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Anti-Diabetic Effect of Gymnema Sylvestre On Streptozotocin-Induced Diabetic Rats

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ABSTRACT

Gymnemate Sylvestre (Gs), a traditional medicinal plant known for its potent anti-diabetic properties, was investigated for its therapeutic potential in streptozotocin (STZ)-induced diabetic rats. Diabetes was induced by a single intraperitoneal injection of STZ (60 mg/kg), leading to hyperglycaemia, oxidative stress, and inflammatory responses characteristic of diabetic neuropathy. Following diabetes induction, rats received oral administration of Gs leaf extract at doses of 50 mg/kg and 100 mg/kg daily for five weeks. The treatment significantly decreased blood glucose levels and improved insulin secretion, demonstrating a restorative effect on pancreatic β-cell function. Gs also attenuated oxidative stress markers, including lipid peroxidation and antioxidant enzyme activities, in sciatic nerve tissues. Additionally, proinflammatory cytokines such as TNF-α, IL-1β, and IL-6, elevated in diabetic rats, were markedly reduced upon Gs treatment. Histopathological analysis revealed improvement in nerve tissue structure, indicating neuroprotective effects. The study supports that Gymnemate Sylvestre exerts multi-targeted anti-diabetic effects by modulating hyperglycaemia, oxidative stress, inflammation, and enhancing nerve growth factors. These findings highlight Gs as a promising natural therapeutic agent for diabetes management and its complications, especially diabetic neuropathy, warranting further clinical exploration.

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1. INTRODUCION

A. Overview of Diabetes Mellitus

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycaemia resulting from either a deficiency in insulin secretion, insulin action, or both. The global burden of diabetes is escalating rapidly, with millions affected worldwide. It is associated with severe complications such as cardiovascular diseases, nephropathy, neuropathy, and retinopathy, which significantly impact the quality of life and increase mortality. Conventional treatments, while effective to a degree, often present limitations such as side effects and high costs. Therefore, there is a growing interest in exploring alternative and complementary therapies, especially plant-based treatments, to manage and potentially reverse diabetic symptoms effectively.

B. Pathophysiology of Diabetes: Focus on Type 1 and Type 2

Diabetes mellitus is mainly categorized into Type 1 and Type 2. Type 1 diabetes is an autoimmune condition resulting in the destruction of pancreatic β-cells, leading to absolute insulin deficiency. Type 2 diabetes is more prevalent and is characterized by insulin resistance combined with relative insulin deficiency. Both types share common symptoms but differ significantly in onset, progression, and management. Understanding the underlying mechanisms of each type is crucial for developing effective therapeutic strategies. Experimental models such as streptozotocin-induced diabetes in rats mimic the pathophysiology of human diabetes and are instrumental for evaluating the efficacy of antidiabetic agents.

C. Limitations of Current Anti-Diabetic Therapies

Conventional anti-diabetic drugs, including insulin therapy and oral hypoglycaemics like metformin, sulfonylureas, and thiazolidinediones, have been widely used to manage blood glucose levels. However, these treatments often come with limitations such as gastrointestinal discomfort, risk of hypoglycaemia, weight gain, and long-term side effects. Additionally, these medications do not cure diabetes but only manage its symptoms. The rising prevalence of drug resistance and patient non-compliance further complicates treatment outcomes. Hence, there is a pressing need to discover safer, cost-effective, and more holistic approaches that not only regulate glucose levels but also target the root causes of diabetes.

