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## Review Article

### Pharmacological Review of *Euphorbia hirta* L. in Dyslipidemia Management: Focus on In Vitro Lipid and Enzyme-Based Assays

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#### Abstract

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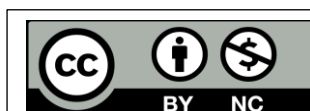
*Euphorbia hirta* L. .  
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A traditional medicinal plant known as *Euphorbia hirta* L. . has lately gained a lot of interest for its potential use in the treatment of dyslipidemia, a leading cause of cardiovascular disease. In this review, we examined the pharmacology of *Euphorbia hirta*, focusing on the findings of in vitro lipid- and enzyme-based analyses that explain how the plant functions as an enzyme inhibitor and lipid-lowering agent. The medicinal value of *Euphorbia hirta* L. lies in the fact that it contains numerous bioactive chemicals with antioxidant, anti-inflammatory, and lipid-modulating characteristics. Its hypolipidemic effects may be due to its inhibitory effects on enzymes involved in lipid metabolism, such as lipase and 3-hydroxy-3-methylglutaryl coenzyme A reductase, as shown by enzyme tests. In vitro lipid experiments also demonstrated that the plant may reduce triglyceride and cholesterol levels. This study compiled and analyzed the available experimental evidence to provide a mechanism-based understanding of the effectiveness of *Euphorbia hirta* L. in treating dyslipidemia. It did so by defending the plant's traditional use and encouraging more pharmaceutical and clinical studies on the subject. For researchers and clinicians exploring supplementary and alternative approaches to lipid management, this list has been an invaluable resource.

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## Introduction

Dyslipidemia, an irregular concentration of lipids in the blood, is a major contributor to the onset of cardiovascular diseases (CVDs), the leading global killer. Abnormal cholesterol, triglyceride, and/or low HDL-C levels, as well as elevated total and low-density lipoprotein cholesterol levels, are hallmarks of this condition. Therefore, dyslipidemia should be treated to mitigate the effects of atherosclerosis, coronary artery disease, stroke, and other cardiovascular problems. While traditional medical treatments, such as fibrates, bile acid sequestrants, and statins, may help control cholesterol levels, their prolonged use has certain drawbacks, and patients often do not adhere to the prescribed treatment regimen[1]. Consequently, there has been an increase in the search for natural, alternative, and complementary treatment agents that are effective and have lower risk profiles. *Euphorbia hirta L.* a plant belonging to the Euphorbiaceae family, has a long history of medicinal use across many cultures to treat a variety of ailments, including those affecting the respiratory system, digestive tract, and immune system. In recent years, scientists have begun to investigate its potential use in managing dyslipidemia and lipid metabolism. Studies have shown that the plant's bioactive phytochemicals, including tannins, alkaloids, flavonoids, and phenolic compounds, have antioxidant, anti-inflammatory, and lipid-lowering effects. Because of these qualities, *Euphorbia hirta L.* might be used to create novel drugs to treat lipid diseases[2].

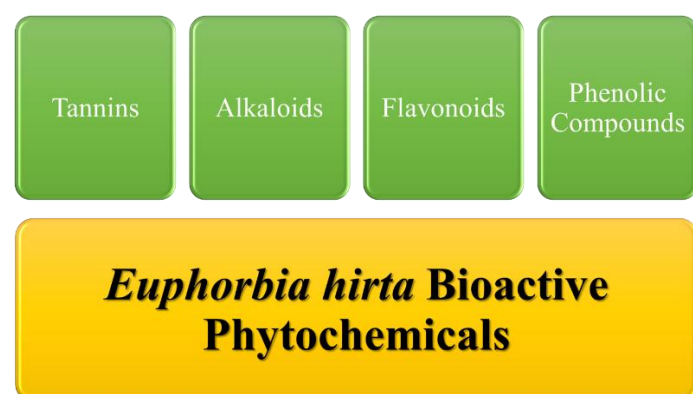


Figure 1 Bioactive Phytochemical of *Euphorbia hirta*

A battery of in vitro lipid and enzyme-based assays has been used in the pharmacological investigation of *Euphorbia hirta L.* to elucidate its mechanisms of action. Pancreatic lipase and 3-hydroxy-3-methylglutylglutaryl-coenzyme A (HMG-CoA) reductase are two of the most studied enzymes in lipid metabolism because of their roles in promoting the

absorption of dietary fat and in the rate-limiting step of cholesterol production. A hypolipidemic effect may be achieved by inhibiting these enzymes using extracts or isolated chemicals from *Euphorbia hirta*. This prevents lipid absorption and endogenous cholesterol production. Further supporting the medicinal potential of this plant, in vitro lipid studies have shown its capacity to decrease cholesterol and triglyceride storage in cell models[3]. Understanding the molecular basis of the lipid-modulating characteristics of *Euphorbia hirta L.* is necessary to justify its traditional use and guide future pharmacological and therapeutic investigations. This study compiles current experimental evidence on *Euphorbia hirta L.* as a tool for dyslipidemia treatment from studies that examined phytochemicals, enzyme inhibition, and lipid buildup. In response to questions regarding its therapeutic potential, this report details the plant's safety and toxicological profile. In line with the broader scientific effort to develop plant-based therapies that may supplement or replace existing lipid-lowering drugs, the pharmacological characteristics of *Euphorbia hirta L.* have been investigated. Given the complex pathophysiology of dyslipidemia, it is particularly helpful to use medicines with several functions, such as antioxidant, anti-inflammatory, and enzyme-inhibitory actions. *Euphorbia hirta L.* is an excellent example of a multi-pronged strategy and has several bioactive chemicals that may provide benefits beyond lipid management, such as protection against oxidative stress and inflammation, both of which contribute to the onset of cardiovascular disease[4].

