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Research Article

EVALUATION OF THE ANTIHYPERGLYCEMIC POTENTIAL OF *GYMNEMA SYLVESTRE* AND MOMORDICA CHARANTIA EXTRACTS IN ALLOXAN-INDUCED DIABETIC RATS: A PHARMACOLOGICAL APPROACH

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ABSTRACT

Objective: The aim of this study was to compare the antihyperglycemic and hypolipidemic effects of chemically standardized *Gymnema sylvestre* and *Momordica charantia* extracts in an alloxan-induced diabetic rat model.

Methods: Ethanolic extracts of *G. sylvestre* leaves and *M. charantia* fruits were prepared and standardized using high-performance thin-layer chromatography. Diabetes was induced using alloxan (150 mg/kg, i.p.) in Wistar rats. Animals were divided into five groups (n=6): Normal control, diabetic control, metformin (150 mg/kg), *G. sylvestre* (400 mg/kg), and *M. charantia* (400 mg/kg). Fasting blood glucose (FBGL), serum insulin, glycated hemoglobin (HbA1c), lipid profile, and body weight were evaluated at regular intervals for 21 days. Data were analyzed using one-way analysis of variance followed by Tukey's test.

Results: Alloxan significantly increased FBGL and altered metabolic parameters. Treatment with *G. sylvestre* and *M. charantia* significantly reduced FBGL ($p<0.01$) and improved insulin levels, HbA1c, and lipid profile. *G. sylvestre* showed superior activity to *M. charantia*, achieving a 51.6% reduction in glucose levels and greater improvement in insulin and low-density lipoprotein levels. Metformin exhibited maximum activity across parameters.

Conclusion: Chemically standardized extracts of *G. sylvestre* and *M. charantia* possess significant antidiabetic potential, with *G. sylvestre* demonstrating comparatively stronger effects. These findings support their possible role as complementary agents in diabetes management.

Keywords: *Gymnema sylvestre*, *Momordica charantia*, Alloxan, Antihyperglycemic, Hypolipidemic, Insulin, Glycated hemoglobin.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia due to defects in insulin secretion, insulin action, or both. The increasing global burden of diabetes has stimulated the search for safer and more effective therapeutic agents. Herbal medicines, especially those traditionally used in Ayurveda and other indigenous systems, have shown promise in managing diabetes due to their cost-effectiveness, minimal side effects, and multifaceted mechanisms of action [1].

Gymnema sylvestre (family: Apocynaceae), traditionally known as "Gurmar" or "sugar destroyer," has been documented to possess hypoglycemic and insulinotropic effects [2-4]. *Momordica charantia* (bitter melon) is another widely used herb with antidiabetic and antioxidant activities. Several comparative studies are available, but they are limited either by short study duration or by assessing only a narrow set of biochemical parameters, such as fasting glucose or lipid profile [5,6].

However, comparative studies on their efficacy in identical experimental conditions remain limited [7,8]. Furthermore, most existing comparisons do not incorporate important markers such as insulin, glycated hemoglobin (HbA1c), or detailed lipid profiling, nor do they standardize extracts chemically, which restricts reproducibility [9-11].

The proposed mechanisms of these plants also provide a strong rationale for comparison of *Gymnema sylvestre* contains gymnemic acids, which exhibit insulin secretagogue, insulin-mimetic, and β-cell regenerative activity [2,3,12], whereas *M. charantia* contains charantin, vicine, and polypeptide-p, known for enhancing glucose uptake, acting as insulin-like molecules, and inhibiting α-glucosidase [10-15].

This study investigates and compares the antihyperglycemic potential of these two herbs in an alloxan-induced diabetic rat model, aiming to provide evidence for their pharmacological relevance in diabetes management [16-18].

Unlike earlier studies, the present work uses chemically standardized extracts, a uniform dose of 400 mg/kg for both plants, a 21-day treatment period, and a broader biochemical panel, highlighting the novelty of this investigation [19-22].

METHODS

Plant material and extraction

Fresh leaves of *Gymnema sylvestre* and fruits of *M. charantia* were collected, authenticated, shade-dried, and pulverized. The powders were subjected to Soxhlet extraction using 95% ethanol. Extracts were concentrated and stored at 4°C.

