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EVALUATION OF NOVEL POLYHERBAL EXTRACT COMBINATION ON GLUCOSE AND LIPID DYSREGULATION IN STREPTOZOTOCIN-NICOTINAMIDE-INDUCED DIABETIC WISTAR RATS

RAJKUMAR PATSKER*[1], NAVEEN GUPTA[2], VIKASH GUPTA[3], DHARMENDRA SINGH RAJPUT[2]

[1] RESEARCH SCHOLAR, PATEL COLLEGE OF PHARMACY, MADHYANCHAL PROFESSIONAL UNIVERSITY, BHOPAL, MADHYA PRADESH, INDIA.
[2] PROFESSOR, PATEL COLLEGE OF PHARMACY, MADHYANCHAL PROFESSIONAL UNIVERSITY, BHOPAL, MADHYA PRADESH, INDIA.
[3] PROFESSOR, KAILASH NARAYAN PATEL COLLEGE OF PHARMACY, BHOPAL, MADHYA PRADESH, INDIA.

ABSTRACT

The present research was planned to investigate the efficacy of a newly formulated polyherbal extract combination, derived from the combination of ethanolic extracts of stem bark of *Ficus racemose*, leaves of *Tecoma stans,* and leaves of *Bougainvillea spectabilis* and seeds of *Cyamopsis tetragonoloba*, in mitigating the hallmarks of type 2 diabetes mellitus and associated dyslipidemia in Streptozotocin-Nicotinamide-Induced Diabetic Wistar rat model. After inducing T2DM with an intraperitoneal dose of streptozotocin (60 mg/kg body weight), followed by 120 mg/kg b.w. of nicotinamide in 8-10-week-old Wistar rats. Animals were orally treated with polyherbal extract combination (developed with mixing ethanolic extracts of all four plants) 100, 200, 300, and 400 mg/kg b.w. and standard antidiabetic agent glibenclamide 5 mg/kg b.w. for 7 hours in case of an acute anti-hyperglycemic study. Consecutively, sub-acute study of 28-day was conducted using the best polyherbal extract combination (PEC) strength. The integrity of the pancreatic tissue was evaluated histopathologically at the study endpoint. After scarifying rats, different biochemical parameters including lipid profiles were studied to evaluate the complete effect of PEC treatment. The diabetic control group demonstrated persistent, severe hyperglycemia, significant disruption of the lipid balance, and significant body weight loss. Administration of PEC 100, 200, 300, and 400 mg/kg b.w., in an acute antihyperglycemic study, resulted in a substantial reduction in FBG compared to the untreated diabetic group, improving blood sugar levels. In a sub-acute study of 28 days significant reduction in FBG by PEC 300 and 400 was noted, followed by an increase in body weight compared to the diabetic control group. Furthermore, PEC therapy attenuated dyslipidemia, achieving significant reductions in total cholesterol, triglycerides, and LDL, alongside a favorable increase in HDL. PEC significantly improved HbA1c, HOMA-IR and plasma insulin level to near normal. Histological examination confirmed that PEC preserved the structure and enhanced the cellular mass of the pancreatic Islets of Langerhans in a dose-dependent manner. The results validated the significant antihyperglycemic and antihyperlipidemic actions of the novel PEC in the STZ-NA rat model, establishing it as a promising therapeutic candidate for simultaneously managing blood sugar and lipid abnormalities associated with T2DM.

Keywords: Antihyperglycemic; Antihyperlipidemic; Polyherbal Extract Combination; STZ-NA; Wistar Rats; Diabetes Mellitus.

INTRODUCTION

Diabetes Mellitus (DM) represents a vast, growing health crisis globally, with Type 2 Diabetes (T2DM) accounting for the majority of cases, recent studies indicated that 89.9 million Indians are suffering from diabetes. Beyond mere hyperglycemia, T2DM is frequently accompanied by dyslipidemia, a cluster of abnormal blood lipid concentrations that significantly escalates the risk of severe cardiovascular disease, the leading cause of mortality in diabetic patients [1,2]. Current single-molecule drugs often target one pathway, necessitating polypharmacy to manage both high glucose and dyslipidemia, leading to complexity and potential side effects. Traditional medicine, particularly the practice of polyherbalism, offers a rationale for multi-target therapy. Polyherbal extract

combination (PEC) utilizes the principle of phytochemical synergy, where diverse bioactive compounds from multiple plants interact constructively, potentially yielding greater therapeutic benefits and reduced toxicity compared to individual components [3]. This investigation aimed to provide scientific validation for a novel PEC combining four plants traditionally used for metabolic disorders: stem bark of *Ficus racemose* (SBFR), leaves of *Tecoma stans* (LTS), leaves of *Bougainvillea spectabilis* (LBS) and seeds of *Cyamopsis tetragonoloba* (SCT). *Ficus racemosa* (potentially improves blood sugar, cholesterol, and insulin levels) [4], *Cyamopsis tetragonoloba* (valued for managing diabetes, hyperlipidemia /high cholesterol, and obesity) [5,6], *Tecoma stans* (renowned for its blood glucose regulation, high cholesterol/triglyceride management) [7], *Bougainvillea spectabilis* (known for managing diabetes and hyperlipidemia) [8], and in diabetic animal model. The streptozotocin – nicotinamide (STZ-NA) induced diabetes Wistar rat model was chosen as it reliably mimics the moderate beta-cell destruction and insulin resistance profile characteristic of human type 2 diabetes mellitus (T2DM) [9]. The objective was to scientifically validate the antihyperglycemic and antihyperlipidemic potential of a novel PEC composed of ethanolic extracts from SBFR, LTS, LBS, and SCT.

