

# **EXPLORING ANTIHYPERLIPIDEMIC PROPERTIES OF MEDICINAL PLANTS AND HERBS: A NATURAL APPRPACH TO LIPID MANAGEMENT**

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## **Abstract**

Hyperlipidemia indicated the elevated levels of Total Cholesterol, Very High-Density Cholesterol (VLDL), Low density Lipoprotein (LDL) and triglycerides (TG) with a decreased level of High-density Lipoprotein (HDL). Antihyperlipidemic drugs are medications used to lower lipid levels in the blood, especially to reduce the risk of heart disease, stroke, and other cardiovascular conditions. These medications target cholesterol (LDL, HDL) and triglycerides depending on the lipid abnormality. Natural herbs are often associated with fewer side effects, affordability, and greater accessibility compared to synthetic drugs like statins, making them an attractive option for individuals seeking natural solutions for cholesterol management. The cholesterol-lowering effects of garlic are attributed to its influence on enzymes such as fatty acid synthase and 3-hydroxy-3-methyl-glutaryl-CoA reductase, which are involved in cholesterol metabolism.

Keywords: Hyperlipidemia, statins, natural herbs.

## **1. Introduction**

Hyperlipidemia is a genetic illness characterized by an excess of lipids in the blood, including fats, cholesterol, and triglycerides. Because these lipids/fats penetrate the arterial walls, anemia is more likely to occur, which increases the risk of heart attacks, strokes, pancreatitis, and other cardiovascular conditions.[1] When triglyceride-protein complex concentrations in the blood are abnormally high, the condition known as hyperlipoproteinemia results. In the bloodstream, fat molecules remain liquid. [2] Hyperlipidemia can be classified on the bases of types of lipid such as hypercholesterolemia, hypertriglyceridemia and on the bases of causing factors such as acquired and familial. [3,4] Hyperlipidemia indicated the elevated levels of Total Cholesterol, Very High Density Cholesterol(VLDL), Low density Lipoprotein(LDL) and triglycerides(TG) with a decreased level of High density

Lipoprotein(HDL). The expert panel of the National Cholesterol Education Program found that blood cholesterol concentrations below 200 mg/dL are desirable. 200 to 239 mg/dL of blood cholesterol are borderline while 240 mg/dL of blood cholesterol is called hypercholesteremic [5].

Complications of hyperlipidemia include Atherosclerosis, Angina pectoris, Coronary artery diseases and myocardial infraction. [6, 7] There are many synthetic therapies available for hyperlipidemia, each one carries a unique set of challenges and is not always helpful in treating lipoprotein abnormalities. Because of their higher safety and efficacy, lesser toxicity, and cheaper cost, chemicals obtained from natural sources are being used more and more in non-invasive therapies. The blood fat level may be lowered with the use of antihyperlipidemic medicines. By reducing lowdensity lipoproteins (LDL) cholesterol, reducing triglycerides, and increasing high-density lipoprotein (HDL) cholesterol, several antihyperlipidemic medicines work to improve lipid profiles. Lowering low-density lipoprotein cholesterol helps avoid cardiovascular disease's main and secondary symptoms. While it comes to treatment both statins and fibrates are the first line of choice for treatment of hyperlipidemia. Statins can reduce LDL cholesterol by up to 60% in a dose-dependent manner, though reductions of 20% to 25% are more common with the doses generally used in clinical practice to treat most individuals with hypercholesterolemia [8]. Some of clinical side effects of statins are Statin Associated Muscular symptoms (SAMS), Diabetogenic potentials, Hepatotoxicity, Neurotoxicity; Immune mediated necrotizing, Increases serum Transaminase.