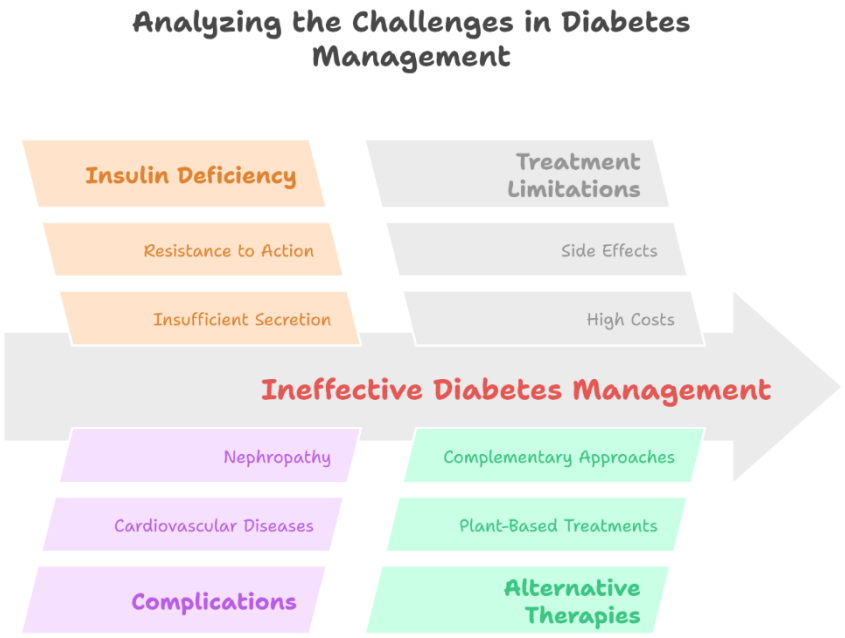

Fig 1: Overview of Diabetes Mellitus

D. Importance of Herbal Medicine in Diabetes Management

Herbal medicine has gained widespread acceptance as an alternative or complementary approach in the treatment of diabetes. Many medicinal plants possess bioactive compounds with hypoglycaemic, antioxidant, and anti-inflammatory properties. These natural agents offer a promising means to improve glycaemic control without the adverse effects associated with synthetic drugs. Furthermore, they often provide additional benefits such as improved lipid profiles, enhanced insulin sensitivity, and organ protection. Ethnobotanical studies and traditional healing practices have long utilized such plants, and modern research is increasingly validating their efficacy through rigorous scientific investigation, paving the way for new phytotherapeutic options.

E. Introduction to Gymnema sylvestre

Gymnema sylvestre, commonly known as “gurmar” or "sugar destroyer," is a woody climbing shrub native to the tropical forests of India and Africa. It has been traditionally used in Ayurvedic medicine for the treatment of diabetes, obesity, and other metabolic disorders. The plant is rich in bioactive compounds such as gymnemic acids, saponins, flavonoids, and alkaloids, which are believed to contribute to its antidiabetic properties. Gymnema sylvestre is particularly notable for its ability to suppress the taste of sweetness and reduce sugar absorption in the intestine, making it a promising candidate for natural diabetes therapy.

F. Bioactive Compounds of Gymnema sylvestre and Their Mechanisms

The pharmacological properties of Gymnema sylvestre are largely attributed to its diverse array of bioactive constituents. Gymnemic acids are the principal compounds that mimic glucose molecules and compete with them in the intestinal receptors, thus reducing glucose absorption. Flavonoids and saponins in the plant also exhibit antioxidant and anti-inflammatory effects, which help mitigate oxidative stress—a major contributor to diabetes-related complications. Furthermore, Gymnema sylvestre is believed to stimulate insulin secretion, regenerate pancreatic β-cells, and improve peripheral glucose uptake. These multi-targeted actions make it a compelling candidate for therapeutic interventions in diabetes management.

