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PHARMACOLOGICAL EVALUATION OF CINNAMOMUM VERUM FOR THE ANTIDIABETIC ACTIVITY

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ABSTRACT

Background: The increasing prevalence of diabetes and related complications has prompted the exploration of alternative treatments. This study investigates the effects of an herbal formulation on various biochemical markers and its potential as a therapeutic agent for diabetes management. **Aim:** To evaluate the phytochemical properties, glucose-lowering effects, and safety profile of the herbal formulation in streptozotocin (STZ)-induced diabetic rats. **Research Methodology**: The polyherbal formulation was analyzed for moisture content, crude fiber, and ash values. Phytochemical screening revealed the presence of tannins, saponins, flavonoids, and alkaloids. The formulation was administered orally at different dosages, and its effects on fasting blood glucose (FBG), serum insulin levels, liver and renal profiles, and enzyme activities (alpha-glucosidase and alpha-amylase) were assessed over four weeks. Histopathological examinations were also conducted to evaluate organ integrity. **Conclusion:** The polyherbal formulation demonstrated significant reductions in FBG levels and improvements in serum insulin and enzyme activities, indicating its potential as an effective antidiabetic agent. The formulation also showed minimal adverse effects on liver and kidney functions. Histopathological analysis confirmed the therapeutic benefits. A promising candidate for diabetes management.

KEYWORDS: Diabetes, herbal, Phytochemicals.

INTRODUCTION

A metabolic condition known as diabetes mellitus (DM) is defined by persistently high blood sugar levels (hyperglycemia) due to insufficient insulin production or ineffective insulin action. With millions of victims of all ages and a high death toll, it ranks high among the world's most pressing public health concerns. The World Health Organization (WHO) predicts that the number of individuals living with diabetes will climb from 463 million in 2019 to 700 million by 2045, a figure that reflects the persistently increasing prevalence of the disease. This concerning pattern highlights the critical need for efficient treatment approaches, particularly those that might forestall or postpone the development of diabetes and its consequences.

Type 2 diabetes mellitus (T2DM) is more prevalent and is more commonly linked to insulin resistance and relative insulin deficiency; Type 1 diabetes mellitus (T1DM) is mainly an autoimmune disease that destroys pancreatic beta cells. The foundation of diabetic therapy is pharmaceutical therapies, but dietary and activity changes are essential. However, there is a rising interest in natural treatments and complementary therapies due to the negative effects commonly linked with long-term usage of antidiabetic pharmaceuticals.

The antidiabetic potential of Cinnamomum verum, or genuine cinnamon or Ceylon cinnamon, has been the focus of much research among the many natural compounds studied. The inner bark of the little evergreen tree Cinnamomum verum, which is indigenous to India and Sri Lanka, is a popular spice in Indian and Sri Lankan cuisine. In addition to its culinary purposes, cinnamon has a rich history of usage in traditional medicine. It is highly esteemed in Ayurveda and Traditional Chinese Medicine for its many health advantages, including its potential to lower blood sugar levels.

METHODOLOGY

Wistar rats will be divided into 5 groups of six animals each = Total **30** rats.

GROUPS	DRUGS	DOSES
GROUP 1	Distilled water	1ml/kg-p.o
GROUP 2	Control	500mg/kg-p.o
GROUP 3	Control + standard drug	200mg/kg-p.o
GROUP 4	Control + Extract	400mg/kg-p.o
GROUP 5	Control + Extract	600mg/kg-p.o

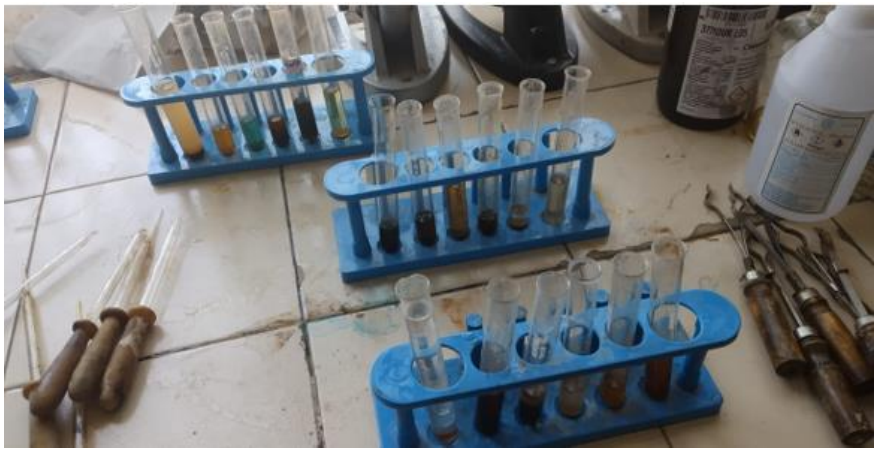
This above dosing schedule will be carried for 14 days and at the end of the Experiment, animals will be sacrificed and the stomach will be dissected out and kept in 10% formalin buffered solution for histopathological examinations.