MATERIALS AND METHODS

Collection and Authentication of plants: Plant materials selected for the research study were identified and authenticated by a botanist of Vindhya Herbal Testing and Research Laboratory, Van Parisar, Barkheda Pathani, Bhopal, M.P., India. Four different herbarium specimens of each plant i.e., stem bark of *Ficus racemose,* leaves of *Tecoma stans*, leaves of *Bougainvillea spectabilis* and seeds of *Cyamopsis tetragonoloba* were prepared and deposited, voucher specimen number MFP/BP/PA/2024/1471/01-04, was received for future reference.

Extractions and Polyherbal Extract Combination Development: Plant materials collected were dried and pulverized. 80% ethanolic solvent was used for extraction by continuous hot extraction using Soxhlet apparatus. The extracts were filtered, concentrated using a rotary evaporator, and lyophilized to yield the final powder extracts [10]. The PEC was prepared by mixing the individual plants extracts in an optimized ratio of 1:1:1:1 and suspended in 0.5% Carboxymethylcellulose for oral administration [11].

Pharmacological Screening

Animals: Antidiabetic study was performed using Wistar rats of both sex weighing 180-250 g were housed under standard laboratory conditions (12-h light/dark cycle) with free access to water. The study protocol was approved by the Institutional Animal Ethics Committee ref. no: RKDF/2024/AD-045 dated 23/07/2024.

Induction of Diabetes: Experimental rats were fasted overnight. T2DM was induced by using an intraperitoneal (i.p.) injection of STZ 60 mg/kg b.w. dissolved in 0.1 M cold citrate buffer of pH 4.5, followed by an i.p. administration of NA 120 mg/kg b.w. after 15 minutes. Rats with fasting blood glucose (FBG) 300 mg/dL or above, 72 hours post-induction were considered diabetic and included in the study [11].

Anti-hyperglycemic Studies

For detailed research two acute and sub-acute anti-hyperglycemic studies, were performed simultaneously.

Acute Anti-hyperglycemic Studies: it was of 7 hours, here blood samples were evaluated at 0, 1, 3, 5, and 7 hours after the treatment PEC 100, 200, 300, and 400 mg/kg b.w. and GLB. In acute anti-hyperglycemic study, animals were randomly divided into seven groups (n=6). Normal control and diabetic control groups, received normal saline, standard group received glibenclamide 0.5 mg/kg b.w. whereas PEC 100, 200, 300 and 400 groups were treated with 100, 200, 300 and 400 mg/kg b.w. Before administering GLB and PEC of different strengths were suspended using 1% CMC and were administered orally using an intragastric tube only once. After treatment, blood samples were analyzed for blood glucose level at 0, 1, 3, 5, and 7 hours [12].

Group I	Normal control	Received normal saline
Group II	Diabetic control	Diabetic rats received normal saline
Group III	Standard treated	Diabetic rats treated with glibenclamide 0.5 mg/kg b.w.
Group IV	PEC 100 treated	Diabetic rats treated with PEC 100 mg/kg b.w.
Group V	PEC 200 treated	Diabetic rats treated with PEC 200 mg/kg b.w.
Group VI	PEC 300 treated	Diabetic rats treated with PEC 300 mg/kg b.w.
Group VII	PEC 400 treated	Diabetic rats treated with PEC 400 mg/kg b.w.

Sub-acute Anti-hyperglycemic studies: In 28 consecutive days sub-acute study, the standard drug GLB and the best two strength test solutions out of PEC 100, 200, 300, and 400 were administered once daily. The effect on fasting blood glucose level (FBGL) was studied at 0, 7th, 14th, 21st, and 28th day. In sub-acute anti-hyperglycemic study, animals were randomly divided into five groups. Normal and diabetic control group, received normal saline, GLB (0.5 mg/kg b.w.) and two best PEC 300 and 400 group received 300 and 400 mg/kg b.w., based on the acute hyperglycemic study, were further studied in detail due to their significant result. GLB and PEC were administered orally using an intragastric tube, once daily for 28 days, and FBGL levels were measured on every seventh day, i.e., on 0, 7th, 14th, 21st, and 28th day by using a glucometer [12].

Group I	Normal control	Animals received normal saline.
Group II	Diabetic control	Diabetic rats received normal saline
Group III	Standard treated	Diabetic rats treated with glibenclamide (0.5 mg/kg b.w.)
Group IV	PEC 300 treated	Diabetic rats treated with PEC 300 (300 mg/kg b.w.)
Group V	PEC 400 treated	Diabetic rats treated with PEC 400 (400 mg/kg b.w.)

Effect of PEC on body weight and food and water intake: During the study, the mean change in body weight, changes in food and water intake were also noted.

Biochemical estimations: After the detailed research study of 28 days, rats were sacrificed by cervical dislocation under mild anesthesia. Blood was collected for serum analysis. Following biochemical parameters were analyzed using standard commercial kits: plasma insulin, HOMA-IR, HbA1c, total cholesterol, triglycerides, HDL, LDL, and VLDL cholesterol.

Histopathological study: It was performed were pancreatic tissue was fixed in 10% buffered formalin, embedded in paraffin, sectioning was done at a thickness of 5-7 µm, and was stained using Hematoxylin and Eosin (H&E) for microscopic examination and finally histological changes were observed and noted [12-14].

All the results were expressed as mean ± SD for six rats in each experimental group. The data obtained were evaluated using a one-way analysis of variance (ANOVA) followed by Dunnett's Test for multiple comparisons *p*-values < 0.05 were considered as statistically significant, $p<0.01$ as very significant and $p<0.001$ as extremely significant.

