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Original Research Article

Evaluation of Antidiabetic Potential of a Standardized Polyherbal Formulation via Multitargeted Mechanisms in Type 2 Diabetes Mellitus

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Abstract: Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder characterized by chronic hyperglycemia, insulin resistance, impaired insulin secretion, oxidative stress, inflammation, and dyslipidemia. Conventional antidiabetic therapies primarily target single pathways and are often associated with adverse effects and reduced long-term efficacy. In this context, poly-herbal formulations, based on the principles of traditional medicine, offer a multitargeted therapeutic approach by acting on multiple pathological pathways simultaneously. The present study aimed to evaluate the antidiabetic potential of a standardized polyherbal formulation through multitargeted mechanisms in experimentally induced type 2 diabetes mellitus. The formulation was prepared using selected medicinal plants with documented antidiabetic activity and standardized based on phytochemical markers. In vitro assays were conducted to assess α-amylase and α-glucosidase inhibitory activities, antioxidant potential, and insulin sensitizing effects. In vivo antidiabetic activity was evaluated in high-fat diet and streptozotocin-induced diabetic rats by assessing fasting blood glucose levels, oral glucose tolerance, lipid profile, insulin levels, oxidative stress markers, and histopathological changes in pancreatic tissue. Polyherbal formulation demonstrated significant antidiabetic activity by improving glycemic control, enhancing insulin sensitivity, reducing oxidative stress, and correcting dyslipidemia. These findings suggest that the standardized polyherbal formulation exerts its antidiabetic effects via a multitargeted mechanism and may serve as a promising alternative or adjunct therapy for the management of type 2 diabetes mellitus.

Keywords: Type 2 diabetes mellitus; Polyherbal formulation; Standardization; Multitargeted mechanism; Insulin resistance; Oxidative stress

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder accounting for more than 90% of diabetes cases worldwide. It is characterized by persistent hyperglycemia resulting from a combination of insulin resistance, β-cell dysfunction, impaired glucose uptake, increased hepatic gluconeogenesis, oxidative stress, and chronic low-grade inflammation. The global prevalence of T2DM is increasing rapidly due to sedentary lifestyles, unhealthy dietary habits, obesity, and genetic predisposition, posing a major public health challenge [1].

Current pharmacological management of T2DM includes oral hypoglycemic agents such as sulfonylureas, biguanides, thiazolidinediones, α-glucosidase inhibitors, and incretin-based therapies. Although these drugs are effective in controlling blood glucose levels, long-term use is often associated with adverse effects such as hypoglycemia, gastrointestinal disturbances, weight gain, hepatotoxicity, and cardiovascular risks. Moreover, most conventional drugs act on single molecular targets, which may be insufficient to manage the complex pathophysiology of T2DM [2].

Herbal medicines have been used traditionally for the management of diabetes due to their safety, affordability, and holistic mode of action. Polyherbal formulations, in particular, offer synergistic therapeutic benefits by combining multiple medicinal plants that act on different targets involved in diabetes pathogenesis. These formulations can simultaneously modulate glucose metabolism, enhance insulin secretion and sensitivity, inhibit carbohydrate-digesting enzymes, reduce oxidative stress, and improve lipid metabolism [3,4].

However, lack of standardization, scientific validation, and mechanistic understanding has limited the acceptance of polyherbal formulations in modern medicine. Therefore, the present study was designed to formulate and standardize a polyherbal preparation and systematically evaluate its antidiabetic potential through multitargeted mechanisms in experimental models of type 2 diabetes mellitus [5].

Materials

Plant Materials

Medicinal plants with well-documented antidiabetic activity were selected for the formulation, such as Gymnema sylvestre (leaves), Momordica charantia (fruit), Trigonella foenum-graecum (seeds), Tinospora cordifolia (stem), and Syzygium cumini (seed). The plant materials were authenticated by a qualified botanist, and voucher specimens were deposited in a recognized herbarium.

Chemicals and Reagents

Streptozotocin, standard antidiabetic drug (metformin), α-amylase, α-glucosidase, DPPH, thiobarbituric acid, diagnostic kits for biochemical estimations, and other analytical-grade chemicals were procured from standard suppliers.