RESULTS

Phytochemical screening tests

Preliminary phytochemical screening

Screening tests of extracts of Polyherbal formulation (P.H.F.) in a ratio of 25:25:25:25. based on the standard methods as follows

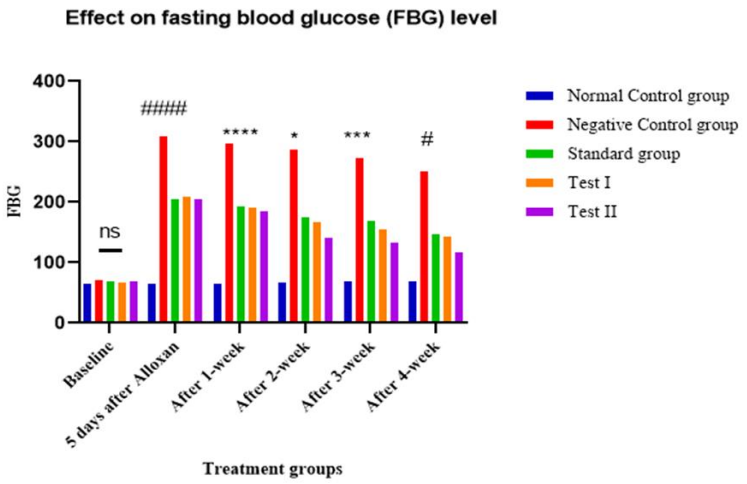


Polyherbal formulation (P.H.F.)	
Parameters	**Values in (% w/w)**
1. Moisture content	82.46
2. Loss on drying	5.47
3. Ash value	
a. Total ash	5.63
b. Acid-insoluble ash	0.29
c. Water-soluble ash	4.17
d. Sulphated ash	1.19
4. Crude fibre contents	8.26

Phytochemicals	*Qualitative*	*Quantitative (%)*
Tannins	++	4.13
Saponin	++	6.14
Flavonoid	++	2.22
Alkaloids	+	1.56
Steroids	+	0.67
Phenol	+	0.84
Anthraquinone	++	2.63
Phlobatannin	+	0.39
Glycosides	+	0.27
Terpenoides	+	0.67

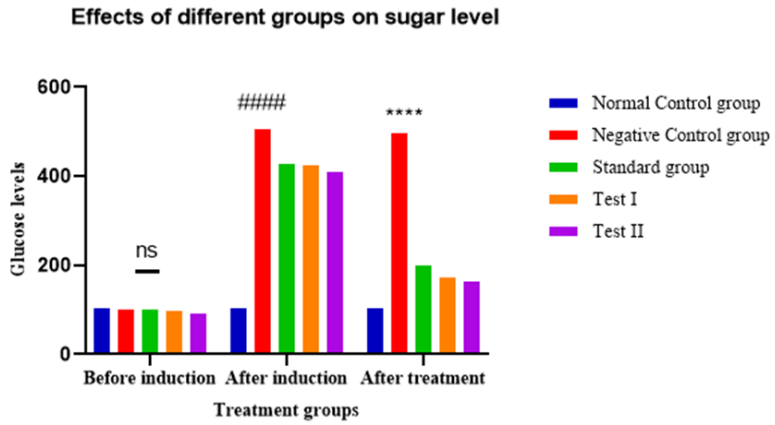
Effect on fasting blood glucose (FBG) level

