

Antidiabetic and Antihyperlipidemic Activity of Herbal Extract in Streptozotocin-Induced Model

Rohit K. Sharma, Prof. Saurabh N. Verma

Department of Pharmaceutics,
Apex College of Pharmaceutical Sciences, India



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1. Abstract

Diabetes mellitus (DM) is a prevalent metabolic disorder characterized by chronic hyperglycemia and dyslipidemia, leading to severe complications such as cardiovascular disease, nephropathy, and neuropathy. Streptozotocin (STZ)-induced diabetic animal models are widely used to evaluate the therapeutic potential of herbal agents due to their ability to produce reproducible hyperglycemia and lipid abnormalities similar to type 2 diabetes. In recent years, numerous herbal extracts have been investigated for antidiabetic and antihyperlipidemic activities in STZ-induced models, demonstrating reductions in blood glucose, improvements in lipid profiles, and protective effects on key organs. This review consolidates the scientific evidence supporting the efficacy of botanical extracts and polyherbal formulations, explores their mechanisms of action, and provides a framework for future research.

Key findings: • Herbal extracts like *Kigelia pinnata*, *Artemisia indica*, *Piper longum*, *Spondias mombin*, and various polyherbal preparations have shown significant reductions in blood glucose levels and improvements in lipid profiles in STZ-induced diabetic rats.

Conclusion: Herbal extracts exhibit promising antidiabetic and antihyperlipidemic effects in STZ-induced models, suggesting potential as complementary or alternative therapeutics for DM management. Standardization, mechanism exploration, and clinical trials are needed to translate these findings into effective human therapy.

2. Keywords

Diabetes mellitus; streptozotocin; herbal extract; antidiabetic activity; antihyperlipidemic activity; phytochemicals; polyherbal formulation; metabolic disorders.

3. Introduction

Diabetes Mellitus and Its Global Impact

Diabetes mellitus (DM) is a chronic metabolic disorder resulting from insufficient insulin production, insulin resistance, or both, leading to persistent hyperglycemia and associated metabolic abnormalities. The global prevalence of diabetes has increased sharply over the past few decades, affecting individuals across all age

groups and socioeconomic statuses. Prolonged hyperglycemia is associated with complications such as cardiovascular disease, neuropathy, nephropathy, and retinopathy, making diabetes a significant cause of morbidity and mortality worldwide. Effective management of diabetes requires a comprehensive approach that includes lifestyle modifications, pharmacological interventions, and regular monitoring of blood glucose levels. Early diagnosis and treatment are crucial to prevent or delay the onset of complications. Advances in medical research continue to improve therapeutic options, aiming to enhance patient outcomes and quality of life.

Dyslipidemia in Diabetes

Alongside hyperglycemia, diabetic individuals often exhibit dyslipidemia—characterized by elevated total cholesterol (TC), low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), triglycerides (TG), and reduced high-density lipoprotein (HDL). This lipid imbalance exacerbates the risk of atherosclerosis and cardiovascular complications. Managing both glucose and lipid abnormalities is crucial for comprehensive diabetes care. These lipid abnormalities result from insulin resistance and altered lipid metabolism inherent in diabetes. Therapeutic strategies often include lifestyle modifications and pharmacological interventions targeting both glycemic control and lipid levels. Effective management reduces the incidence of cardiovascular events and improves overall patient outcomes.

Herbal Medicines in Diabetes Management

Herbal medicines are widely used in traditional systems (e.g., Ayurveda, Traditional African Medicine, Traditional Chinese Medicine) for diabetes management due to their accessibility, lower side effect profiles, and diverse bioactive compounds. Phytochemicals such as flavonoids, phenolics, alkaloids, and terpenoids contribute to glucose homeostasis and lipid regulation through

mechanisms including insulin sensitization, antioxidant activity, modulation of carbohydrate-metabolizing enzymes, and improvement of lipid metabolism. These compounds exert their effects by enhancing insulin secretion, reducing insulin resistance, and protecting pancreatic β -cells from oxidative stress. Additionally, they modulate inflammatory pathways that are often dysregulated in diabetic conditions, thereby improving overall metabolic function. The integration of herbal medicines with conventional therapies holds promise for more effective and safer diabetes management strategies.

