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Review Article

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Review on Antidiabetic Effects of *Euphorbia hirta L.* via Digestive Enzyme Inhibition

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Abstract

A lot of people are curious about the antidiabetic properties of the medicinal plant Euphorbia hirta L., which has a long history of usage in traditional medicine. Focusing on its ability to block digestive enzymes that assist in glucose metabolism, this article critically examines the mechanisms of action underlying Euphorbia hirta's antidiabetic efficacy. Euphorbia hirta's bioactive substances reduce glucose absorption and improve glycemic management by inhibiting α-amylase and α-glucosidase enzymes. Multiple studies, both in the laboratory and in living organisms, have demonstrated that this plant can help diabetic patients lower their blood glucose levels, increase their insulin sensitivity, and reduce their levels of oxidative stress. Phytochemical studies have shown the presence of phenolic chemicals, alkaloids, tannins, and flavonoids, all of which are responsible for these effects. In addition to its potential as a natural alternative or complementary agent in the control of diabetes, the safety profile and therapeutic uses of Euphorbia hirta are also discussed. To ensure that Euphorbia hirta is as useful as possible in antidiabetic treatment, this review will go over the current evidence, any gaps in the literature, and where researchers should go from here.

Introduction

Chronic hyperglycemia, caused by defects in insulin production or activity, or both, characterizes diabetes mellitus, a metabolic condition that persists over time. Worldwide, the prevalence of diabetes is increasing, posing serious health and economic concerns. The major sequelae of diabetes, including cardiovascular illnesses, neuropathy, nephropathy, and retinopathy, increase the risk of morbidity and mortality when they occur together. The goal of diabetes treatment is to control blood glucose levels, which can be achieved through dietary and exercise changes, medication, or the use of antidiabetic herbs and other natural remedies[1]. *Euphorbia hirta L.* L., an ancient medicinal plant with a wide range of applications, including the treatment of respiratory infections, gastrointestinal disorders, and inflammation, is currently being explored as a natural remedy for diabetes. Newer research has demonstrated that it may have antidiabetic effects, mostly by blocking key digestive enzymes involved in glucose metabolism, specifically α-amylase and α-glucosidase. Enzymes play a crucial role in the breakdown of complex carbohydrates into glucose, a form that may be absorbed into the bloodstream. Suppressing these enzymes is one way that *Euphorbia hirta L.* helps with glycemic control; by reducing postprandial blood glucose levels, it achieves this[2]. Phytochemical studies on *Euphorbia hirta L.* have revealed that it contains a wide variety of bioactive chemicals with potential medicinal uses, including tannins, alkaloids, phenolics, and flavonoids. In addition to blocking digestive enzyme activity, these chemicals have antioxidant properties that lessen oxidative stress, a key factor in the development and progression of diabetes and its consequences. Another reason why *Euphorbia hirta L.* is useful as a medicine is because of its antioxidant properties, which help pancreatic β-cells perform their job and make insulin more effective. Researchers have demonstrated that extracts from the *Euphorbia hirta L.* plant can alleviate diabetic symptoms in mice, including high blood sugar, insulin resistance, and oxidative stress, in both laboratory and animal studies[3]. These findings demonstrate the plant's potential as an adjunct to or replacement for conventional antidiabetic drugs, which can have undesirable side effects, be expensive, and lose some of their efficacy over time. Additionally, there have been few reports of toxicity with therapeutic doses of *Euphorbia hirta L.* and its safety profile is generally positive, making it an ideal target for future clinical investigations[4]. Despite these promising results, our understanding of the full therapeutic potential of *Euphorbia hirta L.* and its mechanisms of action remains incomplete **fig:1**. Thorough research is required in several areas, including the standardization of extracts, identification of the most active components, optimization of dosage schedules, and evaluation of extract safety over the long term. For the benefit of people with diabetes, it is important to translate preclinical findings into clinical trials[5].