Level	Group 1	Group 2	Group 3	Group 4	Group 5
Baseline	65.8±0.05	70.6±0.08	69.7±0.04	67.4±0.04	68.3±0.12
5 days after STZ	65.8.42±0.06	308.6±0.04	204.2±0.05	208.3±0.05	205.5±0.17
After 1-week	65.6±0.09	296.5±0.08	192.8±0.08	190.5±0.05	185.5±0.13
After 2-week	66.7±0.04	286.8±0.07	175.8±0.06	166.5±0.02	141.5±0.12
After 3-week	68.5±0.05	272.5±0.04	168.5±0.04	154.5±0.03	133.5±0.05
After 4-week	68.9±0.05	250.5±0.03	146.7±0.05	142.6±0.09	117.5±0.08

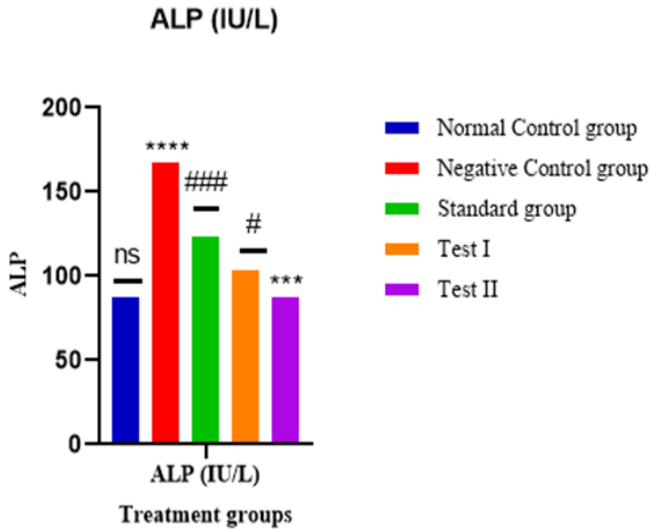


Effects of different groups on sugar level of STZ- induced diabetic rats.

Treatment groups	Dosage (m)	Glucose levels (mg/dl) post treatment with the extracts			
Groups		***Before induction***	***After induction***	***After treatment***	***% Sugar Reduced***
Group 1	(1%w/v CMC), orally	104.50±10.50	505.70±24.30	245.70±6.30	51.41%
Group 2	(1%w/v), orally	100.40±3.60	106.50±4.50	95.60±2.23	10.23%
Group 3	(10mg/kg orally)	101.55±2.45	427.90±10.10	200.50±7.50	53.14%
Group 4	(50mg/kg orally)	97.56±9.44	423.50±45.50	173.50±30.50	59.00%
Group 5	(100mg/kg orally)	92.50±9.50	410.80±45.20	163.60±30.40	60.17%
SD		**00.45436**	**1.5460**	**1.54959**	**00.2077**
SEM		**00.20319**	**00.69140**	**00.2457**	**00.92908**



