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Research Article

ANTIDIABETIC AND ANTIHYPERLIPIDEMIC ACTIVITIES OF A NOVEL POLYHERBAL FORMULATION IN STREPTOZOTOCIN-NICOTINAMIDE-INDUCED DIABETIC WISTAR RATS

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ABSTRACT

Objective: The objective of the study was to investigate the antidiabetic and antihyperlipidemic activities of polyherbal formulation (PHF) containing seven plants, namely, *Cassia auriculata, Cassia fistula, Syzygium cumini, Cyperus rotundus, Saussurea lappa, Terminalia arjuna,* and *Salacia reticulate* in streptozotocin (STZ)-nicotinamide (NC)-induced diabetic rats by administering oral doses (200 and 400 mg/kg body weight).

Materials and Methods: Animals were divided into diabetic and non-diabetic groups. Rats were fed with normal laboratory diet and induced with a single intraperitoneal injection of 60 mg/kg of STZ, and thereafter, 120 mg/kg NC was injected after 15 min. Diabetic rats were treated with formulation (200 and 400 mg/kg) and glibenclamide 5 mg/kg. Blood glucose levels were measured using blood glucose test strips with ACCU CHEK glucometer. Glycosylated hemoglobin (HbA_1C), total haemoglobin (Hb), lipid profiles, lipoproteins, and hepatic marker enzymes activity were determined in normal and STZ-NC-induced diabetic rats after oral administration of the PHF for 28 days. Histopathological changes in normal and diabetic rat pancreas organs were also observed after PHF treatment. The statistical analysis of results was carried out using one-way analysis (ANOVA) followed by Dunnett's *post hoc* multiple comparison tests.

Results: Treatment of diabetic rats with PHF (200 and 400 mg/kg) and glibenclamide (5 mg/kg) indicates significant decreased blood glucose level and significant improvement in body weight. PHF-treated rats showed significant ($p<0.01$) decrease in the level of *glycosylated* Hb, total cholesterol, triglycerides, low-density lipoprotein, very low-density lipoprotein, aspartate amino transaminase, alanine amino transaminase, and alkaline phosphatase while a significant increment in the level of Hb and high-density lipoprotein cholesterol was observed. Furthermore, the PHF-treated rats have a favorable effect on the histopathological changes of the pancreas in STZ-NC-induced diabetes.

Conclusion: These findings suggested the antidiabetic and antihyperlipidemic properties of the PHF and thus help in preventing future complications of diabetes.

Keywords: Glibenclamide, Polyherbal formulation (PHF), Antidiabetic, Antihyperlipidemic, Type 2 diabetes.

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INTRODUCTION

In recent years, there has been renewed interest in the treatment against different diseases using herbal drugs, as they are generally non-toxic and the World Health Organization has recommended its effectiveness rather than the precarious modern drugs. Plant derivatives with hypoglycemic properties have been used in folk medicine and traditional healing systems around the world from ancient time [1]. Herbs and phytochemicals play a major role in the discovery of new therapeutic agents and have received attention as sources of antioxidants, hypoglycemic, and antihyperlipidemic agents. There are numerous traditional plants mentioned in Siddha and Ayurvedic system of medicine which are used as antidiabetic agents. *Sharangdhar Samhita*, an Ayurvedic literature from 1300 AD, has stressed the importance of polyherbalism [2].