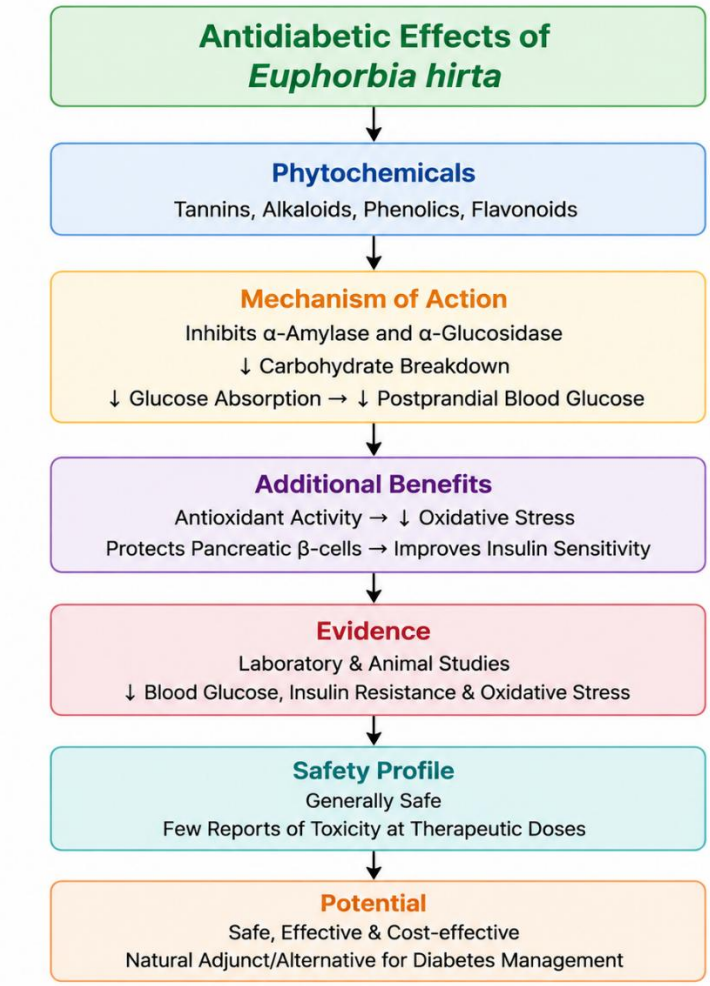

Figure 1 Antidiabetic Pathways of *Euphorbia hirta:* Mechanisms & Benefits

This review aims to summarize the current knowledge on the antidiabetic effects of *Euphorbia hirta L.* with a focus on its effects on digestive enzymes. It explores the potential clinical implications, provides an outline of laboratory and animal studies that have investigated these effects, explains the phytochemical components that cause them, and assesses safety issues. To maximize the potential of *Euphorbia hirta L.* in the management of diabetes and ultimately lead to the establishment of a safe, effective, and cost-effective natural medicine against this

worldwide health concern, this review also suggests future research options by noting present research gaps[6].

Phytochemical Composition of *Euphorbia hirta*

The plethora of phytochemical substances in the medicinal plant *Euphorbia hirta L.* affords it a broad pharmacological profile. Flavonoids, tannins, alkaloids, phenolic compounds, saponins, terpenoids, glycosides, and countless other bioactive substances contribute to the plant 's medicinal qualities, most notably its antidiabetic effects. Flavonoids are prominent components of E. hirta. The strong antioxidant potential of these polyphenols is essential for lowering oxidative stress associated with diabetes. The plant contains flavonoid chemicals, such as quercetin, kaempferol, and their glycosides. The pancreatic β-cells and insulin sensitivity are enhanced by their ability to scavenge free radicals and reduce inflammation, leading to better control of blood sugar levels. Tannins are an important group of phytochemicals in E. hirta because they aid the plant in inhibiting enzymes. The ability of tannins to bind to proteins and enzymes allows these polyphenolic chemicals to alter their activity. The ability of tannins to inhibit digestive enzymes, such as α-amylase and α-glucosidase, which are responsible for breaking down carbohydrates and absorbing glucose, has been proven. Lowering postprandial hyperglycemia is an important part of diabetes care, and tannins can help with this by regulating these enzymes. E. hirta contains alkaloids, which are nitrogen-containing chemicals with a wide range of biological activities. In addition to the pharmacology of the plant, these chemicals can disrupt several biochemical processes and receptors. Research has demonstrated that the alkaloids found in E. hirta have antioxidant and anti-inflammatory properties[7]. These properties allow E. hirta to indirectly aid in the fight against diabetes by safeguarding pancreatic cells and improving metabolic processes. Phenolic chemicals, including simple phenols and complex polyphenols, are found in E. hirta. These chemicals not only provide additional enzyme inhibitory methods but also boost the plant's antioxidant capability. Phenolic acids help to reduce oxidative tissue damage in diabetic tissues, thereby avoiding the problems associated with chronic hyperglycemia. Although present in lower concentrations, saponins and terpenoids are also present in E. hirta. Saponins, which have been found to have hypoglycemic and lipid-lowering properties, have an antidiuretic function that complements the plant's antidiabetic activity. Terpenoids enhance the medicinal potential of E. hirta, which also has anti-inflammatory and antioxidant benefits. Some of the pharmacological actions of E. hirta may be due to glycosides, which modulate glucose metabolism-related enzyme activity and cellular communication pathways[8]. Typically, these substances work in tandem with other phytochemicals to provide a more comprehensive therapeutic effect. E. hirta offers a multimodal approach to diabetes management by combining these bioactive substances. Together, they suppress enzymes that break down carbohydrates and protect against oxidative stress and inflammation, two key factors in the development of diabetes and its consequences. Chromatography and mass spectrometry are examples of phytochemical methods used to establish the presence and concentration of these chemicals in extracts of E. hirta. The part of the plant, location, time of harvest, and method of extraction are some of the variables that can cause phytochemical variations. Extracts must be standardized to ensure consistent medicinal efficacy and safety[9].

