Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

Effectiveness of Novel Polyherbal Combinations in Reducing Hyperglycemia in a "Streptozotocin (60 mg/kg) Induced" Diabetic Rat Model: A Sustainable Alternative for Low-Resource Settings

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(Received: 16 July 2025 Revised: 20 August 2025 Accepted: 20 September 2025)

KEYWORDS

Herbal combination, Anti-diabetic effects, Streptozotocin, serum glutamate pyruvate transaminase (SGPT), lipid profile parameters.

ABSTRACT:

Introduction: Diabetes mellitus is a chronic metabolic disorder associated with hyperglycemia, dyslipidemia, and hepatic dysfunction. Polyherbal formulations have gained interest due to their synergistic therapeutic potential. Despite the availability of synthetic drugs, adverse effects and limited accessibility necessitate safer, affordable alternatives.

Objectives: This study aimed to develop and evaluate a polyherbal extract (PHE) formulation comprising *Coriandrum sativum* (stalk), *Mucuna pruriens* (seed), and *Juglans nigra* (fruit) for its antihyperglycemic, hypolipidemic, and hepatoprotective activities in streptozotocin-induced diabetic rats.

Methods: Plant materials were authenticated, shade-dried, powdered, and standardized through organoleptic, microscopy, FTIR, NMR, and UV–Visible analyses. Granules were formulated using dry granulation and optimized for uniformity and stability. Diabetes was induced in Wistar rats (STZ 60 mg/kg, i.p.), and animals were grouped into normal control, diabetic control, PHE (250 mg/kg), PHE (500 mg/kg), and glibenclamide (5 mg/kg). Biochemical parameters including serum glucose, protein, lipid profile, lipoproteins, and liver enzymes were evaluated.

Results: PHE treatment significantly reduced serum glucose levels ($p < 0.01$) and restored total protein. Lipid abnormalities were markedly improved, with reduced cholesterol, triglycerides, LDL, and VLDL, along with increased HDL. Elevated liver enzymes (ALP, SGOT, SGPT) in diabetic rats were normalized, confirming hepatoprotective effects. The 500 mg/kg dose showed efficacy comparable to glibenclamide, without adverse effects in normoglycemic rats.

Conclusions: The developed polyherbal formulation demonstrated significant antihyperglycemic, hypolipidemic, and hepatoprotective effects in diabetic rats. These findings suggest its potential as a safe, effective, and sustainable herbal alternative for diabetes management.

1. Introduction

Diabetes mellitus is the most prevalent endocrine disorder worldwide, affecting an estimated 150 million individuals, a number projected to exceed 300 million by 2025 (King & Aubert, 1998). According to the International Diabetes Federation, more than one-fifth of diabetic patients are of Indian origin, emphasizing the significant burden in this region. India has been declared the "Diabetes Capital of the World" (Bezbaruah, 2003).

Polyherbal formulations, which combine multiple plant extracts in a single preparation, represent a particularly promising approach. By capitalizing on the synergistic interactions among phytoconstituents, polyherbal combinations can potentially enhance therapeutic outcomes compared to single-plant products. Such formulations may exert multiple beneficial effects improving glycemic control, modulating lipid metabolism, reducing oxidative stress, and protecting pancreatic function.

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JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

The present research is designed to develop and evaluate a standardized polyherbal formulation incorporating selected medicinal plants with known antidiabetic activities. Through systematic preclinical assessment, this study aims to contribute to the development of evidence-based, plant-derived interventions for diabetes management.

The present study was conducted to investigate the hypoglycemic and antihyperlipidemic potential of selected medicinal plants and to evaluate the efficacy of their standardized polyherbal formulation in an established preclinical model of type 2 diabetes mellitus (Tripathi et al., 2016).

By systematically assessing biochemical and metabolic outcomes, this research aims to provide scientific evidence supporting the development of novel, safe, and effective polyherbal therapies for diabetes management.

2. Objectives

Diabetes mellitus is one of the most prevalent metabolic disorders worldwide, characterized by chronic hyperglycemia, disturbances in carbohydrate, protein, and lipid metabolism, and progressive organ damage. Current therapeutic options such as insulin and oral hypoglycemic agents are effective, yet they often present limitations including side effects, high cost, and reduced patient compliance. This creates an urgent need for alternative, safer, and more sustainable treatment strategies. Herbal medicines and polyherbal formulations, in particular, are gaining increasing attention due to their multi-targeted mechanisms of action, synergistic phytochemical interactions, and lower incidence of adverse effects.

The primary objective of the present study was to develop and evaluate a novel polyherbal extract (PHE) formulation prepared from *Coriandrum sativum* (stalk powder), *Mucuna pruriens* (seed powder), and *Juglans nigra* (fruit powder). These plants were selected based on their traditional use and reported pharmacological activities such as antioxidant, antidiabetic, and hepatoprotective properties. Specific goals included:

1. Standardization of crude drugs through organoleptic evaluation, powder microscopy, and advanced analytical techniques such as FTIR, NMR, and UV–Visible spectrophotometry to ensure authenticity and compatibility of the plant materials.
2. Formulation development of polyherbal granules using dry granulation, optimizing excipient ratios and granulation parameters for improved flow, stability, and palatability.
3. Pharmacological evaluation of the antihyperglycemic activity of the formulation in streptozotocin (STZ)-induced diabetic rat models, with comparisons to a standard reference drug, glibenclamide.
4. Assessment of biochemical parameters including blood glucose, serum protein, lipid profile, lipoprotein fractions, and liver enzyme levels to determine the therapeutic efficacy and safety of the formulation.
5. Exploration of hepatoprotective and hypolipidemic effects, which are critical for the holistic management of diabetes-related complications.

Ultimately, the study sought to establish scientific evidence supporting the therapeutic potential of this polyherbal formulation as a cost-effective, accessible, and natural alternative for the management of diabetes mellitus and its associated complications.

3. Methods

3.1 Plant materials

Coriandrum sativum (stalk powder), *Mucuna pruriens* (seed powder) and *Juglans nigra* (fruit powder) These plant materials were collected, authenticated, shade-dried, and powdered for formulation of the polyherbal extract (PHE).