Polyherbal formulations (PHFs) enhance the therapeutic action and reduce the concentrations of single herbs, thereby reducing the adverse events. Compared to the single herb, the PHF has better and multitargeted therapeutic potential. In the Ayurvedic system of medicine, several plants have been advocated for their hypoglycemic effects and are still in practice. Taking the lead from ancient literature seven plants, *Cassia auriculata, Cassia fistula, Syzygium cumini, Cyperus rotundus, Saussurea lappa, Terminalia arjuna,* and *Salacia reticulate* were selected out of various screened plants carried out for this purpose. In a traditional system, the plants of *Cassia* species are being used for asthma, antidiabetic, urinary disorders, nocturnal emission, antibilious, amebiasis antipyretic properties, etc., *S. cumini* called as "Naaval" is widely used a seed for hyperglycemia and polyuria. These plant parts having many constituents are used as lipid peroxidation in liver, anti-inflammatory, anti-arthritic, antipyretic, and analgesic activities [3]. The extracts of *C. rotundus* have been proved for its neuroprotective [4] and anti-inflammatory, anti-arthritic, analgesic, and anticonvulsant activity [5]. Another species of *S. lappa* have been extensively studied for its ameliorative effects [6] and antiviral efficacy [7]. *Terminalia* species are being proved for antidiabetic [8,9]. Furthermore, *S. reticulate* has been also proved for its antidiabetic [10]. The formulation is IPR protected and is already formulated. This study is to evaluate the antihyperglycemic and antihyperlipidemic activities of the PHF.

MATERIALS AND METHODS

Drugs and chemicals

Streptozotocin (STZ) (HiMedia, Mumbai), nicotinamide (NC) (HiMedia, Mumbai), and glibenclamide (Cipla, Mumbai) were used. All other chemicals and reagents were of analytical grade and enzymatic kits used in this study were obtained commercially.

Composition of PHF

The PHF was formulated into the Kudineer Chooranam as per the patent information of the effective doses by the SKM Siddha and Ayurveda Company India Ltd., Erode, Tamil Nadu, India. Each Kudineer Chooranam contains powders of *C. auriculata* (14.28%), *C. fistula*

(14.28%), *S. cumini* (14.28%), *C. rotundus* (14.28%), *S. lappa* (14.28%), *T. arjuna* (14.28%), and *S. reticulate* (14.28%) [11].

Experimental animals

Wistar albino rats of both sexes weighing (150–200 g) were used for the study [12]. All animals were maintained under standard laboratory conditions (temperature [22±2°C] and humidity [45±5°C]) with a 12 h day:12 h night cycle. The animals were fed with normal laboratory diet and allowed to drink water *ad libitum*. All the experimental protocols were approved by the Institutional Animal Ethics Committee and all the animal experiments were conducted according to the principles and guidelines of Committee for the Purpose of Control and Supervision of Experimentation on Animals, India.

Acute oral toxicity study

Acute oral toxicity study was performed as per organization for economic cooperation and development (OECD) guidelines 425 [13].

Experimental induction of diabetes

The animal model of type 2 diabetes mellitus (non-insulin-dependent diabetes mellitus [NIDDM]) was induced by single intraperitoneal injection of 60 mg/kg of STZ, and thereafter, 120 mg/kg NC was injected after 15 min. Hyperglycemia was confirmed by the elevated blood glucose levels determined at 72 h and then on day 7 of the injection. Only rats confirmed with permanent NIDDM were used in the antidiabetic study [14,15]. The diabetic rats were randomly divided into five groups each consisting of six rats and the study was continued up to 28 days.

Experimental design

Group I: Normal control rat group was fed basal diet throughout the experiment
Group II: STZ-NC-induced diabetic rats were treated with water
Group III: Diabetic rats treated with an oral dose of PHF 200 mg/kg b.w
Group IV: Diabetic rats treated with an oral dose of PHF 400 mg/kg b.w
Group V: Diabetic rats treated with an oral dose of glibenclamide 5 mg/kg b.w.

PHF and glibenclamide were suspended in 2% gum acacia separately. Each dose was orally administered through oral gavage according to the body weight, daily for 28 days. Body weights and blood glucose levels were measured using blood glucose test strips with ACCU CHEK glucometer at weekly on overnight fasted animals. At the end of the experimental period, the animals were fasted an overnight and blood was collected for various biochemical estimations. The animals were sacrificed by cervical decapitation. Organs pancreas was dissected out, immediately rinsed in ice-cold saline, and stored for further biochemical estimations [16,17].