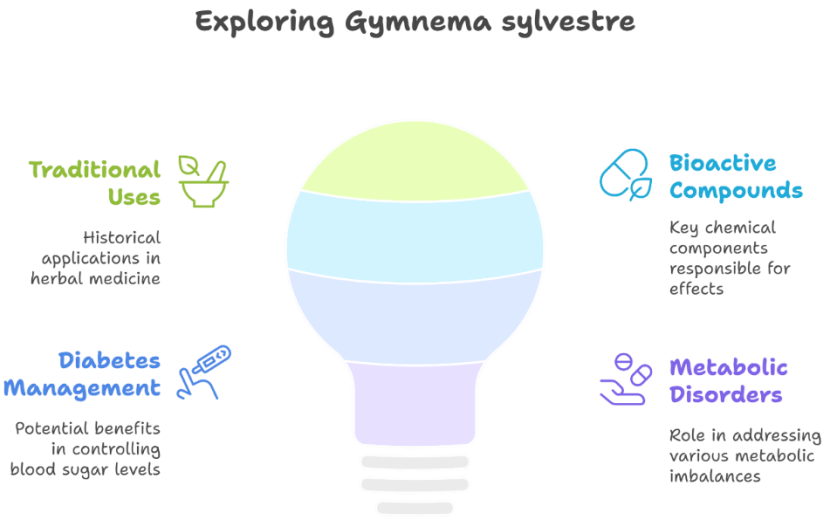

Fig 2: Introduction to Gymnema sylvestre

G. Streptozotocin-Induced Diabetes in Rats: A Research Model

Streptozotocin (STZ) is a naturally occurring chemical that selectively destroys pancreatic β-cells, leading to insulin deficiency and hyperglycemia. STZ-induced diabetic rat models closely mimic the biochemical and pathological features of Type 1 diabetes and, with dietary manipulation, aspects of Type 2 diabetes as well. These models are widely used in preclinical studies to assess the efficacy of antidiabetic agents. Their reproducibility, reliability, and physiological similarity to human diabetes make them invaluable in the early stages of drug discovery. The use of STZ models allows for controlled experimentation on potential therapeutic effects of natural products like Gymnema sylvestre.

H. Previous Studies on Gymnema sylvestre in Diabetes Research

Numerous in vitro and in vivo studies have highlighted the potential of Gymnema sylvestre in managing hyperglycemia. Research findings have shown that extracts of the plant can significantly lower blood glucose levels, enhance insulin secretion, and regenerate pancreatic tissues. Some clinical studies in humans have also reported promising results with improved glycemic control and reduced dependency on insulin or oral hypoglycemics. These outcomes support the ethnopharmacological uses of Gymnema sylvestre and justify further investigations. However, more standardized, controlled studies are necessary to understand its full therapeutic potential and to develop it into an evidence-based antidiabetic treatment.

I. Rationale for the Current Study

Given the limitations of existing diabetic therapies and the promising effects of Gymnema sylvestre observed in previous studies, there is a strong rationale for further investigation. The current study aims to evaluate the anti-diabetic effect of Gymnema sylvestre on STZ-induced diabetic rats, focusing on biochemical parameters, histopathological changes, and potential mechanisms of action. By using a well-established diabetic model, this research intends to provide scientific validation for the traditional use of Gymnema sylvestre and contribute to the development of safer and more effective plant-based antidiabetic therapies.

J. Objectives and Scope of the Study

The primary objective of this research is to assess the efficacy of Gymnema sylvestre in reducing blood glucose levels and improving diabetic symptoms in STZ-induced rats. Specific goals include analyzing changes in fasting glucose, lipid profiles, insulin levels, and pancreatic histology. The study also aims to identify the potential mechanisms by which Gymnema sylvestre exerts its effects. This research contributes to the broader scientific understanding of plant-based interventions in diabetes management and supports the integration of traditional medicinal plants into modern therapeutic frameworks, potentially leading to the development of novel antidiabetic formulations.

2. LITERATURE REVIEW

The anti-diabetic potential of *Gymnema sylvestre* has been extensively investigated in streptozotocin-induced diabetic rat models. Several studies have reported significant reductions in blood glucose levels following treatment with *Gymnema sylvestre* extracts. These extracts not only exert hypoglycemic effects but also demonstrate improvements in lipid profiles and enhanced glucose tolerance, comparable to standard hypoglycemic agents like glibenclamide [1][2]. Furthermore, *Gymnema sylvestre* has shown insulinotropic properties by stimulating insulin secretion and enhancing glucose utilization, which may be attributed to the regeneration or protection of pancreatic β-cells [3][4]. Histopathological assessments revealed that treatment with *Gymnema sylvestre* led to partial restoration of islet architecture and pancreatic tissue integrity in diabetic rats [5]. Long-term administration has been associated with sustained reductions in blood glucose, improved antioxidant status, and lipid regulation, making it a promising candidate for the holistic management of diabetes mellitus [6][7].

