ORIGINAL ARTICLE

Antihyperglycemic and Antihyperlipidemic Effect of Polyherbal Formulation on Alloxan-induced Diabetes in Wistar Rats

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Abstract

Objective: The polyherbal formulation (PHF) containing different herbal extracts has been used to treat diabetic patients by Ayurvedic professionals in India. It has been well documented that the polyherbal plant extracts more productively diminish the elevated blood glucose level as compared with the single plant extract. **Methodology:** The PHF contains the concentrated extracts of *Syzygium cumini*, *Annona squamosa, Momordica charantia, Tinospora cordifolia, Gymnema sylvestre,* and *Curcuma longa*. The present study reports the impact of PHF alone and with metformin on various preclinical models of hyperglycemia. **Results:** PHF treatment with alone and in combination with metformin evoked a noteworthy antihyperglycemic impact on glucose loaded ($P < 0.05$), epinephrine-induced hyperglycemia ($P < 0.05$), and alloxan-induced diabetic rats ($P < 0.05$). PHF treatment also modifies glucose tolerance curve pattern both in normal and in diabetic rats. The treatment with polyherbal formulation was significantly improved architecture of β-islets of Langerhans as compared with the diabetic rats. The PHF significantly decreased ($P < 0.05$) triglyceride, cholesterol, and high-density lipoprotein as compared to diabetic control group. The dynamic phytoconstituents present in this PHF are flavonoids, phenolic compound, triterpene saponins like gymnemic acids, and gymnemasaponins advance the arrival of insulin and postpone the assimilation of glucose. **Conclusion:** PHF treatment in combination with metformin is found to be useful in the management of preclinically induced diabetes mellitus.

Key words: Antidiabetic activity, epinephrine, glucose metabolism, glucose utilization, polyherbal formulation

INTRODUCTION

Diabetes mellitus (DM) is an incessant metabolic condition which prompts increment glucose level in blood, because of non-appearance or imperfection in insulin creation or lack in insulin combination, likewise observed in sugar, fat, and protein metabolism. Prolong and persistent hyperglycemia causes the genuine complications such as nephropathy, retinopathy, and full-scale vascular entanglements such as hypertension, atherosclerosis, cardiovascular failure, and stroke. The WHO revealed that 422 million people across the globe experiencing DM, the quantity of patient, increasing 522 million in the year 2030.[1,2]

The radical change in the present-day way of life, which incorporates sporadic dozing, altered diet regimes, smoking and drinking habits, may cause the lopsidedness between insulin creation and blood glucose which lead to created DM. The enormous exploration on the diabetes and its inconvenience, yet no single hypothesis is accessible for complete treatment for DM and its complication. Traditional herbal assumes a significant job in the treatment of diabetes. It was demonstrated that 5–6 plant extracts detailing has significantly diminished the dose of insulin and hypoglycemic drugs.[3] The various investigations on polyherbal formulation (PHF) have expounded proficient

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likely alternatives for type 2 DM (T2DM). The homegrown medication is regularly utilized with allopathic medications for restorative remedies.[4] Ayurveda has depicted the quantity of extracts or parts of plants and their concentrates for hostile to diabetic potential and against hyperglycemic impacts with lipid bringing down properties. The herbal plants utilized for different cures in India are a typical marvel, Ayurveda explained the act of utilization of natural medications, their mix and line of treatment.[4] In diabetic patient, it has been seen that they take the homegrown plants with the modern allopathic hypoglycemic drugs to control of glucose and its complications. The effectiveness with lowered cost is real gain for the patient, likewise sharpen pancreas for release of insulin, and improves the usage of glucose by peripheral system. *Momordica charantia*, *Syzygium cumini,* and *Gymnema sylvestre* have been in use since long for the glucose-lowering properties, insulin mimic effects,[5-7] and the dynamic constituents of plant extract answerable for glucose-lowering impact in glucose-loaded hyperglycemic rats.[6] Some examination article expressed that *Annona squamosa, Tinospora cordifolia,* and *Curcuma longa* had demonstrated for its antidiabetic response with nerve tonic and lipid-lowering effects.[8-10]

In the present study, PHF contains plant extracts such as *Syzygium cumini*, *Annona squamosa*, *Momordica charantia*, *Tinospora cordifolia*, *Gymnema sylvestre,* and *Curcuma longa*. All the restorative plants were chosen based on their demonstrated antidiabetic, lipid-lowering properties, and insulin-sensitizing mechanisms of individual plants.[11] The newly prepared polyherbal formulation was evaluated to antihyperglycemic effects in Wistar rats and furthermore the formulation was accessed for the acute toxicity study.