Evaluation of biochemical parameters

Serum was analyzed for hemoglobin (Hb), *glycosylated* Hb (HbA_1C), total cholesterol (TC), triglycerides (TGs), high-density lipoprotein (HDL), aspartate amino transaminase (AST) or serum glutamate pyruvate transaminase (SGPT), alanine amino transaminase (ALT) or serum glutamate oxaloacetate transaminase (SGOT), and alkaline phosphatase (ALP) which were analyzed. Very low-density lipoprotein (VLDL) levels and low-density lipoprotein (LDL) were determined by following formula VLDL=TG/5; LDL=TC – (HDL + VLDL) [18-20].

Histopathology

The dissected pancreas was collected in 10% formalin solution and immediately processed by the paraffin technique. Sections of 5 µ thickness were cut and stained by hematoxylin and eosin for histological examination [21].

Statistical analysis

All data were expressed as mean±standard error mean. Results were analyzed by one-way analysis of variance (ANOVA), and significant differences were determined by Dunnett's *post hoc* test using GraphPad Instat version 3.06 computer software.

RESULTS

Effect of PHF on oral toxicity study

In acute oral toxicity studies, a single dose of 2000 mg/kg PHF did not indicate modification of behavior (Table 1). No mortality and signs of toxicity were recorded during 24 h and up to 14 days observation (Table 2). The oral LD_{50} value of PHF must be >2000 mg/kg. Two hundred and 400 mg/kg of the PHF were selected for animal studies.

Effect of PHF on body weight

STZ-NC produced significant loss in body weight as compared to normal animals during the study. Diabetic control continued to lose weight till the end of the study while PHF (both doses) and glibenclamide showed significant improvement ($p<0.01$, $p<0.05$) in body weight by 16.44%, 20.06%, and 21.16%, respectively, compared to diabetic control rat group (Table 3 and Fig. 1).

Effect of PHF on blood glucose level

The antihyperglycemic effect of repeated oral administration of PHF (both doses) on fasting blood glucose levels in STZ-NC diabetic control rat group are presented in Table 4. There was a significant increase in blood glucose level in diabetic control rat group when compared with normal controls due to injection of STZ-NC. The administration of PHF (both doses) and glibenclamide to STZ-NC treated diabetic control rat group caused significantly ($p<0.01$, $p<0.05$) decline the blood glucose level when compared to normal control rats, which was related to dose and duration of treatment. At the end of experiment (the 28th day) blood glucose level was 67.46%, 68.58% at the doses of 200 and 400 mg/kg of PHF respectively. The PHF at a dose 400 mg/kg showed higher ($p<0.01$) efficacy than 100mg/kg dose in diabetic control rat group.

Effect of PHF on HbA_1C and Hb levels

STZ-NC-induced diabetic rats showed a significantly ($p<0.01$) increase in the level of HbA_1C and reduction of Hb level when compared with normal control rat group. Treatment with PHF (both doses) and glibenclamide treated diabetic rat groups caused significantly ($p<0.01$) reduction in HbA_1C level, at the same time, increased in Hb level when compared with diabetic control rat group. The standard drug glibenclamide showed a marked reduction of the HbA_1C level and elevation of Hb level which was similar to the PHF treated with 400 mg/kg (Table 5 and Fig. 2).

Effect of PHF on lipid profile

The result of the serum lipid profile (triglycerides [TG], total cholesterol [TC], low-density lipoprotein cholesterol [LDLC], and high-density lipoprotein cholesterol [HDLC]) revealed that there was elevation in the levels of serum TG, TC, and LDLC compared to the normal control rat group (Table 6). However, the levels of serum TG, TC, and

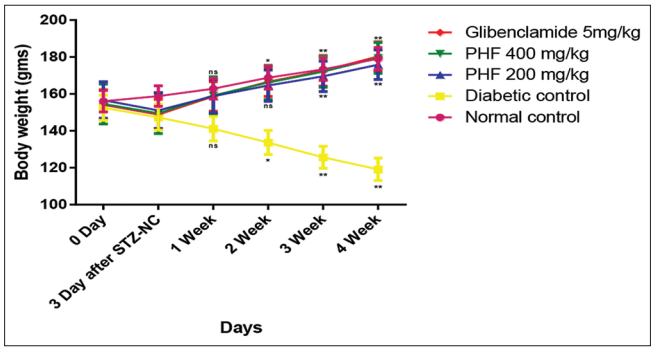

Figure 1: Effect of treatment with polyherbal formulation for 28 days on body weight of control and experimental groups of rats. The values are expressed as mean±SEM for groups of six animals each. Values are statistical significant at *p<0.05, **p<0.01, ns – not significant, when compared to the corresponding values of the normal control. *p<0.05, **p<0.01, ns – not significant, when compared to the corresponding values of the diabetic control

