**Review Article**

**DECODING FENUGREEK’S CHOLESTEROL-LOWERING MECHANISM: A CRITICAL REVIEW OF ITS THERAPEUTIC POTENTIAL**

**ABSTRCT**

**Background:**

 Dyslipidemia is a major modifiable risk factor for cardiovascular diseases, the leading cause of mortality worldwide. The consolidation of interest in plant-based interventions has Spurred further examination of traditional medicinal herbs for their effect on lipid levels. Fenugreek (Trigonella foenum-graecum), an herb found in the traditional Ayurvedic and Chinese matrix, has emerged as a promising functional food. This is based on its phytochemical profile, in addition to its cardioprotective and health-promoting functions.

**Objective:**

 This review sought to evaluate the lipid-lowering effects of fenugreek, describe potential biochemical and pharmacological mechanisms, and evaluate the clinical relevance of fenugreek is dyslipidemia and other metabolic states

**Methods:**

 A comprehensive literature search was conducted using PubMed, Scopus, and Google Scholar, to identify relevant preclinical studies, clinical trials, and imaging and mechanistic studies published in the past 20 years. The key inclusion model was studies examining the effects of fenugreek seed, extract, or derived compounds on lipid profiles and cardiovascular characteristics in human and non-human subjects.

**Results:**

 The chemical analysis revealed that fenugreek seeds are high in soluble dietary fiber (galactomannan), and abundant bioactive constituents, such as, steroidal saponins (e.g., diosgenin), flavonoids, polyphenols, alkaloids (e.g., trigonelline), and amino acids. Such constituents exert numerous lipid-modulating properties, such as: inhibit cholesterol absorption in the intestine; increase bile acid secretion; increase lipolytic enzymes; and downregulate the hepatic HMG-CoA reductase, which is the rate-limiting enzyme in cholesterol biosynthesis. Animal studies show that supplementation with fenugreek has significantly lowered total cholesterol, low density lipoprotein- cholesterol (LDL-C) and triglycerides, while simultaneously raising high density lipoprotein-cholesterol (HDL-C). The relatively few human clinical trials have also shown some encouraging data but sample sizes are too small and the studies too short in duration for any statistically valid claims. However, some literature exists documenting favourable changes in lipid profiles associated with fenugreek in patients diagnosed with hyperlipidemia, type 2 diabetes and metabolic syndrome. Fenugreek was also found to be highly palatable and offer multiple forms of consumption i.e. whole seeds, defatted powder (flour), aqueous extracts and nutraceutical formulations; thus, supporting potential for promotion, uptake and long-term consumption as dietary therapy.

**Conclusion:**

 Fenugreek shows significant potential as an affordable, natural tool for the prevention and treatment of dyslipidemia and cardiovascular disease risk. Its diverse lipid-lowering mechanisms, benign safety profile, and straightforward incorporation into the diet classify it as a candidate for both pharmacological and dietary components of cardiovascular care. However, the present evidence base is limited by methodologic challenges, differences in primary extract type, and a lack of large and well-designed randomized controlled trials. Future research should focus on developing standard doses of fenugreek combined with safety and effectiveness studies designed and executed in large clinical trials to enable evidence-based recommendations for its inclusion in evidence-based treatment protocols.

**Key words:** saponins, flavonoids, fiber, lipid metabolism, hypercholesterolemia, Fenugreek,

 cholesterol-lowering, dyslipidemia, cardiovascular health,

 HMG-CoA reductase, hyperlipidemia.

**INTRODUCTION**

 Cardiovascular diseases (CVDs) are the leading cause of morbidity and mortality worldwide, with dyslipidemia (particularly, hypercholesterolemia) as a major contributing risk factor. Increased total cholesterol, especially low-density lipoprotein cholesterol (LDL-C) plays a major role in the development of atherosclerosis, which can lead to myocardial infarction and stroke. Although statins are now commonly regarded as first-line therapy for the management of dyslipidemia, and are generally prescribed without thought to long-term side effects, some of which may include: hepatotoxicity, the development of myopathy, increased risk of type 2 diabetes, and/or financial costs associated with long-term pharmacotherapy, the exploration of another lipid lowering strategy that is both safe and inexpensive is warranted.

 Complementary and adjunct strategies utilizing plant-based therapies and functional foods have garnered attention in the past few years as methods to assist in achieving and maintaining lipid homeostasis. Trigonella foenum-graecum (fenugreek) is emerging as a promising candidate due to its documented use in historical traditional systems of medicine, as well as its phytochemical complexity. Fenugreek seeds are a unique source of soluble fiber (primarily galactomannan), steroidal saponins, flavonoids, alkaloids, and other bioactive value. These compounds possess lipid lowering, hypoglycemic, and anti-inflammatory properties.