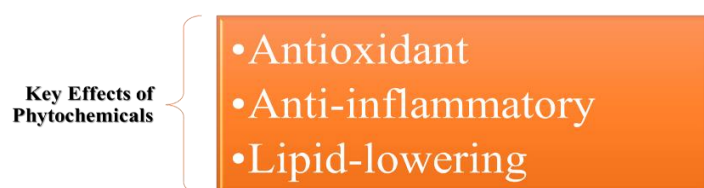


Figure 2 Key Effect of Phytochemicals

## Botanical Description and Traditional Uses

*Euphorbia hirta L.* a small annual herbaceous plant in the family Euphorbiaceae, has a long history of medicinal usage in tropical and subtropical regions. It is a widespread weed in disturbed soils, gardens, and along roadsides because it thrives in a wide range of environments. The morphology of *Euphorbia hirta L.* is characterized by hairy stems, serrated edges on the oval leaves, and tiny, clustered flowers that

lack petals but are encased in bracts. Similar to other members of the family Euphorbiaceae, this plant may grow to a height of 30–60 cm and, when damaged, produces a milky latex. It has found extensive use in traditional medical systems worldwide because of its adaptability and widespread availability. *Euphorbia hirta* L. has a long history of medicinal usage across many civilizations. Ayurvedic, Unani, and traditional African medicine all make use of its expectorant and bronchodilatory properties to treat respiratory disorders, including asthma, bronchitis, cough, and other similar conditions[5]. Its antispasmodic and antibacterial characteristics are further demonstrated by its use in the treatment of gastrointestinal disorders, including dysentery, intestinal parasites, and diarrhea. Because of its anti-inflammatory and antibacterial characteristics, the plant is also used topically to treat wounds, skin diseases, and bug bites. Some people believe that the galactagogue *Euphorbia hirta* L. has diuretic, antipyretic, and analgesic properties; it is also used topically to stimulate breastfeeding. The wide range of traditional applications of the plant serves as evidence of its diverse pharmacological properties and their significance in ethnomedicine. In support of its ethnobotanical significance, *Euphorbia hirta* L. has a rich phytochemical composition that includes terpenoids, alkaloids, saponins, phenolic acids, and flavonoids. The traditional medicinal benefits are believed to be based on these bioactive substances. Flavonoids and phenolic compounds are good examples; they are vital in the treatment of disorders caused by oxidative stress because of their anti-inflammatory and antioxidant capabilities. The plant is used to treat gastrointestinal and infectious disorders because its alkaloids and tannins have antibacterial and antiparasitic actions. It is thought that the combination of these phytochemicals makes traditional medicine preparations of *Euphorbia hirta* L. more effective[6]. The preparation methods for *E. hirta* vary according to cultural norms and medicinal goals. Many people make decoctions, infusions, or powders from the dried leaves and aerial parts. Depending on the therapeutic need, these medications may be administered topically or taken orally. In certain cultures, the plant's juice is used once; however, in others, dried extracts are preferred because they last longer in storage. Typically, traditional healers rely on their empirical knowledge and the patient's reaction to determine the dose and regimen. These traditions show that people have a good grasp of the plant's therapeutic properties and a long history of knowledge about them. However, they also highlight the

need for regulated formulations and dose regimens to ensure the safety and effectiveness of the plant[7]. A more recent development in the ethnopharmacological profile of *Euphorbia hirta* L. is its potential use in the management of dyslipidemia and risk factors for cardiovascular disease. While most of its traditional applications have focused on inflammatory and infectious illnesses, current research is beginning to explore its potential to modulate lipid levels. The desire to identify natural items that might complement or provide alternatives to synthetic lipid-lowering drugs, as well as the worldwide trend toward cardiovascular illnesses, are the driving forces behind this shift. These investigations are supported by evidence that *Euphorbia hirta* L. has a history of use in specific cultures for metabolic and circulatory health treatments. However, to support and optimize its medicinal use, thorough botanical and phytochemical analyses are necessary[8]. To guarantee consistent and high-quality medical goods, it is necessary to identify and authenticate *Euphorbia hirta*. Incorrect identification or mixing with other, similar species of *Euphorbia* may affect therapeutic efficacy and safety. Herbarium and botanical surveys rely on morphological traits as taxonomic identifiers, such as leaf form, stem hairiness, and flower structure. Microscopic examination, chromatographic fingerprinting, and molecular techniques are some of the most advanced tools used to identify certain species. Pharmacological research benefits from this level of rigorous botanical characterization because it provides experimental investigations using standardized plant material. Native American healing practices sometimes include the verbal transmission of information about *Euphorbia hirta* L. from one generation to the next. The medical applications, harvesting times, preparation techniques, and contraindications are all included in this material. Preserving this ethnobotanical history is crucial for cultural preservation and because the pharmacological characteristics of plants may guide scientific study. The sustainable use and conservation of *Euphorbia hirta* L. are achieved through the collaborative efforts of ethnobotanists, pharmacologists, and local populations. This cooperation documents and validates the traditional applications of the plant[9]. *Euphorbia hirta* L. is important not only for its medical uses but also has ecological and economic implications. Soil stability and biodiversity are two outcomes of this resilient species' capacity to adapt to a wide range of environments. Rural communities that rely on traditional medicine can economically benefit from the plant's exploitation and sale in local herbal markets. Herbal

