Assessment of *Momordica charantia* and *Gymnema sylvestre's* Anti-Diabetic Potential in Streptozotocin-Induced Diabetic Rats

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ABSTRACT:

Introduction: Hyperglycemia due to insulin resistance or decreased insulin production characterizes diabetes mellitus, a chronic metabolic condition. Due to its promise in managing diabetes with fewer adverse effects, herbal treatments have received interest. The anti-diabetic effects of *Gymnema sylvestre* and *Momordica charantia* have long made them popular medicinal herbs. Their effectiveness in rats with diabetes caused by streptozotocin (STZ) is the focus of this investigation.

Materials and Methods: The use of streptozotocin (50 mg/kg, intraperitoneally) was used to produce diabetes in Wistar rats. Rats were randomly assigned to one of five groups: normal control, diabetic control, *G. sylvestre* (250 mg/kg), *M. charantia* (250 mg/kg), or combination (250 mg/kg each extract). In this four-week trial, researchers looked at participants' oxidative stress markers, body weight, lipid profiles, and fasting blood glucose (FBG) levels. Additionally, pancreatic tissue was examined histopathologically.

Results: *G. sylvestre* and *M. charantia* both considerably decreased FBG levels when contrasted with the diabetic control group ($p < 0.05$). The hypoglycemic impact was particularly noticeable in the combo treatment. Lipid profile indicators, such as total cholesterol and triglycerides, improved in the treated groups. The levels of antioxidant enzymes (SOD, CAT, and GSH) were found to be significantly higher, and histological analysis showed that the treated groups had regenerated pancreatic β-cells.

Conclusion: According to the results, both *Momordica charantia* and *Gymnema sylvestre* have strong anti-diabetic effects, but the combination is even more effective. Possible supplementary use of these herbal extracts in the treatment of diabetes is being considered. To confirm their medicinal efficacy, additional clinical trials are necessary.

Keywords: *Gymnema sylvestre, momordica charantia,* diabetes mellitus, streptozotocin, blood glucose, antioxidants

INTRODUCTION:

One of the most pressing issues in world health today is diabetes mellitus (DM), a metabolic disease that affects people over the long term. Hyperglycemia that does not go away, whether from insulin resistance or inadequate secretion, is a hallmark of this condition [1, 2]. With an anticipated 643 million persons impacted by 2030, the International Diabetes Federation (IDF) reports that the prevalence of diabetes is rising at a rapid pace. Severe consequences such as cardiovascular diseases, nephropathy, neuropathy, and retinopathy can develop from uncontrolled diabetes, which has a profound impact on quality of life and increases healthcare burdens [1-3].

The possible anti-diabetic properties of *Gymnema sylvestre* and *Momordica charantia*, two medicinal herbs, have been the subject of much research. Another name for the woody climbing shrub *Gymnema sylvestre* is "sugar destroyer" or "Gurmar." Its native habitats include Africa and India. The presence of gymnemic acids in it has been linked to improved insulin secretion and inhibition of intestinal glucose absorption. Bitter melon, or *Momordica charantia*, is another famous medicinal plant that helps with diabetes. Its hypoglycemic action is due to the presence of bioactive substances such vicine, polypeptide-p, and charantin, which enhance insulin sensitivity and promote glucose uptake [2-4].

There are various causes of diabetes mellitus, a metabolic illness that can manifest in two main forms: type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). Insulin resistance, relative insulin insufficiency, and progressive β-cell dysfunction are hallmarks of T2DM, in contrast to T1DM, an autoimmune disorder that causes the loss of pancreatic β-cells and absolute insulin deficiency. Type 2 diabetes is by far the most common kind of diabetes, making up between 90 and 95 percent of all cases globally [3-5].

Two medicinal herbs that have been examined extensively for their potential anti-diabetic effects are *Gymnema sylvestre* and *Momordica charantia*. Ayurvedic practitioners have long relied on Gymnema sylvestre for the treatment of diabetes and obesity. Research has demonstrated that the active ingredients, especially gymnemic acids, can reduce the absorption of glucose in the intestines, improve the release of insulin, and encourage the regeneration of pancreatic β-cells. *Momordica charantia* has a similar history of use due to its hypoglycemic properties in numerous traditional medical systems. It has been found that the bioactive chemicals included in this plant can regulate lipid metabolism, increase glucose absorption by peripheral tissues, and function as insulin mimics [4-6].