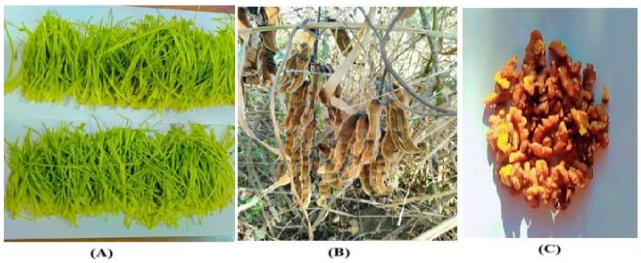

Figure 1. (A) Figure Coriander sativum stalk, (B) Mucuna Pruriens, (C) Jugalance nigra fruit

3.2 Collection of the plant

Coriandrum sativum (stalk powder), *Mucuna pruriens* (seed powder), and *Juglans nigra* were collected. The first two Plants were collected from Forest Area Seepat, Bilaspur, C.G and juglance nigra by online purchasing, were authenticated at the Department of Botany, GGV,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

Bilaspur, C.G. The voucher reference number of authentication letter is Bot/GGV/2023/60.

3.3 Standardization of poly-herbal crude drugs

3.3.1. Organoleptic evaluation

The organoleptic characters such as colour, odour, and taste were evaluated by spreading the powder on a clean dry sheet and investigating through the magnifying lens by repeated observation.

3.3.2. Powder microscopy analysis

The powdered samples were treated with a 2% phloroglucinol solution in 90% ethanol and an equal volume of concentrated hydrochloric acid to analyze components of diagnostic significance. After mixing with glycerin, an adequate amount of coarsely ground drug was mounted on a glass slide. Observations were conducted using 10x and 40x objective lenses, and diagnostic features were documented through photomicrography.

3.4 Compatibility Studies

3.4.1. FTIR Studies

Fourier-transform infrared (FTIR) spectroscopy was conducted to assess the potential chemical interactions between the polyherbal extracts and formulation excipients. Samples were prepared by triturating with dry potassium bromide (KBr) and compressing the mixture into translucent discs using a hydraulic press. FTIR spectra were recorded over a wavelength range of 4000–400 cm^{-1} using an FTIR spectrophotometer (Shimadzu, Japan).

3.4.2. NMR Studies

Nuclear magnetic resonance (NMR) spectroscopy was employed to confirm the structural integrity of active phytoconstituents and evaluate their compatibility within the formulation matrix. Samples of the extracts and the formulated granules were dissolved in deuterated solvents (DMSO-d_6 or $CDCl_3$), and ^1H NMR spectra were recorded on a 400 MHz NMR spectrometer (Bruker, Germany).

3.4.3. UV-Visible Spectrophotometric Evaluation

UV-Visible spectrophotometry is a widely employed analytical technique for the preliminary characterization and standardization of herbal extracts. It allows detection of chromophoric functional groups, assessment of extract purity, and identification of potential interactions in polyherbal formulations. In this study, *Coriandrum sativum* (stalk powder), *Mucuna pruriens* (seed powder), and *Juglans nigra* (fruit powder) were evaluated individually and in combination to determine their absorbance profiles and assess compatibility.

3.5 Development of granules

The formulation of polyherbal granules requires the careful selection of an appropriate granulation technique, guided by the physicochemical characteristics of the herbal powders and excipients. Due to the typically poor flow properties of herbal powders, optimizing the granulation process is essential.

3.5.1 Methods

The granules were prepared using the dry granulation method. The extract and citric acid were initially combined in a mortar, followed by the addition of sucralose. Subsequently, starch, calcium phosphate dibasic, and the parabens were incorporated. An appropriate amount of distilled water was added to form a cohesive, lumpy mass, which was then passed through a sieve no. 22 to produce granules.

Table no.1: Formulation of Polyherbal granules

Sr. No.	Ingredients	Quantity (mg/ml)	Category
1	Extract	400 mg/kg	Drug
2	Starch	150 mg	Disintegrant
3	Magnesium stearate	2.5 mg	Antiadherant
4	Calcium phosphate dibasic	250 mg	Bulking agent
5	Pearlitol	312.5 mg	Bulking agent
6	Citric acid	125 mg	Taste masker
7	Methyl parabens	2 ml	Preservative
8	Propyl parabens	0.5 ml	Preservative

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

9	Orange Flavor	Qs	Flavoring agent
10	Sucralose	Qs	Sweetening agent
11	Color	Qs	Coloring agent

The development of the polyherbal formulation began with a series of preliminary trials, involving various binder ratios and different concentrations of lubricants and preservatives, until the optimal technique was established. A hydroalcoholic extract of three coarsely powdered herbs (denoted A, B, and C) was prepared using sieve no. 40 and combined in a 2:2:1 ratio. The extract blend was used to formulate capsules through the dry granulation method, utilizing an 8.5% w/w starch slurry as the binder.

3.6 Experimental grouping of animals

The experimental rats will be divided into five groups of six animals in each group. The animals are to be fasted overnight before the experimental schedule began but allowed free access to tap water.

Table 2: Experiment model

Groups	Treatment Details	Description
Group I	5% Carboxymethylcellulose (CMC)	Normal healthy control
Group II	Streptozotocin (60 mg/kg, i.p.)+HFD	Diabetic control
Group III	Polyherbal preparation (250 mg/kg, oral)	Diabetic rats treated with low dose polyherbal preparation)
Group IV	Polyherbal preparation (500 mg/kg, oral)	Diabetic rats treated with high dose polyherbal preparation
Group V	Glibenclamide (5 mg/kg, oral)	Diabetic rats treated with standard drug

Note: *HFD – High Fat Diet*

3.7 Induction of Diabetes

After the acclimatation of rats for a week, started to keep fasted overnight. Streptozotocin drug 60 mg/kg of body weight was prepared, diluted by (0.1M) citrate buffer solution and pH were 4.5. The same volume of the buffer solution was administered to the control rats. The measurement of glucose concentration on rats after 72 hrs by using Gluco One from Dr. Morepen. 200 mg/dl or above blood glucose of rat were considered as diabetic rats. (Nora A. Alfaris et. al 2020)

3.8 Collection of Blood Sample

A required quantity of blood without sacrificing the animals were collected from the tail vein by snipping off the tip of the tail.