MATERIALS AND METHODS

The required extracts of herbs were procured from Green Chem Phyto Pvt. Ltd., Bengaluru. Glucose estimation strip was purchased from local market, total cholesterol estimation kit, high-density lipoprotein (HDL) cholesterol estimation kit, and triglyceride estimation kit manufactured by BeneSphera Diagnostics, India, were used for the study. All other chemicals and reagents used were of analytical grade and procured from approved vendors.

Preparation of PHF

The all extracts were weighed as per Table 1 in motor, added water, and mix it well to form a homogeneous liquid mixture; adjust volume up to 20 ml purified water.

Animals

Adult Wistar rats of either sex (200–250 g) were procure from Padro Laboratories Pvt. Ltd., Pune, which were maintained at 25 ± 1 temperature and relative humidity of 45–50%. The animals were housed in spacious polyacrylic cages having free space for food and access the water; maintain the standard pellets and water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethical Committee of Dr. D.Y. Patil Institute of Pharmaceutical Science and Research, Pimpri, Pune (DYPIPSR/IAEC/2019-01-10), accordance with the guidelines of IPCSEA. All preparations were prepared in distilled water and water used as a vehicle for solution.

Table 1: The composition table of polyherbal formulations

Herbal extract	Composition of herbal extract mg/kg		
	PHF-225	PHF-450	PHF-850
Aq. extract of *Tinospora cordifolia*	52.5	87.5	175
Aq. extract of *Syzygium cumini*	30	50	100
Aq. extract of *Gymnema sylvestre*	45	75	150
Aq. alcoholic extract of *Annona reticulata*	52.5	87.5	175
Aq. alcoholic extract of *Momordica charantia*	45	75.5	150
Alcoholic extract of *Curcuma longa*	30	50	100
Total dose (mg/kg *p. o.*)	225	425	850

Acute toxicity study

Acute oral toxicity of the PHF was carried out as per the guidelines 425 set by the Organization for Economic Cooperation and Development. Healthy female Wistar rats were divided into three groups consisting three animals in each group. The animal fed with PHF with dose range from 1, 1.5, to 2 g/kg p.o. body weight, respectively. The animals were observed for their neurological (reactivity, touch response, spontaneous activity, gait, and pain response), behavioral (restlessness, alertness, irritability, and fearfulness), and autonomic (urination and defecation) continuously for 48 h, the animals were observed for 14 days for mortality.

Experimental designing

Oral glucose tolerance test (OGTT) for evaluation of antihyperglycemic activity

The OGTT was completed to discover appropriately to a glucose challenge. The OGTT was performed on overnight

fasted rats. The animal was pretreated for the everyday for the period of 7 days. Animal was divided into five groups, Group no. 1 positive control was received 0.5 ml/100 g of 1% suspending agent, Groups no. II, III, and IV were pretreated with PHF (225, 450, and 850 mg/kg., p.o., respectively), and Group no. 5 was received metformin (500 mg/kg route), glucose (2 g/kg) was loaded 30 min after pre-treatment. Blood glucose levels were measured at 0, 2, 4, and 6 h after glucose load to access the effect of polyherbal formulation on blood glucose levels of the glucose-loaded animals. The blood glucose was measured with the help of glucometer (Accu-Chek Active TM Test Meter).[12,13]

Epinephrine-induced hyperglycemic Wistar rats (prophylactic treatment)

Overnight fasted Wistar rats were divided into five groupings (six animals/group): Group I as hyperglycemic positive control group and received vehicle (0.5 ml/100 g, po of 1% CMC solution), rats of Groups II, III, and IV were treated with PHF (225, 450, and 850 mg/kg po), and Group no. V treated with metformin (500 mg/kg, p.o). Epinephrine hydrochloride (0.8 mg/kg) was administered intraperitoneally (ip) to rats of all groups, 30 min after the vehicle, PHF, and metformin administration. Blood glucose level was measured at 0, 2, 4, and 6 h after epinephrine inducing agent. The blood glucose was measured with the help of glucometer (Accu-Chek Active TM Test Meter).[13]