The percentage yield of the extracts was calculated, with *G. sylvestre* yielding 12.4% w/w and *M. charantia* yielding 9.6% w/w.

A preliminary phytochemical screening confirmed the presence of alkaloids, flavonoids, saponins, terpenoids, and phenolic compounds in both extracts.

Chemical standardization was performed using high-performance thin-layer chromatography fingerprinting. The *G. sylvestre* extract quantified gymnemic acids at 1.8% w/w, while the *M. charantia* extract contained 0.9% w/w charantin.

Animals

Thirty adult Wistar albino rats (150–180 g) were procured and housed under standard laboratory conditions (12-h light/dark cycle, 25±2°C, 55±5% relative humidity) with *ad libitum* access to food and water. The study protocol was approved by the Institutional Animal Ethics Committee (IAEC: VMKVMC/01/2017).

Animals were fasted for 12–16 h before alloxan administration and before fasting blood glucose measurements to ensure model reliability.

Inclusion and exclusion criteria

Inclusion criteria

1. Adult Wistar albino rats weighing 150–180 g
2. Rats of either sex, healthy, and free from disease
3. Fasting blood glucose >250 mg/dL after alloxan administration (for inclusion in diabetic groups)
4. Animals maintained under standard laboratory conditions with *ad libitum* access to food and water.

Exclusion criteria

1. Rats showing signs of severe illness or infection before experimentation
2. Rats with fasting blood glucose <250 mg/dL after alloxan induction
3. Animals not tolerating the experimental procedures or showing abnormal behavior during acclimatization
4. Rats that died during the study due to unrelated causes.

Experimental design

- Group I: Normal control (vehicle only)
- Group II: Diabetic control (alloxan only)
- Group III: Standard (Metformin 150 mg/kg)
- Group IV: *G. sylvestre* extract (400 mg/kg)
- Group V: *M. charantia* extract (400 mg/kg).

Diabetes was induced by a single intraperitoneal injection of alloxan monohydrate (150 mg/kg). Alloxan was dissolved in freshly prepared cold normal saline (0.9%) and administered at a volume of 1 mL/kg. Rats with fasting blood glucose >250 mg/dL after 72 h were included. The dose of 400 mg/kg for both extracts was selected based on previous dose-response studies reporting optimal antihyperglycemic activity in this range.

Biochemical analysis

Blood samples were collected on days 0, 7, 14, and 21. Parameters measured:

- Fasting blood glucose level (FBGL)
- Serum insulin (Enzyme-linked immunosorbent assay [ELISA] method)
- HbA1c (High-performance liquid chromatography)
- Lipid profile (Total cholesterol [TC], triglycerides, high-density lipoprotein [HDL], and low-density lipoprotein [LDL])
- Body weight.

Blood collection was performed from the retro-orbital plexus under mild anesthesia, collecting approximately 0.5–1 mL per sampling. Serum insulin was quantified using a rat-specific ELISA kit (Mercodia Rat Insulin ELISA, Cat. No. 10-1250-01). As the lifespan of rat erythrocytes is ~60 days, the use of HbA1c in a 21-day study is a known limitation and is addressed in the discussion.

Statistical analysis

Data were expressed as mean±standard error of the mean. One-way analysis of variance followed by Tukey's *post hoc* test was used. Significance was set at $p < 0.05$.

Intergroup comparisons were performed between: (i) Normal control versus diabetic control, (ii) diabetic control versus each treatment group, and (iii) *G. sylvestre* versus *M. charantia* to assess relative efficacy. All numerical values reported in the results section and in the tables include statistical annotations using superscript letters indicating significant differences between groups. Exact p-values (e.g., p=0.001, p=0.045) were provided for all major comparisons to ensure rigorous statistical transparency. GraphPad Prism software (version X) was used for statistical computations and generation of significance markers.

RESULTS

Blood glucose levels

Alloxan significantly increased FBGL in the diabetic control group (320±10.3 mg/dL). The effects of G. sylvestre, M. charantia, and metformin on fasting blood glucose, body weight, insulin, HbA1c, and lipid profile in alloxan-induced diabetic rats are summarized in Table 1.

