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Evaluation of the Antidiabetic Efficacy of a Herbal Formulation: Impact on Glycemic Control, Pancreatic Function, and Oxidative Stress Markers in a Preclinical Rat Model

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Abstract: This study evaluated the antidiabetic effects of two herbal formulations, Formulation A and Formulation B, in a preclinical animal model. The formulations were selected based on their traditional use in managing diabetes, with *Momordica charantia* and *Trigonella foenum-graecum* (Formulation A) known for their hypoglycemic effects, and *Ocimum sanctum* and Curcuma longa (Formulation B) recognized for their antioxidant and insulin-sensitizing properties. Both formulations were assessed for their impact on glycemic control, pancreatic function, and oxidative stress. Diabetes was induced in adult male Wistar rats using a high-fat diet and streptozotocin (STZ). The rats were divided into three groups: a control group, a group receiving Formulation A dosage (200 mg/kg/day for 8 weeks), and a group receiving Formulation B dosage (250 mg/kg/day for 10 weeks). Key diabetic parameters, pancreatic function, and oxidative stress markers were measured before and after treatment. Formulation B showed superior results, with a 22.2% reduction in fasting blood glucose, a 30% decrease in postprandial glucose, and a 52.2% increase in insulin sensitivity. Whereas Formulation A resulted reduction in fasting blood glucose and increase in insulin levels, alongside improvements in pancreatic islet area and β-cell density. Additionally, Formulation B significantly reduced oxidative stress markers and enhanced pancreatic health more effectively than Formulation A. Both formulations demonstrated efficacy in managing diabetes, but Formulation B proved to be more effective overall, offering enhanced glycemic control, improved pancreatic function, and greater reduction in oxidative stress.
Keywords: *Diabetes; Herbal Formulations; Glycemic Control; Pancreatic Function; Oxidative Stress; Wistar Rats.*

INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, poses a significant global health challenge due to its increasing prevalence and associated complications [1]. The management of diabetes typically involves lifestyle modifications, pharmacotherapy, and in some cases, complementary treatments. Herbal formulations, with their rich history in traditional medicine, have gained attention for their potential to manage diabetes and its related complications.

Herbal medicine has long been utilized for its therapeutic properties, with numerous plants demonstrating potential benefits in regulating blood glucose levels [2]. The quest for effective, natural treatments for diabetes has led to significant interest in various plant-based remedies. Among these, *Momordica charantia* (bitter melon), *Trigonella foenum-graecum* (fenugreek), *Ocimum sanctum* (holy basil), and Curcuma longa (turmeric) stand out due to their traditional use and emerging evidence supporting their antidiabetic properties [3]. This introduction highlights the potential benefits of these plants in managing diabetes and enhancing metabolic health.

Momordica charantia, commonly known as bitter melon, has been widely recognized in traditional medicine for its ability to lower blood glucose levels. Trigonella foenum-graecum, or fenugreek, is another plant with notable antidiabetic properties. Research indicates that fenugreek supplementation can significantly reduce fasting blood glucose and HbA1c levels, offering a promising natural remedy for diabetes. *Ocimum sanctum*, known as holy basil or tulsi, has exhibits hypoglycemic effects through various mechanisms, such as enhancing insulin activity and reducing oxidative stress. Curcuma longa, or turmeric, is celebrated for its primary active compound, curcumin, which has demonstrated anti-inflammatory, antioxidant, and antidiabetic properties. Curcumin has been shown to improve insulin sensitivity and reduce blood glucose levels by modulating several metabolic pathways. The formulation under investigation combines specific

plant extracts known for their purported antidiabetic effects [4].

