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INSIGHT INTO THE ANTIHYPERLIPIDEMIC PROPERTIES OF TRADITIONAL HERBAL PLANTS: A PHARMACOLOGICAL PERSPECTIVE

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Abstract
Cardiovascular diseases (CVD) remain a leading global cause of morbidity and mortality, with hyperlipidemia serving as a significant risk factor. In frame with statin's side effects, alternative therapeutic options to statins must be explored. Recently, attention has been paid to traditional herbal plants in their potential lipid regulation, and *Clerodendrum inerme* and *Clerodendrum infortunatum Linn.* are likely candidates due to their diversity of bioactive compounds, such as flavonoids, triterpenoids, and sterols. This review examines the antihyperlipidemic mechanisms of *C. inerme* and *C. infortunatum*, particularly focusing on *C. infortunatum* they are composed of inhibition of cholesterol biosynthesis, modulation of lipid metabolism, antioxidant and anti-inflammatory effects, and modulation of lipid transport and excretion. The preclinical studies show that effectively reduces cholesterol and triglycerides making it a viable alternative or an adjunct to conventional lipid-lowering therapies. Although it traditionally has been used as medicine, there are no large-scale clinical trials, nor are its pharmacokinetics and safety profile known. Future research should aim at maximizing the bioavailability of the new drug through novel drug formulation and convenient combinations with currently available lipid-lowering agents. *C. inerme* and *C. infortunatum* integration into mainstream cardiovascular therapy requires standardized extraction techniques, as well as clinical validation.

Keywords: Hyperlipidemia, *Clerodendrum inerme*, lipid metabolism, *Clerodendrum infortunatum Linn*, cardiovascular health, cholesterol biosynthesis

1. Introduction

Cardiovascular diseases (CVD) are major reasons for morbidity and mortality worldwide, as the risk factor for hyperlipidemia is defined as the level of lipids in the blood that is elevated. In 2019, high non-HDL cholesterol was estimated to cause 4.4 million deaths worldwide.

Statins have been effective in reducing low-density lipoprotein cholesterol (LDL-C) to reduce cardiovascular events in general and contain standard care of conventional lipid-lowering therapies. Despite their side effects, however, like muscle pain, liver damage, increased blood sugar, and memory loss or confusion statin intolerance leads some patients to stop using them. In addition, not all patients achieve optimal lipid levels with statin therapy alone, and alternative or adjunctive treatments are needed (Hussain *et al*., 2025).

Lipid regulation is one of the many medicinal properties of traditional herbal plants that have been used in different cultures. Traditional herbal plants possess lipid regulation as one of their multiple medicinal properties. Two Clerodendrum species, namely *Clerodendrum infortunatum Linn.* and *Clerodendrum inerme,* have received extensive research regarding their antihyperlipidemic properties, although they possess different medical applications. These plants possess bioactive compounds that can modulate lipid metabolism by several mechanisms, namely, promoting lipid catabolism, inhibiting lipid synthesis, as well as antioxidant effects. Herbal remedies integration is a complementary approach to the management of hyperlipidemia, especially in those who suffer from adverse effects of conventional therapies or who want to use natural treatment.

Clerodendrum inerme (L.) Gaertn., commonly called garden quinine is a perennial shrub of the Lamiaceae family among these medicinal plants. Extensively used in various traditional medicinal practices for rheumatic pain, arthritis, scrofulous infections, venereal diseases, skin diseases, wounds, fever, cough, and dysentery (Okafor *et al*., 2024).

This study made a phytochemical investigation of *C. inerme* yielding various bioactive compounds, including flavonoids, sterols, and triterpenes. It is believed that these constituents contribute to its medicinal properties.

Herbal plants are used for antihyper lipidemic properties, most particularly *Clerodendrum* inerme. The traditional medicinal uses of the plant will be discussed along with its phytochemical composition and pharmacological activities on lipid regulation as a possible alternative or adjunctive therapy for hyperlipidemia.

1.2 Distribution of *Clerodendrum inerme*

Clerodendrum infortunatum Linn. also has antihyperlipidemic properties, which are similar to those of *C. inerme. C. infortunatum* has a longer history in traditional medicine for hyperlipidemia, but its clinical use needs to be validated further. Its effectiveness should be compared to other herbal remedies such as guggul and fenugreek, as well as conventional lipid-lowering drugs such as statins, in comparative studies (Kaveri *et al*., 2024). The major antihyperlipidemic potential of *Clerodendrum inerme* is reviewed based on its rich phytochemical profile including flavonoids, triterpenoids, sterols, and phenolic glycosides. The bioactive compounds of pomelo affect lipids through inhibition of cholesterol biosynthesis, modulation of lipids metabolism, antioxidant and anti-inflammatory effects, and promotion of lipid transport. It presented preclinical data supporting its capacity to reduce cholesterol and triglycerides, but this needs to be validated clinically at the scale. In addition, focusing on future research to optimize absorption methods and develop new advanced formulations, including nanoformulation, should be made to increase bioavailability. For clinical use, standardization of extraction techniques, dosage optimization measurement, and evaluation of herb-drug interactions. *C. inerme* may be a complementary or alternative approach for hyperlipidemia management. Its inclusion in cardiovascular therapeutics should be explored clinically and mechanistically and be safe and effective.