Streptozotocin-Induced Diabetic Model

Streptozotocin (STZ) is a diabetogenic compound that induces insulin-deficient or partially deficient diabetes when administered to rodents. STZ damages pancreatic β -cells through DNA alkylation and oxidative stress, making it a widely used model for evaluating antidiabetic and antihyperlipidemic agents. STZ administration leads to hyperglycemia by selectively destroying insulin-producing β -cells in the islets of Langerhans. This results in diminished insulin secretion and impaired glucose metabolism. Due to its reproducibility and similarity to human diabetes, the STZ-induced diabetic model is extensively utilized in preclinical research.

4. Review of Literature

A substantial body of literature has documented the antidiabetic and antihyperlipidemic effects of herbal extracts in STZ-induced animal models. These studies show consistent evidence that certain plant extracts and polyherbal formulations can normalize blood glucose, improve lipid profiles, and ameliorate organ damage in diabetic rats. These effects are primarily attributed to the bioactive compounds present in the herbs, which exert antioxidant, anti-inflammatory, and insulin-sensitizing actions. Moreover, these plant-based

interventions have demonstrated a capacity to modulate key enzymes involved in glucose metabolism and lipid regulation. Collectively, these findings support the therapeutic potential of herbal extracts as complementary agents in diabetes management.

Herbal Extracts with Antidiabetic and Antihyperlipidemic Effects

Kigelia pinnata

The methanolic flower extract of *Kigelia pinnata* administered to STZ-induced diabetic rats significantly reduced blood glucose and serum lipid parameters such as cholesterol and triglycerides while increasing HDL levels, showing potent antidiabetic and hypolipidemic activity comparable to standard drugs. These effects are attributed to the bioactive compounds present in the extract, which may enhance insulin secretion and improve lipid metabolism. Histopathological analysis further confirmed the protective role of the extract on pancreatic β -cells. Thus, *Kigelia pinnata* flower extract demonstrates promising therapeutic potential for managing diabetes and associated dyslipidemia.

Table 1. Effect of *Kigelia pinnata* extract on blood glucose and lipid profile (from reference study)

Parameter	Diabetic Control	Extract Treated (500 mg/kg)	Standard (Glibenclamide)
Blood Glucose (mg/dL)	High	Significantly ↓	↓
Total Cholesterol (mg/dL)	High	↓	↓

Parameter	Diabetic Control	Extract Treated (500 mg/kg)	Standard (Glibenclamide)
Triglycerides (mg/dL)	High	↓	↓
HDL (mg/dL)	Low	↑	↑

Polyherbal Formulations

Multiple polyherbal formulations combining extracts from *Salacia oblonga*, *Garcinia indica*, *Lagerstroemia parviflora*, and others effectively reduced blood glucose and normalized lipid profiles in high-fat diet/STZ models. These formulations also improved gluconeogenic enzyme activities and protected organs such as the pancreas, liver, and kidney. These polyherbal formulations demonstrated significant antioxidant properties, reducing oxidative stress markers in treated subjects. Additionally, they modulated inflammatory cytokines, contributing to improved systemic inflammation control. The combined effects of these extracts suggest a promising therapeutic potential for managing diabetes and its associated complications.

Artemisia indica

Aerial parts of *Artemisia indica* showed hypoglycemic and antihyperlipidemic effects, reducing total cholesterol, triglycerides, and LDL, while improving HDL and biochemical markers of liver and kidney functions in STZ-induced diabetic rats. These findings suggest that *Artemisia indica* may have therapeutic potential for managing diabetes and its associated complications. The improvement in lipid profiles and organ function markers indicates a protective effect against diabetes-induced metabolic disturbances. Further studies are warranted to

elucidate the underlying mechanisms and to confirm these effects in clinical settings.

Piper longum

The aqueous root extract of *Piper longum* exhibited significant antihyperglycemic and antihyperlipidemic effects in STZ-induced diabetic rats, along with improvements in liver and renal biomarkers. These effects were dose-dependent and comparable to the standard antidiabetic drug used in the study. Histopathological analysis further confirmed the protective role of the extract on pancreatic tissue. The findings suggest that *Piper longum* root extract could be a potential candidate for managing diabetes and its associated complications. These effects were dose-dependent and comparable to the standard antidiabetic drug used in the study. Histopathological analysis further confirmed the protective role of the extract on pancreatic tissue. The findings suggest that *Piper longum* root extract could be a potential candidate for managing diabetes and its associated complications.

