

Herbal Medicines for Hypercholesterolemia: A Review

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Abstract: Hypercholesterolemia, a major risk factor for cardiovascular diseases, contributes significantly to global morbidity and mortality. Conventional therapies, while effective, are often accompanied by side effects, prompting interest in herbal medicines as alternative or complementary treatments. This review explores the lipid-lowering potential of various medicinal plants, including artichoke, alfalfa, fenugreek, garlic, soybean, milk thistle, red yeast rice, guggul, psyllium, guar gum, and oat. Clinical evidence demonstrates their efficacy in reducing total cholesterol, LDL, and triglyceride levels while improving HDL levels. Mechanisms of action include inhibition of cholesterol synthesis, increased bile acid excretion, and antioxidant properties. However, challenges such as standardization of herbal formulations, optimal dosing, and potential drug interactions persist. Further research is essential to validate the safety, efficacy, and integration of these herbs into mainstream lipid-lowering strategies. The findings highlight the potential of medicinal plants as promising tools in managing hyperlipidemia and mitigating cardiovascular risks.

Keywords: Hyperlipidemia; Herbal Medicine; Cardiovascular health; Review.

INTRODUCTION

Hypercholesterolemia, characterized by elevated levels of cholesterol in the blood, is a critical risk factor for cardiovascular diseases (CVDs), which remain the leading cause of morbidity and mortality worldwide (Illingworth, 2000). The global burden of cardiovascular diseases has risen alarmingly, with deaths attributed to CVD increasing from 14.4 million in 1990 to 17.5 million in 2005, and projections estimating this figure to reach approximately 20 million by 2025 (Mensah et al., 2019). Various circulating agents such as low-density lipoprotein (LDL) free radicals, homocysteine, and nicotine contribute significantly to the pathogenesis of hypercholesterolemia and its associated complications, particularly when coexisting with other conditions like diabetes mellitus and hypertension (Khosravi et al., 2018).

The development of atherosclerosis, the underlying mechanism of many cardiovascular events, is a multifaceted process. It involves LDL accumulation in the arterial intima, LDL oxidation, macrophage-mediated uptake of oxidized LDL through scavenger receptors, foam cell formation, and plaque stabilization (Yang & Vafai, 2006). This sequence of events is perpetuated by inflammatory cytokines, rendering atherosclerosis a chronic inflammatory disease (Griffin et al., 1994). Critical complications arise when plaque causes arterial blockages exceeding 75%, leading to symptoms like angina, and when plaques rupture or

blood clots obstruct downstream blood flow, resulting in heart attacks or strokes (Wang et al., 2020).

Preventive strategies form the cornerstone of managing hypercholesterolemia and atherosclerosis. Conventional medical approaches emphasize lifestyle modifications such as reducing saturated fat intake, engaging in regular aerobic exercise, and quitting smoking. Pharmacological interventions, including cholesterol-lowering and antihypertensive drugs, are also widely employed but are often associated with significant side effects, necessitating the exploration of safer alternatives (Kosmas et al., 2018).

In recent decades, there has been a growing interest in using herbal medicines as complementary or alternative treatments for hypercholesterolemia, along with other metabolic disorders like diabetes and hypertension (Rauf et al., 2022). Medicinal plants have been extensively studied for their lipid-lowering properties, antioxidant effects, and overall cardiovascular benefits (Rauf et al., 2022). However, challenges persist regarding the lack of standardized information on their safety profiles, mechanisms of action, and potential drug interactions.

This review aims to provide an overview of promising medicinal plants used in the prevention and treatment of hypercholesterolemia, highlighting their therapeutic efficacy, mechanisms, and limitations. Additionally, it underscores the need for rigorous research to validate the safety and clinical applicability of these herbal remedies. By bridging the gap between traditional knowledge and

modern scientific understanding, this review aspires to contribute to the development of safer and more effective therapeutic strategies for managing hypercholesterolemia.

METHODOLOGY OF RESEARCH

The evidence from clinical trials, randomized controlled studies, and traditional medicine practices regarding the efficacy of various medicinal plants in treating hyperlipidemia were analysed. Key herbs evaluated include *Cynara cardunculus* (Artichoke), *Medicago sativa* (Alfalfa), *Trigonella foenum graecum* L (Fenugreek), *Allium sativum* L (Garlic), *Glycine max* (Soybean), *Silybum marianum* L, Red Yeast Rice and *Commiphora mukul* (Guggul). The review also considers dietary plant fibers, particularly *Plantago psyllium* and *Cyamopsis tetragonoloba* (Guar Gum), in lipid management.