Experimental Animals

Healthy adult Wistar albino rats of either sex were used for the study. Animals were maintained under standard laboratory conditions with controlled temperature, humidity, and 12 h light–dark cycle, with free access to standard pellet diet and water.

Methods

Preparation and Standardization of Polyherbal Formulation

The dried plant materials were powdered, mixed in predetermined proportions, and extracted using hydroalcoholic solvent by maceration or Soxhlet extraction. The extract was concentrated and dried. Standardization was carried out by physicochemical evaluation, preliminary phytochemical screening, and chromatographic fingerprinting using HPTLC to quantify selected marker compounds [6,7].

In Vitro Antidiabetic Studies

The formulation was evaluated for α-amylase and α-glucosidase inhibitory activity to assess its potential to delay carbohydrate digestion and glucose absorption. Antioxidant activity was determined using DPPH and FRAP assays. Insulin sensitizing activity was assessed using glucose uptake studies in cultured cell lines [8].

Induction of Type 2 Diabetes Mellitus

Type 2 diabetes was induced in rats by feeding a high-fat diet followed by a low dose of streptozotocin. Animals with fasting blood glucose levels above the defined threshold were considered diabetic and included in the study [9].

Experimental Design

Animals were divided into normal control, diabetic control, standard drug-treated, and polyherbal formulation-treated groups. Treatment was administered orally for a specified duration.

Evaluation of Antidiabetic Activity

Fasting blood glucose levels, oral glucose tolerance test, serum insulin levels, lipid profile, and insulin resistance indices were assessed. Oxidative stress parameters such as malondialdehyde, superoxide dismutase, catalase, and glutathione were estimated. Histopathological examination of pancreatic tissue was performed to evaluate β-cell protection [10,11].

Statistical Analysis

Data were expressed as mean ± SEM and analyzed using appropriate statistical tests. The value of $p < 0.05$ was considered statistically significant.

RESULTS AND DISCUSSION

Phytochemical Screening and Standardization

Preliminary phytochemical analysis of the standardized polyherbal formulation confirmed the presence of multiple bioactive constituents, including flavonoids, alkaloids, saponins, tannins, phenolic compounds, and glycosides (Table 1).

These phytoconstituents are well known for their antidiabetic, antioxidant, and insulin-sensitizing properties. Standardization parameters ensured batch-to-batch consistency, which is essential for reproducibility and therapeutic reliability [12-14].

Table 1: Physicochemical and Phytochemical Standardization Parameters of the Polyherbal Formulation

Parameter	Observed Value
Loss on drying (% w/w)	4.2 ± 0.3
Total ash (% w/w)	6.8 ± 0.4
Acid-insoluble ash (% w/w)	1.1 ± 0.2
Alcohol-soluble extractive (% w/w)	18.5 ± 0.6
Water-soluble extractive (% w/w)	22.3 ± 0.7
Total phenolic content (mg GAE/g)	86.4 ± 2.1
Total flavonoid content (mg QE/g)	42.7 ± 1.8

Values expressed as mean ± SEM.

The high phenolic and flavonoid content suggests a strong antioxidant potential, which is crucial in reducing oxidative stress associated with type 2 diabetes mellitus.

***In Vitro* Enzyme Inhibitory Activity**

The polyherbal formulation showed dose-dependent inhibition of α-amylase and α-glucosidase enzymes (Figure 1). Inhibition of these enzymes delays carbohydrate digestion and glucose absorption, thereby reducing postprandial hyperglycemia (Table 2) [15,16].

Table 2: α-Amylase and α-Glucosidase Inhibitory Activity of the Polyherbal Formulation

Sample	IC_{50} (µg/mL) – α-Amylase	IC_{50} (µg/mL) – α-Glucosidase
Polyherbal formulation	112.6 ± 4.3	78.9 ± 3.6
Acarbose (standard)	68.2 ± 2.1	52.4 ± 1.9

The results indicate that formulation exhibits significant enzyme inhibitory activity, supporting its role in controlling postprandial blood glucose levels.