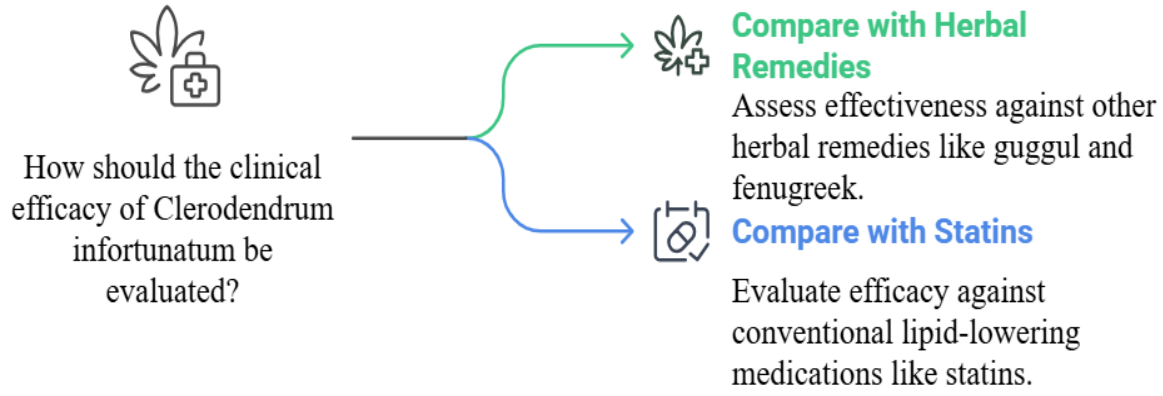

Figure 1: Evaluating the Clinical Efficacy of *Clerodendrum infortunatum* in Hyperlipidemia Management

2. Traditional Uses and Ethnobotanical Importance

Historically, traditional medicine cultures have considered *C. inerme* as an important component. The plant has been used in Ayurveda, Siddha, and traditional Chinese medicine for its diverse therapeutic properties. The leaves, stems, and roots of *C. inerme* are medicinally used to treat rheumatic pain, arthritis, and other inflammatory conditions. Externally, crushed leaves are used to relieve joint pain and swelling (Zheng *et al*., 2020).

Traditional medicine has traditionally utilized both *Clerodendrum infortunatum Linn.* and *Clerodendrum inerme*. The review recognizes two plant species and focuses on the wide range of lipid metabolism regulatory uses of *C. infortunatum*.

SE Asian folk medicine also uses leaves of *C. inerme* as a decoction for the treatment of fever, dysentery, and gastrointestinal infections. Antimicrobial and anti-inflammatory properties of this plant are also used as a remedy for venereal diseases, scrofula, and various skin ailments such as eczema, rashes, and wounds (Patel *et al*., 2014). It may have a hormonal influence, as it has been traditionally used as an abortifacient and to alleviate menstrual irregularities (Das *et al*., 2023).

2.1 Phytochemical Profile and Bioactive Constituents

As of now, at least 95 bioactive compounds have been identified in *C. inerme*, separated as major chemical classes, diterpenoids, triterpenoids, steroids, flavonoids, phenolic glycosides, lignans, iridoid glycosides, through scientific investigations. This study examines *Clerodendrum inerme*, yet research focuses on *Clerodendrum infortunatum Linn*. because its phytochemical composition needs additional investigation. Of these, diterpenoids and flavonoids have been shown to have promising pharmacological activities, including anti-inflammatory and antioxidant activity (Choudhury *et al*., 2017). The plant has the potential to have such antioxidant capabilities as it utilizes bioactive flavonoids such as quercetin, luteolin, and apigenin that have the potential to prevent lipid peroxidation and cardiovascular diseases (El-Tantawy & Temraz, 2019).

There is evidence that triterpenoids and steroids in *C. inerme* have an anti-hyperlipidemic perspective, as they can reduce the amount of cholesterol and triglycerides by targeting the lipid metabolism pathway (Petrović *et al*., 2019). In addition, phenolic glycosides and lignans isolated from *C. inerme* have lipid hypocholesterolemic properties in animal models and hypolipidemic effects in herbal lipid-lowering formulations (Al-Snafi, 2024).

2.2 Potential Pharmacological Applications

Research on the pharmacological properties of *Clerodendrum inerme* exists extensively, It focuses on *Clerodendrum infortunatum Linn*. as an additional subject for lipid metabolism investigation. It has

been recently verified in vitro and in vivo studies that it has antimicrobial, anti-inflammatory, antioxidant, and anticancer properties. Specifically, extraction of *C. inerme* has been shown to inhibit bacterial and fungal growth, as is the case in traditional skin infection and wound therapy (Njeru *et al*., 2016). The antioxidant properties of the plant are attributed to the high flavonoid as well as polyphenol content of the plant, which are believed to neutralize free radicals and prevent oxidative stress-related diseases such as cardiovascular disorders and neurodegenerative conditions (Atef *et al*., 2025).

