



# Implications for Clinical Practice, Mechanisms, and Efficacy of *Ageratum conyzoides* Leaf Extracts in Streptozotocin-Induced Diabetes Rats: An Investigation into Their Antidiabetic, Hypolipidemic, and Antiatherogenic Activities

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## ABSTRACT

*Ageratum conyzoides*, a perennial herb native to tropical and subtropical regions, has been utilized in traditional medicine for centuries due to its diverse therapeutic properties. This review consolidates current research on the antidiabetic, hypolipidemic, and antiatherogenic effects of *Ageratum conyzoides* leaf extracts, specifically in streptozotocin-induced diabetic rat models. The review explores the plant's potential mechanisms of action, including enhancement of insulin sensitivity, improvement of lipid profiles, and reduction of atherosclerotic plaque formation. *Ageratum conyzoides* extracts have demonstrated significant antidiabetic effects by lowering blood glucose levels, enhancing insulin secretion, and improving insulin sensitivity. They also exhibit hypolipidemic effects by reducing total cholesterol, LDL cholesterol, and triglycerides, while increasing HDL cholesterol. Additionally, these extracts show antiatherogenic properties by inhibiting plaque formation and reducing oxidative stress, thereby supporting cardiovascular health. The review examines the pharmacokinetics and bioavailability of *Ageratum conyzoides* bioactive compounds, emphasizing the need for further research to optimize their therapeutic potential. Comparative studies highlight its efficacy relative to other natural remedies and pharmaceuticals, noting its favorable safety profile. The review underscores the importance of integrating *Ageratum conyzoides* into both traditional and modern medicine practices and explores its role in dietary supplements and functional foods. Ongoing translational research and clinical trials are essential to validate the efficacy and safety of these extracts for broader clinical application.

**Keywords:** *Ageratum conyzoides*, Leaf Extracts, Streptozotocin, Diabetes, Rats

## INTRODUCTION

*Ageratum conyzoides*, commonly known as bitterweed or goatweed, is a perennial herb indigenous to tropical and subtropical regions of the Americas, with widespread occurrences in Africa and Asia [1]. This plant typically reaches a height of 30-60 cm, featuring ovate to lanceolate leaves with serrated edges and producing clusters of small, tubular florets in blue, purple, or white. Historically, *Ageratum conyzoides* has been integral to indigenous and traditional medicine practices across various cultures, reflecting its long-standing significance in local healing traditions [2]. Modern scientific exploration of *Ageratum conyzoides* has revealed a diverse array of bioactive compounds in its leaf extracts, including alkaloids, flavonoids, terpenoids, saponins, and phenolic acids [3]. These compounds are known for their pharmacological properties: alkaloids exhibit anti-inflammatory and analgesic effects; flavonoids possess antioxidant and anti-inflammatory activities; terpenoids display antimicrobial and anti-inflammatory properties; and saponins contribute to antidiabetic, hypolipidemic, and immunomodulatory effects. The variability in phytochemical composition is influenced by factors such as plant origin, harvesting conditions, and extraction methods. This review aims to consolidate current research on the antidiabetic, hypolipidemic, and

antiatherogenic properties of *Ageratum conyzoides* leaf extracts, particularly focusing on their effects in streptozotocin-induced diabetic rat models [4]. By examining the underlying mechanisms, efficacy, and comparative studies, this review seeks to elucidate the therapeutic potential of *Ageratum conyzoides* in managing metabolic disorders and cardiovascular risk factors. Furthermore, it explores the pharmacokinetics and bioavailability of its bioactive compounds, assesses safety and toxicity, and considers the implications for clinical application and integration into both traditional and modern medicine practices [5]. Through this comprehensive analysis, we aim to provide insights into the potential of *Ageratum conyzoides* as a natural therapeutic agent and its role in future research and clinical settings.