Inhibition of α-Amylase

As an antidiabetic, *Euphorbia hirta L.* blocks the action of α-amylase, a crucial digestive enzyme that breaks down starch and glycogen into smaller sugars, namely oligosaccharides and maltose. Other enzymes then break them down even further into glucose. Reducing the rate of glucose release and absorption in the small intestine and blocking α-amylase slows down the breakdown of complex carbohydrates. One of the main reasons why diabetics fail to achieve successful glycemic control is postprandial hyperglycemia; this modification can help lower this risk. The bioactive chemicals present in *Euphorbia hirta L.* particularly flavonoids, tannins, and phenolic compounds, exert strong α-amylase inhibitory effects. These compounds alter the structure of the enzyme by reacting with its active or allosteric regions, thereby reducing its catalytic potential. Tannins, for instance, can alter the structure of enzymes or block their access to substrates by complexing with proteins and enzymes. Research has shown that flavonoid derivatives of quercetin and kaempferol bind to α-amylase through hydrogen bonding and hydrophobic interactions, thereby interfering with the enzyme's mechanism of action[10].

In vitro investigations have consistently reported strong α-amylase inhibition by *Euphorbia hirta L.* extracts. To measure the level of inhibition, these studies used enzyme

tests and often compared the results with those of standard α-amylase inhibitors, such as acarbose. The amount of phytochemicals in these plant extracts determines the strength of their inhibitory effects on enzymes, which are dependent on the dose. This indicates that *Euphorbia hirta L.* could be a natural source of α-amylase inhibitors[11].

Animal models of diabetes provide additional in vivo support for these results. Due to the delayed digestion and absorption of starch, blood glucose levels drop after carbohydrate-rich meals when *Euphorbia hirta L.* extracts are administered. Limiting glucose spikes will assist in decongesting pancreatic β-cells and improving rapid glycemic management. Inhibiting α-amylase also aids in improving insulin sensitivity by preventing glucose fluctuations that are too extreme. Reduced oxidative stress and inflammation in diabetes can also be attributed to the inhibition of α-amylase by *Euphorbia hirta L.* . By controlling glucose uptake, the plant reduces the generation of reactive oxygen species (ROS) and advanced glycation end products (AGEs), both of which are known to cause difficulties in diabetes. The modulation of metabolic processes and protection of cells are part of a broader therapeutic action that includes the inhibition of α-amylase. However, it should be noted that if α-amylase is overly inhibited, it could lead to gastrointestinal side effects, such as gas and diarrhea. This is because carbohydrates that the small intestine cannot digest undergo fermentation in the colon. Clinical trials are necessary to confirm the findings from the *Euphorbia hirta L.* study, which suggests that the balanced phytochemical component may mitigate these side effects in comparison to synthetic inhibitors. Finally, flavonoids, tannins, and phenolic substances bound to α-amylase by *Euphorbia hirta L.* decrease its action, which in turn delays carbohydrate digestion. An effective natural medicinal agent in the therapy of diabetes, this process aids the plant in its antidiabetic activity by lowering postprandial glucose levels, enhancing insulin sensitivity, and decreasing oxidative stress[12].