Furthermore, *C. inerme* may play a distinct role in metabolic health and the regulation of Body lipids. The anti-obesity and hypolipidemic effects of the plant are attributed to its capacity to improve lipid metabolism, decrease cholesterol absorption, and regulate key enzymes in fat breakdown (Ly *et al*., 2019). *C. inerme* is a promising candidate for complementary and alternative medicine in the management of hyperlipidemia and metabolic syndrome (Jing *et al*., 2022).

C. inerme has great potential for pharmacological research due to its extensive use in traditional medicine and its diverse bioactive compounds. It has been reported to treat inflammatory diseases, hyperlipidemia, and microbial infections in several preclinical studies, but rigorous clinical trials are required to prove the therapeutic efficacy and safety of using it for human beings. Future research would be necessary into its bioactive extracts, which should be standardized for further research and elucidate the mechanisms of action of this traditional medicine, and its use in modern medicine should be explored. *C. inerme* may be incorporated into nutraceuticals and herbal formulations as a natural and effective alternative to conventional lipid-lowering drugs with fewer side effects.

3.1 Mechanisms of Lipid-Lowering Effects

Clerodendrum inerme, and *Clerodendrum infortunatum Linn.* since both contain similar bioactive compounds but need a separate examination of lipid-lowering mechanisms. These bioactive compounds have been shown to have pharmacological actions that regulate lipids. *C. inerme* inhibits cholesterol biosynthesis, stimulates lipid metabolism using antioxidant and anti-inflammatory pathways, and modulates lipid transport and excretion.

The bioactive compounds in *Clerodendrum infortunatum Linn.* and *Clerodendrum inerme,* including flavonoids, phenolic glycosides, and triterpenoids, help reduce lipids in the body. These medicinal compounds have multiple pharmacological effects, which include blocking cholesterol synthesis together with metabolic lipid improvement, anti-inflammatory and antioxidant activities, and lipid transport management. Recent research indicates that *Clerodendrum infortunatum* shows better hypolipidemic effects compared to *Clerodendrum inerme,* thus becoming a promising candidate for future studies (Kaveri *et al*., 2024).

3.1.1 Inhibition of Cholesterol Biosynthesis

Inhibition of cholesterol biosynthesis is the main mechanism by which *C. inerme* exerts its antihyperlipidemic activity alone. Flavonoids and sterols in *C. inerme* have been shown to downregulate the expression of rate-limiting enzymes of cholesterol biosynthesis in humans and animals (Petrović *et al*., 2019).

In their study, Barman *et al*. (2024) proved that an aqueous extract of *C. inerme* at 500 mg kg-1 body weight decreases total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) and increases high-density lipoprotein cholesterol (HDL-C) in hyper lipidemic rat models. Reduction in cholesterol levels was attributed to the suppression of cholesterol biosynthesis by inhibition of HMG-CoA reductase activity. In addition, *C. inerme* also promotes bile acid excretion and thus contributes to further lowering plasma cholesterol levels by increasing hepatic cholesterol utilization.

3.1.2 Enhancement of Lipid Metabolism

C. inerme also inhibits cholesterol synthesis, but it can complete the job by upregulating the expression of enzymes that regulate fatty acid oxidation. *C. inerme* flavonoids and polyphenols are known to activate peroxisome proliferator-activated receptors (PPARs) mainly PPAR-α, which is very

important for lipid metabolism and energy homeostasis (Zheng *et al*., 2020). The activation of PPAR-α increases the β-oxidation of fatty acids in the liver and decreases the plasma triglyceride levels.
Ly *et al*. (2019) studied Methanolic leaf extract of *C. inerme* and it improved lipid metabolism and lipid profiles in streptozotocin-induced rats, which is often thought to be due to lipid improvement. The study results showed that *C. inerme* extract administration resulted in a highly significant decrease in serum TG and LDL-C levels and an increase in HDL-C levels and, therefore, used and cleared the lipids better. This would be useful to prevent lipid accumulation in the liver, which is often seen in metabolic disorders, especially in non-alcoholic fatty liver disease (NAFLD).