Alloxan-induced diabetic rats (therapeutic treatment)

Diabetes was induced in overnight fasted (six groups) of rats by injecting alloxan monohydrate 120 mg/kg i.p in 0.9% w/v NaCl, whereas the normal control group was received same volume of 0.9% w/v NaCl solution through i.p. Then, 10% glucose solution bottles were kept in the cage to prevent the hypoglycemic events for the period of 24 h. The rats with prominent hyperglycemia were selected and used after 72 h (fasting blood glucose >250 mg/dl).[13] The diabetic animals were divided into six groups each group having six animals and one normal control group. Group I untreated diabetic control group received vehicle (dose of 0.5 ml/100 g); Groups 2 and 3 treated with polyherbal formulation 225 mg/kg p. o. and 450 mg/kg p. o., respectively; Group no. 4 treated standard drug metformin 500 mg/kg; while Groups no. 5 and 6 were treated with polyherbal formulation 225 mg/kg and metformin 250 mg/kg, polyherbal formulation 450 mg/ kg and metformin 250 mg/kg, respectively. The dosing was continuing for 21 days; blood glucose level was measures of days initial, 7, 14, and 21. The body weights of animal were determined on day 21 and ether anesthesia was used for the sacrifices the animals and liver was removed and place in ice-cold 0.9% sodium chloride. The blood was collected through the cardiac puncture and was centrifuged at 3000 rpm for 5 min. Different biochemical parameters such as glycosylated hemoglobin, serum LDL, VDL, cholesterol, triglycerides, and serum creatinine were analyzed, the liver tissue was processed, and liver glycogen level was measured.[14-16]

Histopathological study

All groups of animals were subjected to histopathological studies after euthanasia, the entire pancreas was removed from all groups of animals. The section pancreatic tissue was put in 4% formalin solution. The small piece of tissue of 5 μm thickness was stained with hematoxylin and eosin dye. The histopathological examination of stain section was evaluated for the qualitatively using photo microscope at 10× and 40×.[13]

Statistical analysis

All the values were expressed as mean ± SEM. The data obtained through one-way analysis of variance followed by Duncan's *post hoc* multiple variance test. $P < 0.05$ was considered statistically significant. "P"< 0.05% was considered statistically significant.

RESULTS

Acute toxicity study

There was no sign of morbidity nor mortality and any type of adverse effects in animals given single dose of 2000 mg/kg p.o. of prepared polyherbal formulation.

OGTT for evaluation of antihyperglycemic activity

The oral administration of glucose (1.5 g/kg) was elevated blood glucose levels of positive control rats and reached a peak at 60 min and gradually decreased to 120.16 mg/dl in 4 h. The pre-treatment with PHF (850 and 450 mg/kg) and metformin (500 mg/kg) shown decreased blood glucose level significantly ($P < 0.01$) as compared to the positive control group [Table 2], while polyherbal formulation (225 mg/kg) was significantly ($P < 0.05$) reduced the blood glucose level as compared with the positive control group.

Epinephrine-induced hyperglycemic Wistar rats

The study result shown that antihyperglycemic effect in epinephrine-induced hyperglycemic rats, epinephrine 0.8 mg/kg i.p. was a significant rise in the blood glucose levels of the all groups. PHF 850 mg/kg p.o. and 450 mg/kg p.o. exhibited significant ($P < 0.01$) antihyperglycemic activity at 1, 2, and 4 h after epinephrine induction, compared to positive control group, while PHF (250 mg/kg p. o.) was decreased the elevated blood glucose level significantly ($P < 0.05$) at 1, 2, and 4 h as compared with control animals [Table 3].

Alloxan-induced diabetic rats

Alloxan a chemical moiety has a β-cytotoxic property, it damaging the pancreatic β-cell of Langerhans, the cell responsible for secretion of insulin. The dose-dependent degeneration lesion of pancreatic β-cell of Langerhans causes the diabetes. On 21 days, repeated treatment of the PHF, metformin, and combination of PHF and metformin shown the sustained and significant ($P < 0.05$) lowers in blood glucose level of diabetic rats at dose of 225 mg/kg p.o. and 450 mg/kg p.o. of PHF, respectively, as compared with diabetic control group. The metformin shown the more significant ($P < 0.01$) decrease blood glucose level with the complementary of PHF, this shown that the PHF was express the synergic effect of standard metformin [Table 4]. The combination of PHF and metformin shown significant lowers in blood glucose level at a dose PHF 450 mg/kg along with metformin 250 mg/kg p. o., as compared with the diabetic control group.