Glycemic control is essential for preventing the long-term complications of diabetes, including cardiovascular diseases, neuropathy, and nephropathy. By assessing parameters such as fasting blood glucose, HbA1c, and postprandial glucose levels, this study will evaluate the formulation's effectiveness in maintaining optimal blood glucose levels. Additionally, pancreatic function will be assessed through measurements of insulin levels, C-peptide, β-cell density, and pancreatic islet area to understand how the formulation influences β-cell function and pancreatic health. Oxidative stress plays a critical role in the progression of diabetes, contributing to pancreatic β-cell dysfunction and systemic inflammation. By integrating these aspects into a comprehensive evaluation, this study aims to establish the efficacy of the herbal formulation in managing diabetes and improving overall metabolic health. This study aims to evaluate the antidiabetic efficacy of a novel herbal formulation, focusing on its impact on glycemic control, pancreatic function, and oxidative stress markers in a preclinical model.

RESEARCH METHODOLOGY

Study Design

This study aimed to evaluate the antidiabetic effects of two herbal formulations, Formulation A and Formulation B, using a preclinical animal model as shown in Table 1. The study was designed to assess the impact of these formulations on various diabetic parameters, pancreatic function, and oxidative stress markers over specified durations.

Tab. 1. Plant formulation, its dosage, and its effect as an antidiabetic drug

Plant Formulation	Plant Components	Dosage (mg/kg/day)	Duration of Treatment
Formulation A	*Momordica charantia* (Bitter melon), *Trigonella foenum-graecum* (Fenugreek)	200 mg/kg	8 weeks
Formulation B	*Ocimum sanctum* (Holy Basil), *Curcuma longa* (Turmeric)	250 mg/kg	10 weeks

Experimental Animals

- Species: Adult male Wistar rats.
- Weight Range: 200-250 g.
- Housing Conditions: Standard laboratory conditions with a 12-hour light/dark cycle and free access to water and standard rodent chow.
- Acclimatization Period: 1 week.

Induction of Diabetes

- Method: Diabetes was induced using a high-fat diet and a single dose of streptozotocin (STZ) (50 mg/kg, intraperitoneal injection).
- Confirmation of Diabetes: Rats with fasting blood glucose levels ≥ 200 mg/dL were confirmed as diabetic and included in the study.

Experimental Groups

- Group 1: Control (received vehicle).
- Group 2: Formulation A (*Momordica charantia* and Trigonella foenum-graecum) at 200 mg/kg/day.
- Group 3: Formulation B (*Ocimum sanctum* and Curcuma longa) at 250 mg/kg/day.

Treatment Protocol

- Formulation A: Administered orally at a dose of 200 mg/kg/day for 8 weeks. (Each group consisted of 10 rats).
- Formulation B: Administered orally at a dose of 250 mg/kg/day for 10 weeks. (Each group consisted of 10 rats).
- Vehicle Control: Administered orally for the respective duration of treatment. (Each group consisted of 10 rats).

The varying treatment durations—8 weeks for Formulation A and 10 weeks for Formulation B—were selected based on the differing onset times of the active components. Formulation B, containing *Ocimum sanctum* and Curcuma longa, required a longer duration to fully exhibit its effects, while Formulation A's components, including *Momordica charantia* and Trigonella foenum-graecum, showed faster therapeutic action.

Parameters Assessed

a. Diabetic Parameters

- Fasting Blood Glucose: Measured at baseline and at the end of the treatment period using a glucometer.
- Postprandial Glucose: Measured after a high-carbohydrate meal.
- HbA1c: Determined by blood samples using a specific assay.
- Insulin Levels: Measured by ELISA.
- Insulin Sensitivity Index: Calculated based on fasting insulin and glucose levels.

b. Pancreatic Function

- C-peptide: Measured by ELISA to assess β-cell function.
- Pancreatic Islet Area: Determined from pancreatic tissue sections stained with hematoxylin and eosin (H&E) and analyzed using image analysis software.
- β-cell Density: Quantified from pancreatic tissue sections.

c. Oxidative Stress Markers

- Malondialdehyde (MDA): Quantified as an indicator of lipid peroxidation using the TBARS assay.
- Glutathione Peroxidase (GPX): Measured using a colorimetric assay to assess antioxidant enzyme activity.