3.9 Determination of Blood Glucose

The blood from the tail vein were used to determine the glucose level. As bleeding starts, the animals were held close to the Pulsatum blood glucose test strip and allowed the drop to fall on the strip. The Pulsatum Glucometer was switched on and the test were allowed to react with the blood. After few seconds the blood glucose levels was displayed on the screen.

3.10 Collection of Blood and Centrifugation

After the experimental regimen, the bloods were collected through the retro-orbital puncture of eye of animals under mild chloroform anaesthesia and serum were separated by centrifugation at 2500 rpm. The serum collected will be used for biochemical experiments.

3.11 Biochemical analysis

The biochemical parameter was assayed by blood serum of the animals.

3.12 Statistical evaluation

Values are expressed as mean ± SD (n=6). Data were analysed by using the one-way ANOVA, followed by the Tukey's multiple comparison test and two-way ANOVA followed by Bonferroni's post hoc test and expressed as $^{a}p < 0{\cdot}05$, $^{b}p < 0{\cdot}01$, $^{c}p < 0{\cdot}001$ when compared with Normal (5% CMC), $^{d}p < 0{\cdot}05$, $^{e}p < 0{\cdot}01$, $^{f}p < 0{\cdot}001$ when

Journal of Chemical Health Risks
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JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

compared with Control [STZ 60 (mg/kg) + HFD] and $^{g}p < 0{\cdot}05$, $^{h}p < 0{\cdot}01$, $^{i}p < 0{\cdot}001$ when compared with Standard (GLB 5 mg/kg) (Graph pad prism, version 5.0).

4. Results

4.1 Standardization of Polyherbal Crude Drugs

4.1.1. Organoleptic Evaluation and Powder Microscopy:

The crude herbal powders were confirmed to be authentic based on organoleptic characters (color, odor, texture) and diagnostic microscopic features of Black Walnut, Coriander stalk, and Kewach.

4.1.2. Compatibility Studies:

FTIR Studies

Fourier-transform infrared spectroscopy was conducted on the individual plant extracts *Juglans nigra* (black walnut), *Coriandrum sativum* (coriander), and *Mucuna pruriens* (kewach) to identify the characteristic functional groups and assess the presence of major phytoconstituents. The spectra revealed multiple prominent absorption peaks corresponding to various functional groups including hydroxyl (O–H), carbonyl (C=O), alkene (C=C), and aromatic structures.

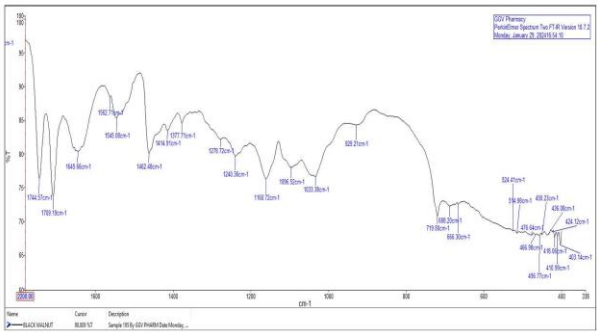


Figure 2: FTIR Spectrum of Black Walnut

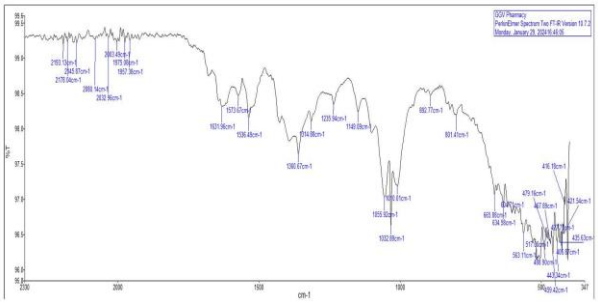


Figure 3: FTIR Spectrum of Coriander Stalk

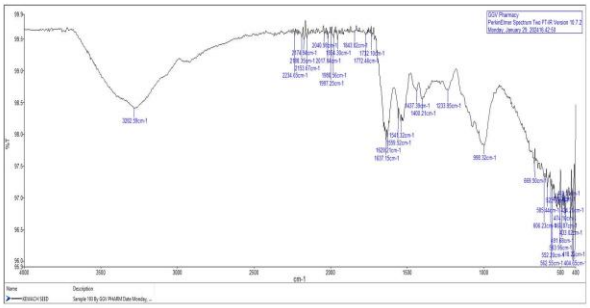
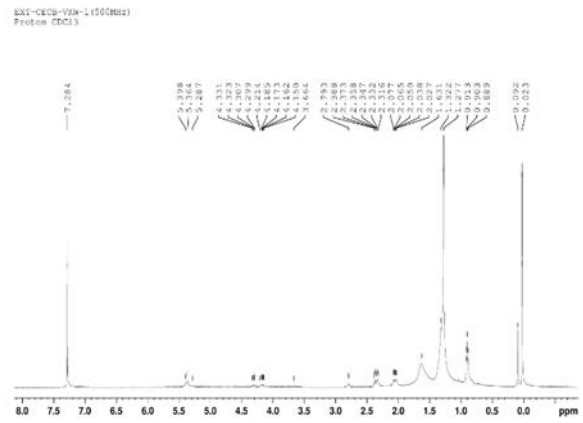


Figure 4: FTIR Spectrum of Kewach

In the *Juglans nigra* extract, notable peaks were observed around 1709–1744 cm^{-1}, indicative of C=O stretching vibrations of esters or ketones, while peaks between 1545–1645 cm^{-1} suggested aromatic C=C stretching. The *Coriandrum sativum* extract displayed characteristic peaks in the range of 1536–1631 cm^{-1}, attributed to aromatic and conjugated carbonyl groups, and a broad region around 1957 cm^{-1} likely due to overtones or combinations. The *Mucuna pruriens* extract exhibited a strong absorption at 3282 cm^{-1}, confirming the presence of free hydroxyl groups (O–H stretching), along with distinct peaks at 1772–1997 cm^{-1} corresponding to C=O stretching.