Biochemical parameters

The estimation of glycosylated hemoglobin, serum HDL, total cholesterol, and serum creatinine of different groups is shown in Table 5. Diabetic rats increase in the level of glycosylated hemoglobin, which was control significantly with the treatment of PHF at different doses. The combine therapy of PHF 450 mg/kg and metformin 250 mg/kg shown more significant ($P < 0.01$) control the glycosylated hemoglobin as compared with diabetic control group. The PHF 225 mg/kg and 450 mg/kg was shown the significant ($P < 0.05$) minimize the serum HDL, total cholesterol, and triglyceride level as compared with diabetic control group. The combine treatment

Table 2: Effect of polyherbal formulation on blood glucose in glucose-induced hyperglycemic rats

Treatment/groups	Blood glucose level (mg/dl)				
	Initial	30 min	60 min	120 min	240 min
Gp. 1 positive control	111.50±9.05	143.50±2.91	161.67±2.18	125.17±5.20	120.16±3.9
Gp. 2 PHF (225 mg/kg p. o.)	103.33±8.26	143.00±2.38	104.17±2.80**	91.50±1.87*	87.5±1.71**
Gp. 3 PHF (450 mg/kg p. o.)	104.50±7.17	150.33±3.77	91.83±1.74**	82.67±1.08**	80.83±2.07**
Gp. 4 PHF (850 mg/kg p.o.)	107.83±7.78	146.50±3.31	88.17±2.24**	76.17±1.33**	76.17±1.70**
Gp. 5 metformin (500 mg/kg p. o.)	109.33±8.28	154.17±3.63	80.50±2.36**	73.83±1.70**	73.83±1.32**

Value are mean±SEM, *n*=6 in each group, significant as ***P*<0.01 versus positive control, **P*<0.05 versus positive control, (one-way ANOVA followed by Dunnett's multiple "*t*-test")

Table 3: Effect of polyherbal formulation on blood glucose in epinephrine-induced hyperglycemic rats

Treatment/groups	Blood glucose level (mg/dl)				
	Initial	30 min	60 min	120 min	240 min
Gp. 1 positive control	109.50±7.17	192.5±3.32	179.33±5.82	135.67±3.32	120.16±3.9
Gp. 2 PHF (225 mg/kg p. o.	112.83±8.79	199.67±5.19	155.17±4.03*	127.17±3.70*	97.5±1.71*
Gp. 3 PHF (450 mg/kg p. o.)	110.66±7.39	189.00±3.70	158.11±4.49*	119.50±3.55*	80.83±2.07**
Gp. 4 PHF (850 mg/kg p. o.)	114.33±8.52	202.83±9.25	136.50±2.80**	103.00±3.90**	73.83±1.70**
Gp. 5 metformin (500 mg/kg p.o.)	107.20±8.09	193.17±4.89	122.83±2.76**	54.167±7.58**	76.17±1.32**

Value are mean±SEM, n=6 in each group, significant as ***P*<0.01 versus positive control, **P*<0.05 versus positive control, (one-way ANOVA followed by Dunnett's multiple "*t*-test")

Table 4: Effect of PHF on blood glucose level in alloxan-induced diabetic rats

Treatment/groups	Serum glucose level (mg/dl)			
	Day 0	Day 7	Day 14	Day 21
Diabetic control	290.33±26.34	294.83±26.99	316.50±17.21	308.50±12.81
PHF-V1 (225 mg/kg p. o.)	312.1±23.98	247.67±12.75#	225.83±12.41#	205.50±19.22#
PHF-V2 (450 mg/kg p. o.)	314.16±26.43	244.16±21.87#	201.50±7.55#	194.83±10.50#
Metformin (500 mg/kg p.o.)	304.00±18.89	215.00±16.77#	179.66±7.84#	165.66±7.61#
PHF (225) + metformin (250 mg/kg p.o.)	316.66±15.34	227.33±12.31#	195.16±4.79#	183.50±17.99#
PHF (450) + metformin (250 mg/kg p.o.)	307.50±10.36	203.5±08.60#	185.83±7.03#	173.66±8.80#
Normal control	110.52+4.32	105.83+5.39	113.33+8.79	107.66+6.52