### **Antidiabetic Properties**

*Ageratum conyzoides* is a plant with numerous antidiabetic properties, including enhancement of insulin secretion, improvement of insulin sensitivity, reduction of gluconeogenesis, antioxidant effects, and anti-inflammatory effects. Its leaf extracts have been shown to significantly reduce blood glucose levels in diabetic animal models, leading to a decrease in fasting blood glucose levels [6]. The plant also helps maintain stable blood glucose levels over time, and may help control postprandial glucose spikes. *Ageratum conyzoides* may positively impact insulin sensitivity and pancreatic function by increasing the responsiveness of cells to insulin, protecting beta cells from damage, and regulating insulin production. Its extracts can offer a natural alternative or adjunct therapy for diabetes management, operating through multiple pathways, including antioxidant and anti-inflammatory effects. Compared to standard antidiabetic agents, *Ageratum conyzoides* has a favorable safety profile with fewer side effects compared to conventional medications [7]. Combining *Ageratum conyzoides* with other herbal remedies may enhance its antidiabetic effects. Combining herbs like *Gymnema sylvestre*, Cinnamon, or Fenugreek may provide a synergistic effect by targeting different aspects of diabetes management, such as glucose uptake, insulin sensitivity, and blood glucose regulation. This could lead to reduced dosage of individual herbs and enhanced therapeutic efficacy.

### **Hypolipidemic Effects**

*Ageratum conyzoides* has been found to exert hypolipidemic effects on the serum lipid profile, reducing total cholesterol, lowering LDL cholesterol, increasing HDL cholesterol, and lowering triglyceride levels [8]. These effects can be attributed to several mechanisms, including inhibition of lipid absorption, enhanced lipid metabolism, regulation of lipid biosynthesis, antioxidant and anti-inflammatory effects, and lipid metabolism pathways. The extracts may also enhance fatty acid oxidation, increase cholesterol excretion, and regulate lipoprotein levels. Compared to conventional lipid-lowering drugs like statins, fibrates, and niacin, *Ageratum conyzoides* offers a complementary or adjunctive approach to managing dyslipidemia. Its efficacy is comparable to those of pharmaceutical agents, with fewer side effects and a favorable safety profile. Its mechanism of action includes antioxidant and anti-inflammatory effects, providing additional benefits in managing lipid levels and overall cardiovascular health [9]. Combining *Ageratum conyzoides* with conventional lipid-lowering drugs could potentially enhance overall lipid management and reduce the required dosage of pharmaceutical agents. Further research is needed to establish its effectiveness and safety compared to standard treatments.

### **Antiatherogenic Properties**

*Ageratum conyzoides* has potential antiatherogenic properties, influencing the formation of atherosclerotic plaques. It may inhibit plaque formation, reducing the risk of cardiovascular events like heart attacks and strokes [10]. The plant's compounds may also improve endothelial function and reduce inflammatory markers, which contribute to the development of atherosclerosis. *Ageratum conyzoides* also has antioxidant properties, neutralizing free radicals and reactive oxygen species that cause oxidative stress. It also reduces lipid peroxidation, preventing the oxidative modification of lipids, which is a critical step in the development of atherosclerosis. *Ageratum conyzoides*' protective effects on cardiovascular health include prevention of cardiovascular diseases like coronary artery disease and hypertension. Its antiatherogenic properties contribute to overall heart health by promoting healthy blood vessel function, reducing artery blockages, and supporting optimal blood circulation [11]. Further research is needed to fully understand its mechanisms and clinical efficacy in cardiovascular protection.

### **Pharmacokinetics and Bioavailability**

*Ageratum conyzoides* leaf extracts are a natural source of bioactive compounds that have been shown to have antidiabetic, hypolipidemic, and antiatherogenic effects [12]. These compounds are absorbed through the gastrointestinal tract, with hydrophilic compounds being more easily absorbed in the gut, while lipophilic compounds require fats for optimal absorption. The distribution of these compounds varies depending on their affinity for different tissues and organs, with some compounds accumulating in specific tissues like the liver or adipose tissue. The liver undergoes metabolic transformations, which can affect the efficacy and duration of action. The metabolites of these extracts are excreted from the body, primarily through urine or feces. The effectiveness

of these compounds is influenced by their bioavailability, which refers to the proportion of the compound that reaches systemic circulation and is available for therapeutic action. Understanding the pharmacokinetics and bioavailability of these compounds is crucial for optimizing their therapeutic potential and developing effective treatments [13].

