INFORMATICS JOURNALS

Research Article

Journal of Natural Remedies
DOI: 10.18311/jnr/2026/55297

eISSN: 2320-3358 | Vol 26(7), 2026 | pp. 1831-1845

Restoration of Metabolic Homeostasis by *Mimosa pudica* Through Modulation of Carbohydrate Metabolism and ATPase Activity

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Abstract

Background: Diabetes Mellitus (DM) is a chronic metabolic disorder characterised by persistent hyperglycemia and associated metabolic dysfunctions. *Mimosa pudica* has been traditionally used for various therapeutic purposes, but its mechanistic antidiabetic potential remains inadequately explored. **Aim:** To evaluate the effect of aqueous and ethanolic extracts of *M. pudica* on carbohydrate metabolism and membrane-bound Adenosine Triphosphatase (ATPase) activity in streptozotocin-induced diabetic rats, supported by molecular docking studies. **Methods:** Wistar rats were divided into five groups: Normal control, diabetic control, diabetic treated with ethanolic extract (400 mg/kg), aqueous extract (400 mg/kg), and metformin (200 mg/kg). Biochemical parameters, including blood glucose, insulin, glycogen content, ATPase activities, and carbohydrate-metabolising enzymes, were assessed. Statistical analyses included One Way Analysis of Variance (ANOVA), correlation matrix, and Principal Component Analysis (PCA). Molecular docking was performed using AutoDock Vina. **Results:** Diabetic rats showed hyperglycemia, reduced insulin, decreased glycogen, impaired ATPase activity, and altered enzyme profiles. Treatment with *M. pudica* extracts significantly restored these parameters, with the ethanolic extract showing superior efficacy. Docking studies demonstrated strong binding affinities of phytochemicals with key metabolic enzymes. **Conclusion:** *Mimosa pudica* exhibits potent antidiabetic effects through modulation of metabolic enzymes, membrane stabilisation, and enhancement of insulin activity.

Major Findings: *Mimosa pudica* significantly restores metabolic and enzymatic alterations in diabetic rats. Ethanolic extract demonstrates efficacy comparable to metformin. Molecular docking supports its multi-target mechanism of action.

Keywords: Carbohydrate Metabolism, Diabetes Mellitus, Membrane-bound ATPases, Metabolic Homeostasis, *Mimosa pudica,* Molecular Docking

(Article Chronicle: Article Received on: 09.03.2026; Revised on: 28.04.2026; Accepted on: 13.06.2026)

1. Introduction

Diabetes Mellitus (DM) is a group of heterogeneous, chronic metabolic disorders primarily characterised by persistent hyperglycemia. This condition arises from either defective insulin secretion or impaired insulin action, ultimately leading to abnormal glucose metabolism and utilisation. According to the International Diabetes Federation (IDF), the global prevalence of diabetes in 2021 was estimated at approximately 537 million individuals[1]. Diabetes not only imposes a significant healthcare burden but also profoundly impacts the quality of life of those affected[2]. In addition, the rising prevalence of type 2 diabetes in developing countries, particularly in India, underscores the urgent need for cost-effective and safer therapeutic

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alternatives that can address both glycemic control and associated metabolic complications[3].

The complications of diabetes are far-reaching. Macrovascular conditions such as cardiovascular disease and microvascular complications, including diabetic nephropathy, retinopathy, neuropathy, and peripheral arterial disease (leading to limb amputations), contribute substantially to increased morbidity and premature mortality among patients with diabetes[3,4]. Beyond these, emerging evidence indicates a potential causal relationship between diabetes and various other conditions, such as cancers, infections, dementia, and liver disease.

Currently, diabetes is managed through a range of pharmacological interventions, including oral hypoglycemic agents and insulin therapy. However, many of these drugs are expensive and may be associated with adverse effects, particularly upon long-term use[5,6]. This has driven a growing interest in identifying safer, more cost-effective alternatives. In this regard, medicinal plants and herbal formulations have garnered attention for their traditional use, multitarget mechanisms, economic viability, and minimal side-effect profiles[5]. Despite the availability of multiple pharmacological agents, most current therapies primarily target single pathways and may not adequately address the multifactorial nature of diabetes, including oxidative stress, membrane dysfunction, and enzymatic dysregulation[6].

One such plant is *M. pudica*, commonly known as the "touch-me-not" plant or shameplant. It is a creeping annual or perennial undershrub belonging to the family Mimosaceae, often found along roadsides, wastelands, and open areas. Phytochemical analyses of *M. pudica* leaves have revealed the presence of diverse bioactive compounds, including flavonoids, terpenoids, glycosides, alkaloids, quinones, tannins, phenols, coumarins, and saponins[7]. These bioactive compounds are known to exhibit antioxidant, anti-inflammatory, and enzyme-modulating properties, which may contribute to improved glucose homeostasis and protection against diabetes-induced cellular damage. Traditionally, extracts of *M. pudica* have been employed in treating conditions such as headache, stomachache, migraine, fever, diarrhoea, dysentery, fistula, piles, and as a sedative[5,7]. Recent investigations have also highlighted its antidiabetic potential.

Given the multifactorial pathogenesis of diabetes and the limitations associated with conventional therapies, *M. pudica* offers promise as a botanical therapeutic due to its pharmacologically active constituents. Flavonoids and alkaloids, in particular, are known for their antioxidant, anti-inflammatory, and hypoglycemic effects, which may collectively aid in restoring metabolic homeostasis. Evaluating the impact of *M. pudica* on carbohydrate metabolism and membrane-bound enzyme activities can offer valuable insights into its mechanistic role in glycemic regulation. Furthermore, such studies serve to bridge traditional medicinal knowledge with modern scientific validation, supporting the development of safe, plant-based antidiabetic agents.

However, despite emerging evidence supporting the antidiabetic potential of *M. pudica*, there is limited information regarding its role in modulating membrane-bound ATPases and integrated carbohydrate metabolism. Furthermore, studies combining *in vivo* biochemical evaluation with in silico molecular docking to elucidate its mechanistic pathways remain scarce.

Hence, the present study aims to investigate the efficacy of ethanol and aqueous extracts of *M. pudica* on glycogen levels, key carbohydrate-metabolising enzymes, and membrane-bound ATPases in streptozotocin-induced diabetic Wistar albino rats, along with molecular docking analysis to support the underlying mechanisms.

2. Materials and Methods

2.1 Plant Material Collection and Authentication

Whole *M. pudica* plants were gathered from Chinthareddypalem, which is located close to Nellore in Andhra Pradesh, India. A professional botanist verified the obtained plant material, and a voucher specimen (Voucher No. 00591) was placed for future reference and verification at the Captain Srinivasa Murti Central Ayurveda Research Institute's herbarium in Chennai, India.

2.2 Preparation of Plant Extracts

The authenticated *M. pudica* plants were thoroughly washed, shade-dried, and coarsely powdered. Two types

of extracts were prepared for the study. The Ethanolic Extract (ME) was obtained using Soxhlet extraction with 10% ethanol, while the Aqueous Extract (MA) was prepared using the cold percolation method with 10% distilled water. Both extracts were concentrated under reduced pressure using a vacuum concentrator. The extraction yield was found to be 10.2% for the aqueous extract (MA) and 6.9% for the ethanolic extract (ME).

2.3 Molecular Docking Analysis

To investigate the interaction between bioactive phytoconstituents of *M. pudica* and diabetes-associated target proteins, molecular docking studies were performed. Selected compounds, including quercetin, stigmasterol, myoinositol, and avicularin, were chosen based on reported phytochemical evidence. The three-dimensional crystal structures of target enzymes—aldose reductase, α-glucosidase, hexokinase, and glucose-6-phosphatase were retrieved from the Protein Data Bank (PDB).

Protein structures were prepared by removing water molecules, adding polar hydrogen atoms, and assigning Kollman charges. Ligand structures were energy-minimised using standard optimisation protocols. Docking simulations were carried out using AutoDock Vina, with grid boxes defined around the active sites of each protein based on the coordinates of co-crystallised ligands.