treatments and natural health products are becoming more popular, which has increased the demand for *Euphorbia hirta*. To prevent the overexploitation of this plant, sustainable harvesting methods for cultivation have been studied. *Euphorbia hirta L.* is a popular plant; however, its safety when used in traditional medicine requires serious consideration. Although bioactive substances, such as latex and diterpenes, may be harmful in the wrong hands, there are few instances of toxicity. Others who practice traditional medicine often advise expectant mothers and others with certain medical conditions to take special care. Chronic and acute toxicity assessments are examples of the scientific toxicological investigations needed to ascertain safe dose levels and potential adverse effects. To establish standard herbal medications, these investigations supplement ethnomedical expertise[10]. *Euphorbia hirta L.* has recently been in the spotlight as a potential candidate for drug discovery and development, thanks to a combination of traditional botanical research and modern pharmacological investigations. With the current trend toward employing plants to treat chronic conditions, such as dyslipidemia, its diverse phytochemical components and adaptable therapeutic effects have been highlighted. Insights into how *Euphorbia hirta L.* may regulate lipid metabolism and related enzymatic activities have come from research on the plant's bioactive components and the mechanisms by which they work. There is a chance that novel molecules may be isolated from this research and used in therapeutic practice[11].

### **Phytochemical Composition**

One plant that has the potential to cure dyslipidemia is *Euphorbia hirta L.* which has a broad variety of phytochemicals that give it its broad pharmacological properties. Various types of bioactive substances, including tannins, alkaloids, saponins, phenolic acids, terpenoids, and essential oils, make up the phytochemical composition of the plant and play different roles in its therapeutic effects. Flavonoids are prominent among the many significant chemicals found in *Euphorbia hirta*. These polyphenolic compounds are known for their antioxidant and anti-inflammatory capabilities, which help alleviate oxidative stress and inflammation caused by lipid metabolic problems. Isolated flavonoids from *Euphorbia hirta L.* include quercetin, kaempferol, and their glycosides. Their presence has been linked to the plant's ability to neutralize free radicals and reduce lipid peroxidation, two processes that protect cellular components from oxidative stress. By

modifying the enzyme activities that control lipid production and catabolism, this antioxidant action not only aids in maintaining cardiovascular health but also helps to manage lipid profiles. Tannins are another important class of phytochemicals found in abundance in *Euphorbia hirta*. The protein-binding properties of these polyphenols provide them with the power to affect enzyme function and microbial growth[12]. Tannins in *Euphorbia hirta L.* have astringent, anti-inflammatory, and antibacterial properties. Their ability to inhibit pancreatic lipase and other digestive enzymes may explain their lipid metabolism by reducing blood lipid levels. Another sign of tannins' function in protecting the cardiovascular system is their capacity to control oxidative activity and chelate metal ions. There are a number of nitrogen-containing chemicals with different pharmacological effects found in the alkaloids of *Euphorbia hirta*. Chemicals with antibacterial, analgesic, and anti-inflammatory properties have been identified. The alkaloids in *Euphorbia hirta L.* contribute to the plant's bioactivity, even if their exact composition is unknown, similar to flavonoids and tannins. By controlling inflammatory responses and enzyme activity, alkaloids may indirectly affect lipid metabolism. *Euphorbia hirta L.* also contains saponins, which are glycosides with surfactant characteristics. By increasing the production of bile acids and cholesterol in the gastrointestinal system, these chemicals have been shown to have cholesterol-lowering effects in the majority of plant species[13]. Saponins also maintain lipid homeostasis by preventing the absorption of lipids and increasing the breakdown of cholesterol to bile acids. Their presence in the phytochemical profile of *Euphorbia hirta L.* suggests that they play a role in the plant's hypolipidemic effect. Another important component of the antioxidant action of *Euphorbia hirta L.* is phenolic acids and other phenolic compounds. Free radical scavenging and inflammation regulation are two functions of compounds with these characteristics, such as gallic acid, caffeic acid, and chlorogenic acid derivatives[14]. Phenolic acids may influence lipid metabolism by influencing the expression of genes involved in lipid synthesis and degradation and by blocking an important stage in atherogenesis the oxidative alteration of lipoproteins. The terpenoids found in *Euphorbia hirta*, including diterpenes and triterpenes, provide the plant with a wide range of medicinal uses. Terpenoids act as cytoprotective, antimicrobial, and anti-inflammatory agents. This plant's lipid-lowering effects are further supported by the assertion that some of its terpenoids inhibit enzymes involved in