Statistical Analysis

Statistical significance was determined using Student's t-test for comparisons between pre-treatment and post-treatment values within each group. For comparisons between different groups, mean and standard deviation values were measured by using statistical software SPSS. Therefore p-value of <0.05 was considered statistically significant.

RESULTS

The results section presents a comprehensive evaluation of the effects of two different plant formulations on diabetes management, including their impact on key diabetic parameters, pancreatic function, and oxidative stress markers. By comparing Formulation A, which combines *Momordica charantia and Trigonella foenum-graecum*, with Formulation B, which includes *Ocimum sanctum* and *Curcuma longa*, this section aims to highlight their relative efficacy in improving glucose control, insulin sensitivity, and pancreatic health, as well as their influence on oxidative stress (Table 2).

Tab. 2. Effects of Formulation A on Diabetic Parameters Post-Treatment

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	Confidence Interval 95%	Percentage Change	P value

Fasting Blood Glucose (mg/dL)	150.6 ± 10.5	132.95 ± 8.4	130.1 - 135.8	↓ 15%	0.01
HbA1c (%)	8.9 ± 0.4	7.4 ± 0.3	7.3 - 7.5	↓ 1.5%	0.01
Insulin Levels (μU/mL)	5.2 ± 0.9	7.1 ± 1.0	6.7 - 7.5	↑ 35.8%	0.001
Total Cholesterol (mg/dL)	210.4 ± 15.7	188.3 ± 12.6	183.6 - 193.0	↓ 17%	0.01
C-peptide (ng/mL)	1.1 ± 0.2	1.3 ± 0.4	1.1 - 1.5	↑ 11.1%	0.001
Pancreatic Islet Area (%)	65.8 ± 5.2	72.25 ± 6.0	69.7 - 74.8	↑ 22%	0.01
β-cell Density (%)	58.7 ± 4.5	71.5 ± 5.7	69.2 - 73.8	↑ 28.6%	0.001
Oxidative Stress Markers					
MDA	158 ±3.6	130±2.6	128.9 - 131.1	↓ 22%	0.001
GPX	103.2±4.1	124±3.8	122.7 - 125.3	↑ 23%	0.001

The results for Formulation A reveal significant improvements in key diabetic parameters and oxidative stress markers. Fasting blood glucose levels decreased by 15%, and HbA1c levels dropped by 1.5%, indicating better glucose control. Insulin levels increased by 35.8%, while total cholesterol levels were reduced by 17%. C-peptide levels showed an 11.1% rise, reflecting improved β-cell function. Additionally, both pancreatic islet area and β-cell density increased by 22% and 28.6%, respectively. In terms of oxidative stress, MDA levels decreased by 22%, and GPX activity increased by 23%, suggesting reduced oxidative damage and enhanced antioxidant defence. These findings underscore the efficacy of Formulation A in managing diabetes and improving pancreatic health. Hence the confidence intervals demonstrate the precision of the estimated effects of Formulation A on diabetic parameters and oxidative stress markers, indicating the range within which the true effect likely falls (Table 3).

Tab. 3. Effects of Formulation B on diabetic parameters, pancreatic function, and oxidative stress markers:

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	CI 95%	Percentage Change	P value
Fasting Blood Glucose (mg/dL)	148.4 ± 9.8	115.5 ± 7.9	112.8 - 118.2	↓ 22.2%	0.01
Postprandial Glucose (mg/dL)	180.2 ± 12.3	126.1 ± 9.5	122.6 - 129.6	↓ 30%	0.001
HbA1c (%)	8.7 ± 0.5	7.1 ± 0.4	6.9 - 7.3	↓ 1.6%	0.01
Insulin Sensitivity Index	2.3 ± 0.2	3.5 ± 0.3	3.4 - 3.6	↑ 52.2%	0.001
Total Cholesterol (mg/dL)	205.6 ± 14.5	162.4 ± 11.2	158.5 - 166.3	↓ 21%	0.01
C-peptide (ng/mL)	1.2 ± 0.3	2.5 ± 0.4	2.3 - 2.7	↑ 108.3%	0.001
Pancreatic Islet Area (%)	66.5 ± 4.8	84.7 ± 5.4	82.3 - 87.1	↑ 27.3%	0.01
β-cell Density (%)	60.3 ± 4.2	77.9 ± 5.2	75.7 - 80.1	↑ 29.2%	0.001
Oxidative Stress Markers					
MDA (nmol/mg protein)	160 ± 3.5	118 ± 2.7	116.9 - 119.1	↓ 26.3%	0.001
GPX (U/mg protein)	105.1 ± 4.3	142 ± 4.0	140.4 - 143.6	↑ 35.1%	0.001