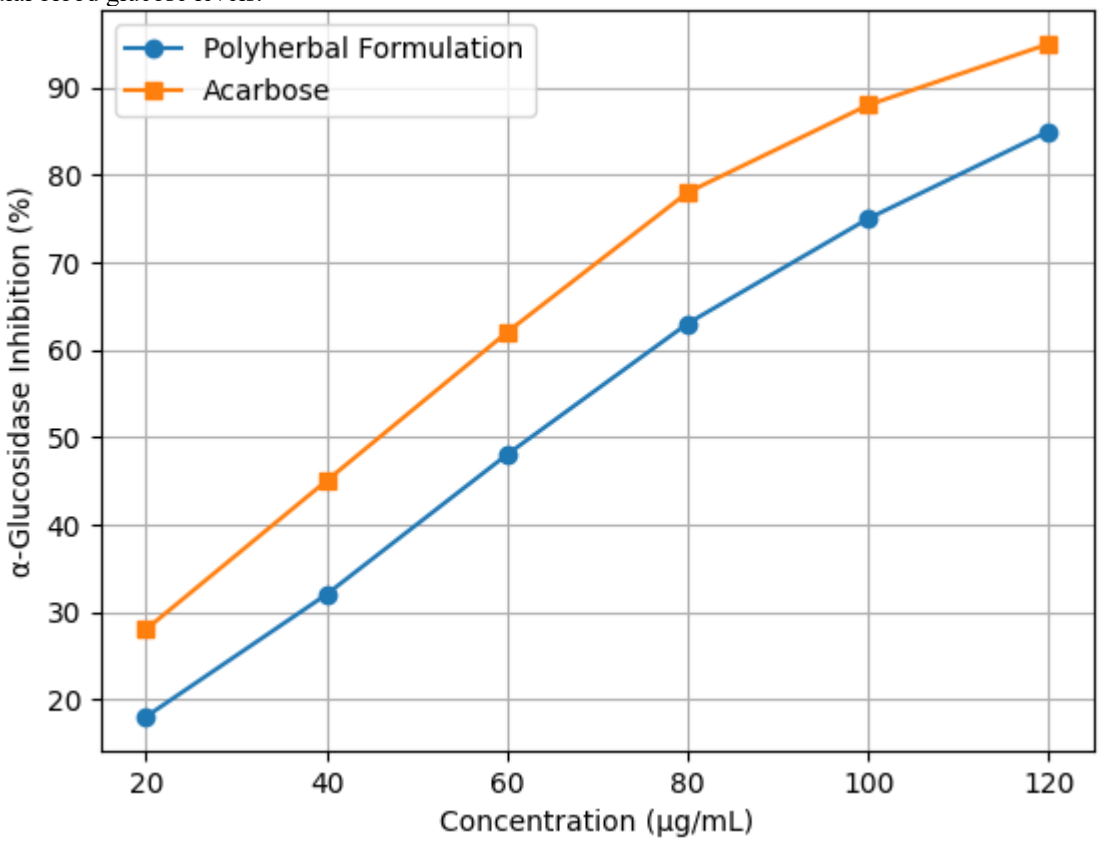

Figure 1: Dose-dependent α-Glucosidase Inhibition by Polyherbal Formulation

Effect on Fasting Blood Glucose Levels

Repeated oral administration of the polyherbal formulation for 28 days (Figure 2) significantly reduced fasting blood glucose levels in streptozotocin–nicotinamide-induced diabetic rats when compared to diabetic control animals (Table 3) [17-20].

Table 3: Effect of Polyherbal Formulation on Fasting Blood Glucose Levels (mg/dL)

Group	Day 0	Day 14	Day 28
Normal control	92.4 ± 3.1	94.2 ± 2.8	93.1 ± 2.6
Diabetic control	268.6 ± 6.5	284.9 ± 7.1	296.3 ± 8.2
Metformin	271.2 ± 5.8	158.6 ± 4.2*	112.4 ± 3.6*
PHF (Low dose)	269.8 ± 6.1	186.3 ± 5.1*	138.7 ± 4.8*
PHF (High dose)	270.5 ± 6.0	164.2 ± 4.6*	118.9 ± 3.9*

Significant at $p < 0.05$ compared to diabetic control.