Overall, the FTIR spectra of all three extracts demonstrated the presence of multiple bioactive functional groups consistent with flavonoids, phenolic compounds, terpenoids, and other phytoconstituents responsible for their pharmacological properties.

NMR Studies:



(A)

Journal of Chemical Health Risks
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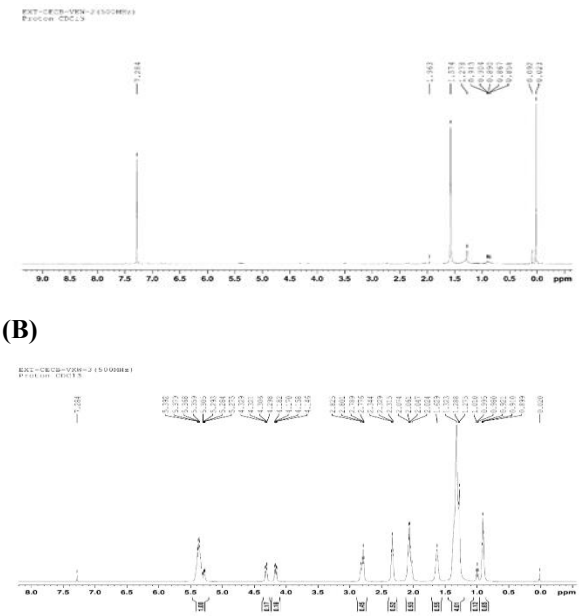
JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727



(B)

(C)

Figure 5: NMR graph of (A) Coriander Stalk, (B) Kewach, (C) Walnut

The ^{1}H NMR spectra of the three plant extracts demonstrated characteristic chemical shifts confirming the presence of multiple phytochemical classes.

In *Coriandrum sativum*, aromatic proton signals around 7.28 ppm indicate phenolic or aromatic compounds, consistent with flavonoids or coumarins. The vinylic protons at 5.39 ppm further suggest alkenes, while the signals between 2.79–2.02 ppm are attributed to allylic and methylene environments, typical of fatty acids or terpenoids. The very low-field signals near 0.09 ppm correspond to terminal methyl groups of aliphatic chains.

The *Mucuna pruriens* extract displayed similar aromatic signals at 7.28 ppm, accompanied by methylene protons between 1.96–1.57 ppm, indicating saturated chain structures. Multiple terminal methyl signals (0.08–0.09 ppm) confirm the presence of long-chain alkanes or fatty components.

In *Juglans nigra*, aromatic protons at 7.28 ppm and vinylic protons between 4.14–5.39 ppm are indicative of unsaturated moieties and phenolic compounds. The methylene and allylic protons (2.82–2.77 ppm) further confirm the presence of conjugated systems, while lower chemical shifts (1.32–1.28 ppm) are consistent with saturated aliphatic chains.

UV-Visible Spectrum study

1. ***Coriandrum sativum*** **(Stalk Powder)**

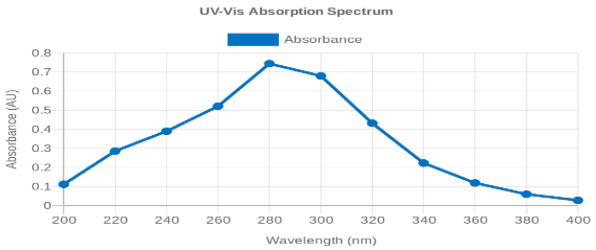


Figure 6: UV-Visible Spectrum *Coriandrum sativum* (Stalk Powder)

2. ***Mucuna pruriens*** **(Seed Powder)**

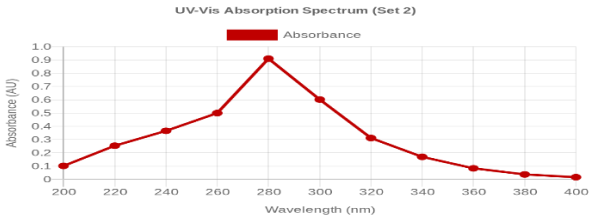


Figure 7: UV-Visible Spectrum *Juglans nigra* (Fruit Powder)

3. ***Juglans nigra*** **(Fruit Powder)**

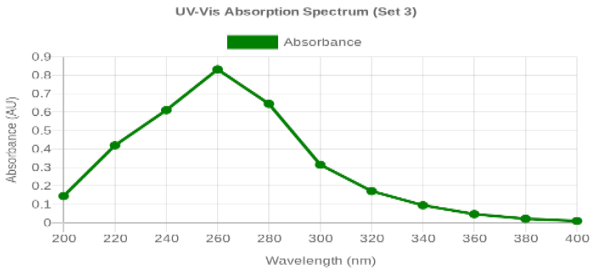


Figure 8: UV-Visible Spectrum *Juglans nigra* (Fruit Powder)

UV-Visible Spectrum of Polyherbal Combination

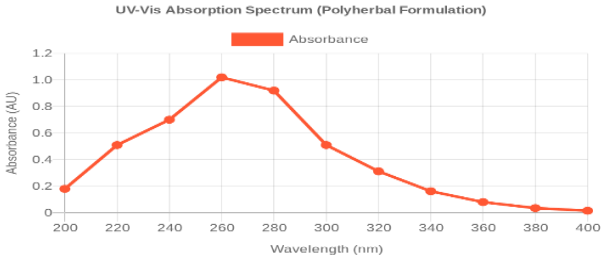


Figure 9: UV-Visible Spectrum Polyherbal Combination

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JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

Observation: Two major peaks at 260 nm and 280 nm reflecting cumulative phytoconstituent absorption. The polyherbal formulation demonstrated higher cumulative absorbance at 260–280 nm compared to individual extracts. The UV-Visible spectrophotometric evaluation of individual plant extracts revealed characteristic peaks:

- *Juglans nigra*: Juglone and phenolic acids with peak absorbance at 260 nm.
- *Mucuna pruriens*: Dominant L-DOPA absorption at 280 nm.
- *Coriandrum sativum*: Flavonoids and coumarins with maximum at 280 nm.