Groups Treatment/Dose	ALP (IU/L)	AST (IU/L)	ALT (IU/L)
Group 1	89.35± 7.12***	83.75± 7.36***	25.52± 1.65***
Group 2	168.96± 9.02	161.92± 9.07	128.37± 7.92
Group 3	121.66± 8.12*	87.31± 7.10**	44.91± 2.36*
Group 4	100.99± 7.96**	89.18± 6.87***	34.68± 2.72**
Group 5	85.94± 6.06***	89.85± 6.84***	28.96± 1.82***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Standard group
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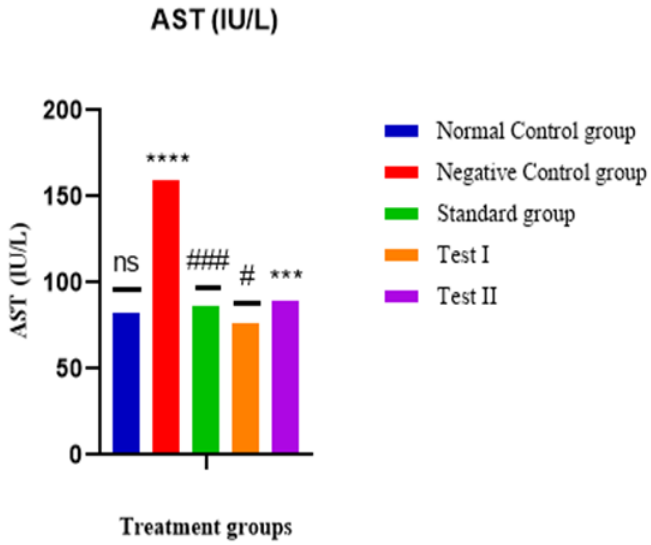
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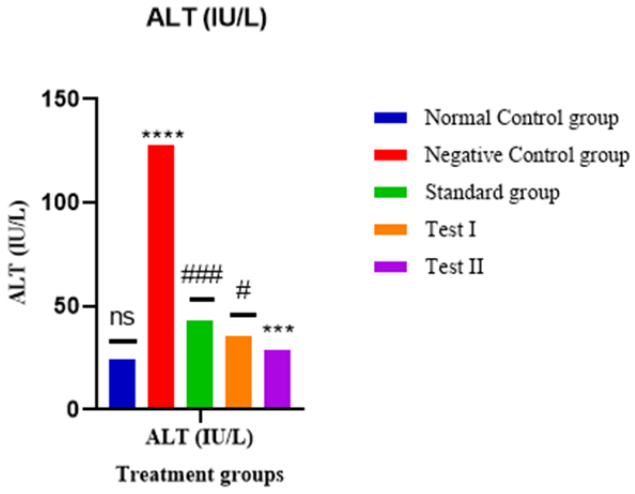
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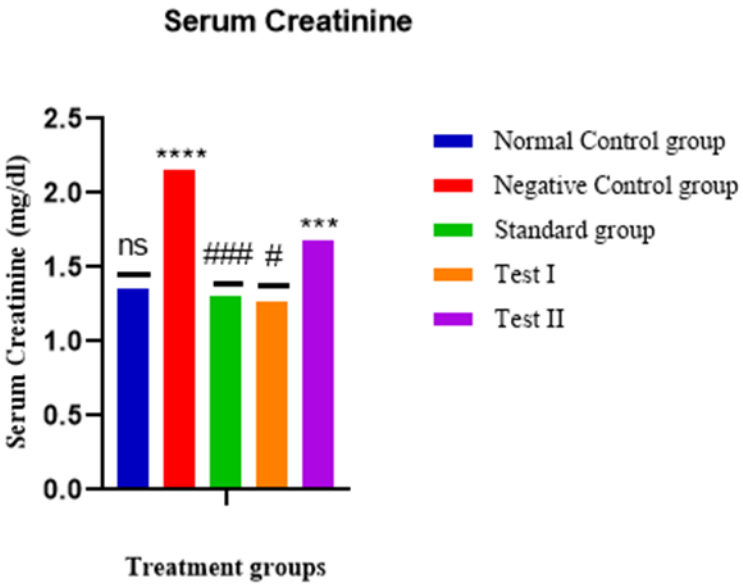
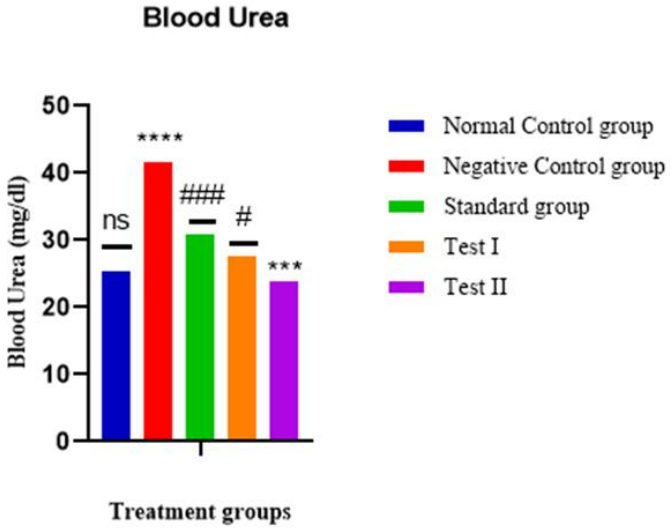
ALT (IU/L)
Treatment groups
Normal Control group
Negative Control group
Standard group
Test I
Test II