Table 1: Acute oral toxicity study of polyherbal formulation

Formulation/ parameters	Alertness	Stereotype	Irritability	Fearfulness	Touch response	Pain response	Spontaneous activity	Grooming	Restlessness	Righting reflex	Limb tone	Grip strength
PHF	N	N	-	-	N	N	N	-	-	N	N	N
Twitching	**Abdominal tone**	**Pinna reflex**	**Corneal reflex**	**Tremors**	**Convulsion**	**Writhing**	**Defecation**	**Urination**	**Heart rate**	**Respiration**	**Pupil size**	**Skin color**
N	N	N	N	-	-	N	N	N	N	N	N	N

(-): Not present, (N): Normal; (+): Present

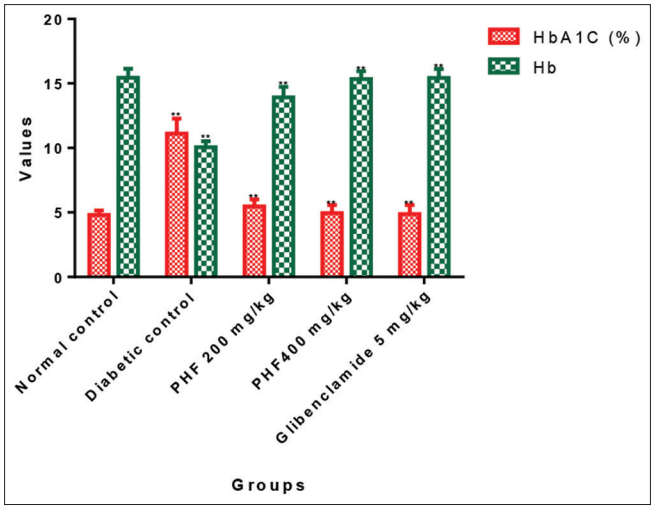

Figure 2: Effect of treatment with polyherbal formulation for 28 days on HbA_1C and total Hb of control and experimental groups of rats. The values are expressed as mean±SEM for groups of six animals each. Values are statistical significant at **p<0.01 when compared to the corresponding values of the normal control. **p<0.01 when compared to the corresponding values of the diabetic control

LDLC were significantly (p<0.01) reduced in groups treated with PHF (both doses) and glibenclamide treated diabetic control rat group. Furthermore, plasma HDLC was reduced in diabetic control rat group when compared with the normal control rat group. However, the level of HDLC was significantly (p<0.05) elevated in PHF (both doses) and glibenclamide treated diabetic control rat groups when compared with diabetic control rat group.

Effect of PHF on serum hepatic marker enzymes profile

The result of the serum hepatic marker enzymes such as AST, ALT, and ALP levels was significantly (p<0.01) increased in the diabetic control rat group compared with the normal control rat group. In treatment with PHF (both doses) and glibenclamide treated diabetic control rat groups, there was a significant (p<0.01) reduction of AST, ALT, and ALP, respectively, as compared with the diabetic control rat group (Table 7). The maximum lowering of hepatic enzymes such as AST, ALT, and ALP in STZ-NC-induced diabetic rats was appeared in PHF 400 mg/kg dose than 200 mg/kg.

Effect of PHF on histopathological study

Histopathology of the pancreas in normal control rat group showed normal pancreatic parenchyma cells and islet cell (Fig. 3a). STZ-NC-induced diabetic rats result in degenerative changed in the islets of Langerhans of the pancreas, such as moderate hyperplasia of islet cells, severe congestion in the pancreatic parenchyma, and mild infiltration of inflammatory cells (Fig. 3b). Treatment with PHF and glibenclamide restored the activity of the islets of Langerhans (Fig. 3c-e).