cholesterol formation and lipid processing. Milky latex from certain species of *Euphorbia* contains diterpenoid esters, which have both medicinal and hazardous potential and must be carefully considered. Essential oils derived from *Euphorbia hirta L.* include volatile chemicals such as monoterpenes and sesquiterpenes. These oils work in tandem with other phytochemicals to combat inflammation and microbes. Essential oils may enhance the health benefits of the plant by controlling inflammation and oxidative stress; however, their effect on lipid metabolism is less well established[15]. To achieve a more potent pharmacological effect from *Euphorbia hirta*, these phytochemicals work in tandem. Together, flavonoids and phenolic acids provide strong antioxidant protection, whereas tannins and saponins restrict enzyme activity and fat absorption, respectively. Alkaloids and terpenoids provide a multi-pronged approach to controlling lipid levels and have additional anti-inflammatory and enzymatic regulatory actions. The observed hypolipidemic actions can be explained scientifically by such a complex phytochemical network, which also supports the traditional use of the plant[16]. Phytochemical extraction of *Euphorbia hirta L.* affects extract yield and bioactive compound composition. Extraction temperature, solvent polarity, and duration all play a role in determining the final concentration of various components, including tannins and flavonoids. Many different types of phytochemicals may be selectively extracted using various solvents; the most popular of them are methanol, ethanol, aqueous mixes, and ethyl acetate. Pharmacological research and therapy require consistent and potent extracts, which can only be achieved through the standardization of extraction techniques. The phytochemical components of *Euphorbia hirta L.* have been identified and quantified using chromatographic and spectroscopic techniques, such as high-performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS), and nuclear magnetic resonance (NMR) spectroscopy. These approaches are useful for quality control and bioactivity correlation studies and allow for the thorough profiling of flavonoid, phenolic acid, alkaloid, and terpenoid compounds[17]. As a phytochemically rich plant, *Euphorbia hirta L.* further emphasizes the need to consider potential interactions and toxicity. Most chemicals have shown beneficial benefits; nevertheless, specific compounds derived from latex or diterpenoids may be unpleasant or even dangerous when used in large quantities. Therefore, understanding the phytochemical composition may aid in developing

therapeutic medicines with an appropriate balance of effectiveness and safety[18].

### **Mechanisms of Dyslipidemia and Therapeutic Targets**

If your blood lipid levels (total cholesterol, low-density lipoprotein cholesterol, triglycerides, and/or decreased high-density lipoprotein cholesterol) are off, you may have dyslipidemia, a metabolic disorder. The development of atherosclerosis, coronary artery disease, stroke, and other cardiovascular illnesses (CVDs) is based on this imbalance. Interventions based on natural products, such as *Euphorbia hirta L.* can only be developed after the underlying processes of dyslipidemia and therapeutic targets are understood. Multiple pathways regulating lipid metabolism, transport, and clearance contribute to the pathophysiology of dyslipidemia. Increased cholesterol and triglyceride synthesis and absorption, impaired lipoprotein clearance, and oxidative lipoprotein modification are associated factors. Lipid homeostasis is largely dependent on the liver's ability to regulate cholesterol and triglyceride synthesis, their encapsulation into lipoproteins, and their subsequent release into the circulation[19]. Damage to the arteries and accumulation of lipids would occur at every level if dysregulation were to occur. The enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase controls cholesterol production and catalyzes the rate-limiting step in the mevalonate pathway. One cause of hypercholesterolemia is an overactive HMG-CoA reductase, which causes an excess of endogenous cholesterol to be produced. An effective way to decrease LDL-C levels is using statin medications, which work by therapeutically inhibiting this enzyme. Similarly, pancreatic lipase is a key enzyme in the breakdown of dietary lipids; it releases monoglycerides and free fatty acids by hydrolyzing triglycerides. By reducing fat absorption, pancreatic lipase inhibition lowers blood triglyceride levels and prevents fat accumulation. Chylomicrons, very-low-density lipoproteins (VLDL), low-density lipoproteins (LDL), and high-density lipoproteins (HDL) are lipid complexes that are involved in lipoprotein metabolism and blood transport. Atherogenesis begins with the oxidative alteration of low-density lipoprotein (LDL) particles, which transport cholesterol to peripheral organs and cause inflammatory responses and the development of foam cells in the artery walls[20]. The reverse cholesterol transfer is made possible by the HDL particles, which carry excess cholesterol from tissues to the

liver for excretion. The risk of cardiovascular disease increases when HDL-C levels are low because this protective mechanism is compromised. Dyslipidemia progresses via a process that includes inflammation and oxidative damage. By modifying low-density lipoprotein (LDL) particles, reactive oxygen species (ROS) exacerbate endothelial dysfunction and pave the way for the secretion of inflammatory cytokines. Lipid metabolism and vascular integrity are both compromised by chronic inflammation. Consequently, lipid-lowering treatments should prioritize antioxidant and anti-inflammatory therapies. Treatment aims for dyslipidemia extend beyond pancreatic lipase and HMG-CoA reductase to include other enzymes and pathways involved in lipid metabolism. To illustrate the impact of acyl-CoA on lipoprotein assembly and storage, consider the enzyme acyltransferase (ACAT), which helps with cholesterol esterification. Cholesterol accumulation in macrophages may be reduced by the ACAT inhibitor. Increased lipoprotein lipase (LPL) activity leads to better triglyceride clearance from the blood, as LPL breaks down the triglyceride in the lipoprotein. Additionally, via binding to the Niemann-Pick C1-like 1 (NPC1L1) protein in enterocytes, cholesterol absorption inhibitors directly block the absorption of dietary cholesterol[20]. The bioactive phytochemical components of the plant *Euphorbia hirta L.* may modulate these therapeutic targets, which include enzymes, antioxidants, and inflammation. In vitro enzyme-based tests have shown that *Euphorbia hirta L.* extracts and isolated chemicals decrease the activities of pancreatic lipase and HMG-CoA reductase. This suggests potential strategies to limit the absorption of dietary fat and endogenous cholesterol generation. Lower circulating cholesterol levels and improved lipid profiles are possible outcomes of these inhibitory activities. Furthermore, flavonoids and phenolic acids are antioxidants found in *Euphorbia hirta*, which inhibit lipid peroxidation and oxidative LDL particle modification. This activity has the significant side effect of decreasing inflammatory responses and endothelial dysfunction, two key components in the development of atherosclerosis. The anti-inflammatory properties of the plant, which inhibit the production of vascular inflammation-inducing cytokines and enzymes, amplify these effects[21]. According to in vitro lipid studies, *Euphorbia hirta L.* has hypolipidemic properties, as it reduces cellular cholesterol and triglyceride levels. Based on these findings, it is reasonable to assume that the bioactive chemicals in the plant may influence cellular lipid intake, synthesis, and storage, as well as their function in systemic