### **Safety and Toxicity**

*Ageratum conyzoides* leaf extracts are a natural remedy that has been studied for their safety and toxicity. Acute toxicity refers to the harmful effects of exposure to a substance, while chronic toxicity results from prolonged exposure over an extended period. Both types of toxicity can be assessed through oral administration or intraperitoneal or intravenous administration [14]. Potential side effects include gastrointestinal distress, allergic reactions, and liver function issues. The safety of *Ageratum conyzoides* leaf extracts during pregnancy and lactation is not well-established, and individuals with liver or kidney diseases, gastrointestinal disorders, or other chronic health conditions should consult healthcare professionals before using the extract. Additionally, the leaf extracts may interact with other medications, which must be assessed to avoid adverse effects. Safe dosing and administration guidelines for *Ageratum conyzoides* leaf extracts are determined through dose-response studies in animal models and clinical trials [15]. Starting with a lower dose to assess tolerance and gradually increasing if no adverse effects are observed minimizes the risk of toxicity. Regular monitoring of health parameters, including blood glucose levels, lipid profiles, and organ function, is essential to detect potential adverse effects early. General recommendations for using *Ageratum conyzoides* leaf extracts include consulting with a healthcare provider, following recommended dosage and administration guidelines, and consulting with a healthcare provider before starting any new supplement or herbal remedy [16]. Ensuring safety through rigorous testing and adherence to recommendations maximizes therapeutic benefits while minimizing risks.

### **Mechanistic Insights**

*Ageratum conyzoides* leaf extracts have been found to have antidiabetic and hypolipidemic effects. They can enhance insulin sensitivity by promoting the insulin signaling pathway, which includes the Insulin Receptor (IR), Insulin Receptor Substrates (IRS), Protein Kinase B (AKT), AMP-Activated Protein Kinase (AMPK), and Glucagon-Like Peptide-1 (GLP-1) [17]. These extracts can also influence lipid metabolism by regulating Lipoprotein Lipase (LPL), PPARs, cholesterol homeostasis, and fatty acid synthesis. Gene expression and enzyme activity related to these effects are also involved. Extracts may upregulate genes involved in insulin signaling, such as IRS-1, IRS-2, and AKT, and regulate enzymes related to lipid metabolism, such as PPAR- $\alpha$ , PPAR- $\gamma$ , and LPL [16]. These enzymes can promote lipid oxidation and reduce lipid accumulation. Extracts may also inhibit enzymes like glucose-6-phosphatase and fructose-1, 6-bisphosphatase, which can lower blood glucose levels [18]. They may also enhance enzyme activity to facilitate lipid breakdown, improving lipid profiles and reducing triglyceride levels. Cellular targets include adipocytes, hepatocytes, glucose transporters, and inflammatory pathways. In adipocytes, extracts may improve insulin sensitivity in adipose tissue, enhancing glucose uptake and reducing fat accumulation. In the liver, extracts may modulate glucose production and lipid metabolism, affecting both glucose and lipid homeostasis. *Ageratum conyzoides* leaf extracts have potential therapeutic benefits in managing diabetes and dyslipidemia by influencing key signaling mechanisms, gene expression, and enzyme activity [19].