DISCUSSION

The present investigation discusses the antidiabetic and antihyperlipidemic potential of the PHF in STZ-NC-induced diabetic rats. The use of STZ to induce DM in rat models is widely accepted and STZ-induced diabetes is reported to resemble human DM [22] which is characterized by glycosuria, hyperglycemia, polyphagia, polydipsia, and body weight loss when compared with normal rodents [18]. In our study, we used STZ-NC for induction of type 2 DM. STZ causes selective cytotoxicity effect on pancreatic beta cells and thus it affects the endogenous insulin release and as a result increases blood glucose level [23]. Due to an antioxidant property of NC, it exerts protective effect on the cytotoxic action of STZ by scavenging free radicals and causes only minor damage to pancreatic β-cell mass producing type 2 DM [14].

Table 2: LD_{50} determination of polyherbal formulation

Group	Dose (mg/kg)	Dose difference (a)	Dead	Mean mortality (b)	(a×b)	Σ (a×b)	LD50=dose (max)-(Σ (a×b)/ No. of animals)
1	175	-	00	-	-	0	2000mg/kg
2	550	375	00	-	-		
3	2000	1450	00	-	-		

Table 3: Effect of treatment with polyherbal formulation for 28 days on body weight of control and experimental groups of rats

Group	Treatment	Dose (mg/kg)	Body weight (g)					
			Treatment days					
			0 day	3 days after STZ	1st week	2nd week	3rd week	4th week
I	Normal control	-----	156.00±5.82	158.83±5.55	162.83±5.63	168.83±6.19	173.33±6.05	179.00±6.11
II	Diabetic control	------	152.50±6.78	147.33±6.93	141.16±6.59^{ns}	133.66±6.51*	125.66±5.99**	119.16±6.05**
III	PHF	200	156.66±9.85	151.00±9.74	158.83±9.16^{ns}	164.50±8.43^{ns}	169.50±8.18**	175.83±8.04**
IV	PHF	400	154.50±10.83	149.50±10.92	159.16±10.11^{ns}	166.16±9.32*	172.00±8.34**	179.50±8.38**
V	Glibenclamide	5	154.16±8.14	148.83±8.22	158.66±8.00^{ns}	166.50±7.84*	172.50±8.28**	180.33±7.91**

The values are expressed as mean±SEM for groups of six animals each. Values are statistical significant at *p<0.05, **p<0.01, ns – not significant, when compared to the corresponding values of the normal control. *p<0.05, **p<0.01, ns – not significant, when compared to the corresponding values of the diabetic control

Table 4: Effect of treatment with polyherbal formulation for 28 days on fasting blood glucose level of control and experimental groups of rats

Group	Treatment	Dose (mg/kg)	Fasting blood glucose level (mg/dL)					
			Treatment days					
			0 day	3 days after STZ	1st week	2nd week	3rd week	4th week
I	Normal control	-----	88.83±7.38	91.66±8.22	88.66±8.13	86.16±5.61	87.50±6.91	84.66±4.44
II	Diabetic control	------	91.66±5.77	331.50±48.03	338.33±40.86**	346.83±44.72**	357.33±36.06**	360.16±28.62**
III	PHF	200	89.50±8.30	326.83±50.70	280.33±36.88^{ns}	216.16±25.18*	127.33±16.01**	106.33±10.81**
IV	PHF	400	86.83±7.02	312.00±32.19	258.66±34.50^{ns}	185.33±20.28**	110.66±15.39**	98.00±1246**
V	Glibenclamide	5	90.33±6.20	334.33±29.48	240.66±36.79^{ns}	172.16±21.37**	108.50±±14.83**	97.16±13.08**

The values are expressed as mean±SEM for groups of six animals each. Values are statistical significant at **p<0.01 when compared to the corresponding values of the normal control. *p<0.05, **p<0.01, ns – not significant, when compared to the corresponding values of the diabetic control

Table 5: Effect of treatment with polyherbal formulation for 28 days on glycosylated hemoglobin and total hemoglobin of control and experimental groups of rats