RESULTS AND DISCUSSION

Extraction and percentage yield of extracts

The percentage yield of aqueous extract of stem bark of *Ficus racemose*, leaves of *Tecoma stans*, leaves of *Bougainvillea spectabilis*, and seeds of *Cyamopsis tetragonoloba* was found to be 11.50%, 19.25%, 11.18% and 26.40%, whereas ethanolic extract yield was found to be 9.60%, 11.22%, 10.90% and 13.50% respectively.

Pharmacological Screening

Acute antihyperglycemic study: In study, the diabetic rats treated with PEC showed a significant ($p<0.05$) reduction in FBG. It has been noted that after 7 hours of a single dose of PEC 100, 200, 300 and 400 blood glucose was reduced by 33.17 %, 41. 49 % 48. 97 % and 49.25 % respectively. This was comparatively better than the standard drug, which showed 41.01 % reduction. By result it was summarized that PEC 400 followed by PEC 300 showed a significant reduction in blood glucose level in diabetic rats, which was highly significant ($p<0.001$)

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Table 1: Acute anti-hyperglycemic study of PEC in diabetic rats

Groups name	Blood glucose level (mg/dL) at different time intervals (in hours)				
	0	1	3	5	7
Group I Normal control	76.53±2.55	75.66±1.26	77.00±1.50	75.33±3.06	76.33±4.20
Group II Diabetic control	349.00±5.00	331.66±2.70	329.00±3.00	330.66±2.45	325.00±2.00
Group III Standard treated	344.66±4.30	293.50±2.20	266.33±4.70	235.00±3.50**	203.33±4.23**
Group IV PEC 100 treated	341.66±3.50	322.05±4.90	280.60±5.20	263.33±3.15*	228.33±3.25*
Group V PEC 200 treated	342.00±5.10	323.33±4.00	262.50±5.40	232.50±4.00**	200.10±4.25**
Group VI PEC 300 treated	343.15±3.50	311.67±2.79	254.30±3.55	218.33±3.10**	175.10±3.05***
Group VII PEC 400 treated	335.66±2.10	319.60±4.50	261.50±5.16	221.33±4.00**	170.33±3.00***

Values are expressed as mean ± SD (n=6); * ($p< 0.05$) significant; ** ($p< 0.01$) very significant; *** ($p< 0.001$) highly significant compared with normal control

TPM Vol. 32, No. S1, 2025
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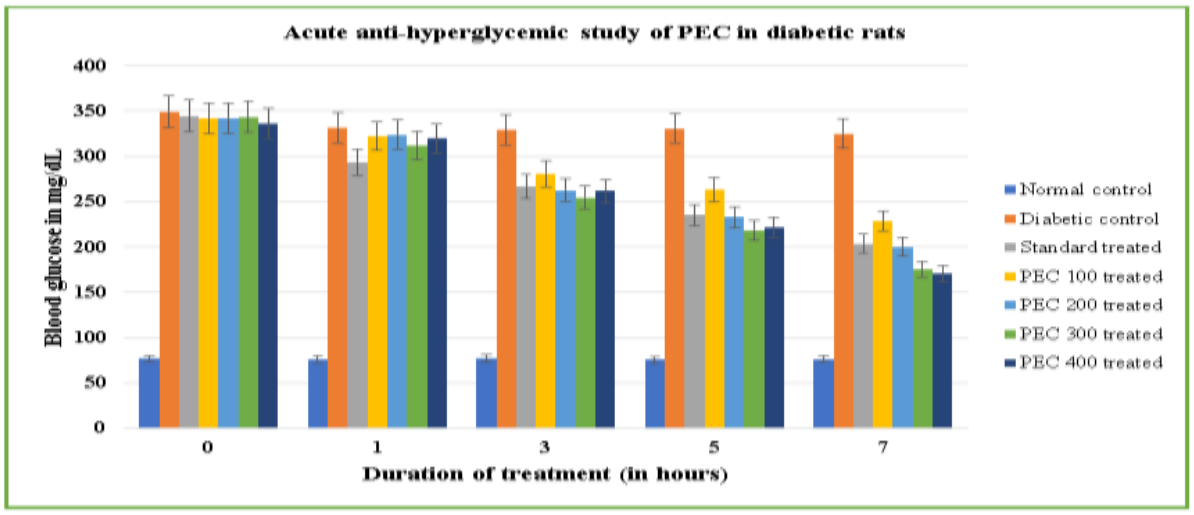

Figure 1: Acute anti-hyperglycemic study of PEC in diabetic rats

Sub-acute anti-hyperglycemic study: 28 days activity was performed using highly effective strength PEC 300 and PEC 400. As a result, it has been revealed that a single daily dose of PEC 300 reduced blood glucose by 75.69 %, PEC 400 showed a reduction by 74.73%. By study, it can be summarized that PEC 300 showed a comparatively significant reduction in blood glucose level in diabetic rats than PEC 400, followed by standard treatment of GLB that showed reduction in FBG by 73.39 %.