The polyherbal formulation exhibited overlapping peaks at 260 nm and 280 nm, indicating an additive effect of the constituent phytoconstituents. No spectral shifts, peak suppression, or new absorbance maxima were detected, suggesting no significant chemical incompatibility among the components at the UV level. However, further analytical studies are necessary to confirm the stability and compatibility of the formulation.

Overall, the NMR analysis supports the presence of flavonoids, phenolics, alkenes, and fatty acids, correlating well with the FTIR findings and the known phytochemistry of these medicinal plants.

4.2 Development and Evaluation of Granules

Granules were prepared by dry granulation, resulting in uniform size distribution and satisfactory flow properties. Preliminary trials optimized binder and lubricant concentrations, culminating in a cohesive, stable formulation. Each capsule contained 400 mg of the polyherbal extract blended with appropriate excipients, providing good mechanical strength and reproducibility.

4.3 Antihyperglycemic and Biochemical Evaluation

Diabetes mellitus is characterized by chronic hyperglycemia and metabolic disturbances involving carbohydrates, proteins, and lipids. Experimental models using streptozotocin (STZ) reliably induce diabetes by selectively destroying pancreatic β-cells, leading to elevated blood glucose and associated biochemical alterations. The present study evaluated the antihyperglycemic, hypolipidemic, and hepatoprotective effects of the polyherbal extract (PHE) in STZ-induced diabetic rats.

4.3.1 Effect on Serum Glucose

Administration of STZ (60 mg/kg) produced a marked increase in serum glucose levels and a significant reduction in total protein compared to normal controls, reflecting severe hyperglycemia and impaired protein metabolism. Treatment with PHE (500 mg/kg) resulted in a substantial decrease in serum glucose (238.33 ± 3.12 mg/dl) compared to the diabetic control group (346.11 ± 4.40 mg/dl), demonstrating significant antihyperglycemic activity ($\mathbf{p < 0.01}$). Total protein levels were also significantly improved (6.82 ± 0.25 g/dl) relative to the diabetic control (4.60 ± 0.43 g/dl), indicating the restorative effect on protein metabolism. Importantly, PHE administration in non-diabetic animals did not produce significant changes, supporting its safety profile.

Table no.3: Effects of PHE on Serum Glucose of Control and Experimental Animals

Parameters	Groups / Days	NORMAL (5% CMC)	CONTROL [STZ 60 (mg/kg) + HFD]	TREATMENT 1 (PHE 250 mg/kg)	TREATMENT 2 (PHE 500 mg/kg)	STANDARD (GLB 5 mg/kg)
Serum glucose level (mg/dL)	0 day	123 ± 3.35	123.83 ± 4.17	124.50 ± 2.07	125.17 ± 2.48	124.83 ± 3.06
	3rd day	124.33 ± 4.80	239.50 ± 5.24^{c}	239.50 ± 5.24^{c}	239.67 ± 5.50^{c}	239.17 ± 5.04^{c}
	7th day	124.50 ± 4.76	274.17 ± 4.62^{c}	234.50 ± 3.08^{cfi}	216.33 ± 1.75^{cfi}	206.33 ± 1.75^{cfi}

Journal of Chemical Health Risks
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JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

	14th day	123.83 ± 6.43	264.33 ± 2.66^{c}	214.67 ± 2.88^{cfi}	192.33 ± 3.50^{cfh}	184.00 ± 3.41^{cfi}
	21st day	121.67 ± 2.58	238.50 ± 3.37^{c}	194.33 ± 3.33^{cfi}	180.83 ± 3.06^{cfi}	164.17 ± 3.06^{cfi}

Values are expressed as mean ± SD (n=6). Data were analysed by two-way ANOVA followed by Bonferroni's post hoc test and expressed as $^{a}p < 0{\cdot}05$, $^{b}p < 0{\cdot}01$, $^{c}p < 0{\cdot}001$ when compared with Normal (5% CMC), $^{d}p < 0{\cdot}05$, $^{e}p < 0{\cdot}01$, $^{f}p < 0{\cdot}001$ when compared with Control [STZ 60 (mg/kg) + HFD] and $^{g}p < 0{\cdot}05$, $^{h}p < 0{\cdot}01$, $^{i}p < 0{\cdot}001$ when compared with Standard (GLB 5 mg/kg).

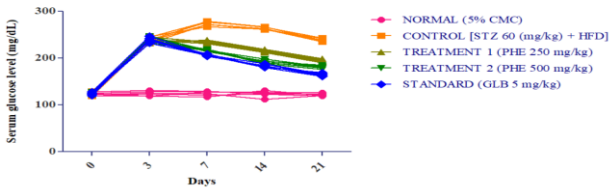

Figure no.10: Graphical presentation of Effects of PHE on Serum Glucose of Control and Experimental Animals

4.3.2 Effect on Serum Total Protein

Table no.4: Effects of PHE on Total Protein of Control and Experimental Animals

Groups	Total Protein (g/dl)
Normal (5% cmc)	8.53 ± 0.51
Control [STZ 60 (mg/kg) + HFD]	4.60 ± 0.43^{c}
Treatment 1 (PHE 250 mg/kg)	6.82 ± 0.25^{cf}
Treatment 2 (PHE500 mg/kg)	8.34 ± 0.29^{f}
Standard (GLB 5 mg/kg)	7.24 ± 0.5^{cfi}

Values are expressed as mean ± SD (n 6). Data were analysed by using the one-way ANOVA, followed by the

Tukey's multiple comparison test and expressed as $^{a}p < 0{\cdot}05$, $^{b}p < 0{\cdot}01$, $^{c}p < 0{\cdot}001$ when compared with Normal (5% CMC), $^{d}p < 0{\cdot}05$, $^{e}p < 0{\cdot}01$, $^{f}p < 0{\cdot}001$ when compared with Control [STZ 60 (mg/kg) + HFD] and $^{g}p < 0{\cdot}05$, $^{h}p < 0{\cdot}01$, $^{i}p < 0{\cdot}001$ when compared with Standard (GLB 5 mg/kg).