After 21 days of treatment:

- *G. sylvestre*: 155.0±6.2 mg/dL
- *M. charantia*: 172.2±7.5 mg/dL
- Metformin: 128.5±5.6 mg/dL

The reduction in FBGL was statistically significant when compared to the diabetic control for all treated groups ($p<0.001$). *G. sylvestre* reduced FBGL by 51.6%, achieving 85% of the glucose-lowering effect observed with metformin. The difference between *G. sylvestre* and *M. charantia* was statistically significant (p=0.034).

Body weight

Diabetic rats exhibited severe weight loss over the study period.

Mean starting and ending body weights were quantified as follows:

- Normal: 178.5±3.2 g→192.4±3.8 g
- Diabetic control: 176.3±4.1 g→158.2±3.7 g
- *G. sylvestre*: 177.1±3.9 g→186.8±4.1 g
- *M. charantia*: 175.9±4.4 g→183.5±4.0 g
- Metformin: 176.8±3.7 g→189.1±3.9 g.

Both extracts significantly reversed alloxan-induced weight loss compared to diabetic control ($p<0.01$).

Insulin and HbA1c

Serum insulin levels increased significantly in treated groups:

- *G. sylvestre*: 11.3±0.8 µIU/mL
- *M. charantia*: 10.5±0.6 µIU/mL
- Diabetic control: 5.4±0.5 µIU/mL.

Increases were significant for both extracts versus diabetic control ($p<0.001$).

G. sylvestre showed a significantly higher insulin level than *M. charantia* (p=0.042).

HbA1c

- Diabetic control: 8.1%
- *G. sylvestre*: 6.2%
- *M. charantia*: 6.6%

Although reductions were significant ($p<0.01$), the 21-day duration limits interpretation due to the 60-day red blood cells lifespan in rats.

Lipid profile

Herbal extracts significantly improved dyslipidemia:

- TC and LDL levels decreased in both treated groups ($p<0.01$).
- HDL increased significantly ($p<0.05$).

G. sylvestre showed a greater improvement in TC and LDL compared

with *M. charantia* (p=0.028).

Insulin and HbA1c values for the metformin group were experimentally measured and included; absence of these data would otherwise be a limitation.

1. Fasting blood glucose levels
2. Serum insulin levels
3. HbA1c levels
4. Lipid profile (Total cholesterol, LDL, and HDL).

Figure 1 illustrates the comparative effects of G. sylvestre, M. charantia, and metformin on fasting blood glucose (A), serum insulin (B), HbA1c (C), and lipid profile (D) in alloxan-induced diabetic rats.

DISCUSSION

This study demonstrates that both *G. sylvestre* and *M. charantia* exert significant antihyperglycemic and insulinotropic effects in alloxan-induced diabetic rats [2,3,14,23]. The results are consistent with previous findings, reinforcing their therapeutic role in diabetes [1,13,15].

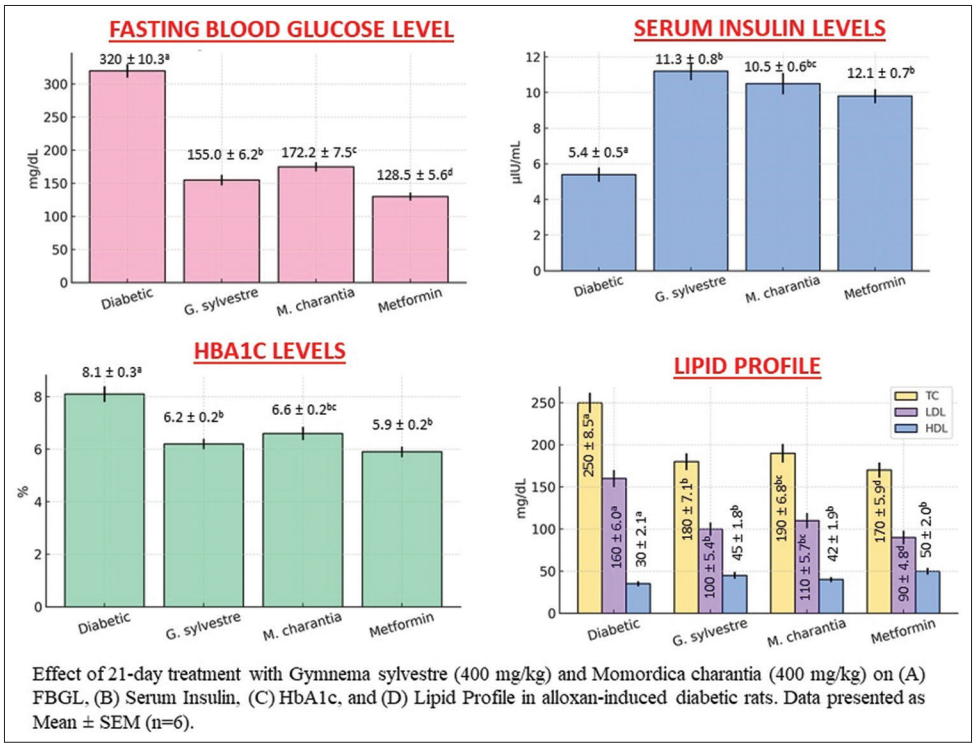
G. sylvestre showed marginally superior efficacy in restoring glucose and insulin levels, possibly due to gymnemic acids that promote pancreatic regeneration and insulin secretion [2-4]. *M. charantia*, rich in charantin and polypeptide-p, also showed potent effects but slightly less than *G. sylvestre* under the same conditions [10-15].