Inhibition of α-Glucosidase

Inhibiting alpha-glucosidase, an enzyme located in the small intestine's brush border that catalyzes the final step in carbohydrate digestion the breakdown of oligosaccharides and disaccharides into absorbable monosaccharides is another important mechanism through which carbohydrate is metabolized by *Euphorbia hirta L.* . In this instance, blocking α-glucosidase slows the release of glucose into the blood, which in turn reduces postprandial hyperglycemia and improves glycemic regulation. The phytochemicals of *Euphorbia hirta L.* including flavonoids, tannins, alkaloids, and phenolic compounds, exert strong α-glucosidase inhibitory effects. Various binding modes, such as hydrogen bonding, hydrophobic interactions, and van der Waals forces, allow these compounds to interact with the enzyme. These interactions alter the enzyme's active site or conformation, resulting in a decrease in substrate affinity. Because of their polyphenolic composition, tannins and flavonoids form strong interactions with the enzyme and serve as potent natural inhibitors.Research conducted in vitro has shown that the 0-glucosidase activity can be inhibited by extracts of *Euphorbia hirta L.* and this suppression is dose dependent. The inhibitory capacity of the extracts for pharmaceutical α-glucosidase inhibitors, such as acarbose, and the use of synthetic substrates are common ways in which these assays quantify enzyme activity. *Euphorbia hirta L.* extracts have consistently shown considerable inhibitory effects, supporting the claim that carbohydrate digestion is modified[13].

In vivo confirmation of the 1-α-glucosidase inhibitory action of *Euphorbia hirta L.* was also achieved using diabetic animal models. Evidence demonstrates that plant extracts are effective enzyme inhibitors in physiological contexts, as they reduce postprandial blood glucose levels after carbohydrate consumption. Crucial for diabetes care, this action reduces glucose fluctuation and increases insulin sensitivity. Additionally, the inhibition of oxidative stress associated with diabetes is aided by the α-glucosidase inhibitory action of *Euphorbia hirta L.* . By blocking glucose uptake, the plant reduces inflammation and oxidative damage caused by glucose. These are the main causes of diabetes complications, such as neuropathy, nephropathy, and retinopathy. The antioxidant effects of phytochemicals, which aid in the elimination of free radicals and improvement of cellular defense systems, augment this impact[14]. The inclusion of α-glucosidase inhibition in combination therapy is due to the fact that the phytochemicals of *Euphorbia hirta L.* have multiple bioactive properties. The antidiabetic effects of the plant are enhanced by the action of alkaloids and phenolic compounds, which slow down digestive enzymes and influence glucose metabolism and insulin response signaling pathways. *Euphorbia hirta L.* is also associated with good safety as an α-glucosidase inhibitor. The balanced phytochemical composition of *Euphorbia hirta*

L. may aid in preventing the negative effects of gastrointestinal discomfort caused by surplus glucose fermentation, in contrast to artificial inhibitors. However, comprehensive clinical evaluations are necessary to determine long-term safety and effectiveness[15].

In Vitro and In Vivo Evidence of Antidiabetic Effects

Numerous in vitro and in vivo investigations have evaluated the antidiabetic effects of *Euphorbia hirta L.* including its ability to control blood sugar levels, improve insulin sensitivity, and reduce oxidative stress associated with diabetes. The pharmacological efficacy of the plant, the processes that may account for its medicinal value, and the historical use of the plant can all be better understood with the help of the data provided by these experimental investigations[16].

In Vitro Studies

The inhibitory activities of *Euphorbia hirta L.* extracts on major digestive enzymes, such as α-amylase and α-glucosidase, can primarily be ascertained through in vitro experiments. An established method for controlling postprandial hyperglycemia is the inhibition of these enzymes, which play an essential role in carbohydrate metabolism. The inhibition of these enzymes by extracts of various parts of the *Euphorbia hirta L.* plant, including the leaves, stems, and whole plant, has been demonstrated to be dose-dependent in multiple studies. Traditional pharmacological inhibitors, such as acarbose, have more side effects than potent Euphoria hirta extracts against α-amylase and α-glucosidase activity. Enzymes are engaged in this process because certain phytochemicals, such as tannins, flavonoids, and phenolic compounds, can bind to the enzyme's active sites or alter their conformation in a way that makes them less effective. According to research on enzyme kinetics, the phytochemical composition of the extract determines whether these bioactive substances inhibit enzymes competitively or non-competitively[16].

