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Antidiabetic Activity of an Optimized Polyherbal Dispersible Tablet of *Terminalia arjuna*, *Moringa oleifera*, and *Syzygium cumini* in Streptozotocin-Induced Diabetic Rats

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Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and associated metabolic complications. The present study was conducted to evaluate the antidiabetic activity of a polyherbal dispersible tablet containing Terminalia arjuna, *Moringa oleifera*, and *Syzygium cumini* in streptozotocin (STZ)-induced diabetic rats. Acute oral toxicity was evaluated according to OECD guideline No. 423, and no mortality or severe toxic effects were observed up to 2000 mg/kg, indicating that the polyherbal tablet formulation was found to be safe. Diabetes was induced using streptozotocin (35 mg/kg, i.p.), and animals were treated orally with the polyherbal formulation (PHF) and polyherbal tablet (PHT) at a dose of 150 mg/kg for 14 days. Body weight, blood glucose levels, and histopathological changes in pancreatic tissue were evaluated. The diabetic control group showed significant hyperglycemia and reduction in body weight, whereas treatment with PHF and PHT significantly reduced blood glucose levels and improved body weight compared to diabetic control animals. Histopathological studies revealed restoration of pancreatic architecture and partial restoration of pancreatic islets in treated groups. The study concludes that the optimized polyherbal dispersible tablet possesses significant antidiabetic activity and may be useful for diabetes management.

Keywords: Antidiabetic activity; Polyherbal tablet; Streptozotocin; Terminalia arjuna; *Moringa oleifera*; *Syzygium cumini*; Histopathology

1. Introduction

Diabetes mellitus (DM) is one of the most common endocrine disorders affecting the endocrine function of pancreatic islets. It is characterized by the complete absence or relative deficiency of insulin. DM is a major cause of blindness, myocardial infarction, stroke, kidney failure, and lower limb amputation worldwide [1]. The rapidly increasing prevalence of diabetes worldwide has created an urgent need for safer and more effective therapeutic strategies [2]. In recent years, medicinal plants and polyherbal formulations have gained considerable attention in the management of diabetes due to their natural origin, therapeutic efficacy, and comparatively lower adverse effects [3].

Terminalia arjuna, *Moringa oleifera*, and *Syzygium cumini* are medicinal plants reported to possess antidiabetic and antioxidant activities through enhancement of insulin secretion, glucose utilization, and protection of pancreatic β-cells. Polyherbal dispersible tablets provide advantages such as rapid disintegration, improved bioavailability, and better patient compliance. In our previous study, an optimized polyherbal dispersible tablet containing aqueous extracts of these plants was successfully formulated [4].

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Streptozotocin (STZ)-induced diabetes is a widely used experimental model that selectively damages pancreatic β-cells and produces hyperglycemia. Therefore, the present study was undertaken to evaluate the antidiabetic activity of the optimized polyherbal dispersible tablet in STZ-induced diabetic rats.

2. Materials and Methods

2.1. Plant Materials

The optimized polyherbal formulation (PHF) and polyherbal tablet formulation (PHT) containing aqueous extracts of Terminalia arjuna, *Moringa oleifera*, and *Syzygium cumini* were used in the present study. The formulation was previously developed and optimized in our earlier research work.

2.2. Experimental Animals

Adult male Wistar rats weighing 150–200 g were obtained from the animal house facility of Pinnacle Biomedical Research Institute (PBRI), Bhopal, India. The animals were maintained under standard laboratory conditions at a temperature of 22 ± 2°C with a 12 h light/dark cycle and relative humidity of 55 ± 5%. Standard pellet diet and water ad libitum were provided throughout the experimental period. Animals were acclimatized to laboratory conditions for seven days prior to the study. All experimental procedures were conducted in accordance with CPCSEA guidelines and approved by the Institutional Animal Ethics Committee (IAEC) (Approval No.: PBRI/IAEC/09-05-25/001).

2.3. Acute Oral Toxicity Study

Acute oral toxicity study of the polyherbal tablet formulation was performed according to OECD guideline No. 423 [5]. The formulation was administered orally at doses of 5, 50, 300, and 2000 mg/kg body weight. Animals were observed for mortality, behavioral changes, toxic symptoms, and body weight variations for 14 days.

2.4. Induction of Diabetes

Experimental diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ, 35 mg/kg, i.p.) prepared in cold citrate buffer [6]. Animals were provided with 5% glucose solution overnight to prevent initial hypoglycemia. After seven days, rats showing fasting blood glucose levels above 250 mg/dLwere considered diabetic and selected for the study.