The review identifies various medicinal plants with significant lipid-lowering effects, supported by clinical and preclinical evidence. These herbs have been shown to reduce total cholesterol, LDL cholesterol, and triglycerides, while improving HDL levels, through mechanisms such as inhibiting cholesterol synthesis, enhancing bile acid excretion, and preventing LDL oxidation. Their potential as natural and complementary treatments for hypercholesterolemia offers promising alternatives to conventional therapies.

***Cynara cardunculus* (Artichoke):**

Artichoke has a rich source of polyphenolic compounds and phytosterols which was believed to exhibit the hypocholesterolemic effect. In a randomized, double-blind trial with 143 high-cholesterol patients, artichoke dry extract decreased total cholesterol by 18.5% versus 8.6% in placebo, reduced LDL cholesterol by 23% versus 6%, and improved LDL/HDL ratios by 20% versus 7%. The compounds cynarin and luteolin in artichoke leaves appear to play key roles in reducing cholesterol synthesis and total levels (Fallah Huseini et al., 2012). The main potential of Artichoke leaf extract (ALE) administration observed on lipid profile shows decreased serum LDL cholesterol, Total cholesterol and Triglyceride with no effect on HDL cholesterol levels. Also evidence shows administration of 2 to 3 g/dL of ALE showed decrease of 8–49 mg/dL for LDL cholesterol, 12–55 mg/dL for total cholesterol and 11–51 mg/dL for triglycerides with its key components Luteolin and Chlorogenic acid playing the key role (Heitor Oliveira santos et al., 2018). ALE consumption resulted in a modest but favourable statistically significant difference in total cholesterol after 12 weeks (Rafe Bundy et al, 2008).

***Medicago sativa* (Alfalfa):**

Research indicates that alfalfa seeds can effectively lower blood cholesterol levels in laboratory animals. A long-term study on cynomolgus monkeys demonstrated that alfalfa consumption led to regression of

atherosclerotic lesions without side effects. The study showed correlation between hydroxyproline and glycosaminoglycan concentrations with lesion severity, suggesting alfalfa's role in aortic remodeling during atherosclerosis regression (Shah et al., 2020). Hypocholesterolemic and Anti-atherosclerotic properties of ethanolic (1% and 2%) and aqueous extracts of Alfalfa was also found in rabbits after induction of hypercholesterolemia with cholesterol enriched diet shown by significant decrease in plasma Total cholesterol by 85.1% and LDL-C by 88%. Also a remarkable inhibition of progression of intimal thickness and normalisation of aortic walls was found on histopathological study after treatment of Alfalfa extract for 28 days (Khaleel A.E et al, 2005).

***Trigonella foenum graecum* L (Fenugreek):**

Studies show fenugreek effectively reduces blood sugar in diabetic patients while also lowering cholesterol levels. In clinical trials, it decreased triglycerides and increased HDL levels. The plant's saponins increase biliary cholesterol excretion, while its phytoestrogens indirectly increase thyroid hormones. It also prevents LDL oxidation, a major component in atherosclerosis development (Geberemeskel et al., 2019).

***Allium sativum* L (Garlic):**

Garlic has shown mixed results in cholesterol reduction studies. However, a 12-week clinical trial showed significant decreases in total cholesterol and LDL cholesterol in patients taking garlic supplements. Studies also indicate garlic's effectiveness in inhibiting atherosclerosis formation and improving aorta elasticity. In a 4-year study with 152 participants, 900mg daily of garlic powder significantly decreased atherosclerosis plaque formation (Sun et al., 2018).

***Glycine max* (Soybean):**

Research demonstrates soybean's effectiveness in reducing LDL cholesterol. Meta-analyses show soy protein intake (average 47g/day) resulted in a 9.3% decrease in total cholesterol, 12.9% decrease in LDL cholesterol, and 10.5% decrease in triglycerides. While some studies suggest isoflavones play a role in cholesterol reduction, others indicate soy proteins may be more significant (Ahmad et al., 2014).

***Silybum marianum* L (Milk Thistle):**

Clinical research shows silymarin can effectively reduce blood cholesterol in patients with hypercholesterolemia. At 420mg daily, it decreased cholesterol concentration in bile and improved HDL levels. In diabetic patients with hyperlipidemia, silymarin treatment resulted in decreased total cholesterol, LDL, and triglyceride levels (Tajmohammadi et al., 2018).