3.1.3 Antioxidant and Anti-Inflammatory Pathways in Lipid Regulation

Oxidative stress and chronic inflammation have a strong role in the pathophysiology of hyperlipidemia and atherosclerosis. LDL-C is oxidized to form oxidized LDL (ox-LDL), which is a major contributor to atherosclerotic plaque formation and cardiovascular diseases. *C. inerme* is known to contain good amounts of phenolic compounds, flavonoids, and terpenoids that are powerful antioxidants and anti-inflammatory (Patel *et al*., 2014).
Atef *et al*. (2025), in an in vitro study, revealed the extract of *C. inerme* had a good free radical scavenging activity against DPPH and ABTS indicatives of potential antioxidant capacity. *C. inerme* can scavenge reactive oxygen species (ROS) to prevent lipid peroxidation and oxidative modification of LDL-C.
In addition, it has been shown to have an anti-inflammatory effect by suppressing pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β. In addition, some pro-inflammatory cytokines may also affect lipid homeostasis and promote lipid accumulation in macrophages, forming foam cells and atherosclerosis. Because *C. inerme* downregulates these inflammatory markers, it may be protective of the cardiovascular system.

3.1.4 Modulation of Lipid Transport and Excretion

C. inerme also has a role in lipid regulation by regulating lipid transport and excretion. Studies have shown that the plant's phytochemicals, namely saponins and sterols, inhibit the absorption of cholesterol in the intestine, prevent dietary ingestion, and excrete it (Al-Snafi, 2024).
According to Njeru *et al*. (2016), supplementation of *C. inerme* extract increased the institutional of cholesterol and bile acids in hyperlipidemic rats. This effect was attributed to the presence of steroidal saponins, which form insoluble complexes with cholesterol in the intestinal lumen and prevent its absorption. In addition, *C. inerme* has been shown to increase the expression of efflux transporters involved in transporting the excess cholesterol out of the enterocytes into the intestinal lumen for excretion, the ATP binding cassette (ABC) transporters ABCG5 and ABCG8.
Furthermore, *C. inerme* may also affect reverse cholesterol transport (RCT), the process of transporting excess cholesterol from peripheral tissues to the liver for excretion of cholesterol. *C. inerme* flavonoids are believed to increase SR-B1 and ABCA1 expression, which are important proteins related to HDL-mediated cholesterol efflux (Raju *et al*., 2016). This effect helps to clear cholesterol from the body and facilitates the cardioprotective potential of C. inerme.
In addition to inhibition of cholesterol biosynthesis, *C. inerme* has multiple mechanisms of antihyperlipidemic effects including enhancement of lipid metabolism, antioxidant and anti-inflammatory actions, and modulation of lipid transport and excretion. In many ways, *C. inerme* is a promising candidate for the treatment of hyperlipidemia and the prevention of cardiovascular diseases.
While preclinical studies have shown efficacy, there is a need for further clinical trials to determine whether the safety and efficacy of this drug can be established in human subjects. Future research should come back in identifying the bioactive compounds involved with their lipid-lowering effects and delineation of their molecular function.