In vitro antioxidant experiments showed that *Euphorbia hirta L.* extracts have a strong capacity to scavenge free radicals and reduce oxidative stress biomarkers, such as reactive oxygen species (ROS), in addition to inhibiting enzymes. Because oxidative stress contributes to the pathogenesis of pancreatic β-cells and insulin resistance in diabetes, the capacity to fight oxidative stress is crucial. Experiments on an pancreatic 8-cell line and adipocyte cell cultures corroborated the findings that *Euphorbia hirta L.* extracts boost glucose absorption and decrease oxidant-induced cell damage, demonstrating a direct impact on insulin sensitivity[17].

In Vivo Studies

Animal models of diabetes, often produced by streptozotocin or alloxan, have been extensively used to examine the antidiabetic benefits of *Euphorbia hirta L.* A significant reduction in fasting and postprandial blood glucose levels is a consistent effect of the oral administration of *Euphorbia hirta L.* extracts to diabetic rats. These effects vary with dosage and may be comparable to or even enhance the effectiveness of standard antidiabetic medications. The slowing of carbohydrate digestion through the inhibition of α-amylase and α-glucosidase, and increased peripheral glucose metabolism, can be attributed, mechanistically speaking, to in vivo hypoglycemic effects. Multiple studies have shown that *Euphorbia hirta L.* can increase insulin sensitivity and concentrations, suggesting that it may either maintain or stimulate pancreatic 8-cell function[18]. Pancreatic tissue histopathology in treated rats shows improved islet architecture and less 8-cell destruction, suggesting a protective effect against diabetic-induced cellular damage. In addition, increased levels of endogenous antioxidant enzymes, such as glutathione peroxidase, superoxide dismutase (SOD), and catalase, as well as lower levels of lipid peroxidation products, such as malondialdehyde (MDA), indicate that *Euphorbia hirta L.* has strong antioxidant activity in vivo. One of the main causes of diabetes-related complications, such as nephropathy and neuropathy, is oxidative stress; however, this antioxidant enhancement inactivates this damage. Better lipid profiles, reduced levels of total cholesterol, triglycerides, and low-density lipoprotein (LDL), and increased levels of high-density lipoprotein (HDL) are among the other metabolic benefits observed in animal models. The overall cardioprotective action of *Euphorbia hirta L.* in diabetics is aided by these benefits. When tested therapeutically, *Euphorbia hirta L.* extracts were found to be safe in animal models, with no negative effects on markers of liver or kidney function and low toxicity overall. Its favorable safety profile suggests that it could be used for long-term treatment of diabetes[19].

Summary of Evidence

Euphorbia hirta L. has complex antidiabetic characteristics, as shown by the in vitro and in vivo data taken together. Inhibition of glucose absorption and

postprandial hyperglycemia is a result of the plant's bioactive components that block digestive enzymes. Concurrently, antioxidant activity improves glycemic management by preserving insulin sensitivity and insulin-insensitive pancreatic 8-cells. Additionally, animal studies have shown that *Euphorbia hirta L.* has favorable effects on lipid metabolism and organ protection, which expands its medicinal potential. Despite the promising preclinical results, several obstacles must be overcome before these results can be applied in a clinical context. The need for standardization arises from the fact that different preparations of extracts, dosage schedules, and phytochemical compositions can produce different effects. Extensive safety, appropriate dosage, and therapeutic effect trials in human diabetic patients should also be conducted through clinical trials[20].

Safety and Toxicity Profile

An important factor to consider when assessing *Euphorbia hirta L.* as a potential medicinal agent for the treatment of diabetes is its safety and toxicity profile. Thorough toxicological evaluations are necessary to guarantee its appropriateness for therapeutic use, even though conventional wisdom and preclinical research imply a generally favorable safety margin[21].

