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Invivo Evaluation of a Polyherbal Formulation in Streptozotocin-Induced Diabetic Rat

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KEYWORDS

Polyherbal extract, Antidiabetic, OGTT, Metformin, Blood glucose level

ABSTRACT:

Objective: To evaluate the *invivo* antidiabetic efficacy of a polyherbal formulation in streptozotocin-induced diabetic rat. **Methods:** Polyherbal formulation (PHF1) was tested for oral glucose tolerance test (OGTT) (2 h) in non-diabetic rats and antidiabetic activity (28 days) in non-diabetic and STZ-induced diabetic rats. Further, liver function test and kidney function test were also carried out. **Results:** The study demonstrate that Polyherbal formulation (PHF1) administered at a dosage of 400 mg/kg followed by 200 mg/kg exhibits significant antidiabetic activity. PHF1 significantly decreases the total cholesterol, triglyceride, LDL, VLDL level along with kidney function parameters. The data suggests that the PHF1 consistently improved hepatic and renal function in the treatment groups. The administration of PHF1 at a dosage of 400 mg/kg has demonstrated significant improvements in diabetic complications, indicating its efficacy as a therapeutic agent.

Conclusion: These findings suggest that PHF1 has the potential to serve as a source for the development of novel antidiabetic drugs.

1. INTRODUCTION

Type 2 Diabetes Mellitus presents a significant health challenge in numerous countries, with its prevalence and associated macrovascular and microvascular complications gathering substantial concern. In India, the incidence of diabetes is rapidly increasing day by day. It is projected that 67% of deaths in India in the year 2020 will be attributable to diabetes. Despite advancements in glycemic control through various pharmacological interventions, diabetes remains a primary health issue due to its considerable impact on mortality and morbidity rates. Severe hyperglycemia, hyperlipidemia, and related complications adversely affect the quality of life for individuals affected by the condition. According to the World Health Organization (WHO), diabetes mellitus is projected to become the single largest non-communicable disease globally by the year 2025, with India expected to have the largest diabetic population. Current pharmacotherapies often

fail to completely reverse hyperglycemia, exhibit limited tolerability, and may induce undesirable side effects. Consequently, there is a growing demand for alternative therapies, particularly those derived from natural plant sources known for their minimal side effects. The popularity of natural plant-based therapies has driven by the need for effective and safe treatment options [1]. In the present investigation, the focus lies on examining dried and powdered mixtures of

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combined medicinal herbal plants i.e, *Lycopersicon pimpinellifollium L (Solanaceae)* [2], *Moringa oleifera (Moringaceae)* [3], *Abelmoschus esculentus L (Malvaceae)* [4], *Artocarpus heterophyllus Lam (Moraceae)* [5] *and Brassica oleracea var. italica (Brassicaceae)* [6] for development of antidiabetic formulations. All the plants used for the study have investigated for their antioxidant and antidiabetic activity. This approach aims to address the need for effective and reliable natural therapies while simplifying the complexity associated with polyherbal formulations.

2. MATERIALS AND METHODS

Chemicals and reagents: Streptozotocin (STZ) was purchased from Hi-Media Laboratories, Mumbai, while Metformin was obtained from Sigma-Aldrich. Diagnostic kits used in the study were purchased from ERBA Diagnostic Mannheim (TRANSASIA Bio-medicals Ltd., Solan). All chemicals and reagents utilized in this research were of analytical grade.

Plant material collection & authentication: Herbs used for the research work were Collected from different region of Assam and further authenticated by Dr. Minaram Nath, Professor, Department of Botany, Royal School of life Sciences, The Assam Royal Global University, Guwahati, Assam, India.

Fig 1: Wild Tomato

Fig 2: Lady finger

Fig 3: Broccoli

Fig 4: Drumstick

Fig 5: Jackfruit

Preparation of hydro-alcoholic (HA) extracts: The powder consisting of 100 g each of the dried fruits of *Lycopersicon pimpinellifollium L*, *Moringa Oleifera*, *Abelmoschus esculentus L*, Brassica oleracea var. italica, and the peel of *Artocarpus heterophyllus Lam* was subjected to extraction using a mixture of methanol and water (6:4 ratio) to obtain a hydro-alcoholic extract. The extraction process involved stirring the powder with the solvent mixture using a magnetic stirrer for 15 hours. Subsequently, the mixture underwent centrifugation at 2850 x g, and the supernatant was carefully decanted. This process was repeated with the precipitated pellet to ensure thorough extraction. The collected supernatants were concentrated using a rotary evaporator at room temperature and then freeze-dried in a lyophilizer. The resulting dried extract was stored at -20°C until further use [7].