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### 2. IMPORTANCE OF PLANT BASED TREATMENT:

Herbal remedies have shown an abundance of promise as a natural substitute for pharmacological therapies in the management of hyperlipidemia. Herbs are generally regarded as safe with little adverse effects and are also advised due to their affordability, ease of usage, and advantages for the environment. [9] In general, herbal remedies have a safer profile than statins, which can have a number of adverse effects, such as liver damage and sympathy. [10] Compared to synthetic medicine, herbal remedies may be more affordable, especially for people with high deductible plans or no health insurance [11]. the efficacy of dietary and lifestyle strategies in controlling cholesterol levels can be further enhanced by the easy integration of herbal remedies. Unlike statins, which may be thought of as a stand-alone treatment, this holistic approach can inculcate long-lasting lifestyle changes that contribute to overall heart health. [12]

Herbal plant	Biological Name	Family	Chemical constituent	References
Garlic	Allium sativum	Amaryllidaceae	Alliin	13

Fenugreek seeds	Trigonella foenum	Fabaceae	Diosgenin.	14
Hibiscus Cannabis	Hibiscus cannabinus	Malvaceae	lignans	15
Tejpat	Cinnamomum Tamala	Auraceae	Cinnamaldehyde	16
Aloe Vera	Aloebarbadensismiller	Asphodelaceae	lignans	17
Artichoke	Cynara scolymus	Asteraceae	Cynaroicin Aguerin-B Grosheimin	18
Terminalia pallida	Tamala pallida	Combretaceae	Triterpenes	19
Grapes	Vitis vinifera	Vitaceae	Resveratrol	20

## 2.1 GARLIC

Garlic lowers cholesterol levels by either decreasing the cholesterogenic and lipogenic actions of fatty acid synthase, 3-hydroxy-3-methyl-glutaryl-CoA reductase, malic, and glucose-6 phosphate dehydrogenase in hepatocytes, or by increasing the excretion of acidic and neutral steroids. Garlic was discovered to have a considerable effect on dyslipidemia due to its modestly enhanced HDL cholesterol and dramatically decreased serum levels of TG, TC, and LDL [21].

### 2.1.1 Dose: Garlic and Its Benefits

Garlic has been widely recognized for its cardiovascular benefits, including:

- **Cholesterol Reduction:** When taken with medications like ezetimibe, which inhibits cholesterol absorption in the intestines, garlic can have a synergistic effect, helping lower plasma LDL-C (low-density lipoprotein cholesterol) and total cholesterol (TC). This combination can reduce the risk of cardiovascular diseases.

- **Daily Dosage for Elderly Individuals:** The recommendation of 4 g of raw garlic (or equivalent doses of dried garlic powder) taken 2-3 times a day is based on studies that support its efficacy in lowering cholesterol levels and improving heart health.[22]

### **2.1.2 Toxicity and Side Effects**

As for the toxicity and side effects of garlic:

- **Safety:** A study involving rats at a very high dose (2000 mg/kg body weight for 6 months) showed no negative effects, suggesting that garlic is generally safe in large amounts.
- **Common Side Effects:** The most common side effect of garlic is its strong odor, which is often undesirable.
- **Other Side Effects:** Rare side effects include:
  - Nausea (6% of people in a study)
  - Vertigo (about 1.3%, possibly due to its blood pressure-lowering effect)
  - Allergic Reactions (1.1%)
  - Headaches, excessive sweating, and bloating[23]

## **2.2 METHI**

Fenugreek seeds are rich in a variety of beneficial compounds, including fiber, phospholipids, glycolipids, oleic acid, linolenic acid, linoleic acid, choline, and several vitamins such as A, B1, B2, C, and niacin. These nutrients contribute to its numerous health benefits. Fenugreek is adaptable to different growing conditions, demonstrating moderate tolerance to drought and salinity, and can be cultivated on marginal lands profitably.

When it comes to cholesterol-lowering effects, studies have found that certain component of fenugreek seeds specifically the fiber and saponins are responsible for these benefits. The fiber and saponins extracts were shown to reduce cholesterol levels, while other components like lipid extracts or trigonelline did not have the same effect. The fiber and saponins reduce cholesterol concentrations in both the liver and blood plasma and inhibit the liver's production of cholesterol. Similarly, the defatted fraction of fenugreek seeds also displayed similar cholesterol-lowering properties.[24]

Further research on both animals and humans has demonstrated that fenugreek can help reduce blood triglycerides, total cholesterol, and low-density lipoprotein (LDL), as well as prevent the oxidation of LDL an important factor in the development of atherosclerosis. These benefits are thought to be linked to the plant's saponins and phytoestrogens. Saponins promote the excretion of cholesterol in bile, while phytoestrogens may indirectly boost thyroid hormones, contributing to the cholesterol-lowering effects.

