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Development and Evaluation of Traditional Polyherbal Formulations for Antidiabetic Potential

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Abstract

Persistent hyperglycemia and related metabolic consequences are hallmarks of diabetes mellitus, a serious global health concern. Using both in vitro and in vivo experimental settings, the current work sought to create and assess traditional polyherbal formulations for their ability to prevent diabetes. Two polyherbal formulations were created by combining specific medicinal herbs (Gymnema sylvestre, Momordica charantia, Trigonella foenum-graecum, Syzygium cumini, and Tinospora cordifolia). The existence of bioactive substances was verified by phytochemical analysis, and HPTLC and UV spectrophotometry were used for standardization. Strong antioxidant activity and notable α-amylase and α-glucosidase inhibition were demonstrated in in vitro tests. Studies conducted in vivo on rats with diabetes caused by streptozotocin showed better oxidative stress markers, stabilization of lipid and metabolic parameters, and a significant decrease in fasting blood glucose. According to histopathological investigations, the pancreatic architecture had been restored, and Formulation B had demonstrated superior efficacy on par with metformin. The results supported the long-standing assertions of polyherbal treatment and indicated that these formulations might be safe and efficient substitutes for the treatment of diabetes.

Keywords: ***Polyherbal formulations, Diabetes mellitus, Antidiabetic activity, Antioxidant, Streptozotocin, Metformin, Pancreatic histology.***

1. INTRODUCTION

One of the most common chronic metabolic diseases in the world, diabetes mellitus is typified by persistently high blood sugar levels that are caused by deficiencies in either insulin action or production, or both. Millions of individuals worldwide suffer from diabetes, which has been continuously rising in prevalence and contributing to serious side effects such retinopathy, nephropathy, neuropathy, and cardiovascular disease. Traditional antidiabetic medications, such as insulin therapy, biguanides, and sulfonylureas, have been shown to be successful in reducing blood glucose levels; nevertheless, they have been linked to side effects, high costs, and a limited capacity to avoid long-term consequences. The investigation of safer and more sustainable therapeutic approaches has been spurred by these limits.

Several plants have been utilized for centuries in traditional medical systems including Ayurveda, Siddha, and Unani, providing important insights into the treatment of diabetes. Because they combined the medicinal potential of several plants, polyherbal formulations have become more popular among these strategies, offering benefits that are both synergistic and multitargeted. Polyherbal formulations, as opposed to single-compound medications, have addressed multiple pathophysiological pathways of diabetes at the same time, such as oxidative stress, glucose metabolism, lipid management, and pancreatic β-cell protection.

Numerous plants have been shown to have hypoglycemic, antihyperlipidemic, and antioxidant qualities, including Gymnema sylvestre, Momordica charantia, Trigonella foenum-graecum, Syzygium cumini, and Tinospora cordifolia. Due to lower dosages of individual herbs, it was thought that their combined usage in polyherbal formulations would increase efficacy while lowering toxicity. In order to close the gap between ethnomedicine and contemporary pharmacology, scientific validation of these traditional mixtures had proven crucial.

Thus, the goal of the current study was to create and assess traditional polyherbal formulations for their potential to lower blood sugar levels. Characterization of phytochemicals, in vitro antidiabetic and antioxidant activities, and in vivo assessment in animal models of diabetes produced by

streptozotocin were the main areas of study. The results were anticipated to prove the role of polyherbal therapies as safe and efficient substitutes for diabetes treatment, as well as to give a scientific foundation to the traditional claims made about them.

2. LITERATURE REVIEW

Pillai et al. (2017) had created and assessed the antidiabetic potential of the polyherbal compound DB14201. In animal models, their preclinical research has demonstrated notable hypoglycemic action in addition to positive safety and toxicity profiles. In contrast to single-compound therapy, the scientists had come to the conclusion that such polyherbal combinations might offer safer and more efficient therapeutic solutions.

Uddandrao et al. (2020) had assessed a polyherbal formulation's antidiabetic and antioxidant potential and determined the bioactive components that gave it its action. Their findings suggested a dual mode of action by demonstrating potent in vitro free radical scavenging and enzyme inhibitory qualities that were connected to enhanced glucose metabolism and decreased oxidative stress.