Preclinical Toxicity Studies

To determine the safe dosage limits and potential side effects, researchers have primarily investigated the acute, subacute, and chronic toxicity of *Euphorbia hirta L.* extracts in animals. Acute toxicity testing typically involves administering a high dosage of the extract to rats all at once and observing them for signs of death, abnormal behavior, and physiological issues over the following 24 to 72 hours. Based on these investigations, *Euphorbia hirta L.* does not appear to be acutely poisonous, given its high median lethal dosage (LD50). Standard doses for antidiabetic effects did not cause any significant adverse consequences or death. Subacute and chronic toxicity tests, which involved administering the extract multiple times over several days or weeks, were used to assess the possible cumulative toxicity. This type of research monitors vital signs, such as histopathology of important organs, blood sugar levels, behavioral changes, hematological markers of liver and kidney function, and body weight. At therapeutic doses of *Euphorbia hirta L.* there are no discernible alterations in hepatotoxic, nephrotoxic, or hematotoxic effects, as shown by the findings of hematological indices, renal tests (e.g., creatinine, urea), and liver enzymes (e.g., ALT, AST). Histopathological examinations of many organs have revealed that their tissue architecture is intact and devoid of signs of inflammation, necrosis, or fibrosis. The absence of organ-specific toxicity is supported by these findings, which are in line with biochemical data. The safety profile established by these preclinical models provides strong evidence supporting the need for further clinical trials[22].

Toxicity Related to Phytochemical Constituents

Euphorbia hirta L. is a safe and effective therapeutic option, being rich in tannins, alkaloids, phenolic compounds, saponins, and terpenoids. Despite its beneficial pharmacological benefits, the toxicities of these bioactive substances must be considered. For instance, tannins may have lethal effects at high concentrations, despite their antioxidant and enzyme-inhibitory properties, given that they bind to proteins and interfere with food absorption. However, standardized extracts of *Euphorbia hirta L.* utilized in research typically have levels that are below those considered hazardous. Similarly, alkaloids can have different pharmacodynamics, and some can be toxic; however, there is no evidence that the specific alkaloids found in *Euphorbia hirta L.* cause major adverse effects when administered at therapeutic dosages. Despite their usefulness in hypoglycemic and anti-inflammatory processes, saponins and terpenoids can cause gastrointestinal irritation when consumed in sufficient quantities. Nevertheless, neither in experimental animals nor in humans at therapeutic doses has there been any evidence of significant gastrointestinal damage[23].

Safety in Traditional and Ethnopharmacological Use

Decoctions, infusions, or extracts of *Euphorbia hirta L.* have a long history of usage in traditional medicine across many cultures for the treatment of inflammatory, gastrointestinal, and respiratory disorders. Common use in traditional medicine is typically linked with acceptable tolerance, which provides an indirect indication of safety based on the ethnopharmacological background. Mild side effects, such as temporary stomach pain, are rare and are usually not recorded in traditional settings. Dosage, preparation method, or sensitivity could be the cause of these side effects. In particular, traditional uses of whole-plant preparations raise the possibility that they mediate toxicity via synergistic phytochemical interactions[24].

Potential Adverse Effects and Contraindications

Although the safety profile is good, there are still a few things to consider. GI side effects like gas, distention, and diarrhea can occur when digestive enzymes like α-amylase and α-glucosidase are overly inhibited. This is because the colon ferments carbohydrates that have not been digested. Extracts from *Euphorbia hirta L.* appear to have a more balanced inhibitory action than synthetic inhibitors, which helps alleviate these symptoms; nevertheless, tolerance varies from person to person. Furthermore, certain populations may be at risk from bioactive alkaloids and other substances, including infants, pregnant or nursing women, and those with preexisting conditions related to the liver or kidneys. Exercise caution until these populations have had the opportunity to participate in targeted clinical trials to establish safety. Other things to consider include potential interactions with standard antidiabetic medications. The patient is at risk of hypoglycemia if they use *Euphorbia hirta L.* with a hypoglycemic drug at the same time without medical supervision because the two substances enhance each other's effects. Therefore, it may be necessary to closely monitor and modify dosages in the context of combined therapy[25].

Clinical Safety Data and Research Gaps

Few details about the clinical safety of *Euphorbia hirta L.* are available at this time. Preclinical studies and traditional applications constitute the bulk of the evidence. Determining its safety profile in human subjects, optimal dosage regimens, and side effects in both short- and long-term use requires well-designed clinical trials. Extracts are crucial for ensuring safety and repeatability. The efficacy and toxicity of phytochemicals can be affected by differences in plant source, harvesting conditions, and extraction processes. It will be easier to obtain regulatory approval and use formulations containing standardized amounts of bioactive components in clinical practice[26].