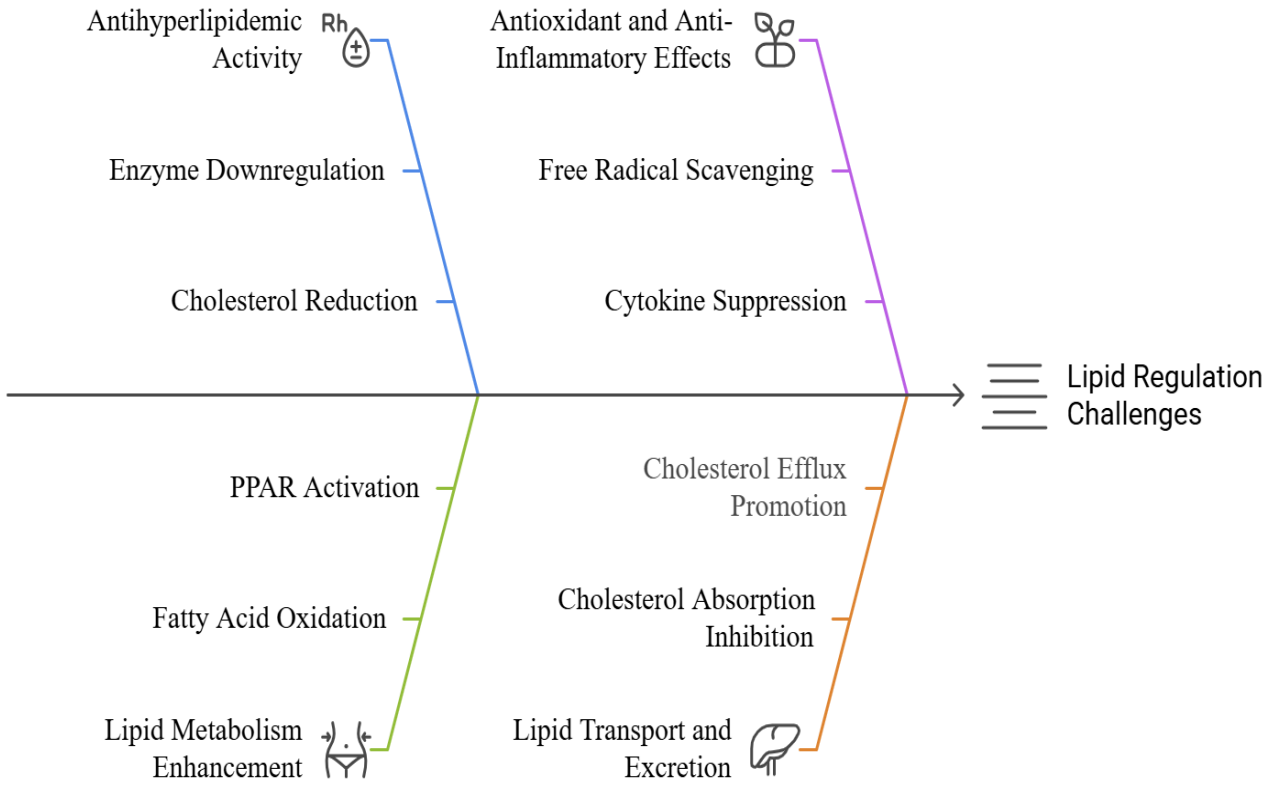

Figure 2: Mechanisms of Lipid Regulation by *C.inerme*

4.1 Comparative Antihyperlipidemic Efficacy of *Clerodendrum inerme* vs. Other Herbal Plants

Hyperlipidemia is one of the main risk factors of cardiovascular diseases that are currently the main cause of mortality worldwide. Some natural compounds extracted from medicinal plants have been extensively investigated as alternatives or adjuncts to traditional therapies, given their lipid-lowering effect. In the current section, *Clerodendrum inerme* is discussed; however, the primary focus of my study is *on Clerodendrum infortunatum Linn*. Future studies should compare the antihyperlipidemic efficacy between these two species and well-established Indian herbs (Ogunlakin *et al*., 2023). Traditionally, Ayurvedic and folk medicine have used *Clerodendrum infortunatum* for metabolic disorders, and it contains flavonoids, triterpenoids, and phenolic glycosides known to influence lipid metabolism (Bhattacharyya *et al*., 2020). Recent studies indicate that *C. infortunatum* may have lipid-lowering effects similar to, or even better than, *C. inerme* because of its better antioxidant and anti-inflammatory properties (Kaveri *et al*., 2024). Nevertheless, there is a lack of comparative evaluations between these two species, and future research should be directed toward determining the efficacy of each of these species through in vitro, in vivo, and clinical trials.

Furthermore, *C. infortunatum* should be compared with well-known lipid-lowering herbs like *Commiphora Mukul* (Guggul), Trigonella *foenum-graecum* (Fenugreek), *Camellia sinensis* (Green Tea), *Allium sativum* (Garlic), and *Curcuma longa* (Turmeric). This will help to evaluate *C. infortunatum* as a potential alternative to these herbs in the management of hyperlipidemia and cardiovascular health. To further consider *C. infortunatum* as a mainstream lipid-lowering therapeutic, standardized extraction methods, bioavailability enhancement strategies, and clinical validation are required (Raju *et al*., 2016; Grewal, 2023).

4.1.1 Guggul (*Commiphora mukul*)

Extensive studies have been conducted on the hypolipidemic effects of guggul, which is derived from the resin of *Commiphora mukul* (Guggul) are the active compounds that act as antagonists to the farnesoid X receptor (FXR) that regulates cholesterol metabolism. Guggul extracts, too have been shown to have cholesterol-lowering effects as shown by clinical trials, including an increase in HDL

cholesterol, a decrease in the level of LDL cholesterol, and a reduction of serum triglycerides (Zheng *et al*., 2020).
Similarly, *C. inerme* also reduced lipid anemia both by regulating hepatic lipid metabolism and by decreasing oxidative stress as well as increasing bile acid excretion (Barman *et al*., 2024). Nevertheless, *C. inerme* has not yet been extensively tested in large-scale clinical trials, while guggul has been extensively tested in human clinical trials (Upadhyay, 2021).

4.1.2 Fenugreek (*Trigonella foenum-graecum*)

Soluble fiber and saponins in fenugreek help in reducing cholesterol levels by binding to bile acids in the gut and removing them. Fenugreek supplementation brings down the total and LDL cholesterol and glycemic control, as has been shown in clinical studies (Petrović *et al*., 2019).
The mechanism of action of *Clerodendrum inerme* is different and it is mainly through its flavonoid and phenolic content which enhances lipid oxidation, reduces lipid peroxidation, and prevents lipid accumulation in the liver (Al-Snafi, 2024). While *C. inerme* has broader antioxidant and anti-inflammatory effects that may complement its lipid-lowering properties, fenugreek primarily acts on cholesterol absorption (Martial *et al*., 2020).