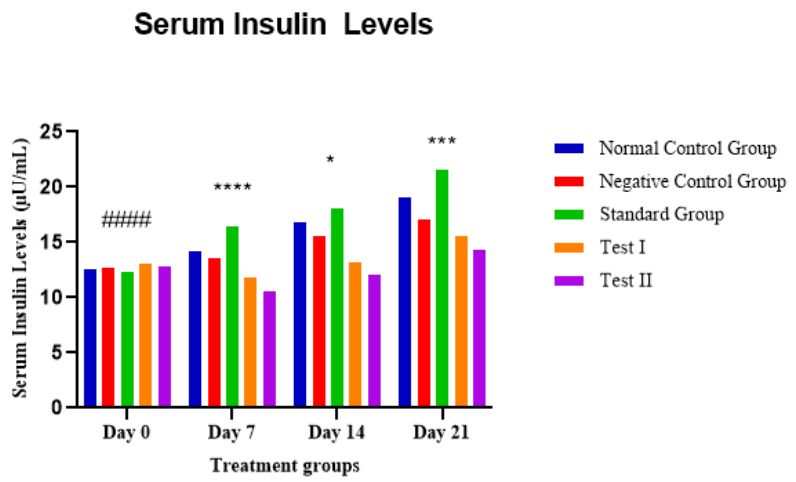
Groups Treatment/Dose	Serum Creatinine (mg/dl)	Blood Urea (mg/dl)
Group 1	1.18±0.08***	25.73± 2.26***
Group 2	2.58± 0.16	41.14± 2.61
Group 3	1.42± 0.12**	30.61± 2.84*
Group 4	1.32± 0.09***	27.86± 2.51**
Group 5	1.27± 0.10***	23.94± 2.08***





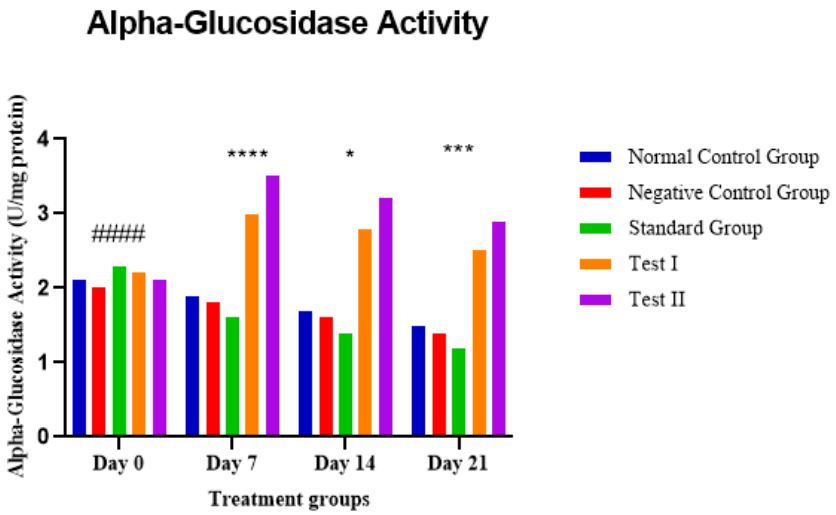
Serum Insulin Levels (µU/mL)

Group	Day 0	Day 7	Day 14	Day 21
Group 1	12.5 ± 1.3	14.2 ± 1.1	16.8 ± 1.0	19.0 ± 1.2
Group 2	12.7 ± 1.2	13.5 ± 1.0	15.5 ± 0.8	17.0 ± 1.0
Group 3	12.3 ± 1.1	16.4 ± 1.3	18.0 ± 1.1	21.5 ± 1.5
Group 4	13.0 ± 1.2	11.8 ± 1.0	13.2 ± 0.9	15.6 ± 1.1
Group 5	12.8 ± 1.3	10.5 ± 1.1	12.0 ± 1.2	14.3 ± 1.4