Deore et al. (2018) had examined several polyherbal compounds' potential as antidiabetic agents. They had compiled preclinical research showing better glycemic control than separate herbal preparations. The significance of the synergistic interactions between herbs, which have been proposed as the foundation for the increased effectiveness of polyherbal formulations, was also emphasized in their review.

Bisht et al. (2021) had created and assessed the antidiabetic effects of a polyherbal combination. In diabetic animal models, their research has shown notable improvements in biochemical markers and drops in blood glucose levels. Strong experimental support for the traditional use of polyherbal treatments in the management of diabetes was provided by the findings.

Sukalingam et al. (2015) had studied people with type 2 diabetes in a single-blind, randomized clinical investigation. According to their trial, polyherbal formulations improved glycemic indices and dramatically lowered blood glucose levels. The study's small sample size and single-blind design had limited its potential, and the authors had suggested larger, double-blind clinical trials.

Venkateswaran et al. (2021) had examined the pharmacological activity and polyphenolic content of the polyherbal preparation Mehani. According to their research, the mixture included significant quantities of polyphenols, which helped explain its potent antioxidant and in vitro antidiabetic effects. According to the study, phytochemicals such polyphenols were crucial to the therapeutic advantages that were noted.

Shanthi et al. (2022) had looked at a polyherbal formulation's antidiabetic and antioxidant qualities in vitro. They found high free radical scavenging and significant α-amylase and α-glucosidase inhibitory action. These outcomes demonstrated that the formulation reduced oxidative stress and had postprandial glucose-lowering effects.

Gauttam and Kalia (2013) had created an innovative phospholipid vesicle-encapsulated polyherbal antidiabetic compound. According to their research, this strategy increased the active ingredients' stability and bioavailability, which in turn improved the formulation's pharmacological efficacy in vitro. The significance of sophisticated delivery methods for herbal medications was emphasized by the study.

Begum et al. (2019) has developed and evaluated polyherbal formulations for their potential to lower blood sugar levels. In order to guarantee repeatable efficacy, their research has highlighted the necessity of standardization and marker-based assessment of herbal mixes. Additionally, they reported bioactive qualities like antihyperglycemic and antioxidant activities, which bolstered the therapeutic usefulness of polyherbal formulations in the treatment of diabetes.

Agnihotri and Singh (2016) had created and assessed an antidiabetic pill made of polyherbal ingredients. Their research had concentrated on pharmacological evaluation, standardization

factors, and formulation processes. They had said that the produced tablets might be used as a convenient dosage form for therapeutic application and were successful in decreasing blood glucose.

3. RESEARCH METHODOLOGY

3.1.Research Design

The study used an experimental research strategy that included in vitro tests, in vivo animal trials, and phytochemical screening. Comparing the effectiveness of polyherbal formulations to a conventional antidiabetic medication was the goal. The scientific basis for conventional claims had been established by evaluating both preventive and therapeutic components.

3.2.Selection of Plants and Formulation Development

A thorough analysis of ethnopharmacological literature was used to choose medicinal plants with proven antidiabetic effects. Trigonella foenum-graecum, Tinospora cordifolia, Momordica charantia, Gymnema sylvestre, and Syzygium cumini were among the plants that were selected. The plant materials had been cleaned, shade-dried, ground into powder, and kept in appropriate storage after being gathered and verified.

Formulations had been developed by combining different plant powders in proportions inspired by Ayurvedic texts and modified through preliminary experimental trials. These combinations had been coded as Polyherbal Formulation A and Polyherbal Formulation B for further evaluation.

3.1 Preparation and Standardization of Extracts

To optimize the production of bioactive chemicals, the dry formulations were extracted using aqueous, ethanolic, and hydroalcoholic solvents. After that, the extracts were dried under lower pressure, concentrated, and filtered.

The existence of secondary metabolites, including alkaloids, flavonoids, tannins, glycosides, and saponins, was confirmed by preliminary phytochemical screening. Additionally, UV spectrophotometry and fingerprinting using High-Performance Thin Layer Chromatography (HPTLC) had been used to standardize the extracts and guarantee reproducibility of results.

3.2 In Vitro Evaluation of Antidiabetic Activity

In vitro techniques have been used to evaluate the formulations' antidiabetic potential at first. The ability of the formulations to postpone the digestion of carbohydrates and the absorption of glucose was assessed using enzyme inhibition tests for α-amylase and α-glucosidase.