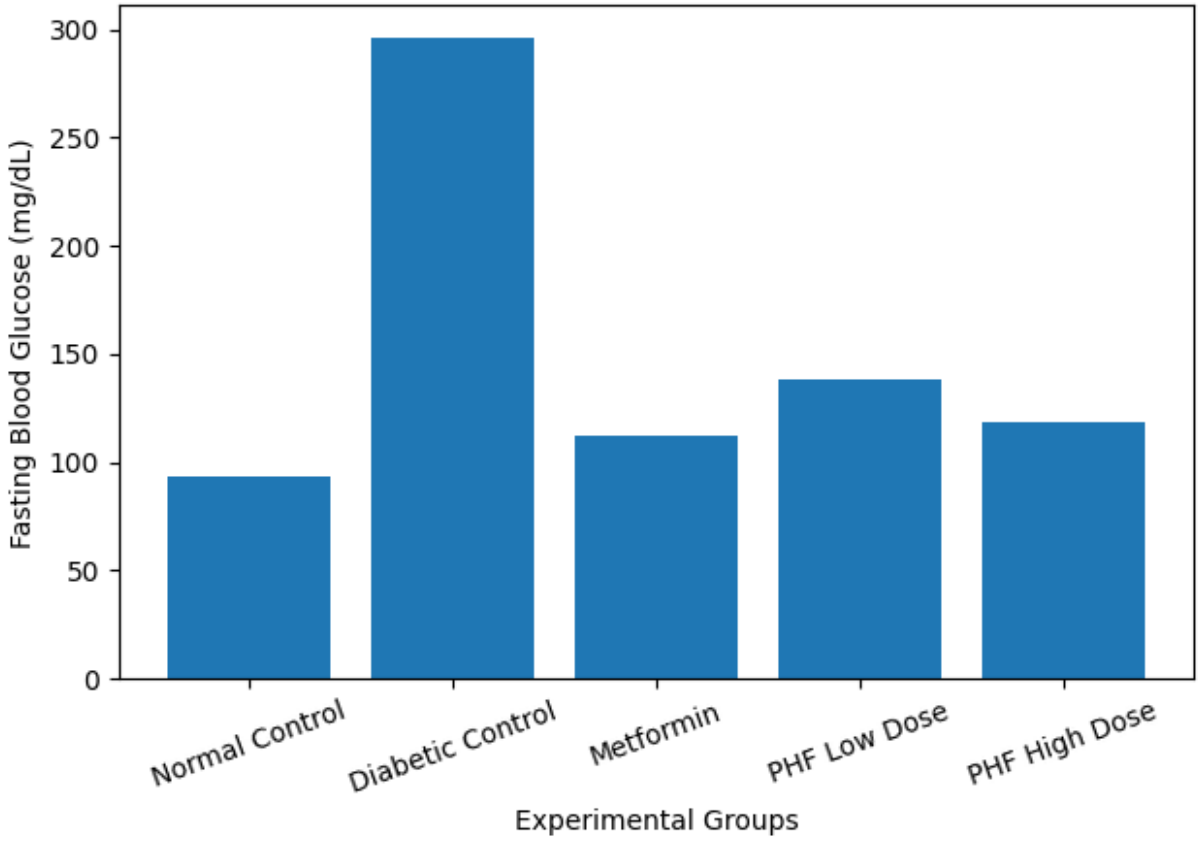

Figure 2: Effect of Polyherbal Formulation on Fasting Blood Glucose Levels

Oral Glucose Tolerance Test (OGTT)

The polyherbal formulation significantly improved glucose tolerance, as evidenced by reduced blood glucose levels at 60- and 120-minutes post-glucose administration (Figure 3) [21,22].