This combination of effects makes fenugreek a promising natural remedy for improving cardiovascular health and managing cholesterol levels. [25]

**2.2.1 Dosage:** The usual dosage is 5 to 30 g of the plant seed powder 3 times per day in the meal time.

**2.2.2 Toxicity:** Fenugreek (*Trigonella foenum graecum* L.) may have a mild stimulatory effect on the gastrointestinal tract when consumed in high doses. However, no toxic effects have been observed in animal studies from consuming this plant. The extract from the seeds has also shown a stimulatory effect on the uterus in guinea pigs. Due to this, it is advised that pregnant women avoid consuming fenugreek, and it should not be used by children or individuals with kidney or liver diseases. [26]

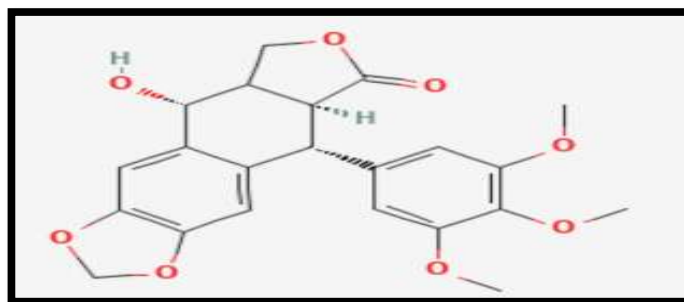
## 2.3 Hibiscus cannabinus

*Hibiscus cannabinus* L., commonly known as "Kenaf" is a fast-growing, herbaceous annual plant with large cream-colored flowers featuring a reddish-purple or scarlet throat. It is primarily cultivated for its fiber and has a woody, prickly stem. Traditionally, it has been used in folk medicine in Africa and India, where it is valued for containing various active compounds such as tannins, saponins, polyphenolics, alkaloids, lignans, essential oils, and steroids. [27]

Historically, the plant has been used as an antidote for poisoning from chemicals (acids, alkalis, pesticides) and venomous mushrooms. It has also been employed in treating bruises, digestive issues, fever, and conditions related to childbirth. The stem peelings were used to address dysentery and disorders of the blood and throat, while the seeds were applied externally for aches and bruises. Additionally, *Hibiscus cannabinus* is reported to have

several other medicinal properties, including being an anodyne, aperitif, aphrodisiac, as well as having fattening, purgative, and stomachic effects. [28]

Limited pharmacological studies have shown that the plant's essential oil exhibits phytotoxic and fungi toxic properties. The aqueous extract of the plant has demonstrated hematinic and antioxidant potential, while the leaf extract has shown hepatoprotective effects, protecting against liver damage induced by carbon tetrachloride and paracetamol in rats. Moreover, an 80% ethanol leaf extract displayed significant immunomodulatory effects in activated macrophages. Lignans isolated from the plant have also exhibited cytotoxic activity against cancer cell lines such as HeLa, Hep-2, and A-549. [29]



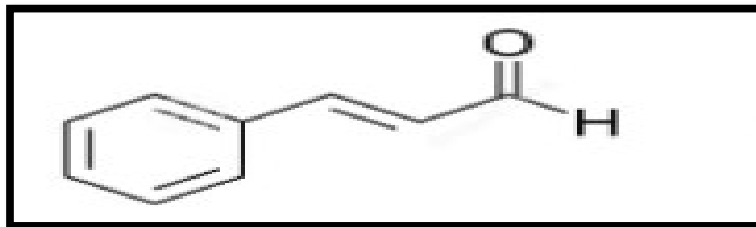
Lignans

## 2.4 Tejpat

Cinnamomum, one of the oldest known spices, is renowned for its sweet fragrance and warm flavor. **Cinnamomum tamala**, also known as Indian bay leaf or Tejpat, belongs to the Lauraceae family. It is widely used as a spice in cooking and is native to regions like India, Nepal, Bhutan, and China. Beyond its culinary use, **C. tamala** is valued in traditional medicine systems worldwide, including Western herbal medicine, for its therapeutic properties.[30]