Red Yeast Rice:

Studies show red yeast rice effectively reduces blood cholesterol through its active compound monacolin K, which works similarly to statins by inhibiting HMG-CoA

reductase enzyme. Clinical trials using 1.2g daily of concentrated extract showed significant decreases in total serum cholesterol, increased HDL levels, and decreased LDL and triglyceride levels (Cicero et al., 2019).

Commiphora mukul (Guggul):

Clinical studies demonstrate Guggul's effectiveness in reducing blood lipids. In a 24-week study, 100mg daily resulted in 11.7% decrease in total cholesterol, 12.7% decrease in LDL, 12% decrease in triglycerides, and 11.1% decrease in cholesterol-HDL ratio. Its effects were comparable to clofibrate in clinical trials, with better results in hypercholesterolemic patients (Singh et al., 1994).

Plantago psyllium:

Clinical studies show significant lipid-lowering effects with psyllium treatment. In patients with hypercholesterolemia, 6-8 weeks of treatment reduced total cholesterol by 3.5-5.6% and LDL cholesterol by 5.1-8.8% compared to placebo. In a study of 125 type 2 diabetic patients with hyperlipidemia, taking 5g psyllium three times daily for 6 weeks decreased total cholesterol, LDL cholesterol, and plasma triglycerides while increasing HDL cholesterol levels after just 2 weeks of treatment (Jovanovski et al., 2018).

Cyamopsis retragonoloba (Guar Gum):

Laboratory studies demonstrate guar gum's ability to significantly reduce blood cholesterol levels in rats through effects on enterohepatic circulation. Its cholesterol-lowering mechanism is attributed to increased steroid excretion in feces and enhanced bile production. Clinical studies on type 2 diabetic patients with hyperlipidemia showed decreases in both blood sugar and lipid levels. Guar gum also helps reduce appetite and triglyceride levels, contributing to weight management (Bahmani et al., 2015).

DISCUSSION

Hyperlipidemia adversely affects lipoprotein levels and the antioxidant balance of various organs, contributing to oxidative stress and promoting the development of atherosclerosis. This process is driven by the oxidation of LDL into ox-LDL, which plays a central role in initiating inflammatory responses, inducing endothelial adhesion molecule expression, foam cell formation, and eventually leading to the formation of fatty streaks and atherosclerotic plaques (Kattoor et al., 2019). Oxidative stress also exacerbates vascular endothelium damage and metabolic disturbances, further increasing the risk of cardiovascular diseases, particularly in individuals with comorbid conditions such as diabetes and hypertension (Incalza et al., 2018).

The antioxidant properties of medicinal plants have been widely recognized as crucial in countering oxidative damage and lowering lipid levels. These plants often contain phenolic compounds, flavonoids, sterols, and

dietary fibers, which scavenge free radicals, reduce LDL oxidation, and protect critical organs like the heart, liver, and kidneys (Akbari et al., 2022). For instance, phenolic-rich plants like *Silybum marianum* and *Allium sativum* have demonstrated notable efficacy in reducing hyperlipidemia while preventing oxidative stress-induced tissue damage. Additionally, the anti-inflammatory properties of these plants help mitigate chronic conditions linked to hyperlipidemia, such as hypertension and diabetes, by lowering markers like C-reactive protein (Guan et al., 2021).

Synthetic antioxidants, including vitamins C and E, though initially promising, have shown limitations due to potential toxicity and inconsistent efficacy in preventing chronic diseases (Forman & Zhang, 2021). This highlights the advantage of plant-based antioxidants, which exhibit minimal toxicity and broader health benefits. Furthermore, several herbal remedies have been shown to enhance lipid metabolism, lower cholesterol, and improve vascular health, underscoring their therapeutic potential.

Despite the extensive data supporting the efficacy of known lipid-lowering plants, there remains significant untapped potential. Many medicinal plants with antioxidant activities have not yet been fully evaluated for their hypolipidemic effects. By targeting oxidative stress and inflammation, these plants represent a promising frontier in the management of hyperlipidemia and associated complications.

CONCLUSION

Hyperlipidemia, a significant risk factor for cardiovascular diseases, is closely linked to oxidative stress. Medicinal plants, rich in antioxidants and bioactive compounds, offer a natural and effective approach to managing lipid levels and reducing oxidative damage. Their dual role in lipid regulation and organ protection emphasizes the need for further exploration of their therapeutic potential.

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