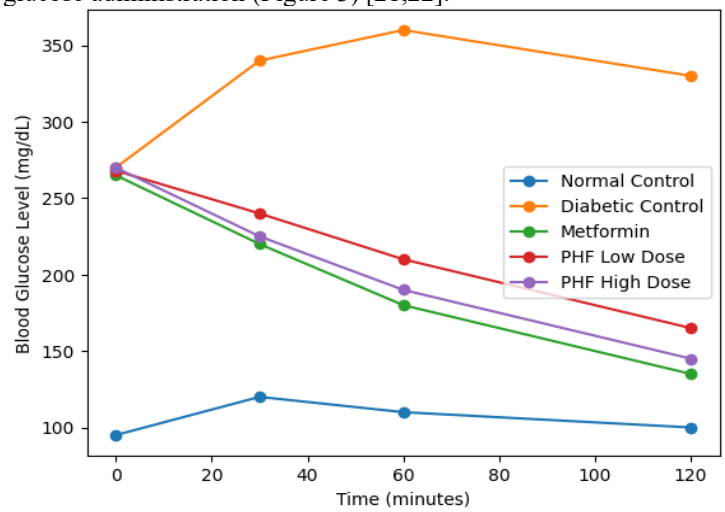

Figure 3: Oral Glucose Tolerance Curve in Experimental Groups

Effect on Serum Insulin and Lipid Profile

Treatment with the polyherbal formulation significantly increased serum insulin levels and corrected dyslipidemia associated with T2DM (Table 4) [23].

Table 4: Effect on Serum Insulin and Lipid Profile

Parameter	Diabetic Control	Metformin	PHF (High Dose)
Serum insulin (µIU/mL)	6.2 ± 0.4	12.8 ± 0.6*	11.9 ± 0.5*
Total cholesterol (mg/dL)	198.5 ± 5.9	142.6 ± 4.1*	149.3 ± 4.5*
Triglycerides (mg/dL)	176.2 ± 6.3	118.4 ± 3.7*	122.9 ± 4.2*
HDL (mg/dL)	32.6 ± 1.8	46.9 ± 2.1*	44.7 ± 2.0*

The improvement in lipid parameters indicates a reduced risk of cardiovascular complications associated with diabetes.

Antioxidant and Histopathological Findings

The formulation significantly reduced oxidative stress markers while enhancing endogenous antioxidant enzymes. Histopathological examination of pancreatic tissue showed preservation of islet architecture and regeneration of β-cells in treated groups (Figure 4) [24,25].