Therapeutic Potential and Clinical Implications

Numerous pharmacological actions, as confirmed by preclinical research, account for the pharmacological properties of *Euphorbia hirta L.* L., which have shown great promise in the treatment of diabetes. The primary mechanism by which it reduces blood sugar levels is through inhibiting two digestive enzymes, α-amylase and α-glucosidase. These enzymes postpone carbohydrate breakdown and glucose absorption, leading to a decrease in postprandial hyperglycemia. By targeting two enzymes simultaneously, rather than just one, blood glucose levels can be more easily managed. *Euphorbia hirta L.* contains many flavonoids, tannins, and phenolic chemicals, which explain why the plant inhibits enzymes and has powerful antioxidant and anti-inflammatory effects. Oxidative stress that leads to insulin resistance and malfunctioning pancreatic cells can be mitigated by these bioactive components. The plant's ability to scavenge reactive oxygen species, regulate inflammatory pathways, preserve β-cells, and improve insulin sensitivity can help alleviate diabetic symptoms and slow their progression[27].

Additionally, in vivo studies have shown that E. hirta improves insulin sensitivity and can maintain or restore pancreatic β-cells, which are crucial in both type 1 and type 2 diabetes, when insulin resistance and insulin insufficiency are present. Regarding lipid metabolism, the plant has demonstrated beneficial effects, including an increase in HDL-C and a decrease in total cholesterol, triglycerides, and LDL-C levels. Cardiovascular protection is a major concern in people with diabetes, and these improvements can help with that[28].

Euphorbia hirta L. may serve as a potential replacement or complement to current antidiabetic drugs, given its clinical promise. Patients seeking plant-based medicines or supplementary therapies to enhance treatment outcomes may find it appealing owing to its natural origin and favorable safety profile. In contrast to synthetic α-amylase and α-glucosidase inhibitors, such as acarbose, which can cause side effects, including bloating and diarrhea, the balanced phytochemical composition of *Euphorbia hirta L.* suggests that it may be an effective enzyme inhibitor with fewer side effects, leading to higher patient compliance. Its accessibility and cost-effectiveness enhance its clinical benefits, which is especially advantageous in low-resource environments where pharmaceutical solutions may be scarce. Although the plant has a long history of medicinal use, rigorous scientific testing is necessary to confirm its efficacy and safety before it can be included in both conventional and alternative medical systems[29].

Owing to differences in phytochemical content among plant parts, harvest times, and extraction methods, there is no universally accepted method for standardized E. hirta extracts. Standardized formulations with defined doses of bioactives are required to obtain consistent therapeutic results. Clinical studies should determine the optimal dose schedule to obtain the maximum benefit from drugs with

the fewest side effects. Close monitoring may be necessary to avoid hypoglycemia because of safety concerns, such as the potential for minor gastrointestinal side effects due to enzyme inhibition and interactions with traditional anti-diabetic medications. The current lack of thorough clinical safety data emphasizes the importance of designing investigations that use human subjects. Randomized controlled trials to validate preclinical findings, elucidate molecular processes, and develop improved formulations with enhanced bioavailability and stability are potential avenues for future studies. The safety and effectiveness of using E. hirta to control diabetes, which has enzyme-inhibitory, antioxidant-protective, insulin-sensitizing, and lipid profile-enhancing properties, must be ensured through pharmacovigilance and post-marketing surveillance. The successful application of this natural antidiabetic agent—which is safe, efficacious, and affordable will depend on resolving the challenges related to standardization, dose, and clinical validation[30].