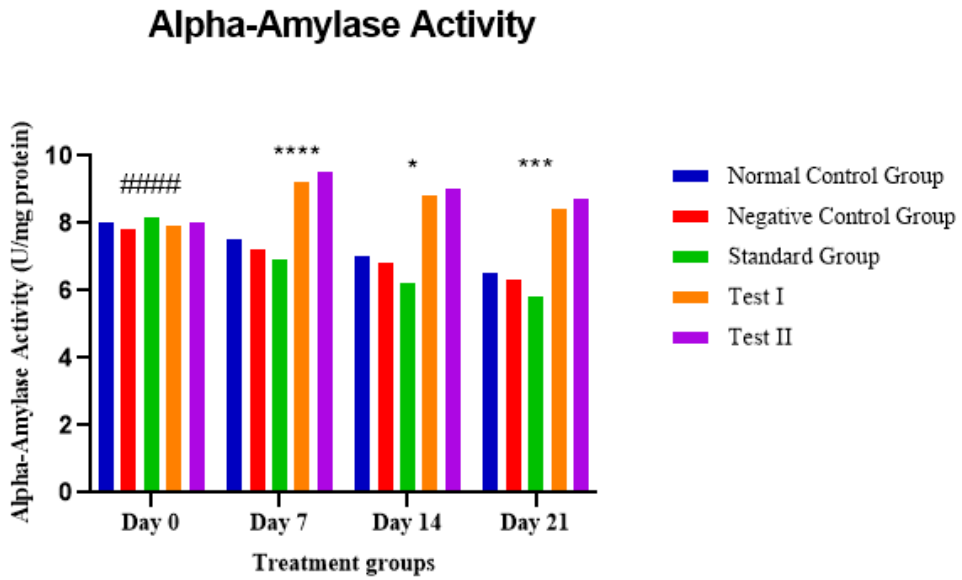
Alpha-Glucosidase Activity (U/mg protein)

Group	Day 0	Day 7	Day 14	Day 21
Group 1	2.1 ± 0.2	1.9 ± 0.1	1.7 ± 0.2	1.5 ± 0.1
Group 2	2.0 ± 0.2	1.8 ± 0.2	1.6 ± 0.1	1.4 ± 0.2
Group 3	2.3 ± 0.3	1.6 ± 0.1	1.4 ± 0.2	1.2 ± 0.1
Group 4	2.2 ± 0.2	3.0 ± 0.4	2.8 ± 0.3	2.5 ± 0.3
Group 5	2.1 ± 0.3	3.5 ± 0.4	3.2 ± 0.3	2.9 ± 0.4



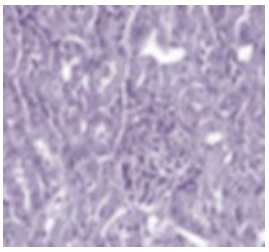
Alpha-Amylase Activity (U/mg protein)

Group	Day 0	Day 7	Day 14	Day 21
Group 1	8.0 ± 0.5	7.5 ± 0.4	7.0 ± 0.3	6.5 ± 0.3
Group 2	7.8 ± 0.4	7.2 ± 0.3	6.8 ± 0.3	6.3 ± 0.2
Group 3	8.2 ± 0.4	6.9 ± 0.3	6.2 ± 0.2	5.8 ± 0.3
Group 4	7.9 ± 0.3	9.2 ± 0.4	8.8 ± 0.5	8.4 ± 0.4
Group 5	8.0 ± 0.3	9.5 ± 0.4	9.0 ± 0.5	8.7 ± 0.5

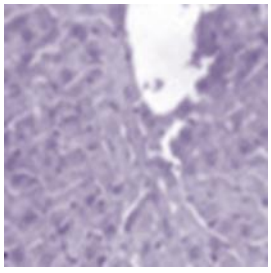


Histopathological studies

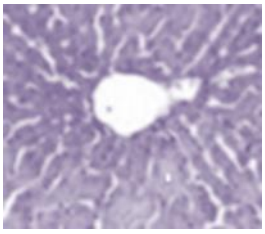
Group 1: Dispersed throughout the tissue were mononuclear cells and epithelial granulomas, both of which are highly inflammatory. Provocative mononuclear cell counts have been tracked around ports and rivers, revealing the spread of settlers. Significant thrombosis of the sciatic nerve.



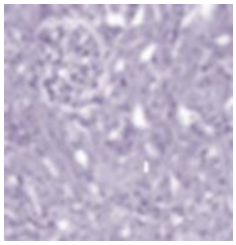
Group 2: Dispersed throughout the tissue were mononuclear cells and epithelial granulomas, both of which are highly inflammatory. Provocative mononuclear cell counts have been tracked around ports and rivers, revealing the spread of settlers. Significant thrombosis of the sciatic nerve.



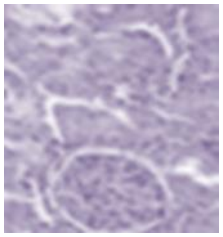
Group 3: The parenchyma included many lymphocytes, macrophages, and histiocytes. There was an apparent deterioration or multiplication of pancreatic cells in the core regions. The mononuclear provocative cells kept an eye on the lymphocytes and histiocytes as they made their way to the periphery.