The plant contains several bioactive compounds that contribute to its medicinal effects. These include Cinnamaldehyde, Trans-Cinnamaldehyde, 3, 4, 5, 7-tetrahydroxyflavone, kaempferol-3-O-rutinoside, quercetin-3-O-sophoroside (flavonoid glycosides),  $\alpha$ -pinene, myrcene, camphene, limonene, and eugenol (4-hydroxy-3-methoxyallylbenzene). The leaf oil of *C. tamala* also contains compounds such as furanogermerone,  $\beta$ -caryophyllene, germacerene D, curcumenol, and curzerenone. These chemicals have been shown to possess various pharmacological activities, including anti-hyperlipidemia, anti-diabetic, gastro

protective, anti-helminthic, anti-protozoal, anti-diarrheal, antifungal, and antibacterial properties, among others. [31]



Cinnamaldehyde

## 2.5 Aloe Vera



The Aloe vera plant has been used for many years due to its medicinal properties, offering benefits such as anti-inflammatory, antioxidant, anti-diabetic, anti-infective, antimicrobial, and immune-boosting effects. The Aloe genus includes over 500 species globally, with Aloe vera being known as the "true aloe" or a desert plant. [32]

In a pilot study conducted over 8 weeks, two aloe products (UP780 and AC952) were tested in patients with prediabetes or metabolic syndrome. The results showed that AC952 led to significant reductions in total cholesterol (TC) and LDL-C levels, along with decreases in blood glucose and HbA1C levels, and improved insulin sensitivity. [33]

However, it did not effectively reduce triglyceride levels or increase HDL-C levels in the serum. This could be attributed to either the chronic hyperglycemia in the patients, which may cause oxidative stress, or the low dose of Aloe vera used in the study. [34]

## 2.6 Artichoke



**Cynara scolymus** (Asteraceae), commonly known as artichoke is cultivated in many countries. Other varieties of artichoke, such as Jerusalem artichoke (**Helianthus tuberosus**) and Chinese artichoke (**Stachys affinis**), are also widely grown. The globe artichoke is the part of the plant that contains the flower buds before they bloom, with the stem removed. Typically, the globe artichoke is cooked, and after discarding the leaves, the edible portion is known as the heart. However, artichoke leaves are often consumed as an herbal supplement, typically in the form of artichoke leaf extract (ALE) [35].

ALE, especially from the *Cynara scolymus* cultivar, has been recognized as an effective phytotherapeutic

Agent for various conditions, including cardiovascular, hepatic, and gastric diseases. Available evidence suggests that artichoke supplementation can enhance the lipid profile in individuals with conditions such as hypercholesterolemia, metabolic syndrome, obesity, type 2 diabetes, non-alcoholic fatty liver disease, and non-alcoholic steatohepatitis [36]

The primary benefits of artichoke in improving the lipid profile are linked to reductions in serum levels of LDL cholesterol (LDL), total cholesterol (TC), and triglycerides (TG). These reductions have been observed as follows: LDL decreased by 8–49 mg/dL, TC by 12–55 mg/dL, and TG by 11–51 mg/dL. However, a study by Lupattelli et al. showed an increase of 9 mg/dL in serum TG concentrations, which contrasts with the overall trend. Table [37]