lipid homeostasis. Dyslipidemia is a complex metabolic and signalling system, much like the diverse functions of *E. hirta*. *Euphorbia hirta L.* modulates lipids in a wide variety of ways using oxidative stress, inflammation, biosynthetic enzymes, and lipid digestion. There may be fewer side effects and better treatment outcomes from this integrated procedure compared to single-target medications[22]. Understanding these processes will aid in the development of more targeted pharmacological studies and clinical trials. It is feasible to create standardized extracts or isolated compounds with enhanced efficacy and safety by identifying the specific bioactive components that induce antioxidant activity and enzyme inhibition. *Euphorbia hirta L.* molecular pathway elucidation also has the potential to provide novel therapeutic targets for dyslipidemia[23].

#### **In Vitro Lipid Assays of *Euphorbia hirta L.***

For a better understanding of how *Euphorbia hirta L.* may help with dyslipidemia treatment, in vitro lipid tests constitute the backbone of lipid-modulating impact assessment. The capacity of the plant to influence the regulation of fat deposition, cholesterol, and triglyceride content in biochemical or cellular systems is the primary focus of these studies. These findings provide the groundwork for the current discussion by demonstrating that isolated bioactive compounds and extracts from *Euphorbia hirta L.* have the potential to exert hypolipidemic effects via various mechanisms[24]. Researchers have shown that in vitro lipid tests may reduce cholesterol and triglyceride levels in several cell types using *E. hirta*. The inhibition of lipid absorption, production, or storage at the cellular level suggests that plant components may have this effect. For instance, it has been shown that extracts from *E. hirta* may inhibit the lipid-accumulating processes of cells by reducing intracellular lipid droplets. This impact is crucial because atherosclerotic plaques and foam cell production are major contributors to the onset of cardiovascular illnesses, and excessive intracellular lipid storage is a cause of both. The lipid-lowering effects shown in these tests are thought to be caused by the diverse phytochemical profiles of *E. hirta*, particularly its flavonoids, tannins, and phenolic acids. Lipid deposition and vascular damage both increase when oxidative lipid modification occurs; these chemicals' antioxidant properties prevent this. By removing ROS and lipid peroxidation, *Euphorbia hirta L.* reduces the atherogenicity of lipoproteins like low-density lipoprotein (LDL). A multifaceted strategy for lipid regulation is

created when this antioxidant mechanism is added to the direct actions that reduce lipids[25]. Lipid studies also show that *E. hirta* affects enzymes involved in lipid metabolism. Enzymes, such as pancreatic lipase and HMG-CoA reductase, may be blocked to reduce dietary fat absorption of cholesterol and endogenous synthesis of cholesterol, respectively. In vitro lipid tests reveal decreased cholesterol and triglycerides in treated cells, which is a downstream effect of this enzyme inhibition. These findings lend credence to the idea that enzymatic and non-enzymatic pathways influence lipid homeostasis via the bioactive chemicals of *E. hirta*. In addition, models that mimic hepatic lipid synthesis or intestinal lipid absorption are often used in in vitro testing; they provide precise information on the plant's action mechanism. One example is the possible effect of extracts from *Euphorbia hirta L.* on intestinal cell line tests. These extracts have the ability to reduce fatty acid and cholesterol absorption, perhaps via changes in membrane fluidity or transporter proteins. Similarly, as a result of interference with the lipogenic pathways, hepatic cell models show a decrease in lipid production or secretion in the treated circumstances. The plant's ability to function at different points in the lipid metabolic cascade is highlighted by all of these discoveries. *Euphorbia hirta*'s dose-dependence in lipid testing is another factor to think about[26]. There seems to be a correlation between the availability of phytochemicals and hypolipidemic activity, since the concentration of extracts has a direct impact on the likelihood of lipid content decreases. In spite of this, the link also shows how important it is to standardize extracts closely in order to increase therapeutic benefits and decrease toxicity. Establishing effective concentration levels in vitro lays the groundwork for subsequent in vivo and clinical trials. It is common practice to compare *Euphorbia hirta L.* to other cholesterol-lowering drugs or controls in in vitro lipid investigations. These comparisons not only demonstrate the plant's efficacy but also put its potency into context. Despite its smaller size compared to manufactured medications like statins, *Euphorbia hirta L.* is a valuable alternative or complimentary agent due to its adaptability in bioactivity and excellent safety record. In addition, it may be able to treat many dyslipidemia pathways at once thanks to the synergistic effects of its phytochemicals[27]. When interpreting these data, it is important to consider the limitations of in vitro lipid tests. They provide a controlled environment to dissect certain processes; however, they can not replicate the intricacy of lipid metabolism in a complete organism, which involves hormonal regulation, interactions

between gut bacteria, and organ crosstalk, among other systemic components. To obtain a complete picture of the medicinal potential of *Euphorbia hirta*, it is necessary to integrate the results of these tests with information from in vivo studies and clinical trials. It is not possible to skip the in vitro lipid assays while doing preliminary pharmacological testing. They facilitate mechanistic investigations, quick screening of plant extracts and isolated chemicals, and candidate selection for future development. The results of these experiments have established the traditional use of *Euphorbia hirta L.* as a treatment for lipid diseases and have identified certain bioactivities that require further research[28].