Docking validation was performed by re-docking the native co-crystallised ligands into the active sites of the respective proteins. The accuracy of the docking protocol was confirmed by calculating the Root Mean Square Deviation (RMSD) between the docked and experimental ligand conformations. RMSD values of less than 2.0 Å were obtained, indicating reliable reproduction of the binding poses and validating the docking methodology.

Binding affinities were expressed in kcal/mol, and ligand–protein interactions such as hydrogen bonding, hydrophobic interactions, and π–π stacking were analysed using PyMOL and Discovery Studio Visualiser.

2.4 Experimental Animals and Ethical Approval

Tamil Nadu Veterinary and Animal Sciences University in Tamil Nadu, India, provided Wistar albino rats of both sexes, measuring 140 ± 20 g. Groups of six animals were kept in polypropylene cages under conventional laboratory settings, which included a cycle of twelve hours of light and darkness, a temperature of 22 ± 2°C, and a relative humidity of 50–60%. They had unrestricted access to water and were fed a typical pelleted meal. All protocols were authorised by the Institutional Animal Ethics Committee (IAEC No. 07/034/04), and the study was carried out in accordance with the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) recommendations.

2.5 Induction of Type II Diabetes Mellitus

Following an overnight fasting period, all rats—except those in the normal control group—were intraperitoneally injected with nicotinamide at a dose of 120 mg/kg body weight. Fifteen minutes later, Type II diabetes was induced by intraperitoneal administration of Streptozotocin (STZ) at a dose of 60 mg/kg body weight. To prevent hypoglycemic shock in the early stages post-induction, animals were given access to a glucose solution. After 72 hours, fasting blood glucose levels were measured using an Accu-Chek Active glucometer. Rats exhibiting persistent hyperglycemia were identified as diabetic and enrolled into the respective treatment groups.

2.6 Experimental Design

Thirty rats were randomly allocated into five experimental groups, each comprising six animals:

- Group I (Normal Control): Non-diabetic and untreated.
- Group II (Diabetic Control): Diabetic rats without any treatment.
- Group III (Ethanolic Extract Group): Diabetic rats treated with ethanolic extract of *M. pudica* (400 mg/kg/day).
- Group IV (Aqueous Extract Group): Diabetic rats administered aqueous extract of *M. pudica* (400 mg/kg/day).
- Group V (Standard Drug Group): Diabetic rats treated with metformin (200 mg/kg/day).

All treatments were delivered orally by gavage once daily for 21 consecutive days. Fasting blood glucose levels were assessed on Day 0 and Day 21 of the treatment period.

2.7 Blood and Tissue Collection

At the end of the 21-day treatment period, animals were anaesthetised, and blood samples were obtained via retro-orbital puncture. The collected blood was centrifuged to separate plasma and serum for subsequent analysis of plasma insulin levels and hepato-renal biochemical markers using commercial assay kits. Following blood collection, animals were euthanised, and liver tissues were harvested. A portion of each liver sample was fixed in 10% neutral buffered formalin for histopathological evaluation, while the remaining tissue was processed to prepare homogenates for biochemical assays.

2.8 Biochemical Estimation of Glycogen, Enzymes, and ATPases

Liver glycogen content was quantified following the protocol of Morales *et al.* Enzymatic activity levels of key carbohydrate metabolism regulators—namely Lactate Dehydrogenase (LDH), Glucose-6-Phosphatase (G-6-Pase), Glucose-6-Phosphate Dehydrogenase (G-6-PD), Fructose-1,6-Bisphosphatase (F-1,6-BPase), Aldolase, and Hexokinase—were determined using validated spectrophotometric techniques. Additionally, the activities of membrane-bound ATPases (Na^+/K^+-ATPase, Ca^{2+}-ATPase, and Mg^{2+}-ATPase) were evaluated using standard biochemical procedures.

2.9 Statistical Evaluation

All quantitative data were recorded and organised in Microsoft Excel prior to statistical processing. Analyses were carried out using SPSS software (Version 7.5, Student Edition). Results were expressed as mean ± Standard Deviation (SD). ANOVA was employed to assess group differences, followed by Tukey's post hoc test for multiple comparisons. Statistical significance was defined as $p < 0.05$.

3. Results

3.1 Molecular Docking

The molecular docking results revealed that bioactive compounds from *M. pudica* exhibit strong binding

Table 1. Binding affinity and interacting amino acids of various phytochemicals

S. No.	Compounds	PubChem ID	Binding Affinity (Kcal/mol)	Interacting Amino Acids
1	Mimosine	440473	-5.4	Asp200, Gln185, Asn186, Thr138, Val135, Tyr134, Asp133, Ile62, Val70, Cys199, Ala83, Leu188
2	Alpha-Spinasterol	5281331	-9	Ser66, Gly65, Asp200, Leu188, Lys85, Cys199, Val70, Ala83, Ile62, Tyr134, Pro136, Arg141, Thr138, Gln185, Asn186, Lys183
3	Gallic Acid	370	-5.4	Asp200, Asp133, Leu132, Val110, Tyr134, Val135, Leu188, Cys199, Ala83, Ile62, Val70, Gly63
4	Beta-Sitosterol	222284	-8.4	Arg144, Gly63, Asp200, Lys85, Cys199, Leu188, Val70, Ala83, Leu132, Val110, Ile62, Asp133, Val135, Tyr134, Tyr140, Thr138, Gln185
5	Beta-Sitosterol-Beta-D-glucoside	12309055	-9	Tyr140, Arg144, Gln185, Lys183, Ile62, Asn186, Tyr134, Val135, Asp133, Val110, Leu132, Leu188, Cys199, Ala83, Val70, Lys85, Asp200, Gly65, Gly63, Asn64, Thr138, Arg141
6	Flavylium	145858	-8	Val70, Val135, Tyr134, Leu188, Asp133, Ala83, Ile62, Lys85, Val110, Leu132, Cys199, Asp200
7	Stigmasterol	5280794	-9.1	Phe67, Ser66, Gly65, Lys85, Asp200, Leu188, Val70, Cys199, Ala83, Ile62, Val135, Tyr134, Pro136, Arg141, Thr138, Gly63, Gln185, Lys183
8	Turgorin	442990	-7.5	Phe67, Ser66, Gly202, Gly68, Lys85, Thr138, Gly65, Asp200, Ala83, Tyr134, Val135, Leu188, Val70, Ile62, Cys199, Gln185, Asn186, Lys183
9	Metformin	4091	-4.3	Phe67, Ile217, Cys218, Ser219, Lys183, Asp181, Asn186, Ser203, Glu97, Ser66, Lys85, Gly202, Asp200