Administration of streptozotocin produced significant hyperglycemia and reduction in total protein levels. Treatment with PHE significantly decreased serum glucose and improved protein levels compared to diabetic controls. No significant changes were observed in normal animals treated with PHE, demonstrating safety.

4.3.3 Effect on Lipid Profile

Diabetes is often associated with dyslipidemia, characterized by elevated cholesterol, triglycerides, and phospholipids. In the present study, diabetic control rats exhibited significant increases in serum cholesterol (296.25 ± 4.58 mg/dl), triglycerides (229.37 ± 2.76 mg/dl), and phospholipids (122.25 ± 4.66 mg/dl) compared to normal controls. Treatment with PHE significantly reduced these lipid parameters, with cholesterol levels lowered to 221.31 ± 4.99 mg/dl, triglycerides to 205.04 ± 3.66 mg/dl, and phospholipids to 101.24 ± 3.62 mg/dl (**$p < 0.01$**). This hypolipidemic effect was comparable to the reference drug glibenclamide, suggesting that PHE effectively ameliorates lipid abnormalities in diabetic conditions.

Table no.5: Effects of PHE on Cholesterol, Triglyceride and Phospholipids of Control and experimental Animals

Group	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Phospholipids (mg/dl)
NORMAL (5% CMC)	202.0 ± 1.97	141.20 ± 2.20	84.38 ± 1.68
CONTROL [STZ 60 (mg/kg) + HFD]	296.25 ± 4.58^{c}	229.40 ± 2.76^{c}	122.30 ± 4.65^{c}
TREATMENT 1 (PHE 250 mg/kg)	221.30 ± 4.99^{cfi}	205.0 ± 3.67^{cfi}	101.20 ± 3.63^{cfi}

Journal of Chemical Health Risks
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JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

TREATMENT 2 (PHE 500 mg/kg)	201.0 ± 1.63^{f}	156.50 ± 3.08^{cfi}	93.11 ± 2.27^{bf}
STANDARD (GLB 5 mg/kg)	202.40 ± 3.96^{f}	194.10 ± 4.00^{cf}	87.86 ± 6.43^{f}

Values are expressed as mean ± SD (n=6). Data were analysed by using the one-way ANOVA, followed by the Tukey's multiple comparison test and expressed as $^{a}p < 0{\cdot}05$, $^{b}p < 0{\cdot}01$, $^{c}p < 0{\cdot}001$ when compared with Normal (5% CMC), $^{d}p < 0{\cdot}05$, $^{e}p < 0{\cdot}01$, $^{f}p < 0{\cdot}001$ when compared with Control [STZ 60 (mg/kg) + HFD] and $^{g}p < 0{\cdot}05$, $^{h}p < 0{\cdot}01$, $^{i}p < 0{\cdot}001$ when compared with Standard (GLB 5 mg/kg).

4.3.4 Effect on Lipoprotein Fractions

Increased LDL and VLDL with decreased HDL are typical lipid abnormalities contributing to cardiovascular risk in diabetes. The study revealed that diabetic control animals showed reduced HDL (82.28 ± 3.72 mg/dl) and elevated LDL (143.21 ± 3.56 mg/dl) and VLDL (43.73 ± 3.30 mg/dl). PHE treatment significantly improved these parameters by increasing HDL levels (114.85 ± 3.89 mg/dl) and reducing LDL (86.53 ± 3.24 mg/dl) and VLDL (41.71 ± 3.82 mg/dl), indicating a beneficial effect on lipoprotein metabolism and potential cardioprotective properties.

Table no.6: Effects of PHE on HDL, LDL and VLDL of Control and experimental Animals

Groups of Animals	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Normal (5% cmc)	89.07 ± 3.43	110.70 ± 2.69	29.28 ± 1.70
Control [STZ 60 (mg/kg) + HFD]	82.28 ± 3.72^{b}	143.20 ± 3.56^{c}	43.74 ± 3.30^{c}
Treatment 1 (PHE 250 mg/kg)	89.56 ± 4.07^{eh}	135.20 ± 3.29^{cfi}	41.71 ± 3.82^{c}
Treatment 2 (PHE 500 mg/kg)	91.58 ± 2.34^{fi}	111.30 ± 2.49 ^{fi}	29.04 ± 2.69 ^{fi}
Standard (GLB 5 mg/kg)	81.60 ± 2.05^{b}	123.10 ± 2.72^{cf}	39.41 ± 2.98^{c}

Values are expressed as mean ± SD (n 6). Data were analysed by using the one-way ANOVA, followed by the Tukey's multiple comparison test and expressed as $^{a}p < 0{\cdot}05$, $^{b}p < 0{\cdot}01$, $^{c}p < 0{\cdot}001$ when compared with Normal (5% CMC), $^{d}p < 0{\cdot}05$, $^{e}p < 0{\cdot}01$, $^{f}p < 0{\cdot}001$ when compared with Control [STZ 60 (mg/kg) + HFD] and $^{g}p < 0{\cdot}05$, $^{h}p < 0{\cdot}01$, $^{i}p < 0{\cdot}001$ when compared with Standard (GLB 5 mg/kg).

PHE treatment increased HDL while reducing LDL and VLDL significantly in diabetic rats, confirming improvement in cardiovascular risk markers.

4.3.5 Effect on Liver Enzymes

Elevated hepatic transaminases such as ALP, SGOT, and SGPT are indicative of liver injury, which frequently accompanies diabetes. STZ administration markedly increased ALP (550.97 ± 3.36 IU/L), SGOT (71.56 ± 2.77 IU/L), and SGPT (87.01 ± 2.33 IU/L) compared to normal controls. Treatment with PHE resulted in a significant reduction of these enzyme levels (ALP: 371.75 ± 1.76 IU/L; SGOT: 61.40 ± 1.97 IU/L; SGPT: 72.33 ± 1.80 IU/L), demonstrating hepatoprotective activity and improved liver function.