### Enzyme-Based Assays Relevant to Lipid Metabolism

To further understand the pharmacological potential of *Euphorbia hirta L.* in treating dyslipidemia, enzyme-based assays relevant to lipid metabolism are essential. The results of these experiments will provide a molecular picture of the interactions between the plant's bioactive chemicals and the main enzymes involved in lipid metabolism, synthesis, and control[29]. The significance of *Euphorbia hirta L.* in regulating enzymatic activity for lipid homeostasis and cardiovascular health is summarized in the discussion, which also includes the findings of other research that inhibited the enzyme. Pancreatic lipase is one of the enzymes investigated in these tests; it plays an important role in the digestion of dietary lipids by hydrolyzing triglycerides into absorbable monoglycerides and fatty acids. Pancreatic lipase inhibition is a recognized therapy approach for hyperlipidemia and obesity, which decreases fat absorption. Studies conducted on *Euphorbia hirta L.* extracts have shown that the plant's phytochemicals may be used to block the absorption of fats in the intestines, as the plant is a strong inhibitor of pancreatic lipase activity. This procedure is in line with the potential use of *Euphorbia hirta L.* as a natural lipase inhibitor and the observed reductions in triglyceride concentrations in in vitro lipid studies. Third, 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in cholesterol production, is another important enzyme that has been investigated[30]. Statins, the most common lipid-lowering drugs, work by inhibiting this enzyme. In enzyme-based experiments, it was shown that *Euphorbia hirta L.* extracts and isolated chemicals inhibited HMG-CoA reductase, which means they may reduce endogenous cholesterol formation. This finding has great significance as it introduces *Euphorbia hirta L.* as a potential vegetable

supplement to conventional statin medication, which has the potential to decrease cholesterol levels with fewer adverse effects[31]. Research on *E. hirta* has focused on lipid metabolism enzymes other than pancreatic lipase and HMG-CoA reductase. For example, acyl-CoA: cholesterol acyltransferase (ACAT) is a therapeutic target. This enzyme prevents atherosclerosis and foam cell development by esterifying and storing cholesterol. Although there is no direct evidence that *E. hirta* affects ACAT, it has been documented in the literature that the plant's phytochemicals, especially flavonoids and tannins, may influence such enzymes, suggesting that there may be indirect benefits. Similarly, the bioactive chemicals of the plant may influence lipoprotein lipase (LPL), an enzyme that increases lipid clearance by degrading circulating lipoprotein triglycerides; however, the exact mechanisms by which particular enzyme assays of LPL with *E. hirta* work remain unclear. The inhibitory activities of *E. hirta* on additional lipid-related enzymes, such as cholesterol esterase (an enzyme that enhances the absorption of cholesterol) and enzymes involved in the production and oxidation of fatty acids, may also be evaluated using these enzyme-based assays. The hypolipidemic effects of *Euphorbia hirta L.* are attributed to its ability to modulate lipid metabolism by regulating the activity of certain enzymes. *Euphorbia hirta L.* contains terpenoids, flavonoids, tannins, and phenolic acids, which act as enzyme inhibitors. Flavonoids, such as quercetin and kaempferol derivatives, may suppress enzyme activities competitively or non-competitively because of their strong binding affinities with enzyme active sites. Tannins may interact with enzymes and reduce their catalytic activity because of their ability to bind proteins. Dose-dependent inhibition has been observed in in vitro enzyme experiments using pure enzymes or enzyme extracts, establishing this relationship[33]. Spectrophotometric analysis of enzyme activity in the presence and absence of isolated chemicals or extracts of *Euphorbia hirta L.* is a common technique in enzyme-based assays. One way to estimate the activity of an enzyme is to observe how quickly it converts substrates into products or consumes cofactors. To quantify the inhibitory strength, assays are designed to assess the IC<sub>50</sub> values, which are the concentrations required to suppress half of the enzyme activity. These results are critical for determining the dosage in future pharmacological studies and for comparing the effectiveness of *Euphorbia hirta L.* to that of standard inhibitors. Important questions include the specificity and selectivity of inhibiting the *Euphorbia hirta*