PHF: Polyherbal formulation, Value are mean ± SEM, n=6 in each group, Significant as #*P*<0.01Drug treatment vs. Diabetic Control, (one-way ANOVA followed by Dunnets multiple 't' test)

Groups no. 5 and 6 were control the HDL, total cholesterol, and triglyceride in the similar pattern of normal control group. The serum creatinine level was elevated significantly in diabetic control group, whereas treatment with PHF 450 mg/kg couple with metformin 250 mg/kg was shown significantly ($P < 0.01$) lowers the serum creatinine.

Effect on body weight

Induction of diabetes by alloxan monohydrate may cause the decrease in body weight of normal control rats, whereas repeated treatment of PHF alone and in combination with metformin sustained improved the body weight as compared with diabetic control groups [Table 6], whereas the repeated oral administration of metformin 500 mg/kg was not improved body weight significantly as compared with diabetic control group. The PHF treated with 450 mg/kg and 225 mg/kg preventing the loss of body weight significantly ($P < 0.01$) of diabetic rats.

Histopathological examines

The photomicrographs of stained pancreas exhibit normal surface topography of acini and in the islets of Langerhans in normal control group [Figure G7]. The alloxan caused severe necrotic changes, karyolitic disappearing of nucleus, reduced dimension of islets, shrunken and distorted islets of Langerhans in diabetic control group on day 21 [Figure G1]. Relative reduction of size and number of islets, especially around the large vessel and severe reduction of β cells, were clearly seen in diabetic rats. Effect of PHF 225 mg/kg and 450 mg/kg treated group on pancreas showed vacuolated cytoplasm and dark stained nuclei of β-cells, respectively [Figure G2 and G3]. The group treated with the metformin was shown the similar architecture of pancreas as normal control group [Figure G4]. After 21 days, combine treatment of PHF and metformin increased cells along with the dark stained nuclease and increase in the size of β-cells of pancreas showed normal architecture of pancreatic β-cells [Figure G5 and G6].

DISCUSSION

The different parts of herbal plant were proven in the management of diabetes. The herbal extract used as complementary with the allopathic medicine to control the diabetic complication, minimized the side effect. The combination of herbal extract

Table 5: Effect of PHF on glycosylated hemoglobin, triglyceride, HDL, and cholesterol in alloxan-induced diabetic rats

Treatment/groups	Biochemical parameters			
	Triglyceride mGs/dL	Cholesterol mGs/dl	HDL mGs/dl	Glycosylated hemoglobin
Diabetic control	146.01±5.53	243.68±19.34	48.74±3.87	9.04±0.66
PHF (225 mg/kg p. o.)	125.57±6.10*	187.35±35.94*	37.47±7.19*	7.25±0.73#
PHF (450 mg/kg p. o.)	96.44±9.14#	138.50±11.62#	27.70±2.32#	5.42±0.64#
Metformin (500 mg/kg p.o.)	107.12±7.90#	112.35±18.77#	22.47±3.75#	7.88±0.65*
PHF (225) + metformin (250 mg/kg p.o.)	85.04±3.41#	117.24±17.58#	23.45±3.52#	4.90±0.51#
PHF (450) + metformin (250 mg/kg p.o.)	80.27±3.62#	98.27±5.23#	19.65±1.05#	4.46±0.43#
Normal control	73.45±6.35	90.35±6.32	17.25±0.75	4.01±0.54

Value are mean±SEM, n=6 in each group, significant as *P<0.05,#P<0.01 versus positive control, (one-way ANOVA followed by Dunnett's multiple "t-test"). PHF: Polyherbal formulation, HDL: High-density lipoprotein