Preparation of polyherbal extract: The hydroalcoholic extracts utilized in this formulation were concentrated to dryness on a water bath operating below 60°C. Polyherbal extract was prepared by mixing the extract of *Abelmoschus esculentus L (*Lady finger), *Artocarpus heterophyllus Lam (Jackfruit), Moringa oleifera* (Drumstick) , *Brassica oleracea var. italic (Broccoli)* and *Lycopersicon pimpinellifollium* L (Wild tomato) in the ratio of 1:1:1:3:1 respectively [8].

Formulation of polyherbal tablets: The polyherbal tablets described in this study were formulated using the direct compression method with a Cadmach CMS-15 No. H/513/11-12 punching machine. The tablet composition, as outlined in Table 1, includes Polyvinyl pyrrolidone (PVP) as the binder, Avicel-101 as the filler, magnesium stearate as the lubricant, and benzoic acid as the antimicrobial preservative.The concentrations of each extract component were determined using D-Optimal mixture design with Design-Expert software (version 8.0).

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Animal selection for the study: Albino rats, wistar strain (150–200 g) and of either sex were obtained from the Girijananda Chowdhury University animal house, Guwahati, Assam (India). The animals were kept in controlled environmental conditions, with a temperature range of 25 ± 2°C, humidity maintained at 65 ± 10%, and a 12-hour light-dark cycle. The animals were provided standard food pellets and drinking water throughout the duration of the study. The study was approved by the Institute Animal Ethics Committee (IAEC) of the Girijananda Chowdhury University (GCU/IAEC/PhD/PRO/1/2023) and all the animal experiments were conducted in accordance with the guidelines set by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), under the Ministry of Environment and Forest, Government of India.

Acute oral toxicity Study: Healthy Wistar rats of either sex were utilized in the experiment, with 3 animals per dose group. Following an overnight fasting period, the rats received oral administration of plant extracts and a polyherbal formulation in increasing dose levels: 5, 50, 300, and 2000 mg/kg body weight, respectively. Continuous observation over a 24-hour period, the animals were observed for their behavioral (alertness, restlessness, irritability, and fearfulness), neurological (spontaneous activity, reactivity, touch response, pain response, and gait), and autonomic (defecation and urination) profiles. Following the initial 24-hour observation period, the animals were monitored continuously for a duration of 14 days to document any occurrences of mortality [9].

***In vivo* antidiabetic activity : Experimental induction of diabetes**

For the study purpose, diabetes was induced in the rats by intraperitoneal injection of freshly prepared streptozotocin (STZ) at a dose of 50 mg/kg body weight dissolved in 0.1 M cold sodium citrate buffer solution of pH 4.5. Diabetes was confirmed in the STZ treated rats by measuring fasting blood glucose levels after 48 h of induction. In order to avoid fatal hypoglycemia following administration of STZ, the animals were permitted to drink 5% (w/v) glucose solution for the next 24 h. The animals with serum glucose level more than 200 mg/dl were measured as diabetic and considered for further study.

The rats were randomly divided into five groups with six in each (n = 6) as mentionedbelow.

Group I–Normal control

(0.9% w/v NaCl solution)

Group II–Diabetic control

(Streptozotocin 50mg/kg b.w. ip.)

Group III– Standard

(Orally with Metformin 100 mg/kg b.w)

Group IV–Test drug

(Orally with PHF 1 200 mg/kg b.w)

Group V–Test drug

(Orally with PHF 1 400 mg/kg b.w)

The polyherbal formulation (PHF1) was suspended in a vehicle consisting of 0.5% w/v carboxymethyl cellulose (CMC) in distilled water. It was then orally administered using an oro-gastric tube once daily for a duration of 28 days. The body weight and food intake capacity of the animals were assessed at the onset of the study and at weekly intervals throughout the 28-day period [8]. Group I animals received intraperitoneal injection of 0.9% w/v NaCl solution (1 ml/kg b.w. i.p.) whereas group II animals received streptozotocin (50mg/kg b.w. ip.), group III received metformin (100 mg/kg) [9] , group IV received PHF1 200 mg/kg and group V received PHF1 400 mg/kg body weight for 28 consecutive days. Blood samples were

collected via retro-orbital venous plexus puncture method on days 0, 7, 14, and 28 following the administration of the formulation. Blood glucose levels were assessed using the glucose oxidase method with a glucometer (Accucheck active).