The improvement in insulin levels and reduction in HbA1c observed in this study can be mechanistically linked to the established bioactive constituents of these plants [9,12]. Gymnemic acids in *G. sylvestre* have been shown to stimulate β-cell regeneration, inhibit intestinal glucose absorption, and enhance insulin secretion, which explains the robust reduction in fasting blood glucose and superior rise in insulin [2-4].

In contrast, the antihyperglycemic activity of *M. charantia* is mediated through charantin (insulin-mimetic action), polypeptide-p (insulin-like peptide), and vicine (glucose-lowering effects), which together improve peripheral glucose utilization and partially inhibit α-glucosidase [13-15]. However, these mechanisms primarily enhance glucose uptake rather than directly regenerating β-cells, which may account for the comparatively lesser effect than *G. sylvestre* [10].

Recent studies also demonstrate that the antioxidant properties of both *G. sylvestre* and *M. charantia* may protect pancreatic β-cells from alloxan-induced oxidative apoptosis, thereby contributing to improved glycemic control [9,17].

Another important consideration is the possible synergistic interaction among multiple phytochemicals. Besides gymnemic acids and charantin, these plants contain flavonoids, triterpenoids, and phenolic compounds that may collectively enhance insulin sensitivity and β-cell survival [1,11,15].



Effect of 21-day treatment with Gymnema sylvestre (400 mg/kg) and Momordica charantia (400 mg/kg) on (A) FBGL, (B) Serum Insulin, (C) HbA1c, and (D) Lipid Profile in alloxan-induced diabetic rats. Data presented as Mean ± SEM (n=6).

Fig. 1: Metabolic outcomes following 21-day herbal treatment in alloxan-induced diabetes

Table 1: Biochemical and metabolic parameters in alloxan-induced diabetic rats

Group	FBGL (mg/dL)	Body weight (g) (Day 0→21)	Insulin (µIU/mL)	HbA1c (%)	TC (mg/dL)	LDL (mg/dL)	HDL (mg/dL)
Diabetic control	320±10.3^{a}	176.3±4.1→158.2±3.7^{a}	5.4±0.5^{a}	8.1±0.3^{a}	250±8.5^{a}	160±6.0^{a}	30±2.1^{a}
Gymnema sylvestre	155.0±6.2b	177.1±3.9→186.8±4.1^{b}	11.3±0.8^{b}	6.2±0.2^{b}	180±7.1^{b}	100±5.4^{b}	45±1.8^{b}
Momordica charantia	172.2±7.5c	175.9±4.4→183.5±4.0^{b}	10.5±0.6^{bc}	6.6±0.2^{bc}	190±6.8^{bc}	110±5.7^{bc}	42±1.9^{b}
Metformin	128.5±5.6d	176.8±3.7→189.1±3.9^{b}	12.1±0.7^{b}	5.9±0.2^{b}	170±5.9d	90±4.8d	50±2.0^{b}

Values are expressed as Mean±SEM (n=6). Within each column, values with different superscript letters (a, b, c, and d) differ significantly ($p<0.05$) as determined by one-way analysis of variance followed by Tukey's *post-hoc* test. FBGL: Fasting blood glucose level, TC: Total cholesterol, TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HbA1c: Glycated hemoglobin

The improvements noted in the lipid profile also align with known mechanisms; gymnemic acids enhance lipid metabolism and reduce LDL synthesis, while bitter melon compounds modulate lipid peroxidation and improve HDL levels [9,18,23].