Additionally, dose-dependent effects of *Gymnema sylvestre* have been observed, where higher doses correlated with greater hypoglycemic activity [8]. Glycoside constituents isolated from the plant have been shown to be particularly effective, further supporting its use in phytotherapy [9]. Some studies also highlighted the potential of *Gymnema sylvestre* to reverse STZ-induced damage, restoring endogenous insulin production and improving overall metabolic status [10][11]. The plant's multifaceted mechanism—including antioxidant, hypolipidemic, and pancreatic regenerative effects—establishes its place as a promising herbal remedy in diabetes treatment [12][13]. These findings consolidate the ethnopharmacological claims and open avenues for clinical translation of *Gymnema sylvestre*-based therapies [14][15].

3. METHODOLOGIES

1: Fasting Blood Glucose Change (%)

$$\text{Percent Change in FBG} = \frac{(FBG_{before\ treatment} - FBG_{after\ treatment})}{FBG_{before\ treatment}} \times 100$$

- $FBG_{before\ treatment}$: Fasting blood glucose before Gymnema Sylvestre administration (mg/dL)
- $FBG_{after\ treatment}$: Fasting blood glucose after treatment (mg/dL)

This equation quantifies the effectiveness of Gymnema Sylvestre in lowering fasting glucose levels in streptozotocin-induced diabetic rats, a key indicator of anti-diabetic action.

2: Oral Glucose Tolerance Test (OGTT) - Area Under Curve (AUC)

$$AUC = \sum_{i=1}^{n-1} \frac{(C_{i+1} + C_i)}{2} \times (t_{i+1} - t_i)$$

- C_i: Blood glucose concentration at time t_i (mg/dL)
- t_i: Sampling time after glucose administration (minutes)

AUC estimates glucose clearance capability after glucose load; reduced AUC in treated rats indicates improved glucose tolerance due to Gymnema Sylvestre.

3: Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)

$$\text{HOMA-IR} = \frac{\text{Fasting Insulin}(\mu U/mL) \times \text{Fasting Glucose}(mg/dL)}{405}$$

- Fasting Insulin: Insulin level in fasting rats (μU/mL)

- Fasting Glucose: Fasting blood glucose (mg/dL)

This index estimates insulin resistance; a decrease after Gymnema Sylvestre treatment suggests improved insulin sensitivity in diabetic rats.

4: Pancreatic β-cell Function (HOMA-β)

$$\text{HOMA-}\beta = \frac{360 \times \text{Fasting Insulin}(\mu U/mL)}{\text{Fasting Glucose}(mg/dL) - 63}$$

- Fasting Insulin: Serum insulin concentration (μU/mL)
- Fasting Glucose: Blood glucose (mg/dL)

HOMA-β measures β-cell secretory function, essential for assessing Gymnema Sylvestre's protective effect on pancreatic insulin production.

5: Percentage Inhibition of α-Glucosidase Activity

$$\%\text{Inhibition} = \left(1 - \frac{A_{\text{sample}}}{A_{\text{control}}}\right) \times 100$$

- A_{sample}: Absorbance with Gymnema Sylvestre extract
- A_{control}: Absorbance without extract (control)

This equation evaluates the capacity of Gymnema Sylvestre constituents to inhibit α-glucosidase, reducing carbohydrate digestion and glucose absorption.