Oral Glucose Tolerance test: Oral glucose tolerance test was performed in overnight fasted (18 h) normal rats. Normal rats were divided into four groups, each consisting of six rats. Group I was normal control (0.9%

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w/v NaCl solution). Group II animals are standard receiving metformin 100 mg/kg body weight. Groups III and IV animals were treated orally with a single dose of PHF1 at a dose of 200 mg/kg and 400 mg/kg p. o. respectively. Doses were fixed thorough toxicological assessments conducted in accordance with OECD guidelines (407, 423). Administration of the drug was executed via the oral gavage method. Additionally, glucose at a dosage of 2 g/kg was orally administered through orogastric tubes 30 minutes post-drug administration. Control animals received an equivalent volume of water. Blood samples were collected from the tail vein at 0, 30, 60, 90, and 120 minutes following glucose administration. Blood glucose levels were assessed utilizing the glucose oxidase method with a glucometer (Accuchek active) [10].

Biochemical analysis: Serum samples were utilized for the quantification of biochemical markers including creatinine, urea, alkaline phosphatase, serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), and serum lipid profile. These markers were measured using a Prietest Easylab - Biochemistry Analyzer manufactured by Robonik [India] Private Limited and the LAB-KITS enzymatic kits.

Statistical Analysis: The results were calculated as mean ± SEM and statistically assessed by two way analysis of variance (ANOVA) followed by Bonferronipost test. The values were considered to be significant when $p< 0.05$.

3. RESULT AND DISCUSSION

Table1: Composition of Polyherbal Tablet

Ingredients	**Quantity (mg) PHF 1**
Broccoli	296.8
Jackfruit	141.4
Ladyfinger	76.3
Drumstick	70.7
Wild Tomato	93.1
PVP	21.7
Avicel 101	478
Magnesium Stearate	12
Benzoic acid	10
Total weight (mg)	1200

Acute toxicity study of polyherbal formulation: Acute toxicity studies did not show any mortality up to 2000 mg/kg given as single oral administration. Hence, the study was carried out at the dose levels of 200 and 400 mg/kg.

Table 2- Effects of polyherbal formulation on body weight of STZ- induced diabetic rat

Treatment	**Body weight (g)**			
	0th day	**7th day**	**14th day**	**28th day**
Normal Control	195.3±6.5	197.0 ± 16.5	203.9 ± 14.9	212.5± 12.7
Diabetic control	196.0 ± 25.7	192.4 ± 17.3 [a]	184.0 ± 22.4 [a]	171.5 ± 17.0[a]
Metformin	195.6 ± 19.3[b]	198.5 ± 17.9[b]	203.6 ± 19.6[b]	196.2 ± 22.4[b]

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(100mg/kg)				
PHF 1 (200mg/kg)	196.2± 15.3	194.9± 12.1[b]	199.1± 13.5[b]	181.6± 17.9[b]
PHF1 (400mg/kg)	198.8 ± 16.7	199.4 ± 16.5[b]	212.4 ± 21.6[b]	194.5± 18.3[b]

Values are mean ± SEM, n = 6, [a] p< 0.001 compared to normal control group, [b] p<0.001 compared to diabetic control group