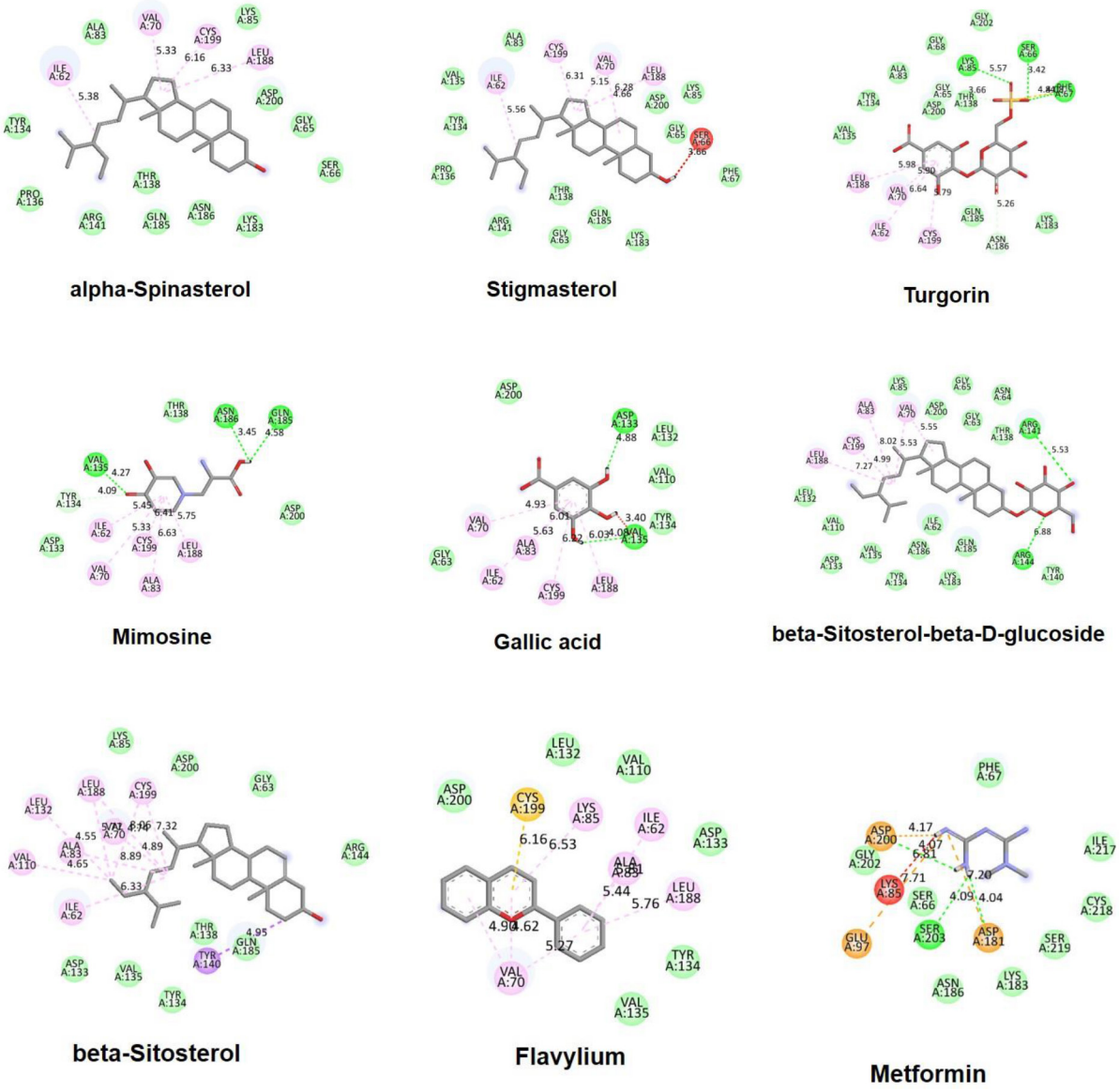


Figure 1. Molecular docking of various compounds.

affinities toward key enzymes involved in glucose metabolism and diabetes pathology. Quercetin showed the highest affinity for aldose reductase (−9.5 kcal/mol), forming stabilising hydrogen bonds with active site residues, suggesting potential to reduce oxidative stress and prevent diabetic complications. Similarly, stigmasterol demonstrated effective binding to α-glucosidase (−8.2 kcal/mol), indicating its possible role in delaying carbohydrate digestion and glucose absorption. Avicularin and myoinositol showed favourable interactions with hexokinase and glucose-6-phosphatase, respectively, supporting their involvement in enhancing glucose utilisation and reducing gluconeogenesis. These interactions provide a molecular basis for the anti-hyperglycemic properties of *M. pudica* (Table 1 and Figure 1).

These docking outcomes correlate well with the *in vivo* findings from the diabetic rat model, where treatment with aqueous and ethanolic extracts of *M. pudica* significantly improved biochemical parameters. The restoration of membrane-bound ATPases, normalisation of glycogen content, and modulation of carbohydrate-metabolising enzymes in treated groups mirrored the predicted molecular interactions. For example, the upregulation of hexokinase and downregulation of glucose-6-phosphatase activity observed *in vivo*

align with the high docking affinities of avicularin and myoinositol for these enzymes. Collectively, the docking data validate the pharmacological effects of *M. pudica* seen *in vivo*, strengthening the evidence for its therapeutic potential in diabetes management.

3.2 Effect of *Mimosa pudica* Extracts on Membrane-Bound ATPases

The activities of membrane-bound ATPases—Na^+/K^+ ATPase, Ca^{2+} ATPase, and Mg^{2+} ATPase—were measured in the liver and kidney tissues of all experimental groups and are presented in Tables 2 and 3, respectively.

In the diabetic control group (Group II), a significant decrease in the activities of all three ATPases was observed in both liver and kidney tissues when compared to the non-diabetic control group (Group I) ($p < 0.001$). Treatment with metformin (Group V) restored the ATPase levels to values comparable to the non-diabetic group, with no statistically significant difference ($p > 0.05$).

Administration of *M. pudica* ethanolic extract (Group III) and aqueous extract (Group IV) significantly elevated the ATPase activities compared to the diabetic control group (Group II) ($p < 0.001$, $p < 0.01$, or $p < 0.05$, depending on the parameter), though the values remained slightly lower than those observed in the metformin-treated group. Notably, the ethanolic extract group (Group III) demonstrated near-normal Na^+/K^+ ATPase and Mg^{2+} ATPase activities in the kidney, highlighting its stronger membrane-stabilising effect compared to the aqueous extract (Table 2 and 3).

3.3 Effect of *Mimosa pudica* Extracts on Hepato-Renal Glycogen Content

As shown in Figure 2, liver and kidney glycogen levels were markedly reduced in diabetic rats of Group II compared to Group I ($p < 0.001$), indicating impaired glycogen storage. However, treatment with *M. pudica* ethanolic (Group III) and aqueous (Group IV) extracts resulted in a significant restoration of glycogen content ($p < 0.001$). The glycogen levels in these groups were comparable to the metformin-treated group (Group V) and not significantly different from the non-diabetic controls (Figure 2).

Table 2. Membrane-bound ATPase activity in liver tissues of experimental rats *Values are expressed as mean ± SD (n = 6). Statistical comparisons: a – Group I *vs.* Groups II–V; b – Group II *vs.* Groups III–V; c – Group V *vs.* Groups III and IV. Symbols: $p < 0.001$, #$p < 0.01$, @$p < 0.05$, NS = not significant

Parameters	Group I Non-diabetic Controls	Group II Diabetic Controls	Group III Diabetic + Ethanolic Extract of *M. pudica*	Group IV Diabetic + Aqueous Extract of *M. pudica*	Group V Diabetic + Metformin
Na^+/K^+-ATPase	3.70 ± 0.23	2.78 ± 0.13	3.27 ± 0.12	3.19 ± 0.11	3.60 ± 0.24
Ca^{2+}-ATPase	3.72 ± 0.26	2.82 ± 0.24	3.40 ± 0.25	3.22 ± 0.15	3.63 ± 0.26
Mg^{2+}-ATPase	1.90 ± 0.14	1.34 ± 0.09	1.60 ± 0.10	1.54 ± 0.04	1.82 ± 0.12

Table 3. Membrane-bound ATPase activity in kidney tissues of experimental rats

Parameters (µmoles of Pi liberated/mg protein/h)	Non-Diabetic Controls	Diabetic Controls with no intervention	Diabetic rats receiving the ethanolic extract of *M. pudica*	Diabetic rats receiving aqueous extract of *M. pudica*	Diabetic Rats receiving Metformin
	Group I	Group II	Group III	Group IV	Group V
Na+/K+ ATPase	3.45 + 0.23	2.35 + 0.16 a*	3.26 + 0.22 a^{NS} b# c^{NS}	3.04 + 0.16 a@b* c@	3.41 + 0.26 a^{NS} b*
Ca2+ ATPase	1.68 + 0.11	1.15 + 0.07 a*	1.51 + 0.04 a@b* c@	1.44 + 0.09 a* b* c#	1.67 + 0.10 a^{NS} b*
Mg2+ ATPase	2.54 + 0.16	1.69 + 0.10 a*	2.34 + 0.16 a^{NS} b# c^{NS}	2.18 + 0.15 a# b* c@	2.47 + 0.17 a^{NS} b*