Table 6: Effect of PHF and standard drug on body weight of hyperglycemic rats

Treatment/groups	Body weight in g			
	Day 0	Day 7	Day 14	Day 21
Diabetic control	233.33±8.76	207.50±16.95	182.50±6.89	174.16±9.70
PHF (225 mg/kg p. o.)	239.17±18.55	225.83±13.93	208.33±14.38*	197.50±13.69#
PHF (450 mg/kg p. o.)	226.66±19.66	230.00±13.10 #	215.83±10.68#	209.17±7.36#
Metformin (500 mg/kg p.o.)	221.83±15.05	213.33±14.72	190.84±12.01	187.50±11.72
PHF (225) + metformin (250 mg/kg p.o.)	234.16±14.28	231.67±12.29#	220.16±12.81#	213.33±10.32#
PHF (450) + metformin (250 mg/kg p.o.)	230.83±15.62	232.50±10.37#	223.33±12.11#	215.00±11.83#
Normal control	220.33±8.32	223.52±7.33	218.66±10.69	221.89±11.29

Value are mean±SEM, n=6 in each group, significant as *P<0.05, #P<0.01 drug treatment versus diabetic control, (one-way ANOVA followed by Dunnett's multiple "t-test"). PHF: Polyherbal formulation

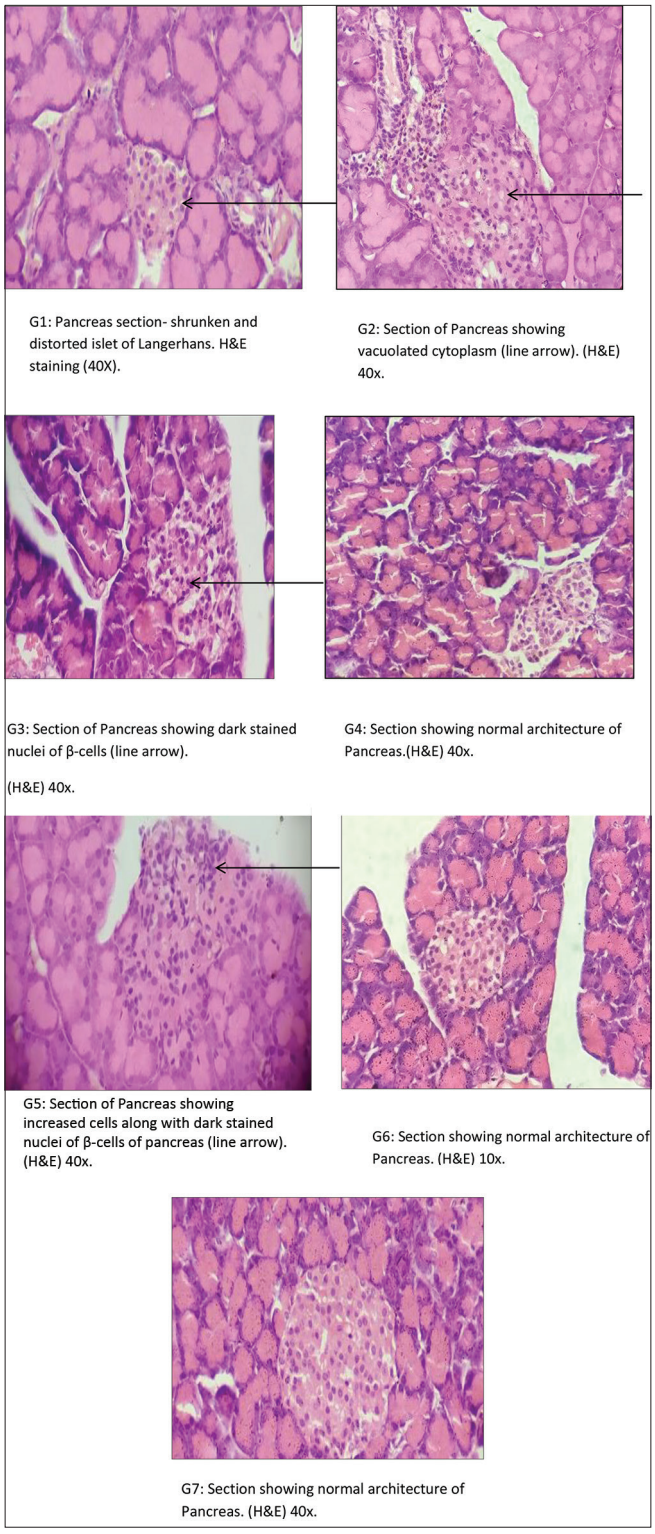

Figure 1: (G1-G7) Histopathological examines of rat pancreas for antidiabetic activity of herbal formulation.