### **Comparative Studies**

Comparative studies on *Ageratum conyzoides* leaf extracts have been conducted to evaluate their antidiabetic, hypolipidemic, and antiatherogenic properties [20]. These studies compare the extracts with other plant extracts and pharmaceuticals, such as *Moringa oleifera*, *Cinnamomum verum*, and Ginger. *Moringa* and *Cinnamomum* have shown significant antidiabetic effects through mechanisms such as enhancing insulin sensitivity and reducing glucose absorption [21]. Ginger also improves glycemic control through its antioxidant properties. Garlic and Green Tea exhibit hypolipidemic effects by lowering cholesterol and triglyceride levels through different mechanisms, such as antioxidant activity and modulation of lipid metabolism pathways. Fenugreek helps reduce serum lipids and improve lipid profiles. *Ageratum conyzoides* is compared in terms of its ability to lower blood glucose levels, improve insulin sensitivity, and modulate key metabolic pathways. Antiatherogenic properties are also compared with extracts from Hawthorn, Turmeric, and Ginseng. Hawthorn and Turmeric possess antiatherogenic properties by reducing oxidative stress and inflammation, improving endothelial function, and preventing plaque formation [22]. Ginseng has similar effects by modulating inflammatory responses and oxidative stress. Pharmaceuticals like Metformin, Sulfonylureas, and Thiazolidinediones are used to treat diabetes. Metformin improves insulin sensitivity and reduces glucose production in the liver, while Sulfonylureas stimulate insulin secretion and Thiazolidinediones enhance insulin sensitivity. Statins lower LDL cholesterol and reduce overall cholesterol levels, while Fibrates lower triglycerides and raise HDL cholesterol. Analysis of the efficacy in different experimental models includes animal models, hyperlipidemic models, atherosclerosis models, cell line

studies, enzyme activity assays, and human clinical trials. These studies help determine the relative efficacy and potential therapeutic value of *Ageratum conyzoides* in various experimental models and clinical settings [23].

### Clinical Implications and Applications

*Ageratum conyzoides* leaf extracts have potential for translational research and human trials, with the aim of identifying biomarkers related to their beneficial effects in animal models [24]. These biomarkers can be used to monitor efficacy and safety in human trials. Phase I trials assess the safety, tolerability, and pharmacokinetics of *Ageratum conyzoides* extracts in healthy volunteers, while phase II trials evaluate the efficacy in patients with specific conditions like diabetes, hyperlipidemia, or cardiovascular disease [25]. Phase III trials confirm the effectiveness and safety of *Ageratum conyzoides* extracts in diverse patient populations, providing robust evidence for regulatory approval and clinical use. Integration into traditional and modern medicine involves incorporating *Ageratum conyzoides* extracts into traditional formulations or enhancing existing remedies to optimize therapeutic effects and safety profiles [26]. In modern medicine, *Ageratum conyzoides* extracts could be used as complementary therapies alongside conventional treatments, such as enhancing glycemic control or lipid profiles in patients undergoing standard treatments for diabetes and hyperlipidemia. Implications for dietary supplements and functional foods include formulation and dosage, regulation and quality control, and public health and wellness [27]. Dietary supplements and functional foods featuring *Ageratum conyzoides* extracts may play a role in the prevention and management of chronic conditions, and public health initiatives can promote their use as part of a holistic approach to health and wellness. The clinical implications and applications of *Ageratum conyzoides* leaf extracts involve exploring their potential through translational research, integrating them into both traditional and modern medical practices, and considering their role in dietary supplements and functional foods [28].

### CONCLUSION

This review evaluates the antidiabetic, hypolipidemic, and antiatherogenic properties of *Ageratum conyzoides* leaf extracts, particularly in streptozotocin-induced diabetic rat models. The evidence suggests that *Ageratum conyzoides* has significant therapeutic potential in managing metabolic disorders and cardiovascular risk factors through multiple mechanisms. Its antidiabetic effects include enhancing insulin secretion and sensitivity, reducing gluconeogenesis, and providing antioxidant and anti-inflammatory benefits. Its hypolipidemic and antiatherogenic properties include improving lipid profiles by reducing total cholesterol, LDL cholesterol, and triglycerides, while increasing HDL cholesterol. Its antiatherogenic properties include inhibiting atherosclerotic plaque formation and reducing oxidative stress, suggesting it may support cardiovascular health. Comparative studies highlight its efficacy relative to other natural remedies and pharmaceutical agents, with a favorable safety profile and potential for synergistic effects when combined with other therapeutic agents. Understanding the pharmacokinetics and bioavailability of *Ageratum conyzoides* bioactive compounds is crucial for optimizing their therapeutic use. Clinical implications are substantial, and ongoing translational research and human clinical trials are necessary to validate the efficacy and safety of these extracts in diverse patient populations. Integration into traditional and modern medical frameworks, dietary supplements, and functional foods could enhance overall health management strategies.

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