Table 2: Sub-acute anti-hyperglycemic study of PEC in diabetic rats

Groups name	Blood glucose level (mg/dL) at different time intervals (in days)				
	0th Day	7th Day	14th Day	21th Day	28th Day
Group I Normal control	76.33±2.00	78.15±1.90	76.80±2.00	78.35±1.50	77.00±1.20
Group II Diabetic control	338.80±3.50	330.50±3.40	334.10±2.80	331.60±2.40	331.80±2.15
Group III Standard treated	335.80±3.90	241.50±2.20	191.30±3.45*	149.33±4.20**	89.33±1.80***
Group IV PEC 300 treated	343.33±4.00	261.66±3.80	204.66±3.56*	145.50±4.55**	83.44±1.90***
Group V PEC 400 treated	341.66±3.66	258.23±3.88	209.69±2.46*	158.50±3.20**	86.33±1.99***
Values are expressed as mean ± SD (n=6); * (p< 0.05) significant; ** (p< 0.01) very significant; *** (p< 0.001) highly significant compared with normal control					

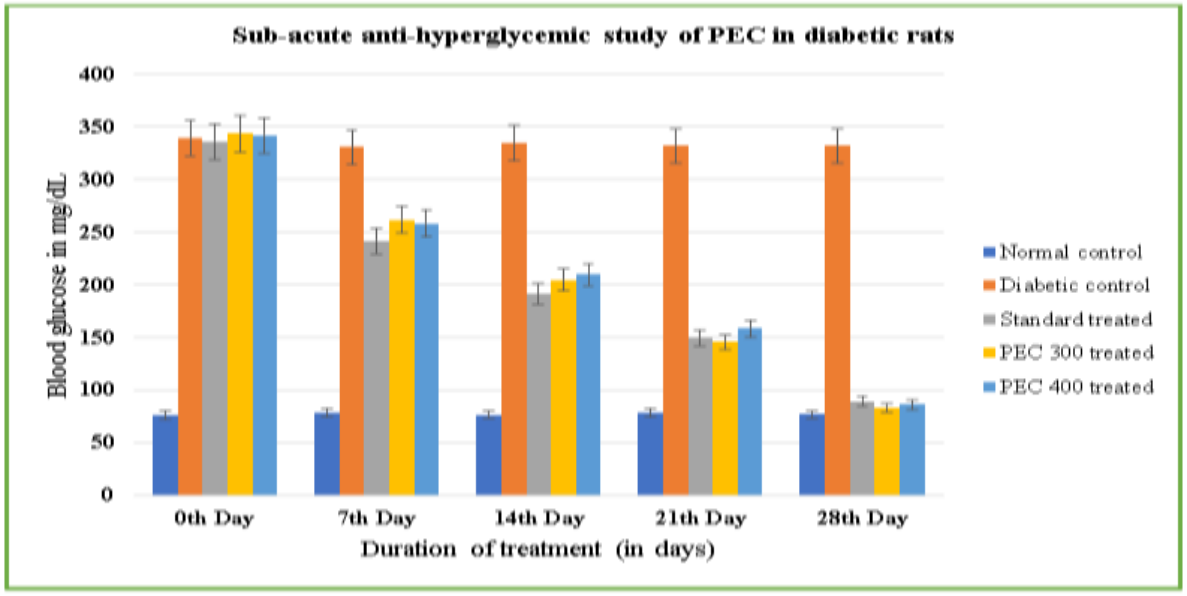

Figure 2: Sub-acute anti-hyperglycemic study of PEC combinations in diabetic rats

TPM Vol. 32, No. S1, 2025
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Effect of PEC on body weight, food, and water intake

After treatment with PEC 300, the mean reduced weight significantly improved by approximately18.19 %, PEC 400 improved weight by 18.65% and GLB improved by approximately 17.79%. Thus, by study, it was revealed that reversing the effect of GLB on body weight was as significant as PEC 300 and 400, leading the body weight to near-normal after continuous treatment of 28 days. The effect of PEC on food and water intake in STZ-induced diabetic rats was studied, and it was depicted that diabetes caused an increase in food and water intake by 50.77 and 77.59 % respectively. After treatment with PEC 300, a significant reduction in the mean food and water intake was noted to be approximately 35.82 and 43.59 % respectively. PEC 400 showed reduction by 50.43% and 41.96%, whereas GLB reduced food and water intake by approx. 45.70 %. Thus, it can be summarized that PEC 300 and 400 significantly normalized the food and water intake to near normal, with the reduction of blood glucose level and activity was comparable to the standard drug's reversing effect.

Table 3: Effect of PEC on body weight of diabetic rats

Groups name	Mean body weight changes (STZ induces hyperglycemia)				
	0th Day	7th Day	14th Day	21th Day	28th Day
Group I Normal control	217.00±3.50	212.00±4.20	223.00±4.50	220.33±4.80	224.66±5.96
Group II Diabetic control	170.69±2.42	168.33±3.10	172.33±2.33	166.84±3.72	165.40±2.48
Group III Standard treated	172.33±1.24	175.23±2.72	187.60±3.01	202.60±2.48*	203.00±4.24***
Group IV PEC 300 treated	171.00±2.30	176.42±2.78	190.33±2.66	196.12±2.54**	202.12±2.48***
Group V PEC 400 treated	174.66±3.24	182.89±1.78	190.60±3.36	197.12±4.78**	207.24±3.48***
Values are expressed as mean ± SD (n=6); * (p< 0.05) significant; ** (p< 0.01) very significant; *** (p< 0.001) highly significant compared with normal control					