4.1.3 Green Tea (*Camellia sinensis*)

Green tea is well known for its catechin content, particularly epigallocatechin gallate (EGCG), which inhibits intestinal lipid absorption and promotes lipid oxidation (Jing *et al*., 2022; Ilie *et al*., 2024). Multiple meta-analyses have confirmed that green tea consumption significantly reduces serum cholesterol and improves cardiovascular health outcomes.
The antioxidant potential of *C. inerme* is comparable to that of green tea, as both contain bioactive flavonoids that scavenge free radicals and reduce oxidative stress-induced lipid peroxidation. However, while green tea is better documented for its lipid-lowering effects in human trials, *C. inerme* has been predominantly studied in preclinical models, necessitating further research in human populations (Ilie *et al*., 2024).

4.1.4 Garlic (*Allium sativum*)

The hypolipidemic effects of garlic have been widely studied, with the sulfur-containing compounds allicin and S-allyl cysteine being the focus of most of the studies. Atef *et al*. (2025) have demonstrated that garlic extracts lower total cholesterol, LDL cholesterol, and triglycerides and increase HDL cholesterol levels.
Clerodendrum inerme possesses bioactive similarity to garlic, which inhibits inflammation-induced lipid accumulation and oxidative stress. The lipid-lowering mechanism of garlic is more well-defined, but the role of *C. inerme* in lipid metabolism is not well-defined.

4.1.5 Turmeric (*Curcuma longa*)

It is reported that Turmeric, especially its active compound Curcumin has been shown to modulate lipid metabolism by manipulating peroxisome proliferator-activated receptor gamma (PPARγ) and interferes with the inflammatory cytokines involved in hyperlipidemia (Njeru *et al*., 2016).
C. inerme and turmeric have strong anti-inflammatory properties, but only *C. inerme* possesses bile acid modulation effects that further aid in lipid-lowering activity. Synergistic benefits in managing lipid disorders may be offered by the combination of *C. inerme* with turmeric.

4.2 Synergistic Effects with Other Medicinal Herbs

Herbal synergy is the interaction of several plant constituents that sum their impact to a greater than the sum of their parts. Full scientific reports demonstrate that *Clerodendrum* inerme, with its broad range of phytochemicals, is a promising candidate in combination therapy.

4.2.1 Enhancing Bioavailability of Active Compounds

Many herbal bioactive compounds have a low bioavailability. Studies also indicate that a combination of *C. inerme* with bio-enhancers like piperine from black pepper or gingerol from ginger will enhance absorption and efficacy (Raju *et al*., 2016). For example, curcumin is sometimes administered with black pepper to increase absorption, so similarly, *C. inerme* extracts could be administrated in combination.

4.2.2 Combining with Other Antioxidants

Because oxidative stress is a big factor in hyperlipidemia, *C. inerme* could amplify the cardioprotective effects of other antioxidants like green tea, grape seed extract, and vitamin E combined with it. Atef *et al*. (2025) studied and found that to have higher efficacy, polyphenol-rich extracts should be used in combination.

4.2.3 Potential Herbal Formulations

The strong lipid-lowering properties of *C. inerme* make it a good candidate for inclusion in polyherbal formulations along with fenugreek, garlic, and turmeric, which would constitute a multi-target approach to the management of dyslipidemia. The attention on polyherbal formulations is due to their ability to target multiple pathways at the same time, thereby reducing the chances of adverse effects as compared to synthetic lipid-lowering drugs.

4.2.4 Reducing Side Effects of Statins

Statins cause muscle pain and liver enzyme abnormalities in many patients. According to studies, administering herbal extracts such as *C. inerme* and turmeric in conjunction with a statin could reduce the oxidative stress-induced side effects with retention of lipid-lowering efficacy (Al-Snafi, 2024).
Clerodendrum inerme, although promising, showing indeed antihyperlipidemic properties, direct comparative studies with well-known medicinal herbs have been scarce. Unlike other lipid-lowering herbs such as guggul, fenugreek, garlic, green tea, and turmeric, it has its mechanisms of action, which include antioxidant activity, lipid metabolism modulation, and bile acid excretion. Future therapeutic potentials of *C. inerme* in hyperlipidemia and cardiovascular disease should seek to identify synergistic herbal formulations and clinical validation.

5. Safety, Toxicity, and Pharmacokinetic Considerations of *Clerodendrum* inerme

5.1 Acute and Chronic Toxicity Studies

Studies have evaluated the safety and toxicity of *Clerodendrum inerme,* This focuses on *Clerodendrum infortunatum Linn* because it requires additional assessments of toxicity and pharmacokinetics assessments are still needed (Akhil *et al*., 2023). Short-term (acute toxicity) studies are done to assess the effects of high doses while long-term (chronic toxicity) studies are conducted to assess the long-term effects of continuous use (Wang *et al*., 2018). Comprehensive toxicity studies on *C. inerme* are, however, limited despite its widespread traditional use. In general, the existing research suggests that aqueous and methanolic extracts of *C. inerme* have a relatively safe profile upon administration at therapeutic doses in animal models. Barman *et al*. experimentally examined the safety of *C. inerme* extract in rats after administration of high doses (up to 2000 mg/kg body weight) which did not yield any significant adverse effects. At supra-therapeutic doses however mild hepatotoxicity and gastrointestinal irritation were seen which implies that standardization of dose in human applications would be required (Rauf *et al*., 2022).