 Several scientific studies have clarified how fenugreek reduces lipid metabolism. Fenugreek modulates lipid metabolism by reducing intestinal cholesterol absorption, increasing bile acids excreted in stools, and inhibiting hepatic HMG-CoA reductase activity, the rate-limiting enzyme in cholesterol synthesis. Moreover, the potential role of fenugreek in improving glycemic control and insulin sensitivity assists us in understanding how fenugreek can disturb integrated and additive pharmacological effects which transcend its lipid-lowering properties in the management of cardiometabolic conditions.

 Hypercholesterolemia is an important risk factor for cardiovascular diseases, which remain the leading cause of morbidity and mortality worldwide. Increases in cholesterol, particularly low-density lipoprotein cholesterol, may lead to atherosclerosis-one of the prime causes of heart attacks or strokes. While statins and other pharmacological agents remain established strategies, side effects complement high prices in the search for alternatives. In plant-based diets and lifestyle interventions, several mechanisms have been proposed that incorporate efficient methods of reinstituting cholesterol homeostasis and ameliorating the high cholesterol condition in the majority of animals.

 These include fenugreek (Trigonella foenum-graecum), which has emerged in recent times as a natural remedy for both medicinal and nutritional purposes. A high lipid-modulating potential of fenugreek usually depends upon developing fenugreek seeds as food and animal nutrition. Fenugreek has a long history of use in traditional medicine and agricultural contexts, treated as a remedy for a wide variety of diseases, from digestive disorders to diabetes. Scientific studies indicate the presence of diverse bioactive constituents in fenugreek, including soluble fiber, saponins, and flavonoids. These active components are responsible for the medicine effects of fenugreek. Its ability to modify lipids together with its potential for assisting in glycemic control points out fenugreek as a multifunctional candidate in the prevention and management of cardiovascular disease.

 Dyslipidemia is one of the most important risk factors for cardiovascular diseases (CVD) that account for a significant share in the mortality count around the world. Some of the currently available therapies have been shown to achieve very good control over cholesterol levels; nevertheless, statins in particular seem to be related to various harmful side effects in some patients. Therefore natural, herbal alternatives are being investigated. This medicinal herb used by various cultures has been found to possess significant lipid-lowering property. The present review hereby thrown to the light of fenugreek involvement in raising the status of blood cholesterol through its mechanism of action, efficacy, and clinical applications which will further promote this natural remedy for clinical use.

 This review highlights the growing body of evidence around the biochemical components, pharmacological mechanisms and clinical effectiveness of fenugreek in the treatment of hypercholesterolemia. A synthesis of in vitro, animal and human clinical study evidence is provided, to bring forth its efficacy and safety as a natural product, as well as, the implications for the development of functional foods / nutraceuticals through the incorporation of fenugreek as one option in combined and multi-targeted systems. This review places fenugreek's lipid lowering impact in a potential clinical rationale and help contextualize fenugreek, from a traditional remedy to a usable evidence-based rational.

**METHODOLOGY**

 This review is grounded in an extensive search of scientific literature, utilizing databases such as PubMed, Scopus, and Google Scholar. The keywords used in the search included "fenugreek," "cholesterol-lowering," "dyslipidemia," and "lipid metabolism." Emphasis was placed on studies published between 2000 and 2023, concentrating on preclinical, clinical, and mechanistic research.

**LITERATURE REVIEW**

 Fenugreek is extensively researched for its anti-lipidemic properties. A reduction in serum total cholesterol, LDL, and triglycerides has been reported in both animal research and in human studies, with a corresponding increase in HDL.

Its peculiar phytochemical composition is described as attributing to these effects.
**BIOCHEMICAL COMPOSITION OF FENUGREEK**

 Fenugreek seeds comprise certain bioactive compounds that drive their health benefits:
Soluble fiber: It is rich in galactomannan soluble fiber, which plays an important role in cholesterol depletion. Saponins:

 These are the substances that bind with cholesterol and bile acids-it reduces their absorption and increases excretions. Flavonoids and polyphenols: Acting as scavengers of reactive oxygen species, antioxidants mitigate oxidative stress and aid lipid metabolism. There are other components too: Proteins, amino acids, and alkaloids also add to the therapeutic potential of fenugreek.

**MECHANISM OF ACTION**

1. Lowering absorption of cholesterol: The soluble fibres present in Fenugreek form with in the gastrointestinal tract a gel-like mass which traps cholesterol and bile acids hence inhibiting absorption.