Group 4: Many hepatocytes were found alive and well inside the typical hepatocytes' nuclei. Sometimes clusters of mononuclear inflammatory cells might be seen deep into the parenchyma. Scattered mononuclear flaming cells, including lymphatic lymphocytes and histocytes, emerge in the portal and perivular sites. The phenomenon of bile duct proliferation has achieved notoriety in specific settings.



Group 5: Pictured as dilated and clogged sinusoids, hepatocytes are shown here. Even though the epitheloid only contains a small number of parenchymas, they are important structural components. Dispersed mononuclear provocative cells have been shown colonising the periportal and perivasive spaces. Inflammation and fire spread to the Sciatic nerve.



DISCUSSION

The polyherbal formulation (P.H.F.) was analyzed for its phytochemical, biochemical, and pharmacological properties, showcasing a significant potential for therapeutic applications, particularly in managing diabetes and its complications.

Phytochemical Screening

Preliminary phytochemical screening of P.H.F. revealed a robust profile of bioactive compounds. Tannins (4.13%), saponins (6.14%), and anthraquinones (2.63%) were present in higher concentrations, whereas glycosides (0.27%) and steroids (0.67%) were less prominent. The presence of tannins, saponins, and flavonoids indicates strong antioxidant and anti-inflammatory potential, aligning with their known biological activities. Comparatively, the moisture content (82.46%) was significantly higher than the ash values, indicating the formulation's freshness and minimal inorganic residue.

Effect on Fasting Blood Glucose Levels

In STZ-induced diabetic rats, the formulation demonstrated a progressive reduction in fasting blood glucose (FBG) levels over four weeks. The highest dose (100 mg/kg) in Group 5 reduced FBG by approximately 60%, outperforming lower doses (e.g., Group 3 at 10 mg/kg with a 53% reduction). This indicates a dose-dependent efficacy of the formulation. The findings suggest that the synergistic action of phytochemicals, particularly saponins and tannins, might enhance glucose uptake and inhibit glucose production.

Effects on Serum Enzymes and Renal Profiles

P.H.F. administration also positively impacted liver and renal profiles:

- **Liver Enzymes**: Group 5 exhibited significant normalization of ALP (85.94 IU/L), AST (89.85 IU/L), and ALT (28.96 IU/L) levels compared to diabetic controls. These results indicate hepatoprotective activity, likely attributed to the antioxidant properties of flavonoids and phenols.
- **Renal Parameters**: Significant improvements in serum creatinine and blood urea levels were observed in Group 5, suggesting renoprotective effects. The reduction in creatinine (1.27 mg/dL) and urea (23.94 mg/dL) correlates with improved kidney function and reduced oxidative stress.

Insulin Levels and Enzyme Activities

The serum insulin levels showed a marked increase in treated groups, particularly Group 5, indicating improved pancreatic β-cell activity. The inhibition of α-glucosidase and α-amylase activities in diabetic rats further highlights the formulation's antidiabetic mechanism, reducing carbohydrate absorption and postprandial glucose spikes.

Histopathological Findings

Histopathological studies corroborated the biochemical results. Group 5 exhibited preserved hepatocyte structures with minimal inflammation compared to the severe inflammatory markers in untreated diabetic rats. The structural integrity of pancreatic cells was also better maintained in the higher dose groups, indicating protective effects against STZ-induced cytotoxicity.

CONCLUSION

The polyherbal formulation (P.H.F.) demonstrates promising phytochemical and pharmacological properties for managing diabetes and its complications. The high tannin, saponin, and flavonoid content provides a strong antioxidant and anti-inflammatory foundation, leading to significant improvements in glucose metabolism, liver enzyme normalization, and renal protection.

In comparison to lower doses, the higher dose (100 mg/kg) of P.H.F. was the most effective, reducing fasting blood glucose by 60%, restoring insulin levels, and improving liver and kidney functions. Histopathological observations further confirmed the protective effects on vital organs, particularly the pancreas and liver.

This study highlights the therapeutic potential of P.H.F. and its bioactive components, emphasizing its role as a multi-targeted approach for diabetes management. Future research could focus on isolating specific active compounds and exploring synergistic mechanisms to optimize its clinical efficacy.

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