Research Gaps and Future Directions

There are several knowledge gaps that must be addressed before the antidiabetic potential and therapeutic use of *Euphorbia hirta L.* can be fully realized. Little is known about actual clinical instances involving humans, and the majority of the available data comes from in vitro and animal studies. This limitation emphasizes the need for adequate clinical trials to establish effectiveness, safety, dose, and long-term consequences in individuals with diabetes. The lack of uniformity in the extraction of *Euphorbia hirta L.* is a major weakness. Because of variations in phytochemical content due to factors such as plant part used, geographical origin, harvest time, extraction method, and others, the therapeutic benefits are not constant. Standardized extraction techniques and concentration definitions of bioactive chemicals are critical for achieving safety and efficacy repeatability. The difficulty in applying preclinical findings to clinical practice stems from the lack of such consistency[31]. The identification and isolation of the phytoconstituents with the greatest anti-diabetic activity is another area that requires additional study. It is necessary to clarify the precise substances and the ways in which they interact with one another; however, flavonoids, tannins, alkaloids, and phenolic compounds have all been suspected. Isolating lead molecules from Phyto transformed leads using bioactivity-directed fractionation and enhanced phytochemical characterization might aid in focused medication development and better formulation methods. Molecular routes other than the inhibition of digestive enzymes have received little attention in mechanistic research. The diverse antidiabetic benefits of phytochemicals from *Euphorbia hirta L.* could be better understood with multifactorial research of their effects on insulin signaling, glucose transporters, inflammation, and pancreatic beta-cell regeneration. These findings could be valuable in developing more effective combination therapies or novel compounds[32].Humans are particularly vulnerable because of the lack of appropriate safety considerations. No information regarding clinical safety, including potential side effects, contraindications, or drug interactions, is available, even though preclinical toxicology tests show a positive safety profile. Longitudinal toxicity and pharmacovigilance studies are necessary to ensure the safe incorporation of E. hirta into diabetes treatment, especially when it is used with conventional antidiabetic medications. Dosage optimization is another significant area of research. There is a lack of information on therapeutic windows and human-equivalent doses; however, the current literature reveals a range of effective doses in animal models. The goal of determining optimal dosage regimens is to maximize therapeutic benefits while minimizing negative effects[33]. The bioavailability and pharmacokinetics of phytochemicals from E. hirta have not been extensively studied. To create formulations and delivery systems that consistently produce therapeutic levels in the plasma, it is crucial to comprehend the absorption, metabolism, distribution, and excretion profiles. Clinical trials on the plant's impact on different age groups, types of diabetes (type 1 and type 2), and comorbidities may be beneficial. Neuropathy, nephropathy, and cardiovascular disease are some of the diabetic consequences that might be treated to expand its therapeutic spectrum[34].

Finally, regulatory concerns are another aspect of healthcare systems that must be addressed when *Euphorbia hirta L.* is integrated. Strict quality control, standard production procedures, and compliance with regulatory standards are required for its approval as a safe, effective, and standardized natural antidiabetic drug[35].

Conclusion

The ability of *Euphorbia hirta L.* to inhibit digestive enzymes α-amylase and α-glucosidase makes it a potential natural antidiabetic drug, and this review provides an overview of the subject. Lowering postprandial

hyperglycemia is a goal of diabetes care, and this dual inhibition decreases carbohydrate digestion and glucose uptake. The phytochemical composition of the plant, which includes tannins, alkaloids, flavonoids, and phenolic compounds, confers enzyme inhibitory activities, strong antioxidant capabilities, and anti-inflammatory properties. In particular, insulin sensitivity is enhanced, pancreatic 1-cells are preserved, and oxidative stress and inflammation are reduced. Researchers have shown that extracts of *Euphorbia hirta L.* can protect the hearts of diabetic rats in several ways, including lowering blood glucose, increasing insulin sensitivity, and positively changing lipid profiles. Traditional use and evidence from animal studies corroborate the plant's generally acceptable safety and toxicity profile, lending credence to its prospective therapeutic use. *Euphorbia hirta L.* can be used instead of synthetic enzyme inhibitors to improve glycemic control and patient compliance, as the latter can have more gastrointestinal side effects. However, challenges remain on the path to clinical translation. Extensive clinical trials confirming efficacy and safety in humans are necessary, as are standardized extracts with established bioactive content and suitable dose schedules. Additional research is required to fully understand pharmacokinetics, potential medication interactions, and molecular mechanisms. Resolving these issues will facilitate the incorporation of *Euphorbia hirta L.* into diabetes management as an affordable, readily available, and easy-to-use supplemental medicine. To manage diabetes holistically, *Euphorbia hirta L.* inhibits enzymes, protects against oxidation, increases insulin effectiveness, and regulates lipids. Owing to its thorough clinical validation and standardization, it shows great promise as a safe, natural, and effective alternative to or supplement to antidiabetic medication treatment.

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Conflict of Interest

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

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