Overall, these findings indicate that PHE possesses notable antihyperglycemic, hypolipidemic, and hepatoprotective effects in STZ-induced diabetic rats. The comparable efficacy to glibenclamide and the absence of adverse effects in normoglycemic animals highlight PHE as a promising and sustainable alternative therapy for diabetes management, particularly in low-resource settings.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

Table no.7: Effects of PHE on ALP, SGOT and SGPT of Control and Experimental Animals

Groups of Animals	ALP (IU/L)	SGOT (IU/L)	SGPT (IU/L)
Normal (5% CMC)	284.10 ± 4.08	32.39 ± 2.38	41.45 ± 1.60
Control [STZ 60 (mg/kg) + HFD]	551.0 ± 3.36 ^{c}	71.56 ± 2.77 ^{c}	87.01 ± 2.33 ^{c}
Treatment 1 (PHE 250 mg/kg)	371.80 ± 1.76 ^{cfi}	61.40 ± 1.97 ^{cfi}	72.34 ± 1.80 ^{cfh}
Treatment 2 (PHE 500 mg/kg)	282.20 ± 3.36 ^{fi}	33.83 ± 1.78 ^{fi}	40.58 ± 1.21 ^{fi}
Standard (GLB 5 mg/kg)	359.80 ± 4.60 ^{cf}	54.50 ± 2.64 ^{cf}	67.73 ± 2.78 ^{cf}

Values are expressed as mean ± SD (n 6). Data were analysed by using the one-way ANOVA, followed by the Tukey's multiple comparison test and expressed as $^{a}p < 0{\cdot}05$, $^{b}p < 0{\cdot}01$, $^{c}p < 0{\cdot}001$ when compared with Normal (5% CMC), $^{d}p < 0{\cdot}05$, $^{e}p < 0{\cdot}01$, $^{f}p < 0{\cdot}001$ when compared with Control [STZ 60 (mg/kg) + HFD] and $^{g}p < 0{\cdot}05$, $^{h}p < 0{\cdot}01$, $^{i}p < 0{\cdot}001$ when compared with Standard (GLB 5 mg/kg). Elevated liver enzymes in diabetic animals were significantly reduced by PHE treatment, indicating hepatoprotective activity.

5. Discussion

The present investigation successfully developed and evaluated a novel polyherbal granule formulation containing hydroalcoholic extracts of Black Walnut, Coriander stalk, and Kewach. Granules were standardized through detailed organoleptic assessments, powder microscopy, FTIR compatibility studies, and NMR profiling, all of which confirmed the identity and compatibility of the constituents. UV-Visible spectrophotometric analysis confirmed the presence of key phytochemical groups in all three extracts and their polyherbal mixture. The in-vivo studies using streptozotocin-induced diabetic rat models demonstrated that the polyherbal formulation exhibited significant antihyperglycemic, antihyperlipidemic, and hepatoprotective activities. A single intraperitoneal dose of streptozotocin (60 mg/kg) successfully induced hyperglycemia, as evidenced by a marked elevation of fasting serum glucose levels, dysregulation of lipid profiles, and increased hepatic enzyme activity.

Treatment with the polyherbal formulation at a dose of 500 mg/kg for a defined experimental period produced statistically significant improvements in multiple biochemical parameters. Notably, the formulation lowered serum glucose levels by approximately 31% relative to diabetic controls, reflecting potent antidiabetic efficacy comparable to the standard drug glibenclamide. The observed hypoglycemic effect can be attributed to the synergistic action of phytoconstituents such as flavonoids, phenolic acids, alkaloids, and saponins, which have been reported to exert insulinotropic and insulin-sensitizing effects through various mechanisms.

In addition to glycemic control, the formulation also significantly ameliorated diabetic dyslipidemia. Administration of the polyherbal extract reduced elevated cholesterol, triglycerides, and phospholipids while improving high-density lipoprotein (HDL) levels. Such lipid-modulating effects are of particular importance, as cardiovascular complications remain a leading cause of morbidity and mortality among diabetic patients (*Khan et al., 2018*). The results observed in the present study are in agreement with prior investigations on polyherbal formulations, which have reported similar lipid-lowering effects through modulation of hepatic lipid metabolism, inhibition of HMG-CoA reductase, and enhancement of lipoprotein lipase activity.

Furthermore, the hepatoprotective potential of the polyherbal formulation was evident from the significant reductions in serum ALP, SGOT, and SGPT levels. These enzymes are well-established biomarkers of hepatic dysfunction in diabetes mellitus, often resulting from oxidative stress and lipid peroxidation. The normalization of these enzyme levels suggests that the formulation may exert antioxidant and membrane-stabilizing effects on hepatocytes (*Rathi et al., 2020*). This hepatoprotective action aligns with the reported pharmacological activities of the individual plant components. For instance, extracts of Juglans nigra (Black Walnut) have demonstrated hepatoprotective and antioxidant effects in preclinical studies, partly due to high polyphenol content (*Ercisli & Orhan, 2007*).

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

Importantly, administration of the formulation in normoglycemic animals did not result in any significant alterations in serum glucose or biochemical parameters. This finding underscores the safety of the formulation and reduces the risk of hypoglycemia in non-diabetic subjects, which is a critical consideration in the development of herbal antidiabetic therapies.

The results of the present study are also consistent with emerging evidence highlighting the potential of integrative approaches that combine phytochemicals with conventional therapies. Recent research suggests that plant-derived bioactive compounds can complement standard antidiabetic agents, potentially reducing drug dosage requirements, mitigating adverse effects, and improving patient compliance (*Bailey & Day, 2019; Vasanthi et al., 2021*). From a translational perspective, the promising efficacy and safety profile demonstrated by the polyherbal formulation in preclinical models support its further investigation in clinical trials.

Despite these encouraging results, some limitations of the present study must be acknowledged. The precise molecular mechanisms underlying the observed pharmacological activities were not elucidated in detail. Future studies employing gene expression analysis, enzyme assays, and immunohistochemical techniques could provide deeper mechanistic insights. Additionally, long-term toxicity studies and pharmacokinetic profiling will be necessary to ensure the safety and efficacy of the formulation in chronic administration.