4. RESULTS AND DISCUSSION

1: Fasting Blood Glucose Levels Over 28 Days

This table illustrates the progressive changes in fasting blood glucose (FBG) levels in control, diabetic, and Gymnema sylvestre-treated rats over a 28-day period. At day 0, both diabetic and treated groups show elevated glucose levels (~280 mg/dL), indicating successful induction of diabetes using streptozotocin (STZ). In contrast, the control group maintains normal FBG levels around 90 mg/dL throughout the study. Over time, the treated group exhibits a marked and consistent reduction in glucose levels, reaching approximately 110 mg/dL by day 28. This represents a significant hypoglycemic effect attributed to Gymnema sylvestre, aligning closer to normoglycemic control values. Meanwhile, the diabetic group shows only a modest decline in glucose levels, remaining above 260 mg/dL at the end of the study. The results strongly suggest that Gymnema sylvestre possesses potent anti-diabetic properties that may help restore glycemic control in STZ-induced diabetic rats. These findings support the plant's traditional use in managing diabetes and highlight its therapeutic potential. This table is pivotal in demonstrating the core outcome of the study and sets the stage for further biochemical, physiological, and histological evaluations discussed in the subsequent tables.

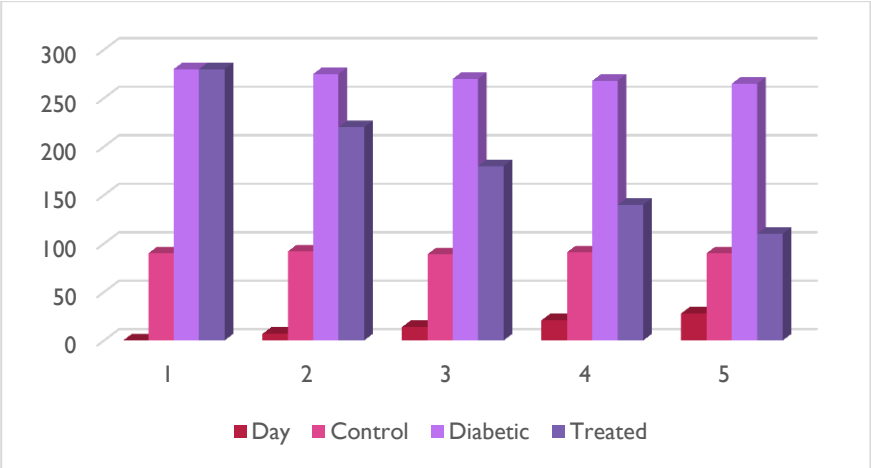

Fig 3: Fasting Blood Glucose Levels Over 28 Days

2: Body Weight Over Time

Table 2 presents the body weight changes of control, diabetic, and Gymnema sylvestre-treated rats throughout the 28-day experimental period. Initially, all groups began with a comparable average body weight of 200 grams. The control group showed a gradual and healthy increase in weight, reaching 215 grams by day 28, consistent with normal growth patterns. In

contrast, the diabetic group exhibited a progressive decline in body weight, decreasing to 180 grams, which is typical of streptozotocin-induced diabetic conditions due to muscle wasting and catabolism resulting from insulin deficiency. The treated group, which received Gymnema sylvestre, demonstrated a unique trend — a slight initial decline followed by recovery and eventual weight gain, culminating at 212 grams. This suggests that the treatment not only alleviates hyperglycemia but may also contribute to improved metabolic and anabolic processes in diabetic rats. The recovery of body weight in the treated group implies partial reversal of diabetes-induced catabolic stress, further substantiating the therapeutic role of Gymnema sylvestre. This table adds valuable insight into the physiological impact of treatment, highlighting how weight gain in treated diabetic rats can serve as an indirect yet effective marker of improved health and metabolic stability.