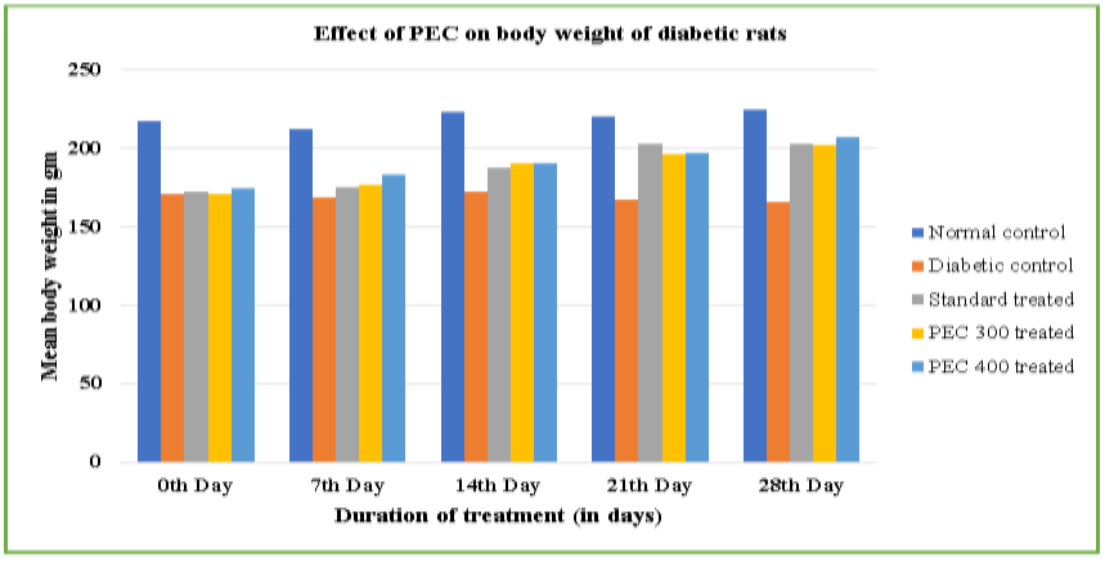

Figure 3. Effect of PEC on body weight of diabetic rats

Table 4: Effect of PEC on food and water intake of diabetic rats

Groups name	Food intake (g/24 hours)		Water intake (ml/24 hours)	
	Initial	Final	Initial	Final
Group I Normal control	13.00±0.90	13.50±0.50	18.30±0.80	19.67±0.50
Group II Diabetic control	19.60±1.15	22.50±0.90	32.50±2.15	35.83±2.50
Group III Standard treated	23.60±2.67	12.80±1.35***	33.50±2.10	18.20±1.60***
Group IV PEC 300 treated	21.50±1.80	13.80±1.12***	36.50±2.50	20.50±1.95**
Group V	23.20±1.15	11.50±1.10***	34.20±2.07	19.85±1.50***

PEC 400 treated				

Values are expressed as mean ± SD (n=6); * (p< 0.05) significant; ** (p< 0.01) very significant; *** (p< 0.001) highly significant compared with normal control