Many researchers utilize streptozotocin (STZ)-induced diabetes as an experimental model to learn about diabetes's etiology and test possible treatments for the disease. STZ causes insulin insufficiency and hyperglycemia, similar to human diabetes, by specifically destroying pancreatic β-cells [5-7]. Fasting blood glucose (FBG), lipid profile, oxidative stress indicators, and pancreatic histology are some of the parameters that will be measured in this study to determine the effectiveness of *Gymnema sylvestre* and *Momordica charantia* in STZ-induced diabetic rats. This study aims to validate the traditional usage of these two medicinal herbs in diabetes care and examine their potential as adjunct therapies to standard anti-diabetic medicines by studying their combined effects [7-9].

MATERIAL AND METHODS:

Materials:

Sigma-Aldrich (USA) supplied the streptozotocin (STZ), which was prepared just before injection in a 0.1 M citrate buffer with a pH of 4.5. An authorized herbal vendor supplied the hydroalcoholic extracts of *Momordica charantia* and *Gymnema sylvestre*, and a botanist verified their authenticity. Commercial vendors supplied the standard diagnostic kits used to measure glucose, lipid profiles, and oxidative stress markers. The solvents and other reagents utilized were all of analytical quality.

Experimental Animals:
A recognized animal breeding institution provided the healthy Wistar albino rats (male, 180-220 g). The animals lived in polypropylene cages in an animal house that had good ventilation and controlled climatic conditions, including a 12-hour light/dark cycle, a temperature range of 22 ± 2°C, and a humidity level of 50 ± 5%. They were given water whenever they needed it and a regular pellet diet. The study adhered to the protocols laid out by the CPCSEA, which is an organization that oversees and controls animal experiments [9-11].

Induction of Diabetes:
After rats fasted overnight, streptozotocin (STZ) was used to induce diabetes. The STZ solution was diluted in freshly made citrate buffer (0.1 M, pH 4.5) and injected intraperitoneally (i.p.) once. The dosage was 50 mg/kg body weight. STZ is a famously diabetogenic substance that causes insulin insufficiency and high blood sugar by specifically destroying pancreatic β-cells. Glucometer readings were taken after 72 hours of STZ treatment to determine fasting blood glucose (FBG) levels. The study included animals that were diagnosed with diabetes when their FBG levels were more than 250 mg/dL [10-12].

Experimental Design:
A total of 30 diabetic rats were randomly divided into five groups, each comprising six animals (n = 6):
Group I (Normal Control): Received distilled water (1 mL/kg) and served as a healthy control.
Group II (Diabetic Control): Received STZ without any treatment and served as a disease control.
Group III (*Gymnema sylvestre* Treated): Received *G. sylvestre* extract (250 mg/kg body weight) orally via gavage once daily for 28 days.
Group IV (*Momordica charantia* Treated): Received M. charantia extract (250 mg/kg body weight) orally via gavage once daily for 28 days.
Group V (Combination Treatment): Received both *G. sylvestre* and *M. charantia* extracts (250 mg/kg each) orally via gavage once daily for 28 days.
Consistent dosing occurred between 8:00 and 10:00 AM each morning. Throughout the trial, the animals were closely observed for any indications of toxicity, changes in behavior, or negative consequences [11-13].

Biochemical Assessments:
Blood samples were collected from the retro-orbital plexus under light anesthesia on days 0, 7, 14, 21, and 28. The collected blood was centrifuged at 3000 rpm for 10 minutes to separate serum, which was used for biochemical analysis.
Fasting Blood Glucose (FBG): Measured using a glucometer at regular intervals (days 0, 7, 14, 21, and 28).
Lipid Profile: Serum levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were estimated using standard biochemical kits.
Oxidative Stress Markers:
Superoxide Dismutase (SOD): Measured based on the inhibition of nitro blue tetrazolium (NBT) reduction.
Catalase (CAT): Determined by assessing the decomposition of hydrogen peroxide (H_2O_2).
Glutathione (GSH): Estimated using the Ellman's reagent method.
Malondialdehyde (MDA): Used as a marker of lipid peroxidation, measured by the thiobarbituric acid reactive substances (TBARS) assay [12-14].

Body Weight and Organ Weight Measurement:
Every week, a digital weighing scale was used to record the animals' body weight. Researchers measured the weights of the pancreas, liver, and kidneys after the rats were euthanized so they could evaluate the efficacy of therapies and the damage that diabetes had caused to these organs [13-15].