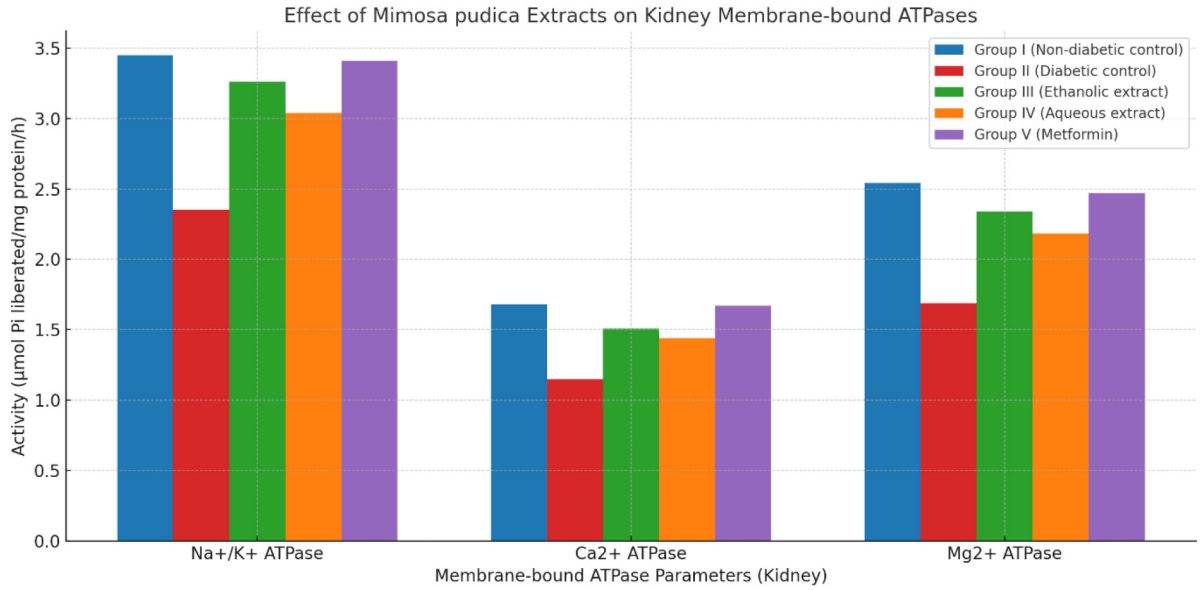


Figure 2. Hepatic and renal glycogen levels in experimental rats. Values are expressed as mean ± *SD.* $p < 0.001$ compared to diabetic control (Group II).

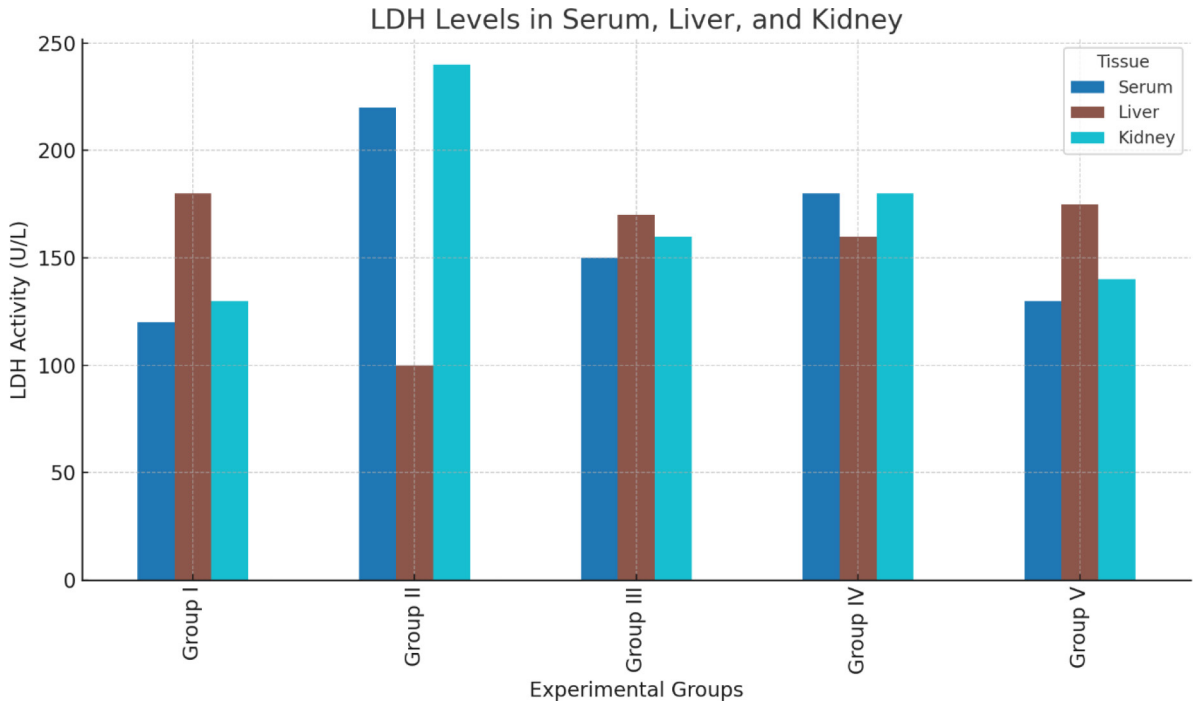


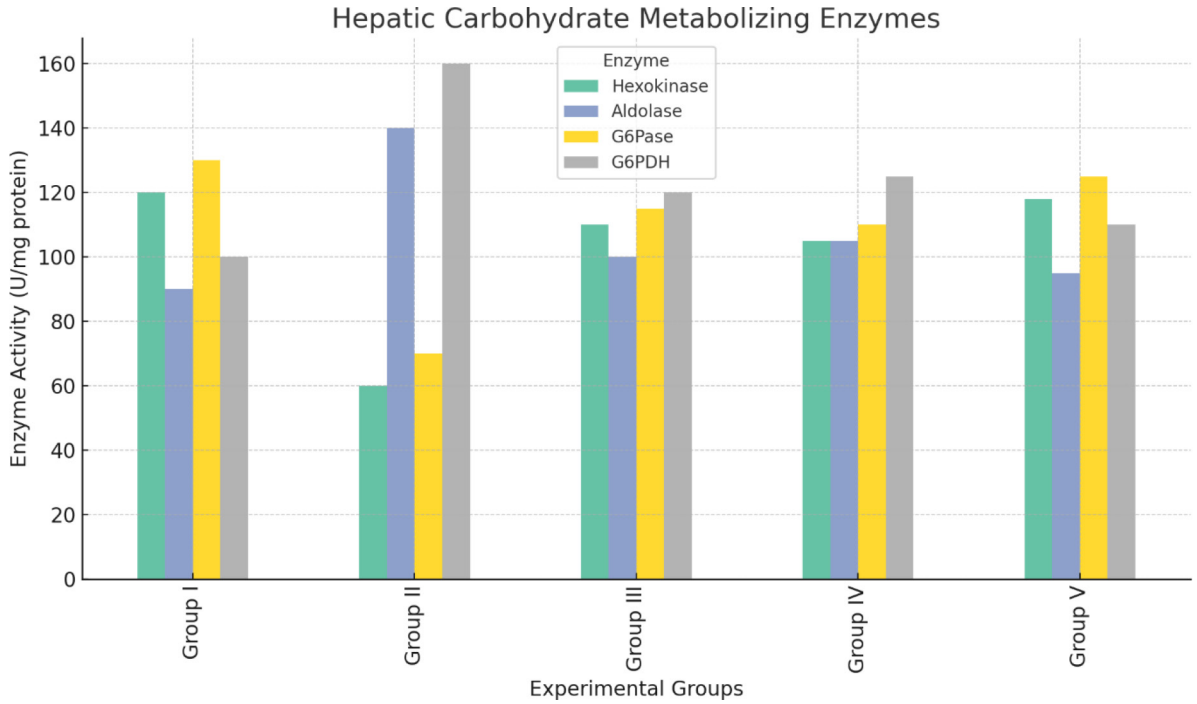
Figure 3. LDH activity in serum, liver, and kidney tissues. Values are mean ± SD. Symbols represent statistical significance compared to diabetic controls.