has more significant results rather than the single plant and shown the antihyperglycemic property without any side effects.[17] Therefore, the polyherbal formulation of five plant extracts was prepared. To select the safe dose of polyherbal formulation for the antidiabetic activity, the formulation was undergoing preliminary toxicological study, which shown the non-toxic, non-harmful, and no any adverse effects up to the dose level 2000 mg/kg.[8] OGTT was performed to check the ability of peripheral tissue to utilize glucose, insulin release pattern, and insulin resistance. The non-significant reduction in blood glucose level in normal rats was treated by standard metformin and PHF at lower doses, while at higher dose of polyherbal formulation slightly decreases the blood glucose level, which is therapeutically conducive.[18] The formulation comprises gymnemic acid, which may be responsible for delayed absorption of glucose molecule and attributes to similar atomic arrangement to that of gymnemic acid, which shown the antihyperglycemic effects,[19] Initially, a rise in blood glucose level in response to infusion of epinephrine, due to increase in rate of gluconeogenesis and enhances the breakdown of hepatic glucose, the PHF contains flavonoids may act through the inhibitory pathway of gluconeogenesis and increase the glycogenolysis.[20,21] Alloxan, β-cytotoxic, causes chemical diabetes, through the destruction of pancreatic ß-cells of the islets of Langerhans and massive reduction in the insulin release.[17] It was responsible for the production of reactive oxygen species, which causes the destruction of pancreatic ß-cells and produced hyperglycemia, metabolic stress, and severe glucose intolerance. In the present study, the polyherbal formulation was significantly lowering the blood glucose level in alloxan-induced diabetic rats. The study was demonstrated that the PHF was responsible for minimize the dose of allopathic medicine significantly due to the enhanced glucose utilization by peripheral tissue,[22,23] sensitize the ß-cells to release the insulin in blood stream, and may prevent the metabolism of metformin through the inhibiting cytochrome P450.[24] The alcoholic extract of *Annona reticulata* has effect on peroxisome proliferate activated receptor-α which is responsible for the insulin releases. Flavonoids also lead to regeneration of pancreatic β-cells, reduce the necrosis and degeneration of pancreatic cells which may lead to increase the insulin released.[26] The phenolic compounds and flavonoids are known as excellent free radical scavenging agents and prevent the free radical chain reaction.[27] The aq. extract of *Tinospora cordifolia* contains isoquinoline alkaloids including palmatine and magnoflorine which have been reported for insulin mimicking and insulin releasing effects. The alcoholic extract of *Tinospora cordifolia*, alcoholic extract of *Gymnema sylvestre* contains saponins, triterpene saponin known as gymnemic acids, gymnemasaponins, and gurmarin phytoconstituents inhibited the enzyme salivary and pancreatic amylase and glucosidase, show sweet inactivation property, which results into the antihyperglycemic effects. The phytoconstituents curcumin presents in curcuma longa, acts as a peroxisome proliferator-activated receptors-α receptor agonist. It stimulates free fatty acid catabolism, which results into suppress the diabetes.[29] Diabetic untreated rats increase level of triglycerides, cholesterol due to enhance the production of very low-density lipoprotein and absence of protein lipase.[25] The polyherbal formulation was responsible to increase the transcription of lipoprotein, which is similar to that of insulin and significantly lowers the triglycerides, cholesterol, and

HDL levels in treatment groups.[28] Alloxan-induced diabetic rats characteristically decrease in body weights, due to muscle wasting.

CONCLUSION

It can be concluded that this PHF may be an ideal alternative medicine for the antihyperglycemic and antihyperlipidemic actions. The polyherbal formulation prevents the loss of body weights may be due to its protective effects in controlling muscle wasting and proper management of diabetes. The histopathological finding shown that the alloxan damaged the pancreatic β-cells and livers, it was reversed by prolong treatment with polyherbal formulation, due to its regeneration of pancreatic β-cells of islets of Langerhans. Medicinal plants contain phytochemicals include alkaloids, terpenoids, flavonoids, cardiac glycosides, and steroids were alternative therapeutic agents for the management of DM. It can be concluded that this PHF may be an ideal alternative medicine for the antihyperglycemic and antihyperlipidemic actions.

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