Histopathological Examination:
Every animal was killed via cervical dislocation while under mild anesthetic as the research period came to a close. The pancreatic tissues were removed and then preserved for 48 hours in 10% neutral-buffered formalin. Afterwards, the tissues were subjected to a succession of progressively stronger alcohols in order to dehydrate them. After that, they were embedded in paraffin, sectioned at a thickness of 5 µm, and stained with hematoxylin. Under a light microscope, the stained sections were checked for histopathological changes, such as β-cell destruction, inflammatory changes, and tissue regeneration [15-17].

Statistical Analysis:
The mean ± standard deviation (SD) was used to express all experimental outcomes. We used GraphPad Prism software to do the statistical analysis. We used one-way ANOVA to compare the groups and then Tukey's post hoc test to account for multiple comparisons. Statistical significance was defined as a p-value below 0.05.

Ethical Considerations:
Ethical standards for research with animals were followed during all experiments. The study was carried out in accordance with the CPCSEA criteria, and the Institutional Animal Ethics Committee granted prior ethical approval. Animals were handled with the utmost care so that they would endure as little pain and suffering as possible throughout the experiment.

RESULTS:
Effect on Fasting Blood Glucose (FBG) Levels:
On days 0, 7, 14, 21, and 28, the fasting blood glucose (FBG) levels of the various groups were assessed. Table 1 displays the outcomes.

Table 1: Effect of *Gymnema sylvestre* and *Momordica charantia* on FBG levels (mg/dL)

Group	Day 0	Day 7	Day 14	Day 21	Day 28
Normal Control	89.2 ± 4.3	91.5 ± 3.8	90.4 ± 4.1	92.1 ± 3.5	91.3 ± 3.9
Diabetic Control	281.4 ± 9.2	295.7± 11.4	312.3± 12.7	328.9 ± 13.5	345.6 ± 15.2
G. sylvestre (250 mg /kg)	278.5 ± 8.6	260.2 ± 9.3	228.9± 10.5	190.3± 8.7	149.5 ± 7.2*
M. charantia (250 mg /kg)	280.1 ± 9.0	268.4± 10.1	239.8± 11.2	202.5± 9.6	160.4 ± 6.9*
Combination (*G. sylvestre* + *M. charantia*)	279.6 ± 9.5	250.1 ± 9.7	205.6 ± 9.3	158.9± 7.8	121.8 ± 5.6**

Values are expressed as mean ± SD (n = 6). $p < 0.05$ vs. diabetic control, $p < 0.01$ vs. diabetic

control.

The fasting blood glucose levels of the diabetes control group rose steadily during the course of the trial. Treatment with *G. sylvestre* and *M. charantia* resulted in a 46.4% and 43.2% decrease in FBG levels, respectively, by day 28 ($p < 0.05$). By day 28, the combo treatment had the most noticeable decline, with a 56.4% decrease in FGB ($p < 0.01$).

Effect on Body Weight:

The control group of diabetics who did not receive treatment for their condition lost weight due to diabetes. But this impact was reduced when *G. sylvestre* and *M. charantia* were administered together.

Table 2: Effect of Treatments on Body Weight (g)

Group	Day 0	Day 7	Day 14	Day 21	Day 28
Normal Control	198.4± 5.2	201.7± 5.5	206.3± 6.1	212.8± 6.5	218.4 ± 7.2
Diabetic Control	196.1± 4.8	182.6± 5.3	170.9± 5.7	158.4± 6.2	149.2 ± 5.8
G. sylvestre	197.2± 5.1	190.4± 5.6	186.8± 5.9	180.3± 6.3	175.7± 6.8*
M. charantia	198.5± 5.4	193.2± 5.9	189.6± 6.1	182.9± 6.5	178.3± 6.9*
Combination	199.1 ± 5.3	195.7 ± 5.8	192.3±6.0	187.5± 6.4	183.9±7.1**

By day 28, 23.9% of the body weight had been dropped by the diabetes control group. A substantial improvement in body weight was seen after treatment with G. sylvestre and M. charantia ($p < 0.05$). With a 22.8% improvement compared to diabetes control, the combo therapy resulted in the highest weight retention ($p < 0.01$).

Effect on Lipid Profile:

In patients with diabetes, dyslipidemia is a result of changes in lipid metabolism. Table 3 displays the results of the lipid profile in its entirety.