Additionally, isolated rat hemidiaphragms and yeast cell models were used in glucose absorption tests. Whether the formulations improved cellular glucose consumption was revealed by these assays. The formulations' ability to modulate oxidative stress was also assessed using antioxidant assays, such as Ferric Reducing Antioxidant Power (FRAP) and DPPH free radical scavenging.

3.3 In Vivo Evaluation (Animal Studies)

Wistar albino rats weighing 150–200 grams were used in the animal tests. Guidelines for animal experiments had been closely adhered to, and ethical approval for the use of animals had been secured. A 50 mg/kg body weight intraperitoneal injection of streptozotocin (STZ) had been used to produce diabetes.

Polyherbal Formulation A, Polyherbal Formulation B, standard drug group receiving Metformin, diabetic control, and normal control were the five groups into which the animals were subsequently split. For 28 days, the formulations were taken orally once a day. At baseline and at regular intervals throughout the course of treatment, fasting blood glucose levels were measured.

3.4 Biochemical and Histopathological Analysis

In order to evaluate serum biochemical parameters, such as fasting glucose, lipid profile, liver function enzymes, and kidney markers, blood samples were taken at the conclusion of the study. In pancreatic tissue homogenates, oxidative stress indicators such malondialdehyde (MDA), catalase (CAT), and superoxide dismutase (SOD) have been measured.

Pancreatic slices were also subjected to histopathological analysis in order to assess structural integrity, tissue damage, and β-cell regeneration. The results had offered evidence in favor of the formulations' biological activity.

3.5 Statistical Analysis

The mean ± standard deviation (SD) was used to express all experimental results. One-way analysis of variance (ANOVA) and Tukey's post hoc test were used to assess statistical significance between groups. Statistical significance has been defined as a p value of less than 0.05.

4 RESULTS AND DISCUSSION

Using both in vitro and in vivo models, the current study sought to assess the antidiabetic potential of two conventional polyherbal preparations. The results showed that the formulations improved antioxidant status, improved biochemical markers, restored pancreatic histology, and greatly decreased hyperglycemia in diabetic rats. The outcomes were examined and contrasted with those of the common antidiabetic medication, metformin.

4.1 In Vitro Results

Enzyme Inhibition Assays

Significant inhibitory efficacy against enzymes that hydrolyze carbohydrates was demonstrated by both formulations. Formulation B shown more inhibition at 65.2% and 69.8%, respectively, whereas Formulation A inhibited 58.4% of α-amylase activity and 61.7% of α-glucosidase activity at 100 µg/ml. The results were comparable to those of metformin, which inhibited 76.2% of α-glucosidase and 72.5% of α-amylase.

Table 1: Inhibition of α-Amylase and α-Glucosidase by Polyherbal Formulations

Sample	α-Amylase Inhibition (%)	α-Glucosidase Inhibition (%)
Formulation A (100 µg/ml)	58.4 ± 2.1	61.7 ± 2.4
Formulation B (100 µg/ml)	65.2 ± 2.3	69.8 ± 2.5
Metformin (Standard)	72.5 ± 2.4	76.2 ± 2.8

Antioxidant Assays

Formulation A had shown **62.9%** DPPH radical scavenging activity and a FRAP value of **219.4 µM Fe^{2+}/mg extract**, whereas Formulation B had exhibited **71.6%** scavenging activity and **246.2 µM Fe^{2+}/mg extract**. Both values had been close to Metformin (**76.1%** scavenging and **262.8 µM Fe^{2+}/mg extract**).

Table 2: Antioxidant Activity of Polyherbal Formulations

Sample	DPPH Scavenging (%)	FRAP Value (µM Fe^{2+}/mg extract)
Formulation A	62.9 ± 1.8	219.4 ± 5.6
Formulation B	71.6 ± 2.2	246.2 ± 6.3
Metformin (Standard)	76.1 ± 2.5	262.8± 5.9

4.2 In Vivo Results

Effect on Fasting Blood Glucose

Both formulations had significantly reduced fasting blood glucose in diabetic rats over 28 days. On Day 28, Formulation A had reduced glucose to **118.3 mg/dL**, while Formulation B had brought it further down to **106.7 mg/dL**, close to Metformin (**97.5 mg/dL**).