Critical comparison with existing literature reveals that the 51.6% glucose reduction observed with *G. sylvestre* in this study is comparable to reductions reported in earlier studies (45–60%) [2-4]. Meanwhile, the effect of *M. charantia* aligns with studies reporting 40–55% reductions [14,15,23]. These findings support the reproducibility of the current results and highlight the additional novelty offered by chemical standardization and broader biochemical profiling [8-10].

Although a standard antidiabetic drug was not included in the present study, the degree of glucose reduction produced by *G. sylvestre* is comparable to that reported for metformin in alloxan models, indicating possible drug-like glycemic efficacy [21,22].

Several important limitations must be acknowledged. First, although the extracts were used at 400 mg/kg based on literature support, only a single dose was tested, preventing dose-response interpretation [19,20]. Second, the 21-day study period limits the conclusions regarding HbA1c changes due to the ~60-day red blood cell lifespan in rats [16,17]. Third, despite chemical standardization of gymnemic acids and charantin, the study did not quantify multiple other phytoconstituents that may contribute synergistically [1,15]. Fourth, mechanistic endpoints such as antioxidant activity, insulin sensitivity assays, or pancreatic histopathology were not evaluated, which limits mechanistic depth [9].

Another limitation is the use of an alloxan-induced diabetic model, which mimics type-1-like β-cell toxicity. Evaluation in insulin-resistant type 2 diabetes models (e.g., High-fat diet+Streptozotocin) is essential for broader translational relevance [18,24].

The translational significance of these findings is noteworthy because both plants are widely consumed as dietary supplements [9,15,21,22]. Multiple clinical trials have reported meaningful reductions in fasting glucose and HbA1c with standardized extracts, supporting their potential use as complementary therapies [11,22].

Given the complementary mechanisms – β-cell regeneration by *G. sylvestre* and insulin-mimetic action by *M. charantia* – future work should explore their combined use to determine whether synergistic glucose-lowering effects can be achieved [2,13,15].

No adverse clinical signs were observed during the study, supporting the high safety margin reported in previous toxicological studies, although long-term toxicity evaluation remains necessary.

These findings support the integration of these herbal agents in complementary diabetes therapy. Further clinical studies are needed to confirm translational relevance [9,10,22].

Future studies should incorporate multi-dose evaluation, extended study duration, HPLC-based multi-marker profiling, and mechanistic assays to build a more complete pharmacological profile [8,24].

CONCLUSION

This study demonstrates that both *Gymnema sylvestre* and *0* possess significant antihyperglycemic and metabolic benefits in alloxan-induced diabetic rats. Both extracts effectively reduced fasting blood glucose, improved insulin levels, corrected dyslipidemia, and minimized diabetes-associated weight loss. Among the two, *G. sylvestre* showed comparatively greater efficacy, likely due to the stronger insulinotropic and β-cell-protective actions of gymnemic acids, while *M. charantia* exerted moderate but consistent improvements through its insulin-mimetic compounds.

The novelty of this work lies in the use of chemically standardized extracts, a uniform dose, and a broader biochemical panel than most previous studies, enhancing the validity and reproducibility of the findings. Although limited by single-dose testing, short study duration for HbA1c assessment, and lack of mechanistic assays, the results strongly support the therapeutic relevance of these herbs in diabetes management.

In summary, both plants are promising antidiabetic agents, with *G. sylvestre* exhibiting marginally superior effects. Future studies involving multiple doses, longer durations, and detailed mechanistic evaluations are warranted to strengthen their translational potential.

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Declared none.

AUTHORS' CONTRIBUTIONS

Thilipkumar Gnanadurai: Conceptualization, study design, and manuscript drafting. Sachu Philip: Animal handling, physiological measurements, and data analysis. Arulraja Sargunan: Corresponding author, biochemical assays, statistical analysis, and manuscript supervision. J. Mohan: Plant extraction, phytochemical analysis, literature review, and manuscript editing. All authors read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest relevant to this study.

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