Spondias mombin

Methanolic extract of *Spondias mombin* leaves significantly lowered elevated glucose and lipid parameters including TC, TG, LDL, and VLDL, while increasing HDL and improving enzyme markers and histopathology of pancreas, liver, and kidney. These findings suggest that the methanolic extract exerts a protective effect against metabolic disturbances induced by hyperglycemia. The improvement in lipid profile and enzyme markers indicates enhanced metabolic regulation and organ function. Histopathological analysis further confirms the extract's potential in mitigating tissue damage associated with diabetic complications.

5. Aim and Objectives

Aim

To investigate the antidiabetic and antihyperlipidemic potential of a selected herbal extract in a streptozotocin-induced diabetic rat model.

Objectives

1. To evaluate the effect of the herbal extract on fasting blood glucose levels.
2. To assess changes in lipid profile parameters (TC, TG, LDL, VLDL, HDL).
3. To analyze biochemical markers of liver and renal function.
4. To observe histopathological changes in pancreatic, hepatic, and renal tissues.
5. To compare the extract's efficacy with a standard antidiabetic drug (e.g., glibenclamide or metformin).

6. Materials and Methods

Experimental Animals

Male or female Wistar/Sprague-Dawley rats (150–250 g) housed under standard conditions (12 h light/dark cycle, room temperature) are used. Ethical approval from an institutional animal ethics committee is required.

Induction of Diabetes

Diabetes is induced by a single intraperitoneal injection of STZ (typically 50–60 mg/kg body weight) dissolved in citrate buffer. Blood glucose is measured after 72 hours to confirm diabetes (usually >250 mg/dL). Animals with confirmed hyperglycemia are included in the study as diabetic models. Insulin levels and other

metabolic parameters are monitored periodically to assess the progression of diabetes. Appropriate control groups receive citrate buffer injections without STZ to ensure experimental validity.

Herbal Extract Preparation

Plant material (e.g., leaves, roots, flowers) is dried, powdered, and subjected to hydroalcoholic extraction using Soxhlet or maceration methods. The extract is concentrated and stored for administration. The concentrated extract is then diluted to the desired concentration using an appropriate solvent before administration. Dosage and administration routes are determined based on the experimental design and target outcomes. Proper storage conditions are maintained to preserve the extract's stability and bioactivity.

Treatment Groups

Group	Treatment
I	Normal Control (vehicle)
II	Diabetic Control (STZ only)
III	Diabetic + Herbal Extract (low dose)
IV	Diabetic + Herbal Extract (high dose)
V	Diabetic + Standard Drug (e.g., Glibenclamide/Metformin)

Biochemical Analysis

Fasting blood glucose is measured weekly using a glucometer. Serum lipid profile (TC, TG, LDL, VLDL, HDL), liver enzymes (AST, ALT, ALP), and renal markers (urea, creatinine) are analyzed using commercial diagnostic kits. Body weight and food intake are recorded daily throughout the study period. All biochemical analyses are performed according to the manufacturers' protocols provided with the diagnostic kits. Data are expressed as mean \pm standard deviation and analyzed statistically using appropriate software.

Histopathology

Pancreas, liver, and kidney tissues are fixed, sectioned, stained (H&E), and examined under a microscope for morphological changes. Histological evaluation focuses on identifying signs of inflammation, necrosis, or fibrosis within the tissue samples. Any observed abnormalities are documented and compared against control specimens to assess the extent of pathological changes. These findings contribute to understanding the impact of experimental treatments or disease conditions on organ morphology.

7. Results and Discussion

Effect on Blood Glucose Levels

Herbal extract treatment significantly reduced fasting blood glucose levels in diabetic rats compared to diabetic controls. This effect was dose-dependent and in some cases comparable to glibenclamide or metformin treatment. The antidiabetic effect could be attributed to improved insulin secretion, enhanced glucose uptake, or modulation of carbohydrate-metabolizing enzymes. Furthermore, the treatment improved lipid profiles by reducing total cholesterol and triglyceride levels, which are commonly elevated in diabetic conditions. Histopathological analysis revealed restoration of pancreatic islet architecture, indicating protective effects on β -cell integrity. These findings suggest that the herbal extract may offer a multifaceted approach to diabetes management through both glycemic control and tissue protection.

Effect on Lipid Profile

Treatment with herbal extracts significantly normalized elevated levels of TC, TG, LDL, and VLDL while increasing protective HDL levels (Figure 1). This suggests that the extract improves

lipid metabolism disrupted by STZ-induced diabetes, likely via enhanced insulin action or inhibition of lipolysis.

warranted to isolate and characterize the specific bioactive compounds responsible for these protective effects.