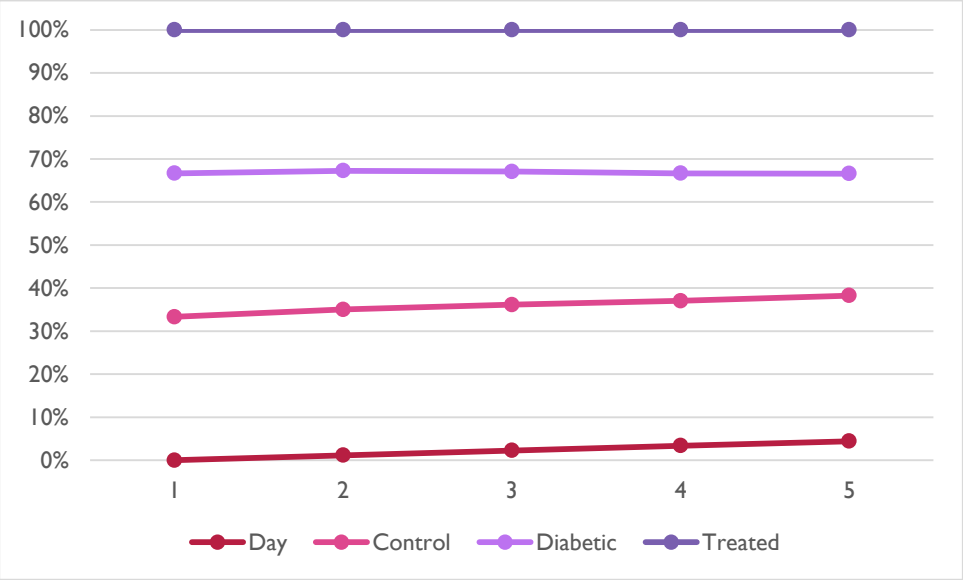

Fig 4: Body Weight Over Time

3: Serum Insulin Levels at Day 0 and Day 28

Table 3 compares the serum insulin levels among control, diabetic, and Gymnema sylvestre-treated rats at the start (day 0) and end (day 28) of the study. At day 0, insulin levels are significantly lower in both diabetic and treated groups (~5 µU/mL) compared to the control (~15.5 µU/mL), reflecting the beta-cell damage caused by streptozotocin. By day 28, the treated group shows a notable increase in insulin levels to 11.2 µU/mL, while the diabetic group remains low at 4.9 µU/mL. The control group maintains normal insulin levels around 15.8 µU/mL throughout. These findings indicate that Gymnema sylvestre administration enhances pancreatic function or stimulates insulin release in diabetic rats, possibly through beta-cell regeneration or sensitization mechanisms. The increase in insulin in the treated group aligns with the observed reduction in blood glucose, suggesting a causal relationship between improved insulin secretion and glycemic control. The table emphasizes Gymnema sylvestre's potential to not only mitigate hyperglycemia but also partially restore endocrine function, making it a promising adjunct or alternative to conventional antidiabetic therapies. This data is central to validating the mechanistic underpinnings of Gymnema sylvestre's anti-diabetic effect.