2.5. Experimental Design

Animals were divided into five groups comprising six animals each. Group I served as normal control, Group II as diabetic control, Group III served as standard control and received metformin (150 mg/kg, p.o.), Group IV received polyherbal formulation (PHF, 150 mg/kg), and Group V received polyherbal tablet formulation (PHT, 150 mg/kg). The dispersible tablet was freshly dispersed in distilled water before oral administration to the experimental animals. All treatments were administered orally for 14 consecutive days.

2.6. Blood Glucose Estimation

Blood glucose levels were measured on day 0, day 7, and day 14 using blood samples collected from the tail vein of experimental rats with the help of a digital glucometer.

2.7. Body Weight Analysis

Body weight of all experimental animals was recorded on 0, 7th, and 14th day to evaluate the effect of treatment on diabetes-induced weight changes.

2.8. Histopathological Examination

Pancreatic tissues were collected and fixed in formalin solution. The tissues were processed, embedded in paraffin wax, sectioned, and stained with hematoxylin and eosin for histopathological evaluation under a light microscope.

2.9. Statistical Analysis

All experimental data were expressed as Mean ± SEM (n = 6). Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Bonferroni's multiple comparison test. Values of $P < 0.05$ were considered statistically significant.

3. Results and Discussion

3.1. Acute Oral Toxicity Study

The acute oral toxicity study of the polyherbal tablet formulation (PHT) was performed according to OECD guideline 423. No mortality was observed in any treatment group during the 14-day observation period, indicating the safety of the formulation up to 2000 mg/kg body weight. Minor behavioral and physiological changes such as mild hair loss, mild yellow discoloration of urine, and nasal discharge were observed at the highest dose level, whereas lower dose groups showed normal behavior and appearance. Body weight of animals remained comparatively stable throughout the study period, suggesting absence of severe toxic effects. The results indicated that the polyherbal tablet formulation was safe for further pharmacological evaluation.

The absence of mortality and severe toxic symptoms suggests that the polyherbal tablet formulation possesses a wide margin of safety. The mild behavioral changes observed at higher doses may be due to transient physiological responses at higher dose levels. Similar findings regarding the safety of herbal antidiabetic formulations have been reported in previous studies.

Table 1 Acute oral toxicity observations of PHT according to OECD 423

Dose (mg/kg)	Mortality	General Behavior	Skin/Fur Changes	Mucous Membrane	Urine Appearance	Body Weight Observation
5	0/3	Normal	Normal	Normal	Normal	Normal increase
50	0/3	Normal	Normal	Normal	Normal	Normal increase
300	0/3	Normal	Normal	Normal	Slight yellow urine	Stable
2000	0/3	Normal	Mild hair loss	Runny nose	Slight yellow urine	Slight variation

No significant toxic effects or mortality were observed in animals treated with PHT up to 2000 mg/kg body weight. Mild behavioral changes were observed only at higher doses.

3.2. Effect on Body Weight

Body weight assessment was carried out on day 0, day 7, and day 14 in all experimental groups. The diabetic control group showed a progressive reduction in body weight throughout the experimental period, which may be attributed to impaired glucose utilization and increased protein catabolism associated with diabetes mellitus. In contrast, animals treated with metformin, polyherbal formulation (PHF), and polyherbal tablet formulation (PHT) demonstrated protection against diabetes-induced body weight loss. Among the treatment groups, the PHT-treated group exhibited comparatively better restoration of body weight during the treatment period, indicating improved metabolic status and glycemic control.

Table 2 Effect of PHF and PHT on body weight in STZ-induced diabetic rats

Group	0 Day	7th Day	14th Day
Normal Control	183.2±6.08	187.3±6.08	191.3±7.12
Diabetic Control	180.3±5.01	172.5±5.21	165.3±7.21
Standard (Metformin 150 mg/kg)	187.7±7.21	191.3±10.40*	196.8±3.10***
PHF (150 mg/kg)	178.2±6.87	179.5±8.21	177.4±6.32*
PHT (150 mg/kg)	193.5±8.38	195.0±5.32*	194.2±9.69**

Values are expressed as Mean ± SD (n = 6). One-way ANOVA followed by Bonferroni's multiple comparison test was applied. *P < 0.05, **P < 0.01, ***P < 0.001 compared with diabetic control group.

Loss of body weight in diabetic animals is commonly associated with excessive protein degradation and defective carbohydrate metabolism. Treatment with PHF and PHT exerted protective effects against diabetes-induced body weight reduction. The observed effect may be attributed to the presence of bioactive phytoconstituents such as flavonoids and phenolic compounds, which are known to enhance insulin activity, improve glucose utilization, and reduce oxidative stress.