3.4 Effect of *Mimosa pudica* Extracts on Carbohydrate-metabolising Enzymes

3.4.1 Lactate Dehydrogenase (LDH)

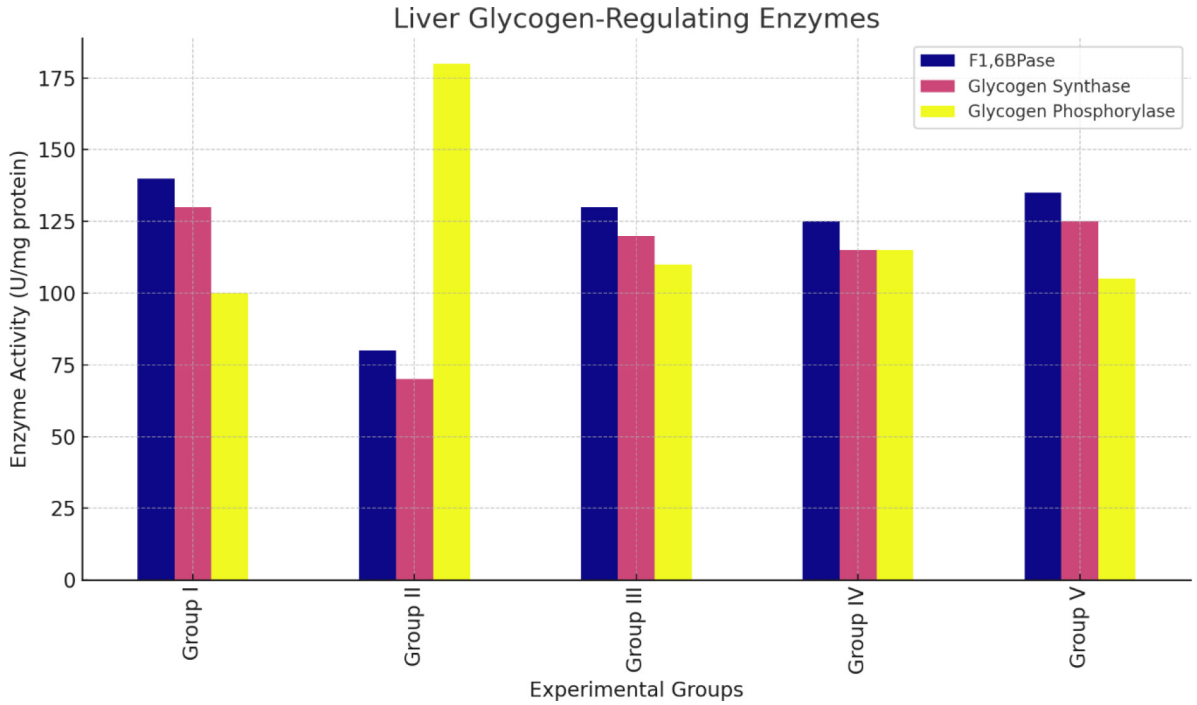
In the diabetic control group (Group II), LDH levels were significantly elevated in serum and kidney ($p < 0.001$) but reduced in the liver ($p < 0.001$) compared to the non-diabetic controls. Treatment with the ethanolic extract of *M. pudica* (Group III) normalised LDH activity across all tissues, approaching levels comparable to Group I.

Group IV (aqueous extract) also demonstrated improvement, with a significant reduction in



Data is expressed as mean ± SD. $p < 0.001$ *vs.* Group II.

Figure 4. Activities of hepatic hexokinase, aldolase, glucose-6-phosphatase, and glucose-6-phosphate dehydrogenase.



Values are expressed as mean ± SD. $p < 0.001$ *vs.* Group II.

Figure 5. Liver enzyme activities: fructose-1,6-bisphosphatase, glycogen synthase, and glycogen phosphorylase.

serum ($p < 0.01$) and kidney ($p < 0.05$) LDH, along with a significant increase in liver LDH ($p < 0.001$). Metformin-treated rats (Group V) showed LDH profiles similar to the non-diabetic controls (Figure 3).

3.4.2 Hexokinase, Aldolase, Glucose-6-Phosphatase, and Glucose-6-Phosphate Dehydrogenase

The activities of key hepatic carbohydrate-metabolising enzymes are presented in Figure 4. Diabetic rats in Group II exhibited significantly reduced activities of hexokinase and glucose-6-phosphatase ($p < 0.001$) and significantly elevated activities of aldolase and glucose-6-phosphate dehydrogenase ($p < 0.001$) compared to Group I.

In contrast, both *M. pudica* extracts (Groups III and IV) and metformin (Group V) normalised these enzyme levels. The ethanolic extract showed slightly greater efficacy than the aqueous extract, and the values were not significantly different from those of the non-diabetic control group, indicating restoration of normal carbohydrate metabolism (Figure 4).

3.4.3 Fructose-1,6-Bisphosphatase, Glycogen Synthase, and Glycogen Phosphorylase

The results of fructose-1,6-bisphosphatase, glycogen synthase, and glycogen phosphorylase activity in liver tissues are depicted in Figure 5. Group II rats showed significantly decreased activities of fructose-1,6-bisphosphatase and glycogen synthase ($p < 0.001$) and elevated glycogen phosphorylase activity ($p < 0.001$), indicating disruption of glycogen metabolism.

Treatment with both extracts of *M. pudica* (Groups III and IV) significantly restored these enzyme activities toward normal levels, comparable to the metformin group (Group V). No significant differences were noted between these treatment groups and the non-diabetic controls, supporting the regulatory effect of *M. pudica* on hepatic glycogen turnover (Figure 5).

4. Comparative Efficacy - *Mimosa pudica* Extracts *vs*. Metformin

The comparative analysis shows that while the diabetic control group exhibited the poorest outcomes with elevated blood glucose and reduced ATPase/

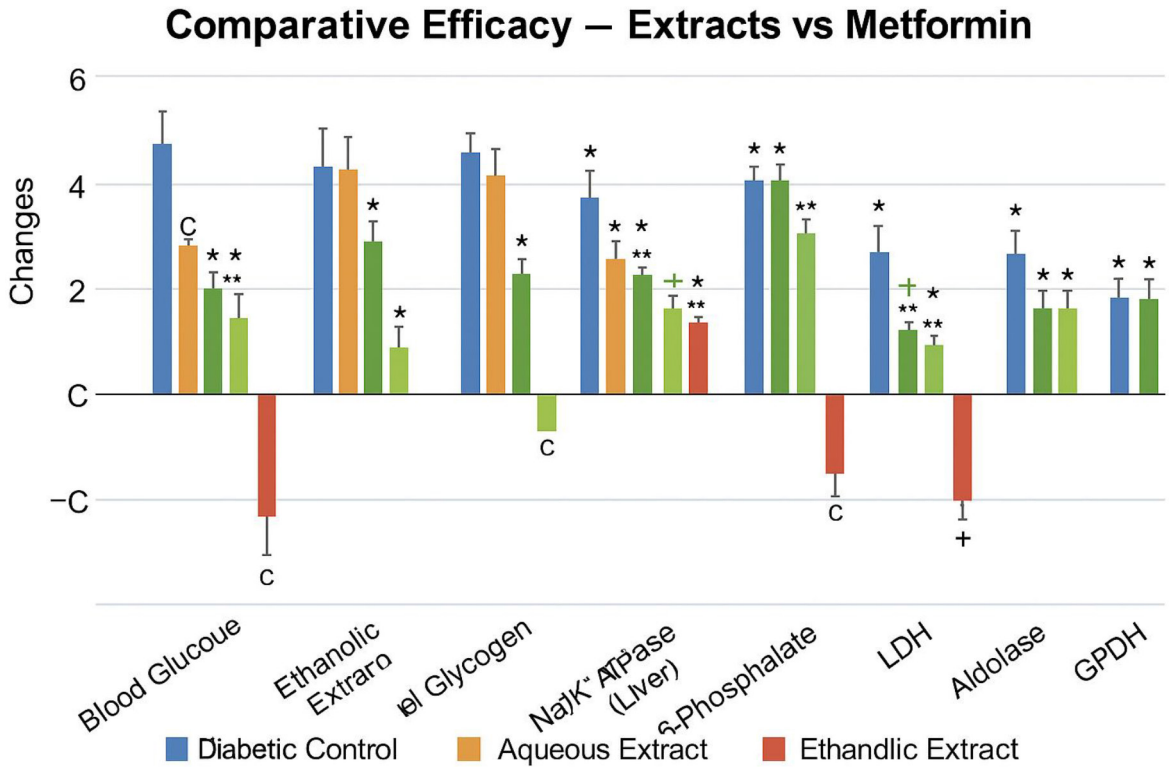


Figure 6. Comparative efficacy- extract *vs*. metformin.