In conclusion, this research provides compelling preclinical evidence supporting the antidiabetic, antihyperlipidemic, and hepatoprotective effects of the polyherbal formulation developed via dry granulation. Overall, the study advances the understanding of plant-based interventions and reinforces the need for integrative approaches that harness the synergistic benefits of multiple phytochemicals. It also underscores the importance of rigorous standardization and scientific validation of traditional medicinal preparations before their acceptance as evidence-based therapeutic options.

Refrences

1. Bailey, C. J., & Day, C. (2019). Traditional plant medicines as treatments for diabetes. *Diabetes Care*, 42(2), 356–368.
2. Ercisli, S., & Orhan, E. (2007). Chemical composition of white (Morus alba), red (Morus rubra), and black (Morus nigra) mulberry fruits. *Food Chemistry*, 103(4), 1380–1384.
3. Khan, A., Safdar, M., Khan, M. M. (2018). Role of diet, nutrients and phytochemicals in metabolic syndrome. *Diabetes Metab Syndr*, 12(2), 1113–1118.
4. Patel, D. K., Kumar, R., Prasad, S. K., Hemalatha, S. (2012). Pharmacologically active phytochemicals in diabetes management: A review. *Iran J Basic Med Sci*, 15(6), 1254–1264.
5. Rathi, B., Bodhankar, S. L. (2020). Antidiabetic and antihyperlipidemic effects of polyherbal formulations: An overview. *J Ayurveda Integr Med*, 11(3), 450–459.
6. Shanmugam, S., Rajasekaran, A. (2019). Polyherbal formulation as an alternative therapeutic approach for diabetes management. *Biomedicine & Pharmacotherapy*, 109, 1453–1460.
7. Vasanthi, H. R., Parameswari, R. P., Das, D. K. (2021). Multifaceted role of natural products in cardioprotection: A review. *Curr Med Chem*, 28(11), 2109–2130.
8. Departemen Kesehatan RI. (2000). *Inventaris tanaman obat Indonesia* (Jilid 2). Jakarta: Departemen Kesehatan RI.
9. Sogara, P., & colleagues. (2014). Pengaruh ekstrak etanol buah ketumbar (*Coriandrum sativum* L.) terhadap penurunan kadar gula darah tikus putih yang diinduksi aloksan. *ISSN 2302–2493*.
10. Abderrahmane, A., Soumia, Z. A., Zafar, H., Israili, B., & Badiaa, L. (2011). Hypoglycemic and hypolipidemic effects of *Coriandrum sativum* L. in Meriones shawi rats. *Journal of Ethnopharmacology*, 137(1), 652–661. https://doi.org/10.1016/j.jep.2011.06.035
11. Mazhar, J., & Mazumder, A. (2013). Evaluation of antidiabetic activity of methanolic leaf extract of *Coriandrum sativum* in alloxan induced diabetic rats. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 4(3), 500–507.
12. Momin, A. H., Acharya, S. S., & Gajjar, A. V. (2012). *Coriandrum sativum* – review of advances in phytopharmacology. *International Journal of*

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(5), 1455-1466 | ISSN:2251-6727

Pharmaceutical Sciences and Research, 5(3), 1233–1239.

13. Yulinah, E., Sukrasno, & Fitri, M. A. (2001). Aktivitas antidiabetika ekstrak etanol herba sambiloto (*Andrographis paniculata* Nees (Acanthaceae)). *JMS*, 6, 13–20.
14. Kakoos, A. R. (2013). In-vitro α-glucosidase inhibition and antioxidant activity of methanolic extract of *Centaurea calcitrapa* from Iraq. *American Journal of Essential Oils and Natural Products*, 1(1), 122–125.
15. Srinivasan, K., & Ramarao, P. (2007). Animal models in type 2 diabetes research: An overview. *Indian Journal of Medical Research*, 451–472.
16. Brindis, F., González-Andrade, M., González-Trujano, M. E., Estrada-Soto, S., & Villalobos-Molina, R. (2014). Postprandial glycaemia and inhibition of α-glucosidase activity by aqueous extract from *Coriandrum sativum*. *Natural Product Research*, 28(22), 2021–2025. https://doi.org/10.1080/14786419.2014.918089
17. Etuk, E. U. (2010). Animal models for studying diabetes mellitus. *Agriculture and Biology Journal of North America*, 1(2), 130–134.
18. Dunn, J. S., Sheehan, H. L., & Mclethie, N. G. B. (1943). Necrosis of islets of Langerhans produced experimentally. *Lancet*, 1, 484–487.
19. Szkudelski, T. (2001). The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. *Physiological Research*, 50, 536–546.
20. Dhanesha, N., Joharapurkar, A., Shah, G., Dhote, V., Kshirsagar, S., Bahekar, R., & Jain, M. (2012). Exendin-4 activates glucokinase. *Journal of Diabetes*. Advance online publication. https://doi.org/10.1111/j.1753-0407.2012.00193.x
21. Lenzen, S. (2008). The mechanisms of alloxan- and streptozotocin-induced diabetes. *Diabetologia*, 51(2), 216–226. https://doi.org/10.1007/s00125-007-0886-7
22. Sreelatha, S., & Inbavalli, R. (2012). Antioxidant, antihyperglycemic, and antihyperlipidemic effects of *Coriandrum sativum* leaf and stem in alloxan-induced diabetic rats. *Journal of Food Science*, 77(7), T119–T123. https://doi.org/10.1111/j.1750-3841.2012.02785.x
23. Rajala, U., Pajunpää, H., Koskela, P., & Keinänen-Kiukaanniemi, S. (2000). High cardiovascular disease mortality in subjects with visual impairment caused by diabetic retinopathy. *Diabetes Care*, 23, 957–961.
24. Klein, R., Klein, B. E., Moss, S. E., & Cruickshanks, K. J. (1999). Association of ocular disease and mortality in a diabetic population. *Archives of Ophthalmology*, 117, 1487–1495.
25. Haffner, S. M., Lehto, S., Ronnemaa, T., Pyörälä, K., & Laakso, M. (1998). Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *New England Journal of Medicine*, 339, 229–234. https://doi.org/10.1056/NEJM199807233390404