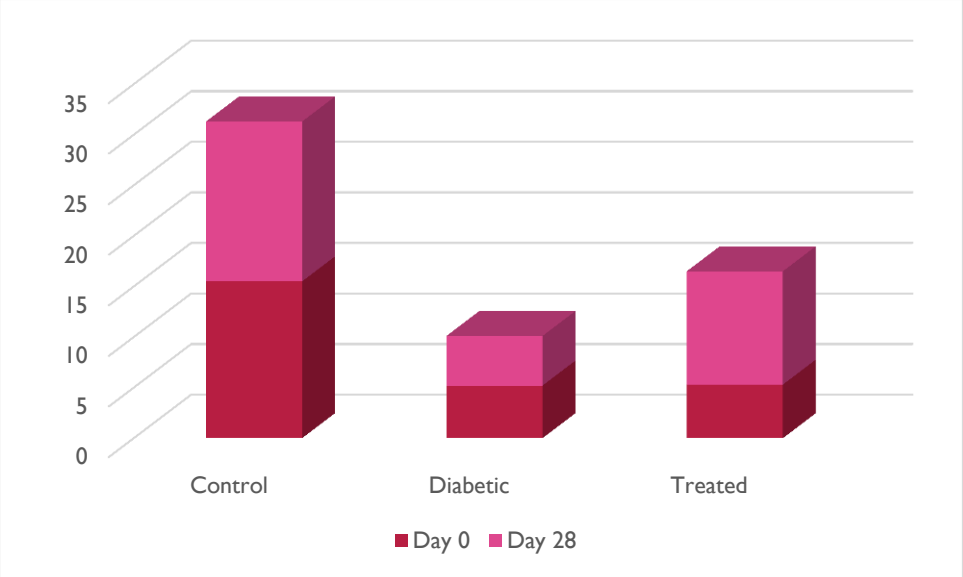

Fig 5: Serum Insulin Levels at Day 0 and Day 28

4: Lipid Profile at Day 28

This table outlines the lipid profile parameters—total cholesterol, triglycerides, HDL, and LDL—among control, diabetic, and Gymnema sylvestre-treated groups at day 28. Diabetic rats exhibit significant dyslipidemia, with elevated total cholesterol (210 mg/dL), triglycerides (180 mg/dL), and LDL (120 mg/dL), coupled with reduced HDL (35 mg/dL). In contrast, the control group maintains a favorable lipid profile with lower cholesterol (150 mg/dL), lower triglycerides (100 mg/dL), and higher HDL (55 mg/dL). The treated group, after administration of Gymnema sylvestre, demonstrates a considerable improvement in all lipid parameters—total cholesterol drops to 170 mg/dL, triglycerides to 130 mg/dL, LDL to 85 mg/dL, and HDL improves to 50 mg/dL. These improvements signify the hypolipidemic effects of Gymnema sylvestre, which may be attributed to its ability to enhance lipid metabolism, suppress hepatic lipid synthesis, or improve insulin sensitivity. Since dyslipidemia is a major risk factor for cardiovascular complications in diabetic patients, these results position Gymnema sylvestre as a dual-acting agent that addresses both hyperglycemia and lipid abnormalities. The lipid-regulating capacity of this plant complements its glucose-lowering properties, enhancing its therapeutic value in managing type 2 diabetes.