Table 3: Lipid Profile (mg/dL) on Day 28

Group	TC	TG	LDL	HDL
Normal Control	98.6 ± 3.5	82.4 ± 3.2	41.2 ± 2.6	52.3 ± 3.0
Diabetic Control	187.2 ± 7.4	155.8 ± 6.9	92.5 ± 4.8	30.6 ± 2.1
G. sylvestre	141.6 ± 6.3*	121.3 ± 5.4*	68.7 ± 3.6*	42.5 ± 2.7*
M. charantia	136.9 ± 6.1*	118.6 ± 5.2*	65.4 ± 3.3*	44.1 ± 2.8*
Combination	120.4 ± 5.8**	98.2 ± 4.6**	53.7 ± 2.9**	48.9 ± 3.1**

Significant vs. diabetic control ($p < 0.05$); $p < 0.01$ vs. diabetic control

High TC, TG, and LDL levels and low HDL levels were seen in the diabetic control group. Lipid profiles improved dramatically after treatment, with combination therapy showing the most improvement.

Effect on Oxidative Stress Markers:

Through the measurement of antioxidant enzyme levels in pancreatic tissues, the oxidative stress that was caused by diabetes was examined.

Table 4: Oxidative Stress Markers on Day 28

Group	SOD (U/mg)	CAT (U/mg)	GSH (nmol/mg)	MDA (nmol/mg)
Normal Control	4.85 ± 0.21	3.67 ± 0.19	5.29 ± 0.26	1.32 ± 0.09

Diabetic Control	2.01 ± 0.17	1.22 ± 0.14	2.18 ± 0.15	4.76 ± 0.21
G. sylvestre	3.42 ± 0.18*	2.56 ± 0.17*	3.89 ± 0.19*	2.78 ± 0.14*
M. charantia	3.51 ± 0.19*	2.72 ± 0.18*	4.02 ± 0.21*	2.65 ± 0.13*
Combination	4.21 ± 0.20**	3.24 ± 0.19**	4.85 ± 0.23**	1.98 ± 0.11**

Combination therapy restored oxidative stress markers closer to normal levels ($p < 0.01$).

The outcomes show that *Momordica charantia* and *Gymnema sylvestre* considerably increase antioxidant defense, lipid metabolism, and hyperglycemia. The combination therapy showed the strongest preventive and anti-diabetic benefits, indicating it could be useful as an additional tool for managing diabetes.

DISCUSSION:

Hyperglycemia, caused by either insulin resistance or inadequate secretion, is a crucial symptom of diabetes. Results showed that FBG levels were much higher in the diabetic rats induced with streptozotocin (STZ) than in the healthy control group. Throughout the trial, the diabetic control group's blood glucose levels steadily rose, reaching 345.6 ± 15.2 mg/dL by day 28, indicating that chronic hyperglycemia was caused by the loss of pancreatic β-cells. After 28 days of treatment, there was a substantial decrease in FBG levels of 46.4% and 43.2%, respectively, when *Gymnema sylvestre* and *Momordica charantia* were administered ($p < 0.05$) [17. 18]. It is worth mentioning that the combined therapy of *G. sylvestre* and *M. charantia* had the most effective effect on lowering glucose levels (56.4% reduction, $p < 0.01$), which could indicate a potential synergistic effect in bettering control of blood sugar levels [17-19]. *M. charantia* is recognized for its insulin-mimetic activity, which helps peripheral tissues absorb glucose, whereas *G. sylvestre's* antihyperglycemic impact is due to its capacity to increase insulin secretion and improve pancreatic β-cell function [19, 20].

An additive or synergistic mode of action, most likely including greater insulin sensitivity, pancreatic protection, and enhanced glucose metabolism, is likely to blame for the combo therapy's superior impact. The inability of insulin to prevent the body from storing fat and breaking down muscle tissue leads to rapid weight loss, a typical consequence of diabetes. With a 23.9% weight loss in the diabetic control group after 28 days, this study confirms the catabolic consequences of diabetes. The combination group demonstrated the maximum weight retention (183.9 ± 7.1 g, $p < 0.01$), while treatments with *G. sylvestre* and *M. charantia* helped limit weight loss. Given that these herbal remedies have the potential to improve glucose utilization and decrease muscle atrophy, they may aid in the preservation of body mass. It is possible that increased insulin activity and metabolic management are responsible for the treated groups' superior weight maintenance [19-21].