The administration of Formulation B led to notable improvements in diabetic parameters, pancreatic function, and oxidative stress markers. Fasting blood glucose levels decreased by 22.2%, and postprandial glucose levels were reduced by 30%, demonstrating enhanced glucose control. HbA1c levels dropped by 1.6%, reflecting better long-term glycemic management. The insulin sensitivity index increased by 52.2%, indicating improved insulin responsiveness. Total cholesterol levels reduced by 21%, while C-peptide levels more than doubled, suggesting enhanced β-cell function.

Pancreatic islet area and β-cell density increased by 27.3% and 29.2%, respectively, highlighting improved pancreatic tissue health. Oxidative stress was significantly reduced, with malondialdehyde (MDA) levels decreasing by 26.3% and glutathione peroxidase (GPX) activity increasing by 35.1%, indicating reduced oxidative damage and improved antioxidant defence. These findings underscore the effectiveness of Formulation B in managing diabetes and mitigating oxidative stress. Therefore, confidence intervals illustrate the reliability of the estimated improvements in diabetic parameters and pancreatic function following treatment with Formulation B, providing a clearer picture of the potential variability in the results.

Thus, both formulations show significant efficacy in managing diabetes and improving related parameters, but Formulation B demonstrates superior overall results. Formulation A led to a 15% reduction in fasting blood glucose levels and improvements in insulin levels and β-cell density. However, Formulation B resulted in a more pronounced 22.2% decrease in fasting blood glucose and a notable 30% reduction in postprandial glucose levels. Additionally, Formulation B showed a greater improvement in insulin sensitivity (52.2% increase) compared to Formulation A. The significant reduction in oxidative stress markers and substantial enhancements in pancreatic function with Formulation B suggest it offers more comprehensive benefits for diabetes management. Thus, Formulation B appears to be the more effective treatment option.

DISCUSSION

The discussion of this study highlights the significant antidiabetic potential of two herbal formulations, each comprised of different plant components, in improving diabetic parameters, pancreatic function, and oxidative stress markers. The comparison between Formulation A, which includes *Momordica charantia* (bitter melon) and *Trigonella foenum-graecum* (fenugreek), and Formulation B, consisting of *Ocimum sanctum* (holy basil) and Curcuma longa (turmeric), reveals critical insights into their relative efficacy in managing diabetes. Formulation B delivered even more significant results, with a 22.2% reduction in fasting blood glucose and a 30% decrease in postprandial glucose, suggesting superior glucose control. The 52.2% boost in insulin sensitivity and more than double C-peptide levels point to improved insulin response and β-cell function. The 27.3% increase in pancreatic islet area and 29.2% rise in β-cell density further affirm its effectiveness in enhancing pancreatic health. The reduction in oxidative stress, shown by a 26.3% drop in MDA levels and a 35.1% increase in GPX activity, underscores the powerful antioxidant effects of Formulation B, offering added protection against diabetes complications. The findings of this study are consistent with previous research that has demonstrated the antidiabetic properties of the individual plant components. In the discussion, Formulation B's herbal components likely exert their antidiabetic effects by enhancing insulin sensitivity, promoting β-cell regeneration, and reducing oxidative stress. The significant increase in insulin sensitivity and reduction in fasting and postprandial glucose levels suggest a mechanism targeting insulin signaling pathways, similar to current diabetes treatments like metformin. Additionally, the reduction in oxidative stress markers and improvement in pancreatic islet function align with therapies aimed at preserving β-cell health, which is crucial in managing diabetes. These findings highlight the potential of Formulation B as a complementary therapy to existing antidiabetic drugs.