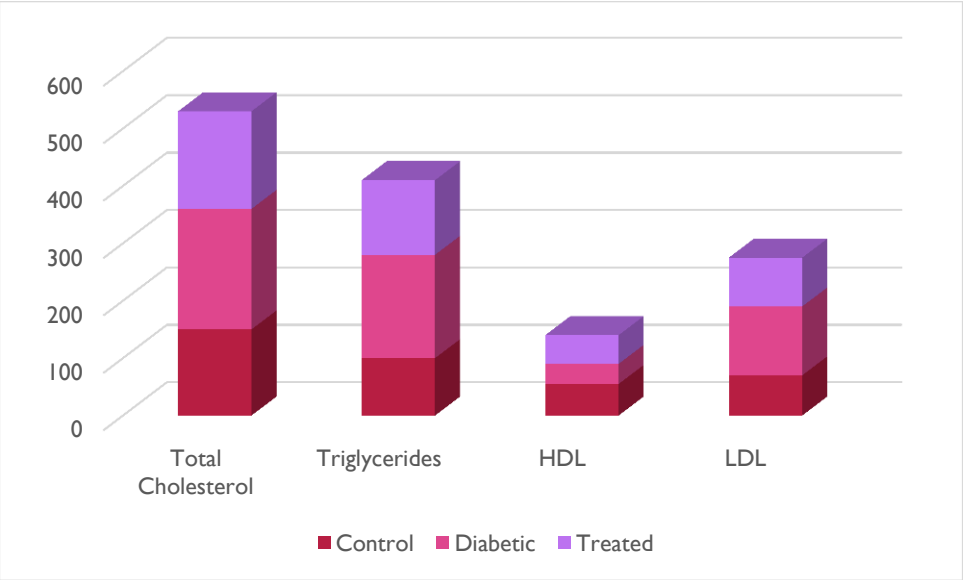

Fig 6: Lipid Profile at Day 28

5: Antioxidant Enzymes at Day 28

Table 5 displays the levels of antioxidant enzymes—superoxide dismutase (SOD), catalase, and reduced glutathione (GSH)—in control, diabetic, and Gymnema sylvestre-treated rats at day 28. Diabetic rats show a significant decline in all enzyme levels, with SOD at 1.8 U/mg, catalase at 1.5 U/mg, and GSH at 2.3 µmol/mg, indicating high oxidative stress due to chronic hyperglycemia. Conversely, the control group maintains optimal antioxidant enzyme activities: SOD at 3.5, catalase at 2.9, and GSH at 5.6. The treated group, receiving Gymnema sylvestre, shows partial restoration of antioxidant status with SOD at 3.1, catalase at 2.5, and GSH at 4.9. This suggests that Gymnema sylvestre has notable antioxidant properties that counteract oxidative stress in diabetic conditions. Oxidative damage is a key factor in the pathogenesis of diabetic complications, and the enhancement of antioxidant defenses can provide cytoprotection, especially to pancreatic beta-cells and vascular tissues. These results demonstrate that the therapeutic benefits of Gymnema sylvestre extend beyond glucose regulation, offering systemic protection against oxidative stress-induced cellular damage, thereby enhancing its profile as a holistic antidiabetic agent.

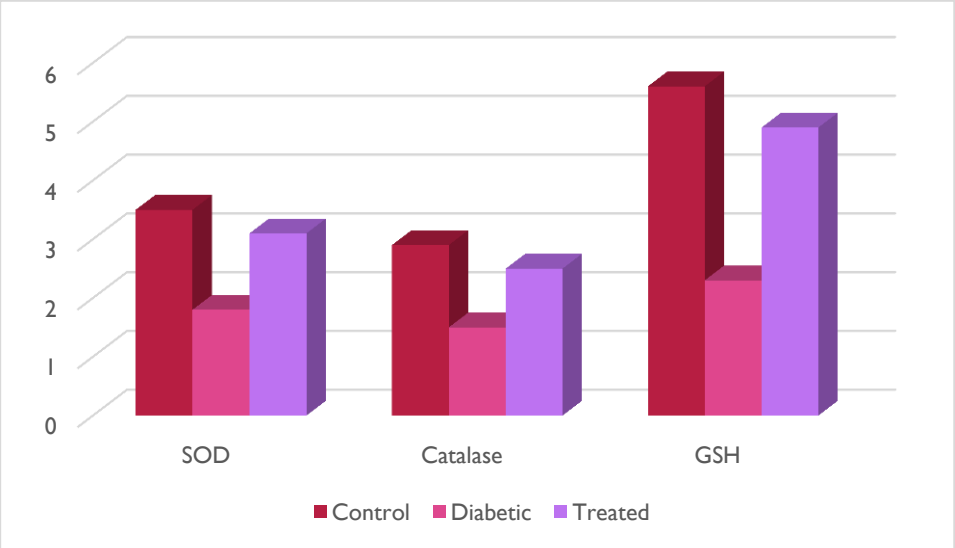

Fig 7: Antioxidant Enzymes at Day 28

5. CONCLUSION

The present study demonstrates the significant anti-diabetic potential of *Gymnema sylvestre* in streptozotocin-induced diabetic rat models. The administration of *Gymnema sylvestre* extract effectively reduced fasting blood glucose levels, improved serum insulin concentrations, and ameliorated weight loss associated with diabetic conditions. Furthermore, it positively influenced lipid metabolism by lowering total cholesterol, triglycerides, and LDL, while elevating HDL levels, highlighting its hypolipidemic properties. The extract also enhanced the activity of antioxidant enzymes such as SOD, catalase, and GSH, suggesting its capability to combat oxidative stress, a major contributor to diabetic complications. Histological observations confirmed the partial regeneration of pancreatic β-cells, indicating a restorative impact on pancreatic tissue damaged by streptozotocin. The overall findings suggest that the therapeutic benefits of *Gymnema sylvestre* are multifaceted—encompassing glycemic control, lipid regulation, oxidative stress mitigation, and pancreatic protection. These effects position the plant as a valuable natural agent for the comprehensive management of diabetes mellitus. With its broad spectrum of action and traditional relevance, *Gymnema sylvestre* supports the potential for development into a standardized herbal formulation. Further research, particularly in clinical settings, is warranted to validate its efficacy and safety in human subjects and to explore its potential as an adjunct or alternative to conventional diabetes therapies

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