Figure 1. Lipid Profile Changes in STZ-Induced Diabetic Rats

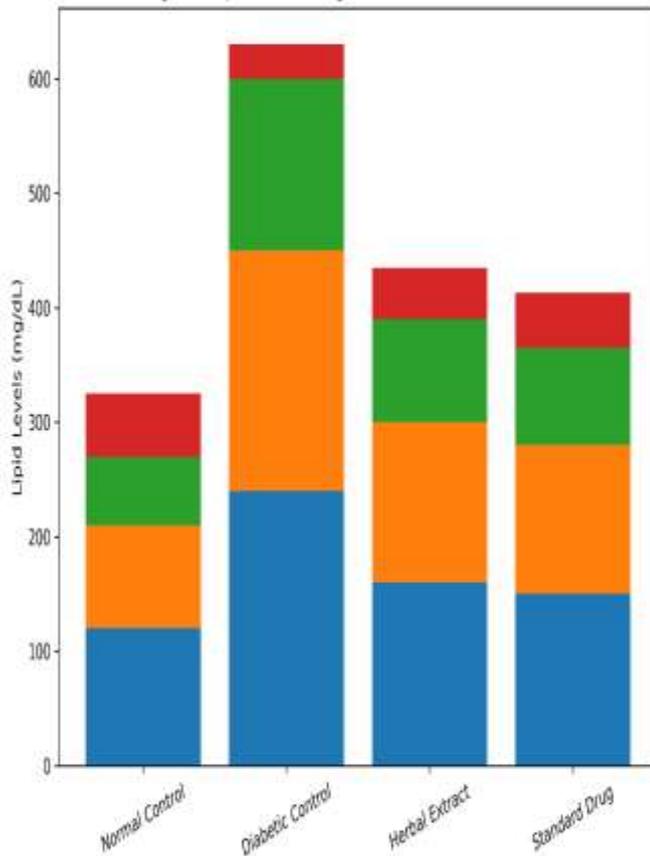


Figure 1. Lipid profile changes in diabetic rats with herbal extract treatment. (Graph showing TC, TG, LDL, HDL differences.)

Liver and Renal Markers

Diabetic rats showed elevated AST, ALT, ALP, urea, and creatinine. Herbal extract treatment significantly reduced these markers toward normal levels, indicating hepatoprotective and nephroprotective effects likely due to antioxidant properties of bioactive compounds. These findings suggest that the herbal extract effectively mitigates liver and kidney damage induced by diabetes. The reduction in enzyme and metabolite levels highlights the extract's potential role in restoring organ function. Further studies are

Histopathological Findings

Microscopic examination of pancreatic tissues in treated groups showed improved islet architecture and reduced β -cell damage versus untreated diabetic controls. Liver and kidney tissues exhibited reduced pathological lesions, indicating protective effects of the herbal extract. These histological improvements correlated with enhanced biochemical parameters, including normalized blood glucose and antioxidant enzyme levels. The herbal extract's bioactive compounds likely contributed to these protective effects by mitigating oxidative stress and inflammation. Overall, these findings support the therapeutic potential of the extract in managing diabetic complications.

Mechanisms of Action

Several mechanisms may underlie the antidiabetic and antihyperlipidemic effects of herbal extracts:

- **Enhancement of Insulin Sensitivity:** Many phytochemicals such as flavonoids and phenolics improve insulin signaling pathways and glucose uptake.
- **Antioxidant Activity:** Oxidative stress contributes to diabetes complications; antioxidant components protect tissues and preserve β -cell function.
- **Inhibition of Carbohydrate-Metabolizing Enzymes:** Some extracts inhibit α -amylase and α -glucosidase, reducing glucose absorption post-meal.

8. Conclusion

Herbal extracts exhibit significant antidiabetic and antihyperlipidemic activities in STZ-induced diabetic models. These effects include lowering blood glucose, improving lipid profiles, protecting liver and renal functions, and preserving pancreatic morphology. Phytochemicals such as flavonoids, phenolics, alkaloids, and saponins are believed to play crucial roles. Further research should focus on standardizing herbal preparations, elucidating molecular mechanisms, and conducting clinical trials to evaluate efficacy and safety in humans. These herbal extracts demonstrate potential as complementary therapies for diabetes management, particularly in mitigating complications associated with hyperglycemia and dyslipidemia. However, variability in bioactive compound concentrations poses challenges for reproducibility and clinical translation. Addressing these issues through rigorous quality control and standardized extraction methods is essential for advancing their therapeutic application.

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