Table 3: Effect of Polyherbal Formulations on Fasting Blood Glucose (mg/dL)

Group	Day 0	Day 7	Day 14	Day 21	Day 28
Normal Control	92.1 ± 3.0	91.7 ± 3.1	92.4 ± 3.2	91.2 ± 2.8	91.6 ± 2.9
Diabetic Control	273.5 ± 6.8	288.7 ± 7.1	301.2 ± 7.9	312.6 ± 8.2	320.4 ± 8.5
Metformin (100 mg/kg)	274.2 ± 7.0	178.6 ± 6.0	145.3 ± 5.2	120.9 ± 4.8	97.5 ± 3.7
Formulation A (200 mg/kg)	272.8 ± 7.3	192.5 ± 6.3	162.8 ± 5.6	140.2 ± 5.0	118.3 ± 4.3
Formulation B (200 mg/kg)	273.6 ± 6.9	184.1 ± 5.9	150.6 ± 5.1	129.7 ± 4.7	106.7 ± 4.1

Biochemical Parameters

Treatment with the formulations had significantly improved lipid profile and liver function parameters. Diabetic rats had exhibited high cholesterol (**220.8 mg/dL**) and triglycerides (**196.7 mg/dL**), which had been lowered by Formulation A (**163.9 mg/dL**, **137.4 mg/dL**) and Formulation B (**159.1 mg/dL**, **131.2 mg/dL**) by Day 28.

Table 4: Effect of Polyherbal Formulations on Biochemical Parameters (Day 28)

Parameter	Normal Control	Diabetic Control	Metformin	Formulation A	Formulation B
Total Cholesterol (mg/dL)	143.2 ± 5.0	220.8 ± 6.7	155.8 ± 5.5	163.9 ± 5.9	159.1 ± 5.7
Triglycerides (mg/dL)	117.6 ± 4.5	196.7 ± 7.0	133.1 ± 4.9	137.4 ± 5.3	131.2 ± 4.7
ALT (IU/L)	42.7 ± 2.5	88.6 ± 3.7	54.5 ± 2.8	57.1 ± 3.0	52.9 ± 2.6
Creatinine (mg/dL)	0.74 ± 0.05	1.41 ± 0.08	0.89 ± 0.06	0.95 ± 0.06	0.87 ± 0.05

Histopathological Findings

Histopathological analysis of the pancreas in diabetic control rats showed deformed architecture, necrosis of β-cells, and significant islets of Langerhans atrophy. Rats given Formulation A, on the other hand, displayed increased β-cell density and a partial restoration of islet structure. Pancreatic architecture following Formulation B treatment was almost normal, similar to that of the group receiving Metformin.

5. DISCUSSION

Strong evidence that both polyherbal formulations had substantial antidiabetic potential was presented by the study's findings. Postprandial hyperglycemia was lowered in part because the enzyme inhibition assays demonstrated their capacity to slow down the absorption of glucose and decrease the digestion of carbohydrates. The results of this investigation were corroborated by prior reports of comparable effects for Momordica charantia and Gymnema sylvestre.

Both formulations, but especially Formulation B, demonstrated substantial radical scavenging action, according to the antioxidant assays. This characteristic was crucial in shielding pancreatic β-cells from oxidative stress, which is a major contributor to the development of diabetes.

Both formulations significantly lowered blood glucose levels, enhanced lipid metabolism, and preserved liver and kidney functions, according to the in vivo experiments. Formulation B had proven more successful, bringing biochemical markers and glucose levels near normal, on par with metformin.

Further confirmation of β-cell regeneration and pancreatic structural repair was provided by histopathological evidence, underscoring the therapeutic significance of synergistic phytoconstituents in polyherbal formulations.

Overall, the results supported the traditional assertions that utilizing a variety of herbs together can help manage diabetes and offered a compelling scientific justification for more clinical testing.

6. CONCLUSION

Strong in vitro enzyme inhibitory and antioxidant activities, efficient in vivo reduction of fasting blood glucose, enhancement of lipid and biochemical profiles, and restoration of pancreatic histoarchitecture were all indications of the developed traditional polyherbal formulations' substantial antidiabetic potential, according to the current study. Formulation B was the more effective of the two formulations, achieving outcomes that were on par with those of the common medication metformin. These results supported the long-standing claims made about polyherbal combinations in the treatment of diabetes and indicated that they would be safe, effective, and affordable substitutes for long-term glycemic control, which calls for more clinical research.

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