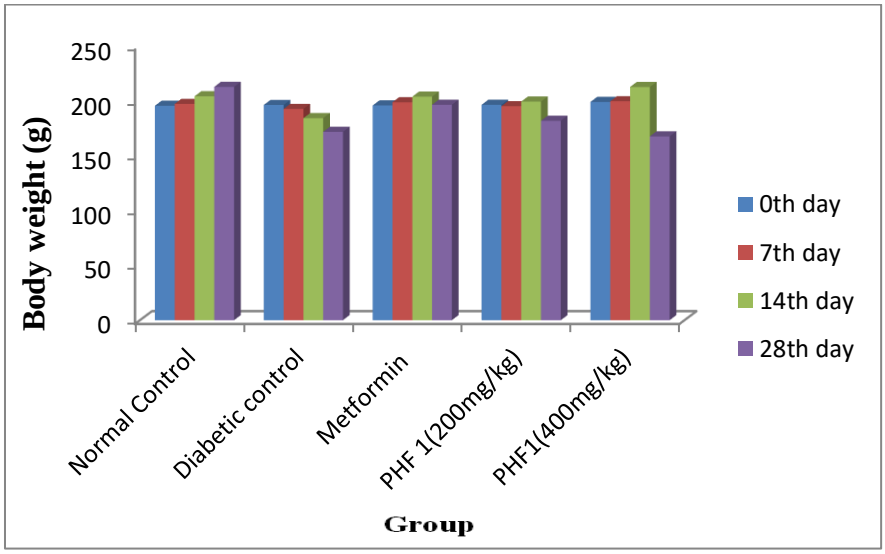

Figure 6: Effect of PHF1 on body weight

The body weight of normal control rats at the beginning of the experiment (195.3±6.5g) and end of experiment (i.e, at 28thday 212.5± 12.7g) was found with normal increase as per growth. A decrease ($p < 0.001$) in body weight was observed in diabetic rats (171.5 ± 17.0g) as compared to the normal control group at the end of the study. It was observed that groups of animals treated with standard drug (metformin 100mg/kg) and polyherbal formulation (PHF 1 200mg/kg and PHF1 400mg/kg) recovered significantly ($p < 0.001$) and their body weight was regained after treatment for 28 days, which may be attributed to improved glycemic control achieved by the administration of the extract and the drug. Here also the results at the dose of 400 mg/kg body weight (194.5± 18.3g) was comparable to the metformin on 28th day (196.2 ± 22.4g) [Table 2].

Table 3- Food consumption in various treatment groups during antidiabetic study

Treatment	**Food consumption (gm/animal)**			
	0th day	**7th day**	**14th day**	**28th day**
Normal Control	12.02±6.15	12.87±5.32	13.85±5.10	17.92±6.03

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Diabetic control	12.69±4.27	16.72±3.19	17.59±4.62	19.95±3.93
Metformin (100mg/kg)	11.95±2.54	12.31±3.73	13.56±2.19	17.24±3.59
PHF1 (200mg/kg)	12.52±6.30	13.94±5.48	14.59±5.27	16.92±6.96
PHF1 (400mg/kg)	11.96±3.49	12.75±4.51	13.79±3.49	17.21±5.52

Values are mean ± SEM, n = 6

Diabetic animals showed significant increase (19.95±3.93gm/animal) in food intake when compared to the treated groups as shown in [Table-3] whereas standard drug metformin and polyherbal formulaton (PHF1) normalizes the food intake capacity of rat at the end of the study.

Table 4- Effects of polyherbal formulation on oral glucose tolerance test

Treatment	**Blood Glucose level in (mg/dl)**				
	0 min	**30 min**	**60min**	**90 min**	**120min**
Normal Control	92.0±3.5	129.0±3.1	115.0±2.5	112.0±1.0	98.7±1.2
Metformin (100mg/kg)	110.0±3.1	119.0±3.0**	109.0±3.6**	107.0±2.1 **	96.5±1.2
PHF1 (200mg/kg)	101.0±2.0	118±2.4*	104.0±1.0*	100.0±4.0*	98.2±5.0
PHF1 (400mg/kg)	98.0±1.3	112.0±1.5**	99.0±2.3**	98.0±2.0*	95.3±1.3

Values are mean ± SEM, n = 6, * p< 0.05, ** p<0.01 compared to normal control group