*L.* enzyme. The potential benefits of broad-spectrum inhibition in targeting different lipid pathways are outweighed by the risks of over- or non-selective inhibition. Consequently, enzyme tests are often used to measure the degree of enzyme inhibition to chart the plant's bioactivity spectrum[34]. The phytochemicals of *Euphorbia hirta L.* are safe and effective because they have balanced inhibitory activity, meaning they act on certain enzymes without affecting many off-targets. We will gain a comprehensive understanding of the processes by which *Euphorbia hirta L.* exerts its effects when the results of the enzyme-based tests, in vitro lipid assays, and phytochemical research are combined. Lipid profiles are improved in part by antioxidant phytochemicals, which prevent lipid oxidation, and by enzyme inhibition, which reduces fat production and absorption. When dealing with many causes of dyslipidemia, a multifactorial approach is superior to treatments that focus on only one issue. The reductionist nature of enzyme-based assays is one of their main drawbacks; that is, they separate enzyme activity from the complex biological environment that contains many regulatory mechanisms and negative feedback loops. Therefore, it is important to demonstrate enzyme inhibition in vitro as a predictor of potential therapeutic results in cellular, animal, and clinical models to verify safety and effectiveness[35]. The need for standardized techniques is further underscored by the fact that variations in extract preparation, phytochemical concentration, and test conditions may affect repeatability. Isolating and characterizing specific bioactive compounds with enzyme-inhibitory capabilities, understanding how they bind using molecular docking and structural analysis, and studying the synergistic effects of phytochemicals are all areas where research is headed in the future. To treat dyslipidemia, these investigations will aid in the production of standardized, effective formulations of *Euphorbia hirta*. We can learn more about these drugs' in vivo effectiveness by investigating their pharmacokinetics and bioavailability[36].

### Pharmacological Activities and Mechanisms

When it comes to treating dyslipidemia, the broad spectrum of pharmacological actions of *Euphorbia hirta L.* lend credence to its efficacy. Several phytochemical components work together to affect different pathways in lipid metabolism, oxidative stress, and inflammation, which explains these effects. To better understand how *Euphorbia hirta L.* contributes to lowering cardiovascular risk and

producing hypolipidemic effects, this section reviews the results of in vitro lipid- and enzyme-based investigations. Among *Euphorbia hirta*'s many pharmacological actions, its capacity to modulate lipid metabolism by directly inhibiting enzymes and modulating lipid production and absorption stands out. Studies on enzyme inhibition have shown that isolated chemicals and plant extracts show promise as pancreatic lipase inhibitors[37]. This may reduce the breakdown and absorption of dietary lipids in the gut. One component of dyslipidemia, hypertriglyceridemia, is alleviated when this mechanism reduces blood triglyceride levels. Another enzyme that *Euphorbia hirta L.* inhibits is 3-hydroxy-3-methylglutylglucone-coenzyme A (HMG-CoA), which is the rate-limiting enzyme in cholesterol production. Reduced levels of atherogenesis-related low-density lipoprotein cholesterol (LDL-C) result from this inhibition, which prevents hepatocytes from producing endogenous cholesterol. By lowering both endogenous and external lipid synthesis and absorption, these enzymatic activities improve lipid profiles[38]. Although *Euphorbia hirta L.* exhibits important enzyme-inhibiting pharmacological activity, its antioxidant impact is more important in preventing the oxidative modification of lipoproteins, particularly low-density lipoprotein (LDL) particles. Endothelial dysfunction, inflammation, and foam cell generation are accelerated by oxidized LDL, which in turn speeds up the progression of atherosclerotic plaques. Tannins, phenolic acids, and flavonoids present in *E. hirta* help fight lipid peroxidation and reactive oxygen species (ROS). Reducing the risk of cardiovascular disease, this antioxidant system aids in maintaining the integrity of vascular tissues and lipoproteins. In addition, it protects hepatic cells from oxidative stress, contributing to healthy lipid metabolism and liver function. The lipid-lowering actions of *E. hirta* are complemented by its anti-inflammatory activities. There is a never-ending loop of vascular damage and metabolic disturbances in dyslipidemia, which is characterized by chronic inflammation. By blocking the action of enzymes like cyclooxygenase-2 and pro-inflammatory cytokines like TNF-alpha and IL-6, phytochemicals like flavonoids and terpenoids control the inflammatory processes. This regulation inhibits endothelial activation and leukocyte recruitment, thereby reducing vascular inflammation and atherogenesis. By simultaneously targeting oxidative stress and inflammation, *E. hirta* combats two interconnected pathological processes that are crucial for cardiovascular risk. Cellular studies have shown that extracts of *E. hirta*

reduce intracellular lipid accumulation, which is a key step in the development of foam cells and fatty liver disease[39]. The bioactive chemicals of the plant change the expression and activity of enzymes involved in lipid metabolism and lipid transport, which in turn affects the amount of lipid intake and storage. It has been suggested that inhibiting sterol regulatory element-binding proteins (SREBPs) may reduce lipid production. These transcription factors control genes involved in cholesterol and fatty acid synthesis. Concurrently, upregulation of peroxisome proliferator-activated receptors (PPARs) may aid in reducing lipid accumulation by promoting fatty acid oxidation and lipid breakdown. In vitro models have demonstrated beneficial effects on triglyceride and cholesterol levels, as well as gene and protein level regulation. Inflammation, dysregulated lipid metabolism, and oxidative damage play roles in the development of dyslipidemia, which is consistent with the multifactorial pharmacological effects of *E. hirta*. The multi-target actions of *Euphorbia hirta L.* allow it to address intersecting processes of lipid diseases, representing an advantage over single-target pharmacotherapies. As the bioactive chemicals of the plant have moderate modulatory effects rather than complete enzyme inhibition, this may lead to improved effectiveness with fewer side effects. We discuss the pharmacological uses of *Euphorbia hirta L.* while keeping safety in mind. Toxicity studies have shown that therapeutic doses of well-prepared extracts have acceptable safety profiles, despite the presence of bioactive diterpenoids and latex, both of which may cause irritation[40]. In addition to reducing the risk of adverse consequences, antioxidant and anti-inflammatory chemicals may have cytoprotective benefits. However, standardization of extraction and dosage is necessary to maximize the advantages with the fewest hazards. The medicinal efficacy of phytochemicals derived from *E. hirta* is dictated by their pharmacokinetics and bioavailability. Flavonoids and phenolic acids may undergo metabolic alterations that impact their biological actions. Bioenhancer formulation or encapsulation, which can boost bioavailability, may have a positive impact on clinical results. Patterns of absorption, distribution, metabolism, and excretion need to be further studied in the field of pharmacology[41]. Recent studies have used computational modelling and molecular docking to reveal how phytochemicals from *Euphorbia hirta L.* bind to certain enzymes, such as pancreatic lipase and HMG-CoA reductase. Structural information on the inhibitory mechanism has been provided by these investigations, which in turn have helped in the formulation of effective