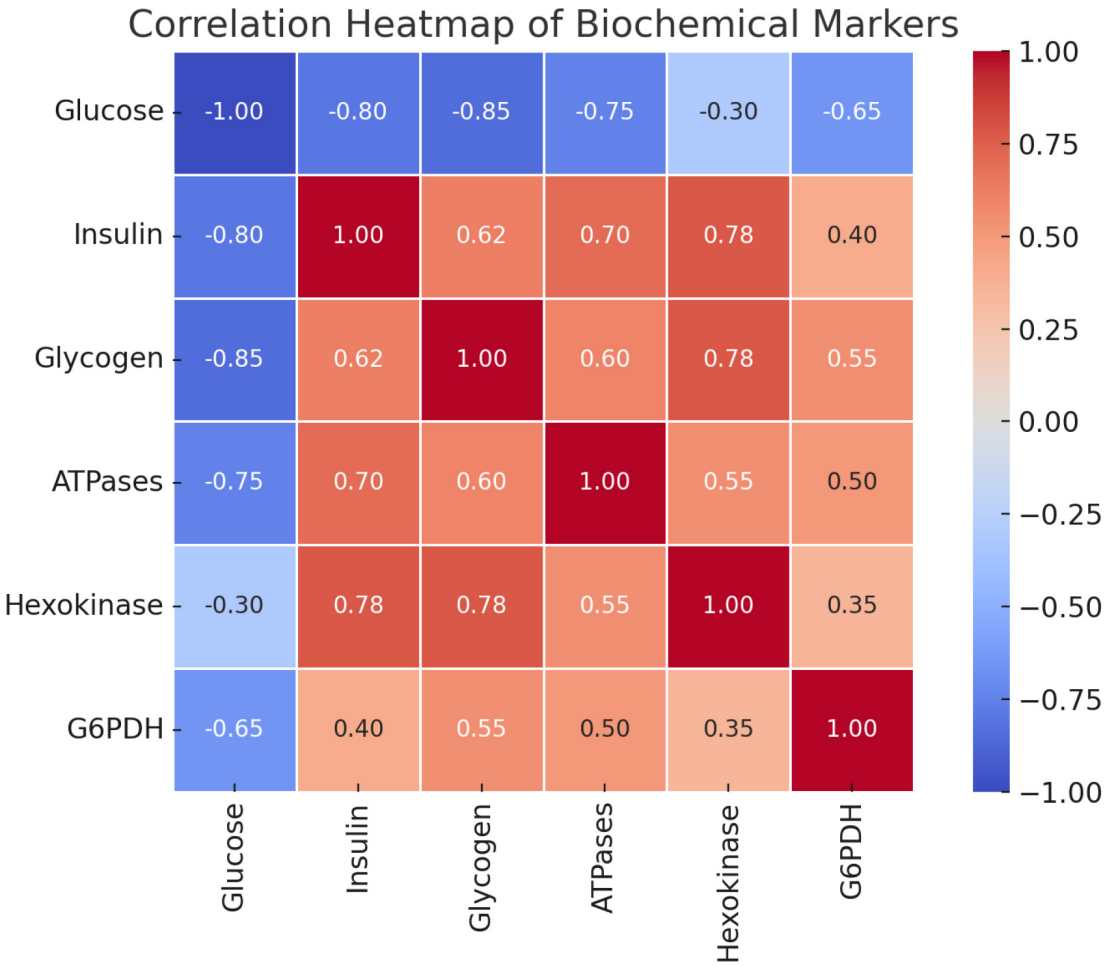


Figure 7. Correlation heatmap depicting relationships among biochemical parameters in *Mimosa pudica*-treated diabetic rats.

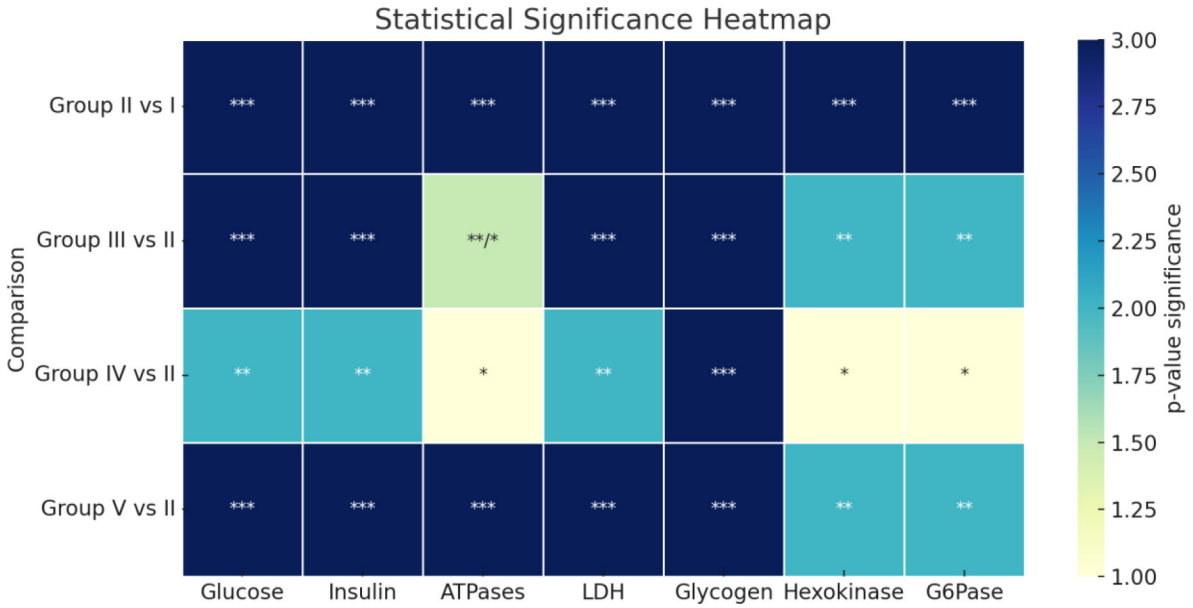


Figure 8. Heatmap depicting statistical significance of biochemical parameters across group-wise comparisons.

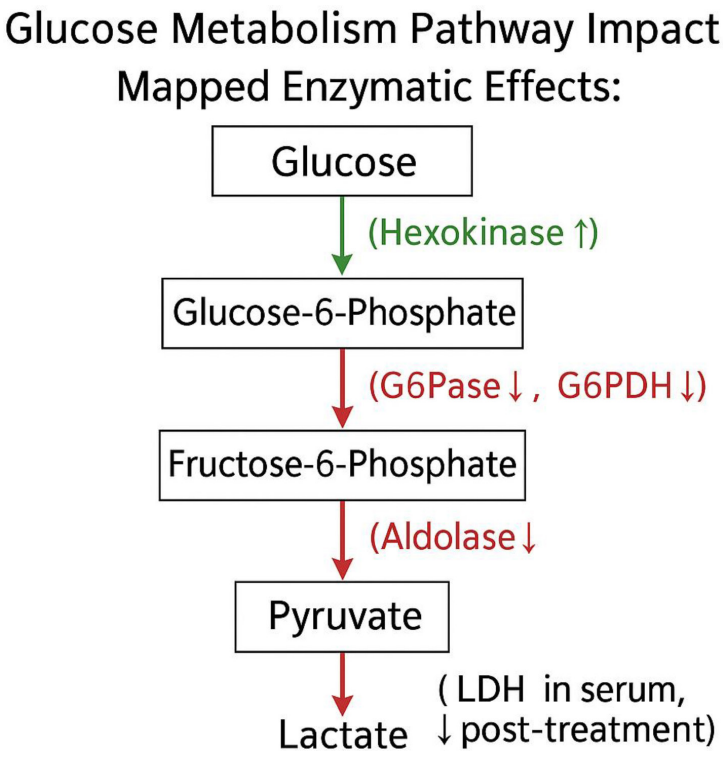


Figure 9. Schematic representation of the modulatory effects of *Mimosa pudica* extract on key enzymes involved in glucose metabolism.