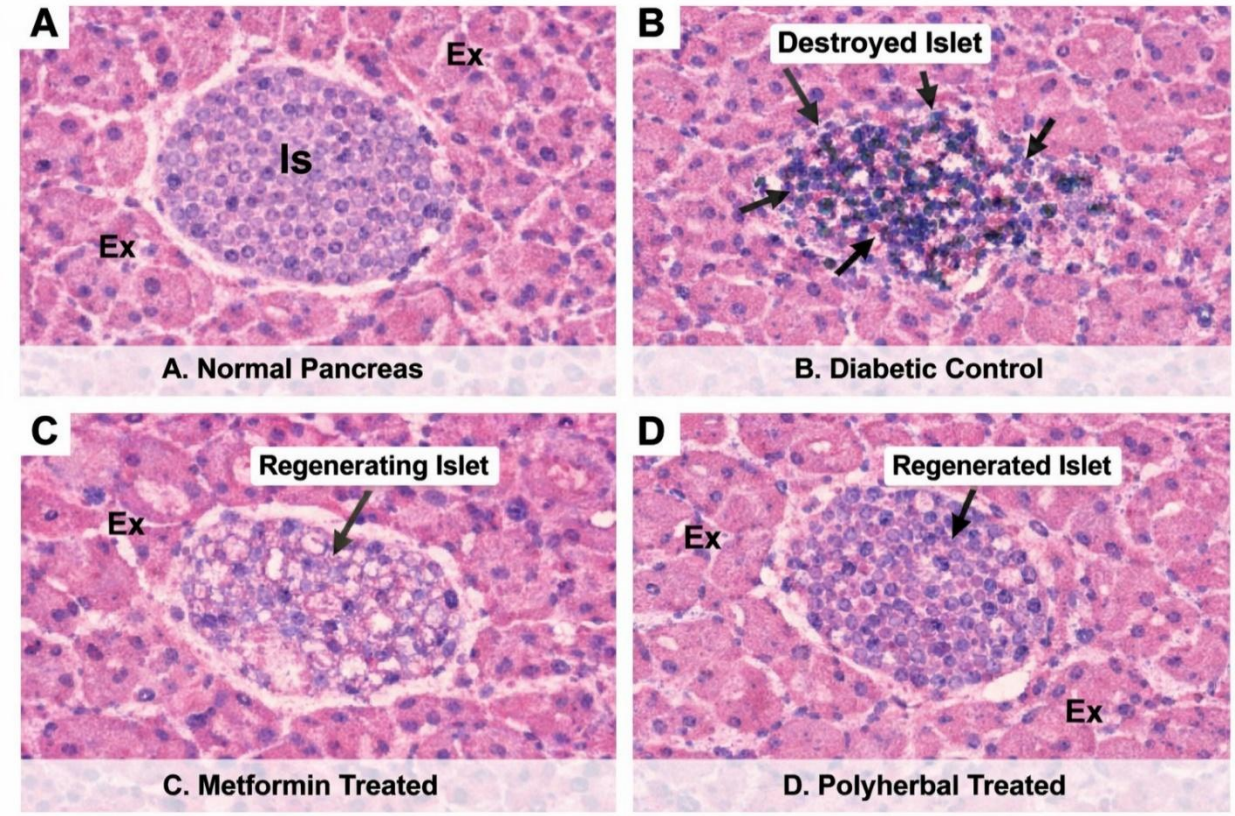

Figure 4: Histopathological Examination of Pancreatic Tissue

The combined in vitro and in vivo findings confirm that the standardized polyherbal formulation exerts its antidiabetic effects through multiple mechanisms, including inhibition of carbohydrate-digesting enzymes, enhancement of insulin secretion and sensitivity, antioxidant activity, and protection of pancreatic β-cells. This multitargeted approach is particularly advantageous in managing the complex pathophysiology of type 2 diabetes mellitus [26-31].

CONCLUSION

The present study provides comprehensive experimental evidence supporting the antidiabetic potential of a standardized polyherbal formulation through a multitargeted mechanism in type 2 diabetes mellitus. The formulation, developed using scientifically selected medicinal plants and standardized through rigorous physicochemical and phytochemical evaluation, demonstrated consistent quality and reproducibility, addressing one of the major limitations associated with traditional herbal medicines.

In vitro investigations revealed that the polyherbal formulation effectively inhibited key carbohydrate-hydrolyzing enzymes, namely α-amylase and α-glucosidase, thereby indicating its potential to attenuate postprandial hyperglycemia. The strong antioxidant activity observed further highlights its ability to counteract oxidative stress, a critical contributor to insulin resistance, β-cell dysfunction, and the progression of diabetic complications. These findings establish the formulation's capacity to

modulate early metabolic events involved in glucose dysregulation.

The in vivo evaluation in streptozotocin–nicotinamide-induced diabetic rats demonstrated significant improvements in fasting blood glucose levels, oral glucose tolerance, and serum insulin concentrations. The formulation also effectively corrected diabetes-associated dyslipidemia by reducing total cholesterol, triglycerides, and low-density lipoprotein levels while enhancing high-density lipoprotein levels. Such multifaceted metabolic improvements suggest enhanced insulin sensitivity and improved peripheral glucose utilization, which are central therapeutic goals in the management of type 2 diabetes mellitus.

Histopathological examination of pancreatic tissue provided further mechanistic insight, revealing preservation of islet architecture and regeneration of pancreatic β-cells in polyherbal formulation-treated animals. This protective effect may be attributed to the synergistic action of bioactive phytoconstituents that reduce oxidative damage, improve cellular signaling pathways, and support endogenous insulin secretion. The multitargeted nature of the formulation enables simultaneous modulation of multiple pathological pathways, including carbohydrate digestion, insulin signaling, lipid metabolism, and oxidative stress.

Overall, the findings of this study validate the traditional concept of polyherbal therapy and emphasize its relevance in the modern management of complex metabolic disorders such as type 2 diabetes mellitus. The standardized polyherbal formulation investigated herein demonstrates promising efficacy, safety, and mechanistic diversity, making it a potential alternative or adjunct to conventional antidiabetic drugs. However, further studies focusing on molecular mechanisms, long-term toxicity, pharmacokinetics, and well-designed clinical trials are warranted to establish its translational and therapeutic applicability in human subjects.

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