33. | Sankhpushpi | Convolvulus pluricaulis Family: Convolvulaceae Part Used: whole plant | Methanol extract | Catabolism of LDL-C through its hepatic receptors and effect on HMGCoA reductase action. | A double blind, randomized controlled trial |
| 34. | Guggal | Commiphora mukul Family: Part used: Leaves | E- and Z-guggulsterone Isomers of the guggal | This lipid-lowering activity may be due to the inhibition of hepatic cholesterogenesis and catabolic conversion of cholesterol to bile acids in the liver. | A double blind, randomized controlled trial |
| 35. | Sparrow grass/ Satavari | Asparagus racemosus Family: Asparagaceae Part Used: root | digitonin and tomatine | bind to the cholesterol and increase its precipitation in vitro and inhibit the cholesterol absorption without bile acid absorption in vivo. | A double blind, randomized controlled trial |
| 36. | Kantakari | Solanum surattense Family: Solanaceae Part Used: leaves | Leaves extract | decreased in the cholesterogenesis and reduced fatty acid synthesis, and this may be also due to the enhancement of the glucose utilization. | A double blind, randomized controlled trial |
| 37. | Tamarind | Terminalia chebula 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. | A double blind, randomized controlled trial |
| 38. | Drumstick | Moringa oleifera Lam Family: Moringaceae Part Used: fruit | Plant sterols | Partial inhibition of cholesterol synthesis by the de novo or by inhibiting the cholesterol absorption. | A double blind, randomized controlled trial |
| 39. | Amla | Emblica Officinalis | Fruit extract | Found to have action on the lipid metabolism. | A double blind, randomized controlled trial |
| 40 | Haritaki | Scientific name: *Terminalia chebula Retz.*, Family: Combretaceae | Bark extract | de novo lipogenesis leading to fatty liver was most probably reduced [60] | A Randomized Double-Blind, Placebo Controlled Clinical Trial [61] |
| 41 | Apamarga | Scientific name: *Achyranthes aspera* Family: Amaranthaceae | Aqueous extract | Low absorption of cholesterol because of rapid excretion of bile acids causing [62] |
| 42 | Barberry | Scientific name: *Berberis orthobotrys* Family: Berberidaceae | Extract of root | Extract might change the activity of diacylglycerol acyltransferase (DGAT), which is a key enzyme in HDL, its flux from the cell membrane into HDL, or might have effect on HMG-CoA reductase [63] |
| 43 | Orchids | Scientific name: *Bauhinia purpurea* Family: Fabaceae | Proanthocyanidines | The cholesterol reducing effect of the extracts most probably due to inhibition of dietary cholesterol esterification [64] |
| 44 | Matura Tree | Scientific name: *Cassia auriculata L.* Family: Fabaceae | Ascorbic acid | It might reduce the endogenous cholesterol biosynthesis by decreasing/stoping the hepatic uptake of cholesterol by the liver [65] |
| 45 | Liquorice | Scientific name: *Glycyrrhiza glabra Linn.* Family: Fabaceae | glycyrrhizin, glycyrrhizinic acid, glabrin A&B, glycyrrhetin, glabrolide, isoglabrolide, | Free radical scavenging activity [67] |
| 46 | Tomato | Scientific name: *Solanum lycopersicum* Family: Solanaceae | Lycopene | It might act on LDL receptor and prevent the binding of cholesterol [68] |
| 47 | Methi | Scientific name: *Trigonella foenum-graecum* Family: Fabaceae | Diosgenin | Diosgenin have a protective effect on blood vessels against oxidative stress via reducing the mRNA expression of MPO [69], [70] |
| 48 | Berry | Scientific name: *Dioscorea nipponica* Family: Dioscoreaceae. | Protodioscin | Most probably it is known to act as a HMG-CoA reductase inhibitor [71] |
| 49 | Vinca | Scientific name: *Catharanthus roseus* Family: Apocynaceae | Vincamine | Reduced the oxidative stress and reactive oxygen species [72], [73] |
| 50 | Yerba Mate tea | Scientific name: *Ilex paraguariensis* Family: Aquifoliaceae | Mate tea aqueous extract | Activation of PPARa stops the formation of macrophage foam cells formation of reactive oxygen species (ROS), and associated lipoprotein oxidative modification, [73] |

**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 [74], 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 Centre 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 [75-77].

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 [78]. 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 intolerant to statin. Still the occurrence of myalgias after the starting of statin is poorly defined, SAMs are a serious note major clinical concern. 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.

In Ayurvedic science the lipids are known as Medodhatu the drug which helps in control medodhatu called as Medooghna 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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