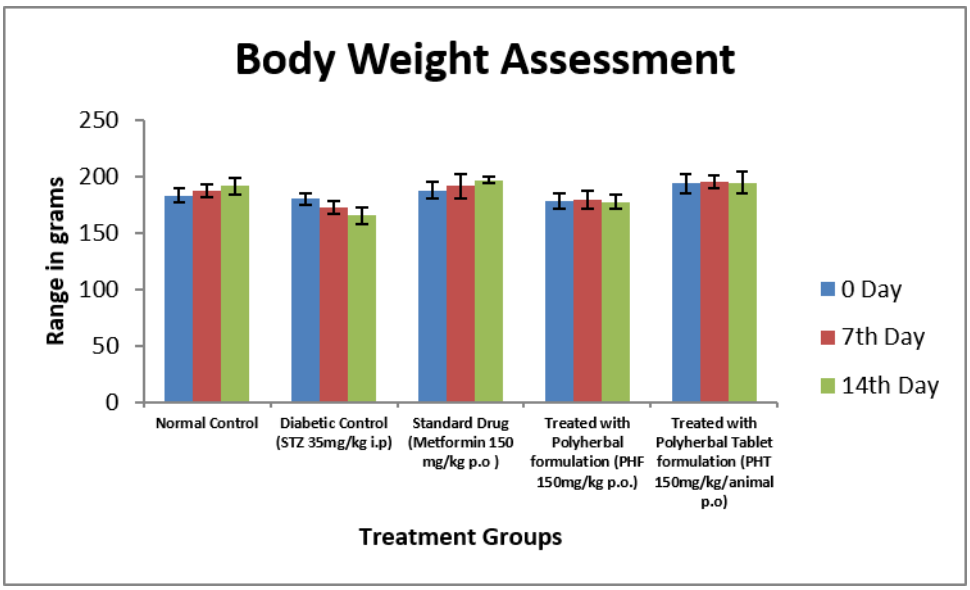


Figure 1 Effect of PHF and PHT on Body Weight

3.3. Effect on Blood Glucose Level

The effect of PHF and PHT on blood glucose levels in STZ-induced diabetic rats is presented in Table 3. Administration of streptozotocin resulted in marked hyperglycemia in diabetic animals compared with the normal control group. Treatment with metformin, PHF, and PHT significantly reduced blood glucose levels throughout the 14-day experimental period. Among the treatment groups, the polyherbal tablet formulation (PHT) produced a greater reduction in blood glucose levels and exhibited an antihyperglycemic effect comparable to that of the standard drug metformin.

The antihyperglycemic activity observed in PHF- and PHT-treated groups may be attributed to the presence of bioactive phytoconstituents present in Terminalia arjuna, *Moringa oleifera*, and *Syzygium cumini*. These phytoconstituents are known to possess antioxidant and antidiabetic properties, which may contribute to improved glucose utilization and glycemic control. Among the tested formulations, PHT demonstrated superior antihyperglycemic activity compared with PHF, as evidenced by its greater reduction in blood glucose levels and better maintenance of body weight in STZ-induced diabetic rats.

Table 3 Effect of PHF and PHT on blood glucose levels in STZ-induced diabetic rats

Group	Day 0	Day 7	Day14
Normal Control	134.5±2.08	129.2±1.20	135.5±2.00
Diabetic Control	397.5±2.74	324.2±9.20	315.5±2.22
Standard (Metformin 150 mg/kg)	355.4±5.74	269.3±2.72*	146.3±2.72***
PHF (150 mg/kg)	333.5±9.19	226.5±1.09**	159.3±3.52***
PHT (150 mg/kg)	359.2±3.24	202.0±4.75***	156.0±3.21***

Values are expressed as Mean ± SD (n = 6). Statistical analysis was performed using one-way ANOVA followed by Bonferroni's multiple comparison test. *P < 0.05, **P < 0.01, ***P < 0.001 compared with diabetic control group.