Author	N	Study Design (Length of the Intervention)	Type of artichoke	Daily dose of artichoke	HDL-c	LDL-c	TC	TG
Barrat et al. [38]	94, subjects with hypercholesterolemia	Randomized placebocontrolled trial (16 w)	Artichoke leaf extract, policosanols and red yeast rice	200 mg	↔	↓22	↓26	↔
Bundy et al. [39]	68, subjects with mild to moderate hypercholesterolemia	Randomized, double-blind placebocontrolled trial (12 w)	Artichoke leaf extract	1280 mg	↔	↔	↓11.6	↔

	erolemia							
English et al. [40]	143, hyperlipoproteinemia patients	Double-blind, randomized, placebo controlled, multi-centre clinical trial (6 w)	Artichoke dry extract	180 mg	↔	↓48.7	↓55.3	↔
Lupattelli et al. [41]	28, moderately hyperlipidemia patients	Nonrandomized interventional study (6 w)	Frozen artichoke juice	20 mL	↔	↓14	↓17	↑9

**2.6.1 Dosage:** Germany's Commission E recommends a total of 6 grams of the dried herb per day, divided into three doses, as the optimal amount for treating dyspepsia. However, they do not specify an optimal dose for hyperlipidemia.

**2.6.2 Toxicity:** No side effects have been reported from using artichoke leaves; however, since research on this is still ongoing, pregnant or breastfeeding women are advised not to use it. Additionally, young children, individuals with severe liver or kidney conditions, and those with gallstones should exercise caution when using the leaves. People who are allergic to artichokes or related plants in the Asteraceae family, such as arnica or chrysanthemums, should avoid artichoke or cynarin-based preparations. [42]

## 2.7 Terminalia pallid

The intake of fruits and vegetables plays a key role in managing hyperlipidemia. The fruits of *Terminalia pallida* Brandis (*T. pallida*), which thrive during the monsoon season, are found primarily in the Tirumala hills of the Rayalaseema region in Andhra Pradesh, India. These fruits, known locally as "tellaraka," mature over a two-month period, changing from light to dark green before turning brown when fully ripe. Tribal communities use these fruits as a remedy for diabetes, and they are also widely used to treat various conditions like diarrhea, ulcers, venereal diseases, and for their

antibacterial and antifungal properties. In addition, *T. pallida* fruits are known for their effectiveness in treating skin diseases and liver ailments [43].

Lipids and lipoproteins were measured using kits from Erba Diagnostics Ltd., India. HDL-C was measured directly, while very low-density lipoprotein cholesterol (VLDL-C) was calculated using the formula  $VLDL-C = TG/5$ , and low-density lipoprotein cholesterol (LDL-C) was determined as  $LDL-C = TC - (HDL-C + VLDL-C)$ . Malondialdehyde (MDA) levels were assessed to evaluate lipid per oxidation (LPO). Reduced serum paraoxonase (PON) activity has been observed in diseases related to hypercholesterolemia, atherosclerosis, and an increased risk of cardiovascular disease (CVD) [44].

PON helps protect against CVD by reducing HDL-C oxidation and shielding plasma membranes from free radical damage. Our previous research highlighted the cardio protective effects of HPLC-standardized *T. pallida* fruit extract (TpFE) on cardiac markers, myocardial lipids, antioxidants, and membrane-bound ATPases in rats with induced myocardial infarction. In this study, we further investigated the beneficial effects of TpFE on lipids, lipoproteins, lipid metabolic enzymes, and PON in rats with induced myocardial infarction [45].

## 2.8 Grapes

Grapes are commonly used in traditional medicine and form an integral part of the Mediterranean diet. Grape seeds are a rich source of antioxidant polyphenols, which include flavonoids, non-flavonoids, anthocyanidins, catechins, and phenolic acids. Based on their chemical structure, five primary classes of polyphenols have been identified: flavonoids, phenolic acids, lignans, stilbenes, and other minor polyphenols. Grape Seed Extracts (GSE) has been extensively studied in several meta-analyses for their hypolipidemic effects. The ways in which grape compounds improve lipid profiles and help combat atherosclerosis include reducing lipid absorption and increasing fecal excretion of lipids, primarily attributed to GSE. Additionally, GSE consumption has been linked to a reduction in early-stage atheromatous plaque. Diets rich in polyphenols are associated with multiple health benefits, likely due to their ability to enhance cardiovascular risk factors by reducing oxidative stress, lowering inflammation, boosting antioxidant capacity, and inhibiting platelet aggregation [46, 47].