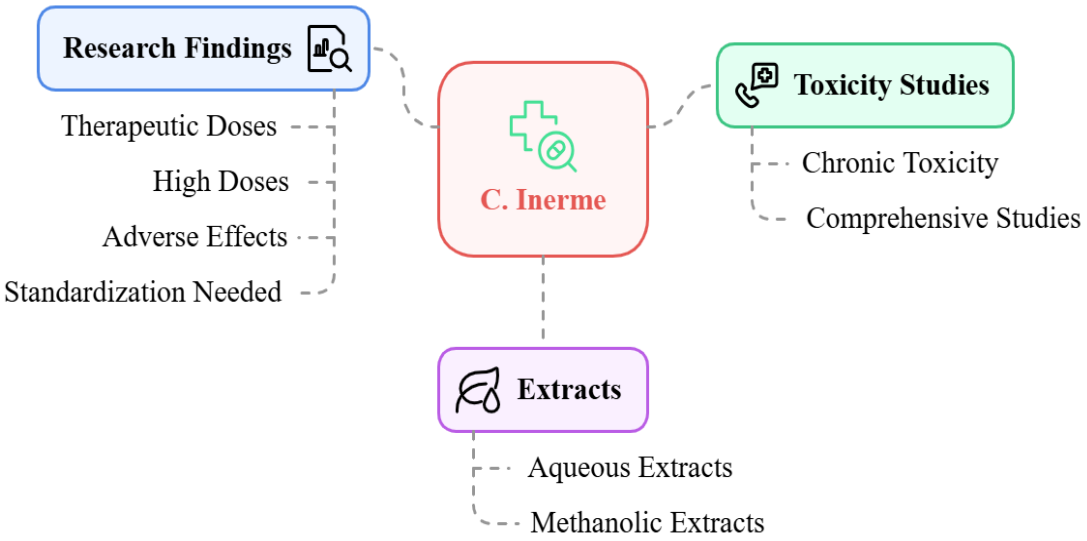

Figure 3: Toxicity and Safety Profile of *C. inerme*

C. inerme has not been subjected to chronic toxicity studies. However, if the herb is long-term therapy, it may cause cumulative toxicity of herbal biologically active compounds mainly in the liver and kidneys as they are rich in these organs. In its recently published review, (Petrović *et al*., 2019). stressed how renal toxic, hepatoxic, and hematological alterations of chronic exposure to herbal medicines should be evaluated. Cytotoxicity of *C. inerme* at higher concentrations is suggested by the presence of bioactive flavonoids, alkaloids, and saponins.

5.2 Potential Side Effects and Contraindications

C. inerme has traditionally been used without serious adverse effects, but its pharmacological activity suggests that some populations should exercise caution. Among the reported side effects were mild gastrointestinal disturbances (nausea and diarrhea) in people who ingested high doses of *C. inerme* extracts. These effects may also be the result of tannins and flavonoids in the tea, causing alterations in gut microbiota and digestive enzyme activity. In addition, some in vitro studies indicate that *C. inerme* flavonoids may inhibit cytochrome P450 enzymes, which are important in drug metabolism. This inhibition is a cause for concern regarding herb-drug interactions, especially in patients on anticoagulants, antihypertensive medications, or statins (Njeru *et al*., 2016).

C. inerme should be avoided by pregnant and lactating women because there is insufficient data on the safety of *C. inerme* on fetal development and maternal health. Preliminary animal studies have suggested that certain alkaloids found in *C. inerme* may cause uterine contractions and thus have the potential to be abortifacient (Al-Snafi, 2024). They should also discuss the use of *C. inerme* with a healthcare professional, as long-term consumption may add further metabolic stress on the liver or kidneys of people who already suffer from such conditions (Ly *et al*., 2019).

5.3 Bioavailability and Pharmacokinetics

Knowledge of *C. inerme* pharmacokinetics is important to maximize the therapeutic efficacy of *C. inerme*. Its bioactive compounds have not been explored in terms of absorption, distribution, metabolism, and excretion (ADME). *C. inerme* has limited bioavailability because flavonoids and polyphenolic compounds are poorly aqueous soluble and prone to rapid hepatic metabolism (Ly *et al*., 2019). Nevertheless, absorption of these compounds can be enhanced by nanoformulation, liposomal encapsulation, and administration with bioenhancers such as piperine (Swiger *et al*., 2013).

In preliminary pharmacokinetic studies, *C. inerme* flavonoids are shown to be extensively first-pass metabolized in the liver resulting in the formation of bioactive metabolites responsible for their pharmacological activity. These metabolites are primarily excreted in the biliary and renal pathways with a half-life in the animal models of approximately 6–12 hours (Raju *et al*., 2016). Optimal dosing

regimens and potential interactions with other therapeutic agents need further study using advanced pharmacokinetic modeling.