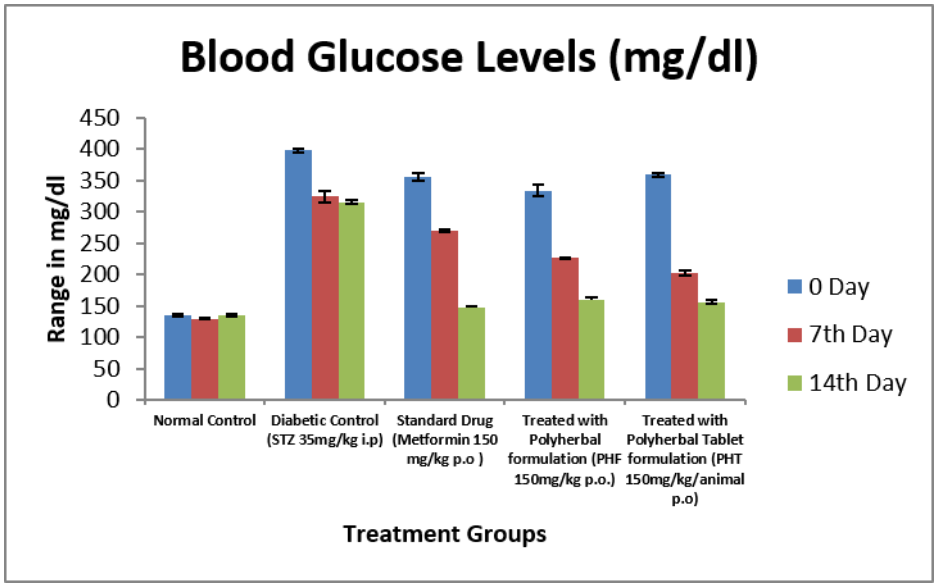
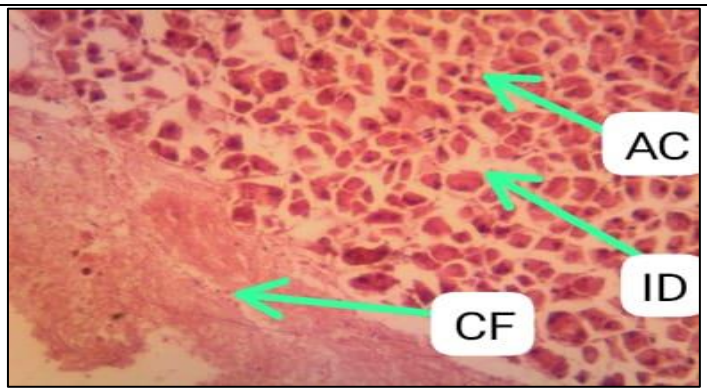
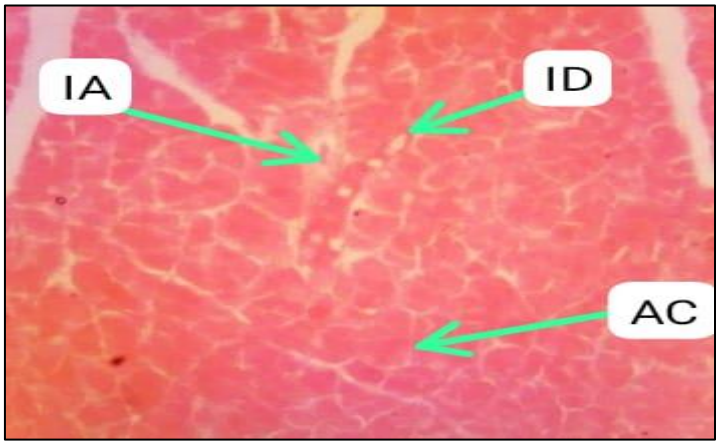


Figure 2 Effect of PHF and PHT on Blood Glucose Levels

3.4. Histopathological Examination

Histopathological examination of pancreatic tissues revealed normal cellular architecture in the normal control group with intact islets of Langerhans and acinar cells. The diabetic control group showed severe pathological alterations including degeneration of pancreatic β-cells, reduced islet size, and cellular necrosis. Treatment with metformin, PHF, and PHT improved pancreatic histoarchitecture with partial restoration of islet cells and reduced tissue damage. The polyherbal tablet-treated group showed marked improvement in pancreatic architecture with improved cellular integrity, indicating protective effects against STZ-induced pancreatic injury.

Group I: Normal Control	
Group II: Diabetic Control (STZ 35 mg/kg, i.p.)	