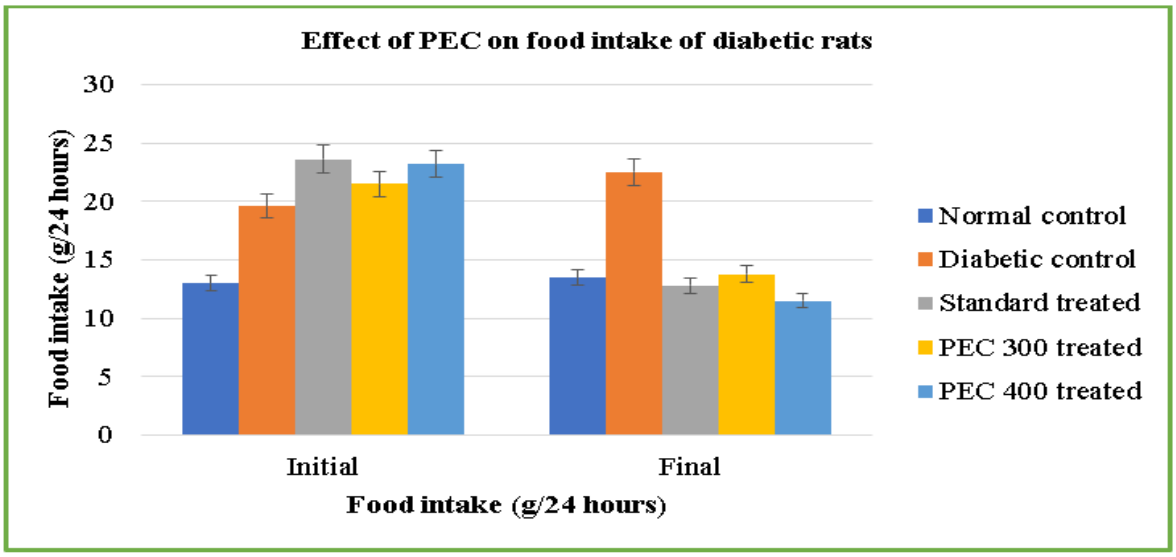

Figure 4 (a): Effect of PEC on food intake before and after treatment

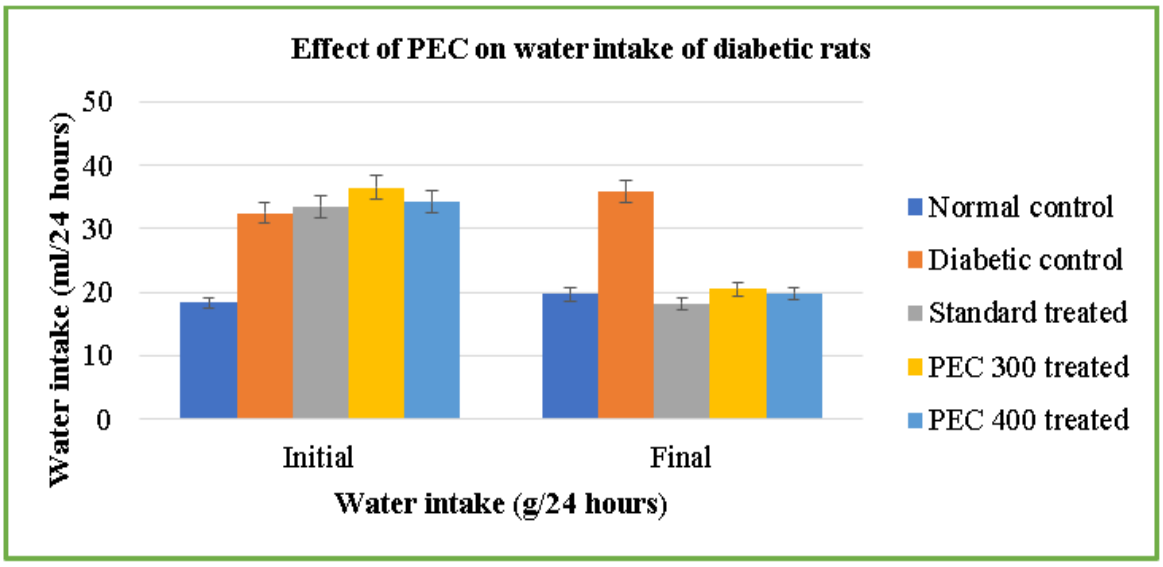

Figure 4 (b): Effect of PEC on water intake before and after treatment

Biochemical estimations:

STZ-induced diabetes decreased approximately 50% plasma insulin level. Administration of PEC 300, 400, and GLB significantly improved the level by approximately 72%, 79% and 85% and brought it to near normal. HOMA-IR levels due to diabetes were elevated by 90.17%, which, upon treatment with PEC for 28 days, significantly decreased to near normal. HbA1c level increased by 132.33% which was significantly reduced by 48.69% and 53.92% by PEC 300 and PEC 400, better than GLB, i.e., 41.74% thus was comparatively significant and better than the standard drug's reversing effect.

STZ-induced diabetes caused a significant rise by 43.17 % in the levels of TC, 116.42 % TG, 57.35 % LDL and 116.42 % VLDL, whereas the level of HDL significantly decreased by 16.55 % as compared to the normal control group. Treatment with PEC 300 and 400 significantly (p<0.001) lowered the levels of TC by 25.62 % and 28.08 %, TGL by 32.93 % and 37.20 %, LDL by 40.94 % and 38.04 %, VLDL by 32.95 % and 37.20 % respectively. Whereas level of HDL showed improvement by 36.32 % and 17.36 %. Treatment with GLB showed reduction of TC by 20.92 %, TGL by 28.70 %, VLDL by 28.69 % and LDL by 30.85 % whereas HDL improved by 22.80 %. Diabetes caused a significant rise in the TC/HDL-c ratio to 5.66, non-HDL-c to 161.05, whereas LDL/HDL-c ratio decreased to 0.58, and HDL/LDL-c ratio 0.28 in diabetic rats compared to normal rats. Treatment with PEC 300 and 400 significantly (p<0.001) significantly reduced the levels of TC/HDL-c ratio by 45.58% and 38.87%. Non-HDL-c by 38.90% and 37.83%, whereas HDL/LDL-c ratio improved by 135.72% and 92.86% and in

TPM Vol. 32, No. S1, 2025
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LDL/HDL-c ratio no changes were noted. GLB reduced TC/HDL-c ratio by 35.69%, Non-HDL-c by 30.31%, whereas improved HDL/LDL-c ratio by 82.14% and no significant changes were noted in LDL/HDL-c ratio. Thus, it was revealed from the result that after 28 days of treatment with two different PEC 300 & 400 comparatively showed better activity in managing dyslipidemia ($p<0.001$) than standard GLB.

Table 5: Effect of PEC on plasma insulin, HOMA-IR and glycosylated hemoglobin level of diabetic rats

Groups	Biochemical analysis		
	Plasma insulin (µU/mL)	HOMA-IR	HbA1c (%)
Group I Normal control	13.75±2.05	2.85±0.32	4.95±0.32
Group II Diabetic control	6.82±1.10	5.42±0.36	11.50±0.20
Group III Standard treated	12.60±0.50***	2.94±0.15***	6.70±0.18*
Group IV PEC 300 treated	11.75±0.75***	3.12±0.36***	5.90±0.12*
Group V PEC 400 treated	12.24±1.40***	3.05±0.20***	5.30±0.36***
Values are expressed as mean ± SD (n=6); * ($p< 0.05$) significant; ** ($p< 0.01$) very significant; *** ($p< 0.001$) highly significant compared with normal control			

Table 6. Effect of PEC on lipid profile of diabetic rats

Groups	**Lipid profile in mg/dL**				
	TC	**TGL**	**HDL**	**VLDL**	**LDL**
Group I Normal control	136.62±2.90	95.00±3.32	41.40±1.25	19.00±0.66	76.22±0.99
Group II Diabetic control	195.60±4.80	205.60±5.30	34.55±1.50	41.12±1.06	119.93±2.24
Group III Standard treated	154.68±3.46	146.58±4.65	42.43±1.32	29.32±0.93*	82.93±1.21***
Group IV PEC 300 treated	145.50±4.64***	137.88±4.30***	47.10±2.85***	27.57±0.86**	70.83±0.93***
Group V PEC 400 treated	140.67±5.32***	129.10±5.5***	40.55±2.44***	25.82±1.10***	74.30±1.78***
Values are expressed as mean ± SD (n=6); * ($p< 0.05$) significant; ** ($p< 0.01$) very significant; *** ($p< 0.001$) highly significant compared with normal control					