5.4 Future Research Directions and Conclusion

Although *Clerodendrum inerme* has promising pharmacological properties, it has to undergo extensive safety and pharmacokinetic evaluations before it can be widely used in clinical practice. Future toxicological research will need to be well-designed, establish safe dosage limits, and detect possible adverse effects. Pharmacokinetic profiling is additionally essential to improve biopharmaceutical drug formulations and to improve the bioavailability of its bioactive compounds. These clinical trials will help to establish if it has the potential to be an alternative or adjunct therapy to treat hyperlipidemia and other metabolic disorders (Amorha *et al*., 2024).

At therapeutic doses, *C. inerme* has a favorable safety profile, but high-dose exposure and extended exposure need further evaluation. It is still poorly understood in terms of its pharmacokinetics; therefore, more studies are needed to elucidate its metabolic pathways, elimination profile, as well as possible drug interactions. Because of its traditional medicinal value, it will be important to integrate modern scientific evaluations to ensure the safe and effective use of the drug in modern medicine (Saad *et al*., 2021).

6.1 Need for Large-Scale Clinical Trials

Previous preclinical studies have suggested *C. inerme* has promising anti-hyperlipidemic effects and large-scale clinical trials confirming these effects in human populations have not been performed. While informative, most of the existing research is limited to in vitro experiments and animal models and does not replicate human physiological conditions — the majority of which. Randomization trials with diverse human cohorts are necessary to assess the efficacy, the best dose for suppression of hyperlipidemia, and the safety of *C. inerme*. Such studies would offer robust evidence needed for its integration into clinical practice (Bhinge *et al*., 2025).

6.2 Potential for Novel Drug Formulations

Because phytochemicals in *C. inerme* are poorly soluble and rapidly metabolized, a significant challenge to bioavailability of phytochemicals exists. These limitations are overcome by novel drug delivery systems such as nanoformulations. For example, the medicinal potential of plant extracts of *Clerodendrum* serratum, a species of the same genus, was improved by formulating them into nanotransferosomal vesicles, especially in anticancer applications. While this study was conducted on a different species, the approach could be applied to *C. inerme* to optimize the delivery and efficacy of its lipid-lowering compounds. Moreover, the biosynthesis of silver nanoparticles from *C. inerme* leaf extracts was also explored suggesting the possibility of its use in nanoparticle-based applications. Such novel formulations could be further researched to produce more effective therapeutic agents from *C. inerme* (Saad *et al*., 2021).

6.3 Integration into Mainstream Lipid-Lowering Therapies

Comprehensive studies are needed to evaluate the efficacy of *C. inerme* compared to other treatments in mainstream lipid-lowering therapies for *C. inerme* to be considered a viable option. Such comparative analyses are made with standard pharmacological agents in use such as statins and other herbal remedies with proven lipid-lowering effects. The third is to understand if the drugs may work synergistically compared to other treatments. Additionally, standardized methods for extraction and dosage forms will be needed to ensure consistency and efficacy in clinical applications (Dwivedi, 2023). These aspects will enable *C. inerme* to be integrated into conventional medical practice for the treatment of hyperlipidemia.

Clerodendrum inerme has some promise in lipid-lowering, however, there are lots of research gaps to do. Its validity and safety in humans, however, require large-scale clinical trials. The therapeutic potential of chrysotile can be improved by exploring new drug formulations, such as nanoformulations. However, its efficacy needs to be compared comprehensively to current lipid-

lowering therapeutic approaches and it must play a role in integrative treatment approaches before it is adopted by mainstream medicine.

Conclusion

Clerodendrum infortunatum Linn. also has antihyperlipidemic properties, which are similar to those of *C. inerme. C. infortunatum* has a longer history in traditional medicine for hyperlipidemia, but its clinical use needs to be validated further. Its effectiveness should be compared to other herbal remedies such as guggul and fenugreek, as well as conventional lipid-lowering drugs such as statins, in comparative studies. The major antihyperlipidemic potential of *Clerodendrum inerme* is reviewed based on its rich phytochemical profile including flavonoids, triterpenoids, sterols, and phenolic glycosides. The bioactive compounds of pomelo affect lipids through inhibition of cholesterol biosynthesis, modulation of lipids metabolism, antioxidant and anti-inflammatory effects, and promotion of lipid transport. It presented preclinical data supporting its capacity to reduce cholesterol and triglycerides, but this needs to be validated clinically at the scale. In addition, focusing on future research to optimize absorption methods and develop new advanced formulations, including nanoformulation(s), should be made to increase bioavailability. For clinical use, standardization of extraction techniques, dosage optimization measurement, and evaluation of herb-drug interactions. *C. inerme* may be a complementary or alternative approach for hyperlipidemia management. Its inclusion in cardiovascular therapeutics should be explored clinically and mechanistically and be safe and effective.

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