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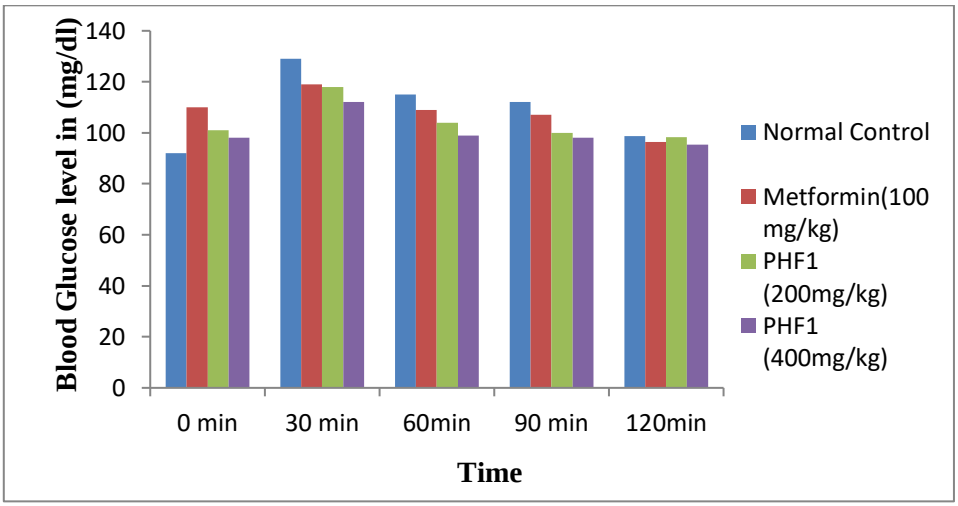

Figure 7: Effect of PHF1 in oral glucose tolerance test

PHF1 (200mg/kg) showed significant decline in blood glucose levels at 30 min (118±2.4 mg/dl) and 60 min (104.0±1.0 mg/dl) ($p<0.05$) in comparison to the normal control group whereas PHF1 (400mg/kg) exhibited significant decrease (112.0±1.5 mg/dl) ($p< 0.01$) in the blood glucose levels after 30 min which was comparable to Metformin (119.0±3.0 mg/dl) [Table 4].

Table 5- The effect of polyherbal formulation on fasting blood glucose levels (mg/dl) on streptozotocin- induced diabetic rats

Treatment	**Blood Glucose level in (mg/dl)**			
	0th day	**7th day**	**14th day**	**28th day**
Normal Control	178.39±3.12	182.08±2.25	187.44±3.46	194.52±3.56
Diabetic control	280.46±7.17	310.25±3.26 [a]	336.42±5.59 [a]	364.03±4.21[a]
Metformin (100mg/kg)	237.26±4.62	160.15±3.50[b]	138.46±2.74[b]	103.21±2.51[b]
PHF1 (200mg/kg)	278.56±5.21	190.61±4.56[b]	162.05±9.12[b]	112.68±3.69[b]
PHF1 (400mg/kg)	269.87±4.65	178.39±5.36[b]	154.18±3.57[b]	107.36±9.67[b]

Values are mean ± SEM, n = 6, [a] $p< 0.001$ compared to normal control group, [b] $p<0.001$ compared to diabetic control g

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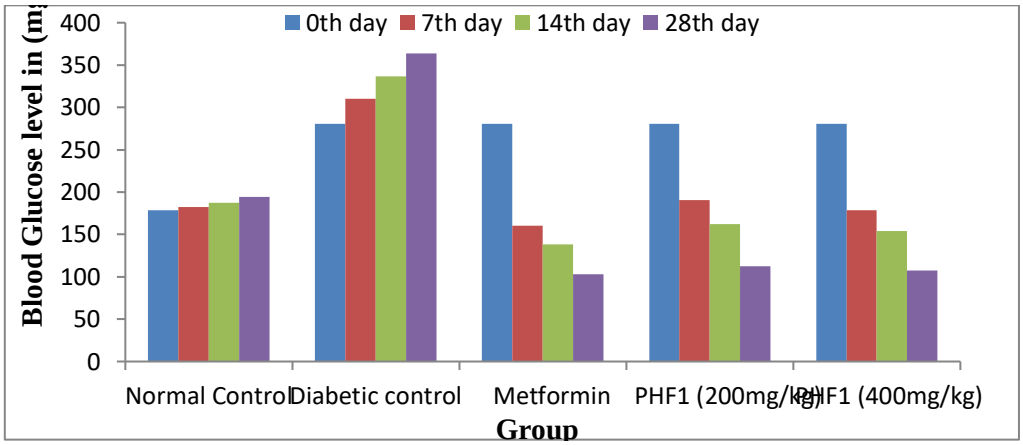

Figure 8: Effect of PHF1 on STZ-induced diabetic rats

The diabetic control group exhibited significant increase ($p<0.001$) in blood glucose levels at all time periods in comparison to the normal control group [Table 5]. The polyherbal formulation (PHF1 200mg/kg and PHF1 400mg/kg) indicated significant decrease($p<0.001$) in blood glucose level at all time intervals of day 7, day 14 day and day 28 against the diabetic control group. The results were more prominent at the dose of 400 mg/kg body weight (107.36±9.67 mg/dl) and was comparable to Metformin (103.21±2.51 mg/dl) at 28day.