compounds or standardized extracts. Research on the synergistic effects of phytochemicals has shown that the combined antioxidant and enzyme-inhibiting capacity of terpenoids, flavonoids, and tannins may be higher than that of the individual substances. Animal models of hyperlipidemia have demonstrated that treatment with *Euphorbia hirta L.* reduces inflammatory indicators, increases antioxidant enzyme activities, and decreases blood cholesterol and triglyceride levels, lending credence to the in vitro findings. The results also indicate better vascular function and less atherosclerotic lesion development. Such preclinical data provide credence to *Euphorbia hirta*'s potential as a natural medicinal agent with translational potential[42]. Further clinical trials are needed to determine whether *Euphorbia hirta L.* is safe and effective for humans. A correct design is essential for randomized controlled trials that assess changes in lipid profiles, inflammatory markers, and cardiovascular outcomes. To develop evidence-based conclusions on the use of *Euphorbia hirta L.* in the treatment of dyslipidemia, it is necessary to combine clinical results with pharmacological data[43].

### Safety and Toxicological Profile

When considering the use of *Euphorbia hirta L.* as a treatment agent, particularly for the treatment of dyslipidemia, its safety and toxicology must be carefully considered. The bioactive components of the plant, including diterpenoids and the characteristic milky latex, have encouraging pharmacological characteristics and are widely employed as traditional medicines; however, they may be harmful if not administered properly. Extracts of *Euphorbia hirta L.* often offer a tolerable margin of safety when properly produced and administered, according to toxicological studies. There have been no notable adverse effects on important organs or biochemical markers at therapeutic dosage ranges determined by acute and sub-chronic toxicity testing in animal models. Based on these findings, it is plausible that the plant's antioxidant and anti-inflammatory phytochemicals possess cytoprotective characteristics that mitigate potential toxicity. Latex contains diterpenoid esters, which are known to have irritating qualities and may cause skin and mucous membrane irritation upon direct contact. This highlights the need for standardized extraction procedures to limit exposure to potentially harmful components and calls for caution when applying topically[44]. Because there is a lack of safety data for certain populations, traditional healers may also advise caution or outright forbid treatment for

pregnant women and people with particular medical problems. The effectiveness and safety of phytochemicals may be affected by variations in the plant part utilized, time of harvesting, and extraction processes. These factors also impact the phytochemical concentration. Therefore, it is critical to use standardized formulations with quality controls in place to ensure the same therapeutic benefit while minimizing side effects[45].

It is necessary to conduct comprehensive toxicological experiments, including chronic toxicity, genotoxicity, and reproductive toxicity tests, on *Euphorbia hirta L.* to ascertain its complete safety characteristics, even if the medicine has shown a favorable safety profile in preclinical trials. Research of this kind will help establish appropriate doses and pave the way for the development of standardized herbal remedies for the treatment of dyslipidemia[46].

### Conclusion

*Euphorbia hirta L.* has an excellent phytochemical profile and exerts several pharmacological effects, making it a promising natural option for the management of dyslipidemia. The bioactive components of the plant, including tannins, alkaloids, saponins, phenolic acids, and terpenoids, work together to reduce lipids by influencing multiple pathways involved in lipid metabolism. Important dietary fat-digesting and endogenous cholesterol-forming enzymes, namely, pancreatic lipase and HMG-CoA reductase, have been shown to be inhibited by enzyme-based tests. Reduced blood triglyceride and cholesterol levels are aided by this two-pronged inhibitory mechanism. At the same time, lab tests on lipids show that *Euphorbia hirta L.* can lower levels of lipids within cells, which means it may control how cells take in, make, and store lipids. Along with its ability to directly inhibit enzymes, *Euphorbia hirta L.* also has powerful antioxidant and anti-inflammatory properties. These are crucial for preventing the oxidative modification of lipoproteins and lowering vascular inflammation, two key factors that lead to the development and advancement of cardiovascular diseases, such as atherosclerosis. Because of its diverse mechanism of action, the plant may be able to address the underlying causes of dyslipidemia more comprehensively than pharmaceuticals targeting a single target. Irritating diterpenoid and latex components warrant caution; however, safety studies reveal that, at appropriate dosages, *Euphorbia hirta L.* extracts are reasonably hazardous. Standardized extraction methods and toxicological testing (including tests for reproductive and chronic toxicity) are required to ensure safe clinical use.

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#### Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare no conflict of interest among themselves. The authors alone are responsible for the content and writing of this article.

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