Grape consumption has been found to enhance flow-mediated dilation and reduce the endothelial dysfunction caused by a high-fat diet [48]. In individuals with metabolic syndrome components, randomized placebo-controlled trials have shown that grape supplementation, provided as powder, juice, or seed extracts for durations ranging from 2 to 24 weeks, improved various metabolic issues. This supplementation significantly lowered blood pressure and reduced markers of oxidative stress, such as oxidized LDL. Notable effects on glucose metabolism were observed after consuming different grape products, including seed extracts, juice, and pomace. However, the impact of grape polyphenols on lipid metabolism remains less conclusive, with some studies showing a significant reduction in lipid levels, while others find no change in lipid profiles [49].

### **3. Conclusion:**

Herbal remedies have emerged as valuable natural alternatives for managing hyperlipidemia, offering several potential benefits over conventional pharmacological treatments. Herbs such as garlic, fenugreek, artichoke, and grape seed extract (GSE) have been extensively studied for their efficacy in lowering cholesterol levels and supporting cardiovascular health. These herbs are often associated with fewer side effects, affordability, and greater accessibility compared to synthetic drugs like statins, making them an attractive option for individuals seeking natural solutions for cholesterol management.

Garlic (*Allium sativum*) is one of the most well-known herbs for cardiovascular health, particularly in lowering levels of low-density lipoprotein (LDL) cholesterol, total cholesterol (TC), and triglycerides (TG). It can also modestly increase high-density lipoprotein (HDL) cholesterol. The cholesterol-lowering effects of garlic are attributed to its influence on enzymes such as fatty acid synthase and 3-hydroxy-3-methyl-glutaryl-CoA reductase, which are involved in cholesterol metabolism. Garlic has been shown to enhance the effects of other medications like ezetimibe, making it a useful adjunct in managing hyperlipidemia. While garlic is generally safe, common side effects include its strong odor, with rarer cases of nausea, vertigo, and bloating.

Fenugreek (*Trigonella foenum-graecum*), another herb with promising cholesterol-lowering properties, contains fiber, saponins, and various bioactive compounds that help reduce cholesterol levels. Fenugreek inhibits cholesterol production in the liver and promotes its excretion in bile, making it an effective remedy for both hyperlipidemia and atherosclerosis

prevention. The recommended dosage of fenugreek is typically 5 to 30 grams of seed powder, taken with meals. However, pregnant women, children, and those with liver or kidney conditions should avoid using fenugreek.

Other herbal remedies like *Cynara scolymus* (artichoke) and *Terminalia pallida* have also shown significant promise in improving lipid profiles. Artichoke leaf extract (ALE) is known to reduce LDL cholesterol, TC, and TG levels, offering a potent natural remedy for individuals with high cholesterol. Artichoke is generally well tolerated, with no major side effects reported, though caution is advised for pregnant or breastfeeding women, young children, and those with severe liver or kidney conditions.

Similarly, *T. pallida*, native to India, has been shown to improve lipid profiles and offer cardio-protective effects in animal models, particularly in rats with induced myocardial infarction. *T. pallida* fruit extract enhances serum antioxidant levels and influences lipid metabolic enzymes, offering a potential remedy for hyperlipidemia and cardiovascular risk factors.

Finally, Grape Seed Extract (GSE) is rich in polyphenolic compounds like flavonoids, catechins, and anthocyanidins. These compounds have demonstrated the ability to reduce lipid absorption, increase fecal excretion of lipids, and combat early-stage atherosclerosis. GSE also improves endothelial function, reduces oxidative stress, and enhances glucose metabolism in individuals with metabolic syndrome. While some studies show significant improvements in lipid levels, more research is needed to understand the full extent of grape polyphenols' effects on lipid metabolism.

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