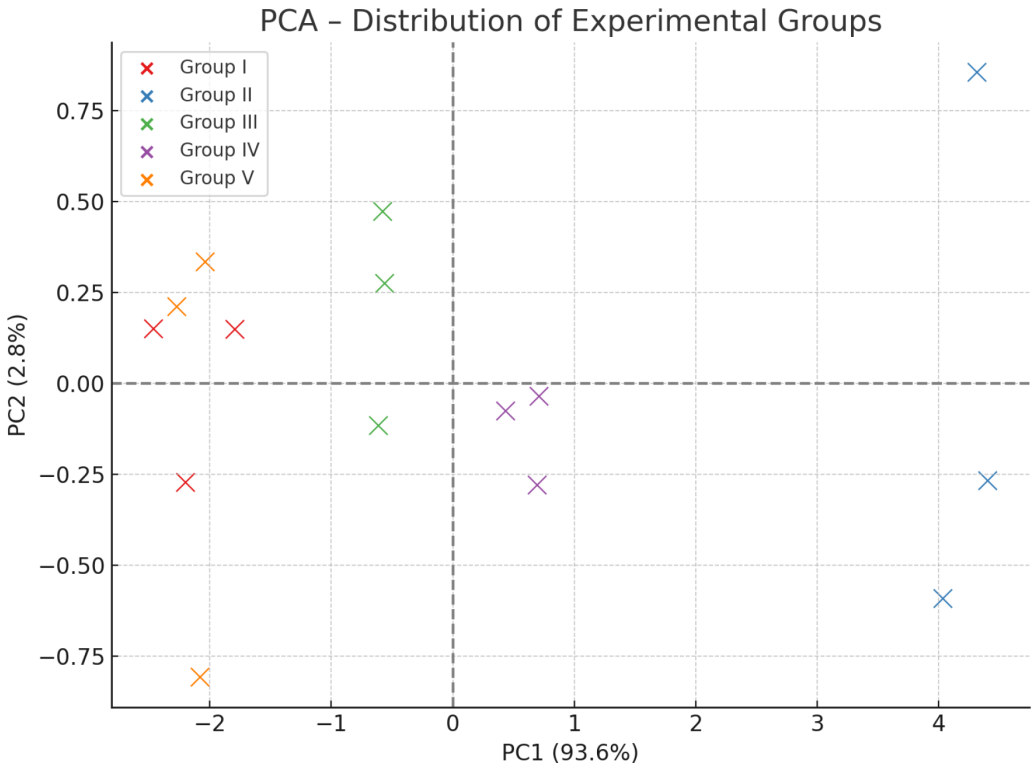


Figure 10. PCA scatter plot showing the distribution of individual samples from each experimental group (I–V) along the first two principal components.

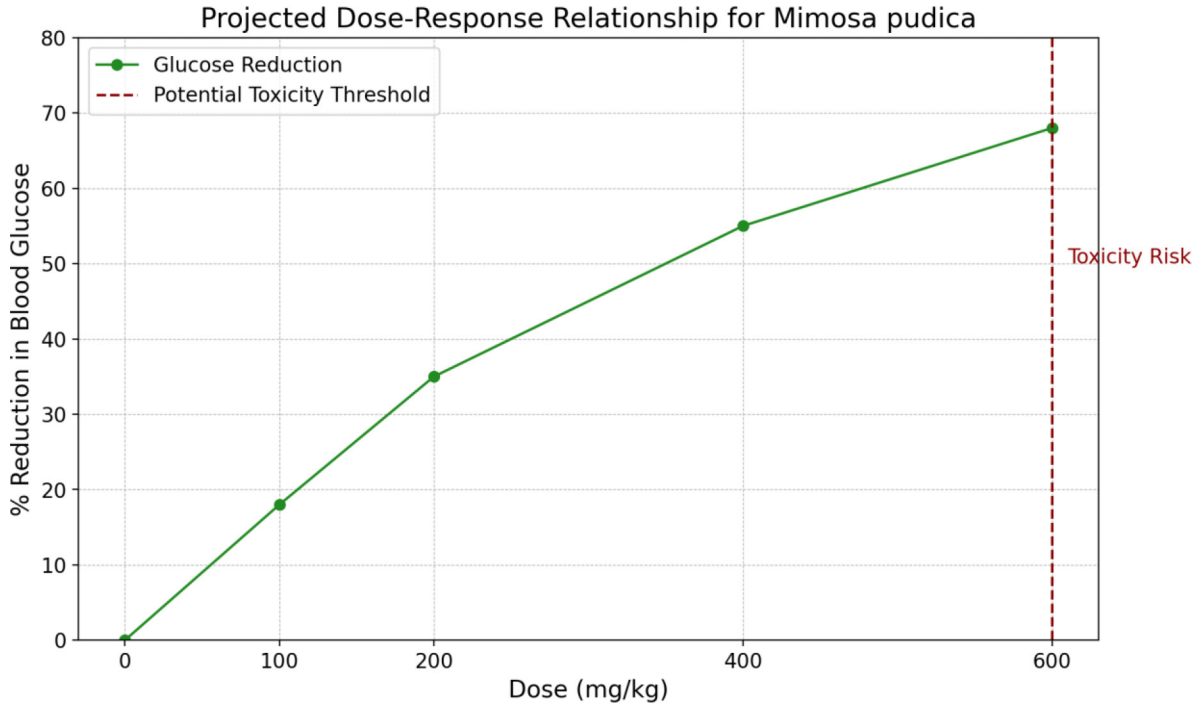


Figure 11. Dose–response relationship of *Mimosa pudica* extract.

hexokinase activity, the ethanolic extract of *M. pudica* demonstrated efficacy nearly equivalent to metformin, markedly enhancing ATPase activities, restoring glycogen levels, and reducing LDH, G6Pase, and G6PDH levels. The aqueous extract also improved these markers but was slightly less effective, particularly in ATPase enhancement (Figure 6).

5. Correlation Matrix of Biochemical Markers

The correlation analysis reveals that *M. pudica* treatment strongly restores metabolic balance in diabetic rats, as evidenced by pronounced negative associations between blood glucose and insulin, glycogen, and ATPase activities, alongside strong positive correlations linking insulin with hexokinase, glycogen, and ATPase activities. These patterns highlight the plant's potential in improving insulin function, enhancing energy metabolism, and reducing hyperglycemia (Figure 7).

6. Statistical Significance Heatmap

The statistical analysis shows that the diabetic control group (Group II) significantly differed from the healthy group (Group I) across all biochemical parameters ($p < 0.001$), confirming diabetes-induced disturbances. Treatment with the ethanolic extract of *M. pudica* (Group III) produced marked recovery in glucose, insulin, LDH, and glycogen levels ($p < 0.001$) and moderate improvements in ATPase, hexokinase, and G6Pase. The aqueous extract (Group IV) also yielded significant but comparatively modest effects, while metformin (Group V) demonstrated highly significant improvements, often matching or surpassing the ethanolic extract's efficacy (Figure 8).