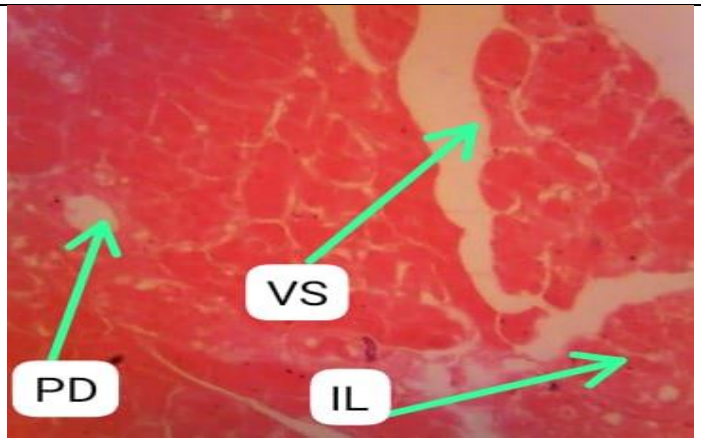
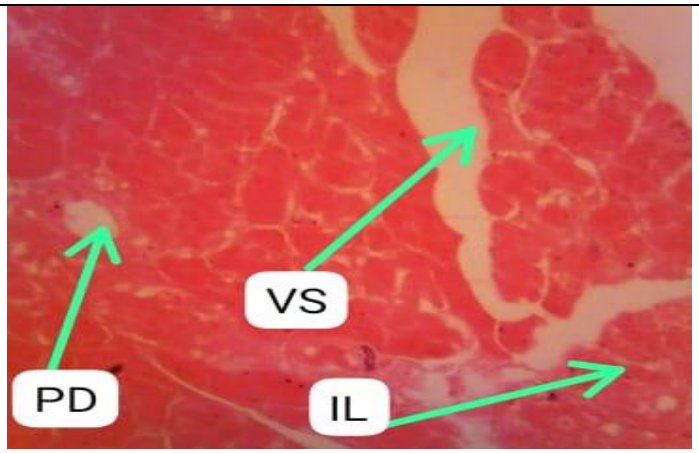
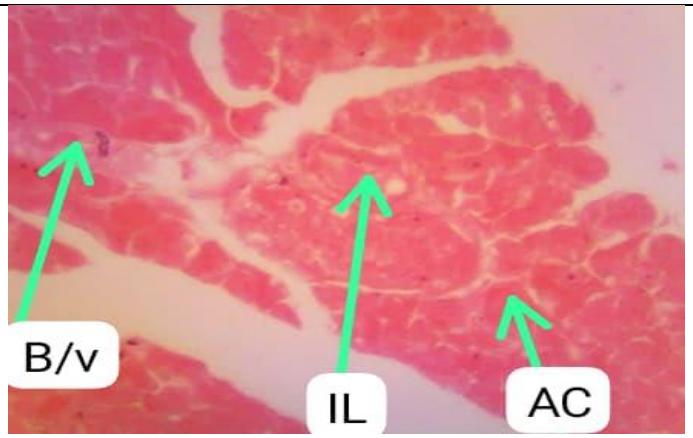
Group III: Standard Drug (Metformin 150 mg/kg, p.o.)	
Group IV: Treated with Polyherbal Formulation (PHF 150 mg/kg, p.o.)	
Group V: Treated with Polyherbal Tablet Formulation (PHT 150 mg/kg, p.o.)	

Figure 3 Histopathological examination of pancreatic tissues in experimental groups. Abbreviations: AC, Acini; ID, Interlobular duct; CF, Collagen fibers; IA, Interlobular artery; VS, Vascular space; PD, Pancreatic duct; IL, Islets of Langerhans; B/V, Blood vessel containing blood

Histopathological improvement observed in treated groups further supports the protective effect of the polyherbal formulation against STZ-induced pancreatic damage. Restoration of islet architecture and reduced cellular degeneration suggest improvement in pancreatic cellular morphology and possible antioxidant-mediated tissue protection. The findings correlate well with the observed reduction in blood glucose levels.

4. Conclusion

The present study demonstrated that the optimized polyherbal dispersible tablet containing aqueous extracts of Terminalia arjuna, *Moringa oleifera*, and *Syzygium cumini* possesses significant antidiabetic activity in streptozotocin-

induced diabetic rats. The formulation significantly reduced blood glucose levels, improved body weight, and restored pancreatic histoarchitecture comparable to metformin treatment. The observed effects may be attributed to synergistic phytoconstituents with antioxidant and pancreatic β-cell protective properties. Acute oral toxicity studies confirmed the safety of the formulation up to 2000 mg/kg body weight. Therefore, the optimized polyherbal dispersible tablet may serve as a potential herbal therapeutic candidate for diabetes management. However, further mechanistic and clinical investigations are necessary to establish its therapeutic efficacy and safety.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this research work.

Statement of ethical approval

The study was approved by the institutional Animal Ethics Committee (IAEC) and was conducted in accordance with CPCSEA guidelines.

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