When you have diabetes, your blood lipid profile may look like this: high levels of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL), with low levels of high-density lipoprotein (HDL). The diabetic control group showed an aberrant lipid metabolism with elevated levels of TC (187.2 ± 7.4 mg/dL), TG (155.8 ± 6.9 mg/dL), and LDL (92.5 ± 4.8 mg/dL), and significantly lower levels of HDL (30.6 ± 2.1 mg/dL) [20-22].

By reducing TC, TG, and LDL levels and boosting HDL levels, the lipid profile was markedly improved ($p < 0.05$) after treatment with *G. sylvestre and M. charantia.* The combined therapy showed the greatest benefit, with a 42% decrease in LDL levels and a 59.8% increase in HDL ($p < 0.01$) [22, 23]. Their lipid-lowering actions are responsible for these benefits, which are presumably conveyed through increased insulin sensitivity, better lipid metabolism, and a reduction in cholesterol production in the liver. One of the key players in the development of diabetes and its consequences is oxidative stress. Oxidative damage, malfunction of β-cells, and insulin resistance are caused by an increase in the formation of

reactive oxygen species (ROS) in diabetes. Cells are shielded against oxidative damage by antioxidant enzymes including glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT). Lipid peroxidation is indicated by malondialdehyde (MDA) [23-29].

Serious oxidative stress was indicated by a marked decrease in antioxidant enzyme levels (SOD: 2.01 ± 0.17 U/mg, CAT: 1.22 ± 0.14 U/mg, GSH: 2.18 ± 0.15 nmol/mg) and an increase in malondialdehyde levels (4.76 ± 0.21 nmol/mg) in the diabetic control group. The combination of *G. sylvestre* and *M. charantia* exhibited the most protective effects on antioxidant levels, with individual treatments restoring levels of 4.21 ± 0.20 U/mg, 3.24 ± 0.19 U/mg, and 4.85 ± 0.23 nmol/mg, respectively ($p < 0.01$). Furthermore, there was a notable decrease in MDA levels (1.98 ± 0.11 nmol/mg, $p < 0.01$), which implies that lipid peroxidation was reduced. The results show that the polyphenolic and flavonoid content of both herbs scavenges ROS and protects pancreatic β-cells from oxidative damage, suggesting that they have a robust antioxidant defense mechanism [30-34].

In addition to the biochemical results, histological analysis of pancreatic sections provided additional support. The normal control rats exhibited well-preserved β-cells and an intact islet of Langerhans. Islet size was reduced, cellular degeneration was seen, and β-cell damage was significant in diabetic control rats. Partial regrowth of pancreatic islets was observed in the *G. sylvestre* and *M. charantia* treatment groups, together with reduced β-cell damage [35-37]. Combination therapy had the best protective benefit, with almost normal pancreatic architecture, which implies that β-cells are regenerating and insulin secretion is improved. The traditional usage of *G. sylvestre* and *M. charantia* in diabetes therapy is supported by our histological findings, which show their protective and regenerative potential. Consistent with earlier studies, these results demonstrate that *G. sylvestre* and *M. charantia* have antidiabetic properties. Nevertheless, the combo therapy showed better results, suggesting a potential synergistic impact. Based on the findings, these botanicals could provide a safer, more effective, and all-natural alternative to current diabetes treatments [38-41].

CONCLUSION:

This study shows that *Gymnema sylvestre* and *Momordica charantia* have strong anti-diabetic effects in rats that have been made to have diabetes by streptozotocin (STZ). Fasting blood glucose levels were lowered, lipid metabolism was improved, and antioxidant defense systems were boosted by both herbal extracts. The strongest results were seen with the combination therapy, which may indicate a potential synergistic interaction between *G. sylvestre* and *M. charantia* in the management of diabetes. Multiple mechanisms, such as protecting pancreatic β-cells, increasing insulin production, inhibiting glucose absorption, improving insulin sensitivity, and having potent antioxidant activity, could be responsible for the observed antihyperglycemic effects. Not only did the combo therapy enhance pancreatic histology, but it also restored metabolic parameters, suggesting β-cell regeneration and protection against damage caused by oxidative stress. These findings provide credence to the long-standing practice of using *Momordica charantia* and *Gymnema sylvestre* as natural antidiabetic medicines, and they emphasize the potential of these plants to supplement established treatments for diabetes. To confirm these findings in human individuals and investigate their potential therapeutic benefits over the long term, additional clinical trials are necessary.

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