Table 6- The effect of polyherbal formulation on serum lipid levels

Group	**Lipid Profile (mg/dl)**				
	Triglyceride (mg/dl)	**Total cholesterol (mg/dl)**	**HDL (mg/dl)**	**LDL (mg/dl)**	**VLDL (mg/dl)**
Normal Control	82.1±2.32	84.3±4.13	56.6±5.96	43.2±5.70	12.12 ± 0.37
Diabetic control	149.4±6.50	158.4±3.24[a]	31.6±4.57[a]	139.2±6.49[a]	39.20 ± 0.23[a]
Metformin (100mg/kg)	85.2±5.91	81.1±6.30[b]	55.7±5.44[b]	41.7±3.40[b]	13.00 ± 0.12[b]
PHF1 (200mg/kg)	93.5±3.67	109.5±5.19[b]	53.0±3.11[b]	52.2±4.76[b]	15.10 ± 0.65[b]
PHF1 (400mg/kg)	86.3±6.30	88.3±3.42[b]	49.7±4.85[b]	46.6 ±5.31[b]	11.50 ± 0.41[b]

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Values are mean ± SEM, n = 6, [a] p< 0.001 compared to normal control group, [b] p<0.001 compared to diabetic control group

On 28th day of the study, diabetic animals showed significant (P < 0.001) rise in total cholesterol, triglycerides, LDL and VLDL levels, and lower HDL level in comparison to normal rats.

The PHF1(200mg/kg), PHF1 (400mg/kg) and metformin (100 mg/kg) treated animals led to a significant (*P* < 0.001) normalization of lipid profile [Table 6].

Table 7: Effect of polyherbal formulation on alkaline phosphatase, SGOT, SGPT, serum creatinine, and urea levels in STZ-induced diabetic rats

Group	**ALP (IU/L)**	**SGOT (IU/L)**	**SGPT (IU/L)**	**CREA TININE (mg/dl)**	**UREA (mg/dl)**
Normal Control	131.8 ± 5.53	67.26 ± 1.74	38.77 ± 0.50	0.64 ± .05	42.80 ± 1.20
Diabetic control	252.0±10.57[a]	134.6 ± 2.31[a]	92.43 ± 1.06 a	1.45 ± .13[a]	63.31 ± 2.60[a]
Metformin (100mg/kg)	187.2 ± 3.31[b]	102.5 ± 6.01[b]	48.30 ± 1.73[b]	0.61 ± .04[b]	24.67±1.70[b]
PHF1 (200mg/kg)	163.3 ± 3.04[b]	89.73 ± 8.80 [b]	60.12 ± 1.86[b]	1.12± .16[b]	37.43 ±1.31[b]
PHF1 (400mg/kg)	157.3 ± 6.03[b]	87.20 ± 2.65 [b]	52.06 ± 1.52[b]	0.61 ± .04[b]	32.57 ±1.14[b]

Values are mean ± SEM, n = 6, [a] p< 0.001 compared to normal control group, [b] p<0.001 compared to diabetic control group

The results in Table 6 showed a significant increase (p< 0.001) in the liver function parameter and level of plasma urea and creatinine in the diabetic groups compared to control level. These results indicated that diabetes might lead to liver and renal dysfunction. While, after treatment of metformin-diabetic rats and polyherbal formulation (PHF1 200mg/kg and PHF1400mg/kg) the level of ALP, SGOT , SGPT and the level of urea and creatinine were significantly (p<0.001) decreased as compared to value of the diabetic group [Table 7].

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CONCLUSION

The research findings suggest that the polyherbal Formulation (PHF1) exhibits significant antidiabetic activity both *in vitro* and *in vivo* at doses of 200 and 400 mg/kg. Its efficacy is comparable to metformin, as evidenced by reduced blood glucose levels, changes in body weight, and food intake. Biochemical analysis further support the efficacy of PHF1. Thus, PHF1 could serve as an alternative treatment for Type 2 diabetes mellitus.