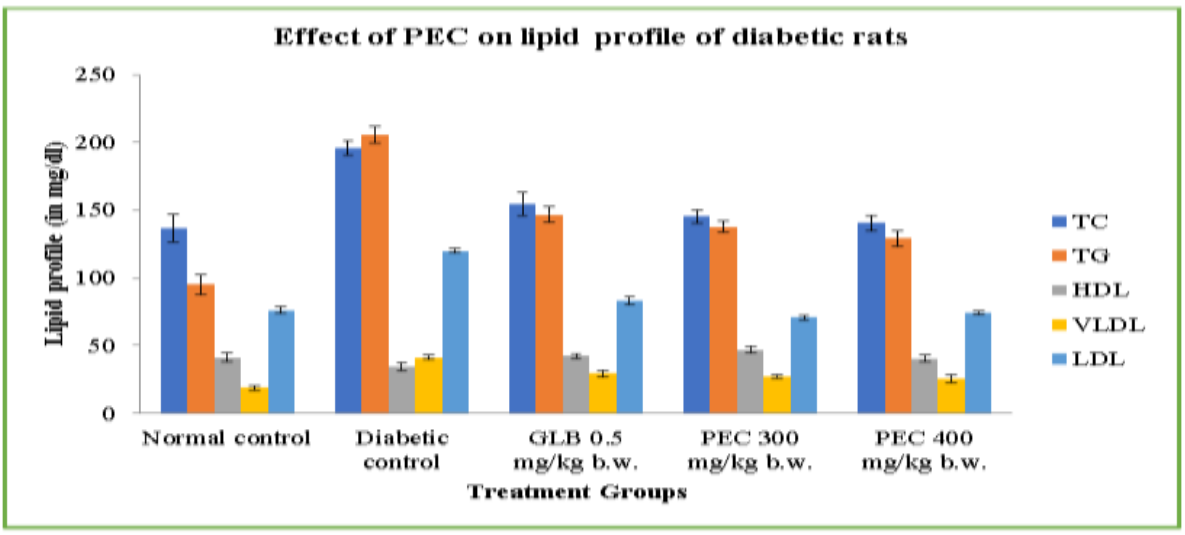

Figure 5. Effect of PEC on lipid profile of diabetic rats

TPM Vol. 32, No. S1, 2025
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Table 7. Effect of PEC on lipid profile (ratio) of diabetic rats

Groups	TC/HDL-c Ratio	LDL/HDL-c Ratio	HDL/LDL-c Ratio	Non-HDL-c
Group I Normal control	3.3±0.03	0.80±0.02	0.54±0.03	95.22±1.65
Group II Diabetic control	5.66±0.14	0.58±0.08	0.28±0.08	161.05±3.30
Group III Standard treated	3.64±0.55***	0.56±0.07***	0.51±0.06**	112.25±2.14***
Group IV PEC 300 treated	3.08±0.91*	0.52±0.03**	0.66±0.04***	98.40±1.79***
Group V PEC 400 treated	3.46±0.90***	0.57±0.05***	0.54±0.05***	100.12±2.88***
Values are expressed as mean ± SD (n=6); * (p< 0.05) significant; ** (p< 0.01) very significant; *** (p< 0.001) highly significant compared with normal control				

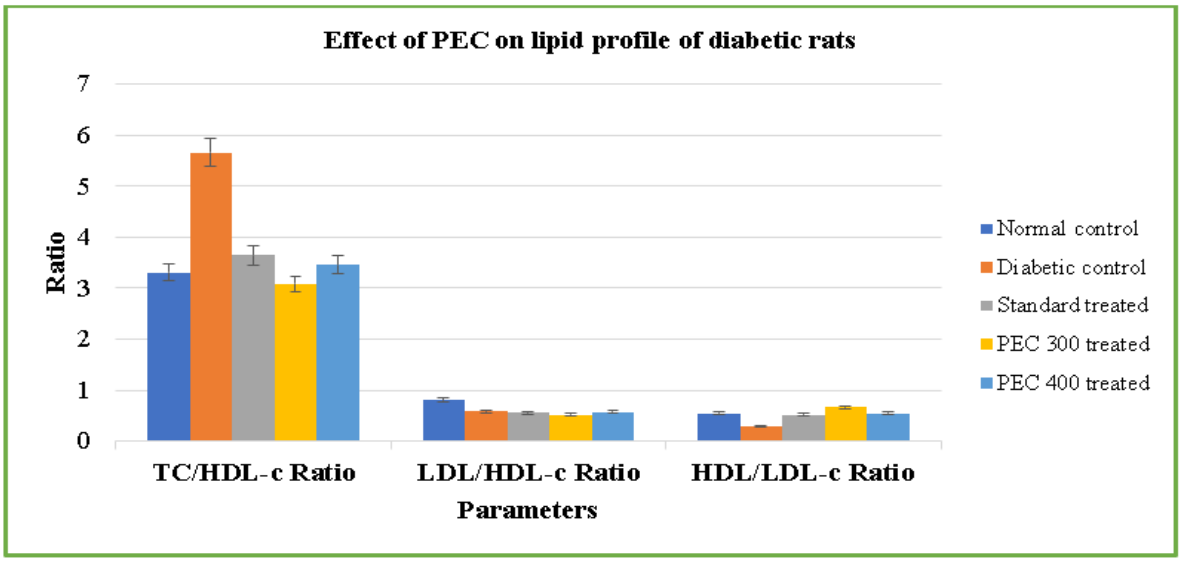
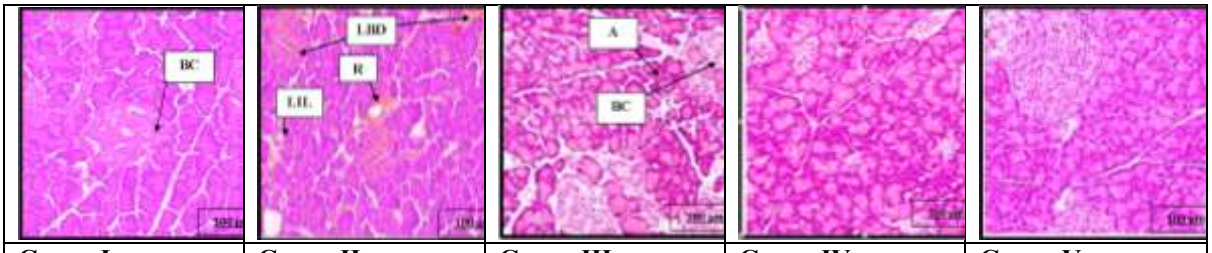