2. Increase bile-acid excretion: The saponins in Fenugreek bind bile acids and assist in their excretion. This causes liver cholesterol to be utilized by the liver for synthesizing new bile acids.

3. Modulation of lipid metabolism: Fenugreek influences the enzymes in lipid synthesis and degradation whereby HMG-CoA reductase is known to reduce the production of LDL-cholesterol.

4. Antioxidant: The flavonoids contained in fenugreek exert beneficial effects via combating oxidative stress-a known contributor in the pathogenesis of dyslipidemia and atherosclerosis.

**PRECLINICAL AND CLINICAL EVIDENCE**

 In vitro and in vivo studies have provided reasonable evidence that fenugreek has a lipid-lowering property. Fenugreek supplementation has been shown in hypercholesterolemic rats and rabbits to markedly reduce total and low-density lipoprotein plus triglycerides while raising high-density cholesterol. This mechanism appears to be increased bile acid excretion and improved lipid metabolism. Several human trials corroborated findings from animal studies. Key highlights include: Clinical study, for example, demonstrated significant lowering of total and LDL cholesterol in fenugreek-supplemented hyperlipidemics. Fenugreek-treated diabetic patients have shown improved lipid profiles and glycemic control, thus indicating dual benefits of fenugreek.

**DOSAGE AND SAFETY**

 The working dose for cholesterol management might range anywhere between 5-25 grams each day, either taken in the form of seed powder or as extracts or capsules. In general, fenugreek is well-tolerated, with some reports of mild gastrointestinal side effects-such as bloating and diarrhea. It has been considered safe in long-term studies as well as an effective one. Uses that can be applicative in Functional Foods Presenting Functional Foods with fenugreek holds the simplest method of leveraging its cholesterol-lowering application. Fenugreek-enriched bread, teas, or supplements are desired by increasingly health-conscious consumers. Fig.1.

**CHALLENGES AND FUTURE DIRECTIONS**

 Challenges and Future Directions Further large-scale and long-term clinical studies will be required to better define the standard treatment dose for its clinical use, and properly to study fenugreek against various groups of patients. Investigating the synergistic effects of fenugreek along with other natural products or drugs could lead to further insights into fenugreek's therapeutic potential. Fig.2. Table.1.



**Fig.1.Dose-response relationship between fenugreek supplementation (in grams per day) and the percentage reduction in LDL cholesterol**.

 

**Fig.2. Effect of fenugreek supplementation on cholesterol levels. It compares total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides before and after supplementation**

**Supplementary table.**1. **Clinical and preclinical effects of fenugreek on blood cholesterol lowering activity.**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **study type** | **population** | **dose** | **duration** | **total cholesterol reduction (%)** | **LDL reduction (%)** | **HDL increase (%)** | **Triglyceride reduction (%)** |
| clinical trail | hyperlipidemic patients | 10 g/day | 8 weeks | 15% | 20% | 5% | 18% |
| clinical trail | diabetic patients | 25 g/day | 12 weeks | 10% | 15% | 10% | 12% |
| preclinical study | hypercholesterolemic rats | 5% of diet | 6 weeks | 25% | 30% | 15% | 20% |

**Fig.3. graphical representation of clinical and preclinical effects of fenugreek on blood cholesterol lowering activity.**

**DISCUSSION**

 Fenugreek is a potent natural alternative for managing dyslipidemia, with a strong evidence base stemming from clinical studies. There is no uniformity regarding the dosage and preparations available in applications. Further, its combinational prowess with any existing drug needs further studies to establish this palette. Figure 1 shows the dose-response association between fenugreek supplementation (in grams per day) and the % reduction in LDL cholesterol. As the dose increases, the reduction in total LDL in the blood decreases, and Figure 2 depicts the effect of fenugreek on LDL, HDL, and triglycerides. It will compare the level of LDL reduced before and after supplementation, and fig. 3 will explain clinical and preclinical data on the effect of fenugreek supplementation in hyperlipidemia, diabetic patients, and a preclinical study on hypercholesterolemic rats, concluding that fenugreek is effective in LDL reduction.

**CONCLUSION**

 Inhibition of cholesterol absorption, induction of bile acid excretion, and hepatic lipid synthesis regulation are different mechanisms of action. The evidence to support the use of fenugreek for hyperlipidemia reduction is found in clinical and preclinical studies. The widespread formulation of fenugreek already provides an alternative dietary intervention that could replace the introducing of hyperlipidemia treatment. Recommendations for future research include dosage standardization, long-term safety and effectiveness, and acceptability in various populations. Therefore, it appears to be economical, widely acceptable, and more promising in the present milieu to provide an answer to modifications in lipid profiles against cardiovascular risk.

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