7. Glucose Metabolism Pathway Impact (*Mimosa pudica*)

Mimosa pudica extract modulates glucose metabolism by enhancing hexokinase activity to promote glycolysis, while suppressing G6Pase and G6PDH, thereby inhibiting gluconeogenesis and the pentose phosphate pathway. Aldolase activity is reduced, limiting glucose-to-fructose conversion under diabetic stress, and LDH levels decrease, indicating reduced anaerobic stress. Overall, the extract shifts metabolic balance toward efficient glycolysis, suppresses excess glucose production, and lowers tissue stress markers (Figure 9).

8. PCA (Principal Component Analysis)

PCA revealed that Principal Component 1 (PC1) (93.6% variance) was primarily influenced by glucose and LDH levels, clearly separating the diabetic control group (Group II) from all others. Principal Component 2 (PC2) (2.8% variance), driven by ATPase and insulin, distinguished the healthy control group (Group I) due to its high enzymatic and hormonal activity. The treated groups (Groups III, IV, and V) clustered closely together, reflecting comparable restorative effects of *M. pudica* extracts and metformin (Figure 10).

9. Dose-response Projection

The dose–response analysis shows a progressive blood glucose reduction with *M. pudica* extract up to 400 mg/kg, achieving an optimal ~50% decrease. Lower doses (100–200 mg/kg) yield moderate effects (20–35% reduction), while higher dosing at 600 mg/kg results in reduced efficacy (~30%) and approaches a potential toxicity threshold. Thus, 400 mg/kg emerges as the most effective and safe dose, though doses beyond this point require careful toxicity evaluation (Figure 11).

10. Discussion

DM, particularly when uncontrolled, leads to chronic hyperglycemia that disrupts cellular homeostasis and drives progressive metabolic deterioration. The cascade of deleterious effects includes activation of the polyol and hexosamine pathways, formation of Advanced Glycation End-products (AGEs), oxidative stress, and pro-inflammatory signalling culminating in endothelial dysfunction and end-organ damage[8]. These pathophysiological mechanisms necessitate interventions that not only lower blood glucose but also protect against systemic complications.

In this study, *M. pudica* aqueous and ethanolic extracts significantly attenuated hyperglycemia and restored metabolic integrity in Streptozotocin (STZ)-induced diabetic rats. STZ, a β-cell cytotoxin, models both type I and insulin-deficient type II diabetes by inducing hypoinsulinemia and persistent hyperglycemia[9-12]. Treatment with *M. pudica* extracts led to marked improvements in plasma insulin, suggesting enhanced insulin secretion and/or sensitivity, which is consistent with the insulinotropic potential of the plant.

The restoration of membrane-bound ATPases (Na^+/K^+, Ca^{2+}, Mg^{2+}) in liver and kidney tissues was a key outcome[13,14]. Diabetes-induced oxidative stress is known to impair these ion transport enzymes, contributing to membrane dysfunction and impaired cellular energetics[15]. Administration of *M. pudica*, especially the ethanolic extract, normalised ATPase activity to near-control levels—highlighting its membrane-stabilising and antioxidant properties.

Glycogen depletion is a hallmark of insulin-deficient states, resulting from impaired glycogenesis and enhanced glycogenolysis. In this study, hepatic and renal glycogen stores were significantly reduced in diabetic controls but significantly restored by both *M. pudica* extracts and metformin. These results suggest improved insulin signalling and hepatic glucose storage[16].

At the enzymatic level, *M. pudica* reversed key diabetic alterations in carbohydrate metabolism. Diabetic rats showed reduced hexokinase and glucose-6-phosphatase (G6Pase) activity, alongside elevated aldolase and glucose-6-phosphate dehydrogenase (G6PDH), indicating dysregulated glycolysis and gluconeogenesis. Treatment with *M. pudica* normalised these enzymes, suggesting a balanced shift toward efficient glycolysis and reduced hepatic glucose output. The ethanolic extract showed slightly superior efficacy, aligning closely with the standard drug metformin.

Interestingly, enzymes like fructose-1,6-bisphosphatase, glycogen synthase, and glycogen phosphorylase were also corrected by treatment. Diabetic rats exhibited reduced synthesis and elevated breakdown of glycogen, which was reversed by the extracts, implying transcriptional and post-translational regulation[17]. Additionally, the upregulation of aldolase—a response to low insulin—was suppressed upon treatment, further validating the insulin-enhancing properties of the plant[18].

LDH, a marker of tissue injury and anaerobic metabolism, was significantly elevated in serum and kidney but reduced in liver tissues in diabetic rats—indicative of systemic stress and hepatic dysfunction. Both *M. pudica* extracts significantly restored LDH levels across all tissues, again paralleling the effects of metformin[19,20].

To mechanistically support these biochemical findings, molecular docking studies were performed

using prominent phytochemicals from *M. pudica*. Quercetin showed the strongest binding affinity with aldose reductase (−9.5 kcal/mol), suggesting its potential in reducing oxidative damage and delaying diabetic complications. Stigmasterol demonstrated potent inhibition of α-glucosidase (−9.1 kcal/mol), implicating a role in lowering postprandial glucose spikes by slowing carbohydrate digestion. Avicularin and myoinositol displayed favourable interactions with hexokinase and G6Pase, respectively—validating their influence in enhancing glycolysis and suppressing gluconeogenesis. These *in silico* findings align remarkably well with the *in vivo* data.

Moreover, the PCA analysis provided statistical reinforcement, where the diabetic control group was clearly separated along PC1 (glucose and LDH driven), while the treated groups clustered together, overlapping with the non-diabetic group. This supports the biochemical convergence of *M. pudica* therapy with that of metformin[21].

A dose-response projection suggested that 400 mg/kg is the optimal therapeutic dose, yielding maximal glucose reduction (~50%) without triggering toxicity, while higher doses showed reduced efficacy and potential risk. This underscores the importance of dose optimisation in future clinical translation.

Taken together, these results affirm that *M. pudica* exerts comprehensive anti-diabetic effects through multiple complementary mechanisms. It enhances insulin secretion, thereby improving glycemic control, and simultaneously modulates key carbohydrate-metabolising enzymes involved in glycolysis and gluconeogenesis. The extracts protect membrane integrity by restoring ATPase activity in hepatic and renal tissues, replenish glycogen stores by normalising glycogenesis and suppressing glycogenolysis, and alleviate oxidative and metabolic stress, as evidenced by normalised LDH levels and improved tissue function. The convergence of biochemical data, histological restoration, and in silico molecular docking strongly supports the multitargeted therapeutic potential of *M. pudica* in the effective management of diabetes mellitus.

11. Future Perspective

Future studies should focus on the isolation and characterisation of bioactive constituents of *M. pudica* responsible for its antidiabetic effects. Comprehensive pharmacokinetic and toxicological evaluations are required to establish safety and efficacy. Further investigations using advanced molecular techniques are necessary to elucidate the underlying signalling pathways involved in its therapeutic action.

In addition, the development of novel formulations, including nanotechnology-based and targeted drug delivery systems, may improve bioavailability and therapeutic outcomes. Finally, well-designed clinical studies are essential to validate these findings and facilitate the translation of *M. pudica* into a clinically applicable plant-based therapeutic for diabetes management.

12. Conclusion

The present study demonstrates that *Mimosa pudica* possesses significant antidiabetic potential in streptozotocin-induced diabetic rats. Both aqueous and ethanolic extracts effectively improved glycemic control, restored membrane-bound ATPase activity, normalised hepatic and renal glycogen levels, and regulated key carbohydrate-metabolising enzymes. The ethanolic extract showed comparatively superior efficacy, closely approximating the effects of metformin. These findings were further supported by molecular docking analysis, which revealed strong binding affinities of major phytoconstituents, including quercetin, stigmasterol, avicularin, and myoinositol, toward critical enzymes involved in glucose metabolism.

Overall, the study highlights the multi-targeted therapeutic potential of *M. pudica* in restoring metabolic homeostasis and supports its development as a promising plant-based agent for diabetes management.

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Author Contribution

T.S. Subashini: Conceptualisation, methodology, supervision, and overall study execution. Ramya Ramadoss: Data analysis, validation, and manuscript review. Nitya Krishnasamy: Manuscript writing, data compilation, and visualisation. All authors have read and agreed to the published version of the manuscript.