Momordica charantia and *Trigonella foenum-graecum* have been shown to improve glucose tolerance and enhance insulin secretion, while *Ocimum sanctum* and Curcuma longa are well-known for their anti-inflammatory and antioxidant properties, which play a critical role in improving insulin sensitivity and reducing oxidative stress. The superior performance of Formulation B in this study aligns with existing literature, suggesting that the combination of *Ocimum sanctum* and Curcuma longa may provide a more comprehensive approach to diabetes management. A study by Horax et al.,(2015)[5] suggested the hypoglycemic effects of *Momordica charantia* in diabetic rats, revealing a significant reduction in blood glucose levels and improved β-cell function. The study's results resonate with our findings, where Formulation A, containing Momordica charantia, exhibited a 15% reduction in fasting blood glucose and a notable enhancement in β-cell density.

Another study by Geberemeskel et al.,(2019)[5] examined the antidiabetic efficacy of *Trigonella foenum-graecum* in diabetic animal models and hence reported an increase in insulin secretion and improved glycemic control, paralleling our study's observation of a 35.8% increase in insulin levels with the use of Formulation A. Similar study conducted by Cohen ,(2016)[6] showed antidiabetic potential of *Ocimum sanctum* and found that it significantly reduced fasting blood glucose levels and improved insulin sensitivity in diabetic rats. This supports our findings with Formulation B, where a 22.2% reduction in fasting blood glucose and a 52.2% increase in insulin sensitivity were observed.A study by Pivari et al. (2019) [9]explored the effects of Curcuma longa on oxidative stress and pancreatic function in diabetic rats. The researchers discovered a significant reduction in oxidative stress markers and an improvement in pancreatic β-cell function, which aligns with our study's results, where Formulation B showed a 26.3% decrease in MDA levels and a 35.1% increase in GPX activity. Saelao et al.,(2023)[10] evaluated the synergistic effects of combining different herbal

components on diabetic parameters. Their findings indicated that multi-herbal formulations could provide a more comprehensive approach to diabetes management by targeting various pathways involved in the disease. This is consistent with our study, where the combination of *Ocimum sanctum* and Curcuma longa in Formulation B resulted in superior overall efficacy compared to the other formulation. These studies provide a solid foundation for the observed effects of the herbal formulations in our research, highlighting the potential of combining specific plant components to achieve enhanced antidiabetic efficacy. The consistency between our results and those of other studies reinforces the credibility of our findings and suggests that these herbal formulations could serve as effective alternatives or complements to conventional antidiabetic therapies. Further clinical research is recommended to explore their therapeutic potential in human populations.

Conclusion: In conclusion, while both formulations exhibit significant antidiabetic effects, Formulation B demonstrates superior efficacy in improving glycemic control, enhancing insulin sensitivity, promoting pancreatic health, and reducing oxidative stress. These findings suggest that Formulation B, which includes *Ocimum sanctum* and Curcuma longa, may offer a more effective treatment option for diabetes management. Further research involving clinical trials is warranted to confirm these results and explore the potential of these herbal formulations in the treatment of diabetes in human populations.

CONCLUSION

In conclusion, while both formulations exhibit significant antidiabetic effects, Formulation B demonstrates superior efficacy in improving glycemic control, enhancing insulin sensitivity, promoting pancreatic health, and reducing oxidative stress. These findings suggest that Formulation B, which includes *Ocimum sanctum* and *Curcuma longa*, may offer a more effective treatment option for diabetes management. Further research involving clinical trials is warranted to confirm these results and explore the potential of these herbal formulations in the treatment of diabetes in human populations.

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