REFERENCES

1. Rohini C. Kolhe., Rajesh Y. Chaudhari., 2023. Development and evaluation of antidiabetic polyherbal tablet using medicinal plants of traditional use. Int J Curr Pharm Res. 15(2), 17-21.
2. Rajnish G., Manas M., Vijay K B., Pawan K., Sunita Y., Raka K., 2012. Evaluation of antidiabetic and antioxidant activity of Moringa oleifera in experimental diabetes. J Diabetes. 4 (2) , 1 6 4 - 7 1 . d o i : 1 0 . 1 1 1 1 /j.1753-0407.2011.00173.x.
3. Subrahmanyam. G.V., M. Sushma., Alekya A., Neeraja Ch., H. Sai Sri H., Ravindra J., 2011. Antidiabetic activity of Abelmoschus esculentusfruit extract. International journal of research in pharmacy and chemistry. 1(1), 17-20.
4. Basaria M., Hadyanto L., Jekson Martiar S., Endy Juli A., Putri C E., Sandeep P., 2 0 2 3 . The Effect of Jackfruit (Artocarpus heterophyllus Lam) Seed Ethanol Extract on Blood Sugar Levels and Anti-Inflammatory Reduction on Wistar Albino Rats Streptozotocin-Induced Gestational Diabetes. Research Journal of Pharmacy and Technology. 1 6 (2) , 8 0 4 - 8 . d o i : 10.52711/0974-360X.2023.00138.
5. Mashood Ahmad S., Md. Moklesur Rahman S., Mohammad Gosuddin I., 2016. Antidiabetic Potential of Brassica Oleracea Var. Italica in Type 2 Diabetic Sprague Dawley (SD) Rats. International Journal of Pharmacognosy and Phytochemical Research. 8(3), 462-469.
6. Charanjit K., Suresh W., Shweta N., Shweta W., Jashbir S., Braj Bhushan S., 2013. Functional quality and antioxidant composition of selected tomato (Solanum lycopersicon L) cultivars grown in Northern India. LWT - Food Science and Technology.50(1) , 139-145.
7. Gauttam V. K., Kalia A. N., 2013. Development of polyherbal antidiabetic formulation encapsulated in the phospholipids vesicle system. J Adv Pharm Technol Res. 4(2), 108-116. doi. 10.4103/2231 4040.111527.
8. Kaskoos RA., Hagop AB., Faraj AB., Ahamad J., 2015. Comparative antioxidant activity of *Gymnema sylvestre, Enicostemma littorale, Momordica charantia* and their composite extract. JPP. 4(1), 95–8.
9. Parasuraman S. 2011. Toxicological screening. J Pharmacol Pharmacother. 2,74-9.
10. Ahmed M. F., Kazim S. M., Ghori Safiullah S., Mehjabeen Syeda S., Ahmed Shaik R., Ali Shaik M., 2010. Antidiabetic activity of Vinca rosea extracts in alloxan-induced diabetic rats. Int J Endocrinol. 2, 1-6.
11. Pourghasem M., Shafi H., Babazadeh Z., 2015. Histological changes of kidney in diabetic nephropathy, Caspian J Intern Med. 6(3), 120-127.
12. Osterby R., Hartmann A., Nyengaard JR., Bangstad HJ., 2002. Development of renal structural lesions in type-1 diabetic patients with microalbuminuria. Observations by light microscopy in 8-year follow-up biopsies. Virchows Arch. 440, 94-101.
13. Petchi RR., Parasuraman S., Vijaya C., 2013. Antidiabetic and antihyperlipidemic effects of an ethanolic extract of the whole plant of Tridax procumbens (Linn.) in streptozotocin-induced diabetic rats. J Basic Clin Pharm. 4, 88-92.
14. Parasuraman S., Kumar E., Kumar A., Emerson S., 2010. Free radical scavenging property and diuretic effect of triglize, a polyherbal formulation in experimental models. J Pharmacol Pharmacother. 1, 38-41.
15. Mandavi, D'Cruz S., Sachdev A., Tiwari P., 2012. Adverse drug reactions and their risk factors among Indian ambulatory elderly patients. Indian J Med Res. 136, 404-10.