Figure 7. Effect of PEC on lipid profile (TC/HDL-c Ratio, LDL/HDL-c Ratio, HDL/LDL-c Ratio, Non-HDL-c) of diabetic rats

Histopathology Study: In histopathology of the Pancreas study the normal control group showed well-defined pancreatic parenchyma and intact Islets of Langerhans with densely packed beta-cells. The diabetic control group exhibited significant pancreatic and acini cells damage, including beta-cell degeneration, reduced islet size, fibrotic changes and vacuolation. Treatment with the PEC 300 and 400 demonstrated a clear protective and regenerative effect. The PEC 400 group showed noticeable restoration of the Islets of Langerhans architecture, with moderate regeneration of the beta-cells and reduced signs of cellular damage, acini cells improvement, comparable to the standard drug-treated group.



Group I Normal control	Group II Diabetic control	Group III Standard treated	Group IV PEC 300 treated	Group V PEC 400 treated

Normal: All normal beta cells structure (BC). **Diabetic:** Loss of beta-cell and degranulations (LBD), Swelling of the intracellular organelles necrosis, atrophy, fibrotic changes, and lesions in the islet of langerhans (LIL), Destroyed pancreatic lobules, acini cells (A), reduced pancreatic cell number and size (R).

Thus, the results demonstrated that the novel polyherbal formulation PEC 300 and 400 effectively ameliorates both hyperglycemia and dyslipidemia in the STZ-NA induced diabetic rat model. This multi-target effect is consistent with the established mechanism of action of its individual herbals present in the PEC.

According to antihyperglycemic mechanism, the observed reduction in FBG and HbA1c can be attributed due to the presence of glycosides, bioflavavonoids, phytosterols, kaempherol, β-sitosterol, quercetin, triterpenes, phenolic compound. PEC might have worked by repairing and regenerating beta cells, which bring blood glucose homeostasis by increasing serum insulin levels, this in turn also improved the reduced body weight, food and water intake [15]. Treatment with PEC, HOMA insulin resistance decreases, leading to improved glucose utilization by the cell and hence blood glucose and HbA1c decreased to near normal values. Plasma insulin level improvement also helped to control the blood glucose level and utilization. The histological evidence of islet protection/regeneration suggests that the PEC acts partly by preserving the structural integrity of the insulin-producing beta-cells [12].

As per antihyperlipidemic mechanism, dyslipidemia in DM results from insulin resistance and hyperglycemia, that leads to increase in free fatty acids, hepatic TG synthesis, LDL formation, VLDL production by liver and a decrease VLDL clearance and HDL levels. The significant lowering of TC, TG, and LDL-C, along with the elevation of HDL-C by PEC, suggests it favorably modifies hepatic lipid metabolism [15]. Phytochemicals like quercetin, phytosterols, flavonoids and triterpenoids present in the formulation may reduce TC and TGs, increase HDL-c, reduce LDL, improve insulin sensitivity, inhibit the lipid accumulation, HMG-CoA reductase enzyme (a key step in cholesterol synthesis) or enhance the fecal excretion of cholesterol. They might alter cholesterol uptake and reduce oxidation of LDL uptake [16].

The synergistic effect of combining herbs is a critical finding, as the multi-pronged approach better manages the complex pathology of T2DM compared to single-drug or single-herb therapies. Both PEC doses demonstrated significantly overall better efficacy comparable to glibenclamide, a known sulfonylurea, without the risk of severe hypoglycemia associated with the standard drug. Furthermore, the improvements in body weight, food and water intake and pancreatic morphology strengthen the potential long-term therapeutic value of the formulation. Further research is warranted to isolate the specific bioactive constituents and elucidate the precise molecular pathways (e.g., PPAR gamma activation, AMPK signaling) responsible for the PEC's potent anti-diabetic and anti-dyslipidemic activities [12,15,17].

CONCLUSION

The novel polyherbal formulation PEC demonstrated significant and dose-dependent antihyperglycemic and antihyperlipidemic potential in STZ-NA induced diabetic Wistar rats. The formulations effectively lowered blood glucose and corrected the adverse lipid profile, while also showing a protective effect on pancreatic tissue. These findings strongly support the use of this PEC as a promising therapeutic agent for the integrated management of T2DM and dyslipidemia.

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