Group	Treatment	Dose (mg/kg)	HbA_1C (%)	Hb (gm/dL)
I	Normal control	-----	4.81±0.34	15.45±0.70
II	Diabetic control	------	11.11±1.17**	10.06±0.47**
III	PHF	200	5.47±0.54**	13.93±0.81**
IV	PHF	400	4.95±0.63**	15.34±0.62**
V	Glibenclamide	5	4.87±0.70**	15.42±0.71**

The values are expressed as mean±SEM for groups of six animals each. Values are statistical significant at **p<0.01 when compared to the corresponding values of the normal control. **p<0.01 when compared to the corresponding values of the diabetic control

Oral administration of PHF to the diabetic rats showed significant reduction of blood glucose levels in a dose-dependent manner and also at 400 mg/kg dose level of PHF exhibited the parallel effect to that of glibenclamide (Table 4). Glibenclamide is a standard antihyperglycemic drug that stimulates insulin secretion from β-cell of islets of Langerhans. From the results of the present study, it may be suggested that the mechanism of action of PHF may be similar to glibenclamide action [24].

In the present investigation, it was observed that the body weight of STZ-NC-induced diabetic control rats group gradually decreased when compared to the normal control rats group indicating the impaired glucose metabolism. Induction of diabetes by STZ leads to loss of body weight due to increased muscle wasting and loss of tissue proteins [25]. Treatment with PHF, gain in body weight was recognized in diabetic control rats group, and the results were comparable with that of the standard drug, glibenclamide (Fig. 1).

The HbA_1C is an essential biochemical parameter in diabetes, which helps to establish the degree of protein glycation during diabetes [26]. In STZ-NC-induced diabetic rats, significantly decreased Hb and increased HbA_1C levels were noticed than control rats. Treatment with PHF and glibenclamide showed downgrading of HbA1C and upgrading of Hb levels was observed. This result might be due to blood glucose lowering effect of PHF probably through reversal of insulin resistance or rising insulin secretion by regeneration of pancreatic β-cells [24] (Fig.2).

Hypercholesterolemia and hypertriglyceridemia are most essential factors of diabetic state involved in the progression of atherosclerosis

Table 6: Effect of treatment with polyherbal formulation for 28 days on total cholesterol, triglycerides, HDL, LDL, and VLDL of control and experimental groups of rats

Group	Treatment	Dose (mg/kg)	Total cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
I	Normal control	-----	128.83±7.09	83.50±5.75	55.00±5.50	57.13±11.39	16.70±1.15
II	Diabetic control	------	241.33±15.95**	210.16±10.46**	28.66±3.16**	170.63±15.00**	42.03±2.09**
III	PHF	200	149.00±12.55**	101.50±8.66**	48.83±7.39*	79.86±13.95**	20.30±1.73**
IV	PHF	400	130.83±9.57**	89.50±9.30**	54.00±5.11*	76.83±9.80**	17.90±1.86**
V	Glibenclamide	5	129.50±7.27**	84.16±5.10**	55.00±5.07**	57.66±3.85**	16.83±1.02**

The values are expressed as mean±SEM for groups of six animals each. Values are statistical significant at **p<0.01 when compared to the corresponding values of the normal control. *p<0.05, **p<0.01 when compared to the corresponding values of the diabetic control

Table 7: Effect of treatment with polyherbal formulation for 28 days on AST, ALT, and ALP of control and experimental groups of rats

Group	Treatment	Dose (mg/kg)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)
I	Normal control	-----	34.16±3.96	47.50±9.26	100.16±7.08
II	Diabetic control	------	147.00±11.05**	157.50±10.25**	250.50±23.38**
III	PHF	200	45.33±11.63**	52.83±9.90**	111.50±14.39**
IV	PHF	400	39.33±12.09**	49.50±10.85**	105.83±10.92**
V	Glibenclamide	5	37.83±11.54**	48.66±10.38**	102.33±8.01**

The values are expressed as mean±SEM for groups of six animals each. Values are statistical significant at **p<0.01 when compared to the corresponding values of the normal control. **p<0.01 when compared to the corresponding values of the diabetic control

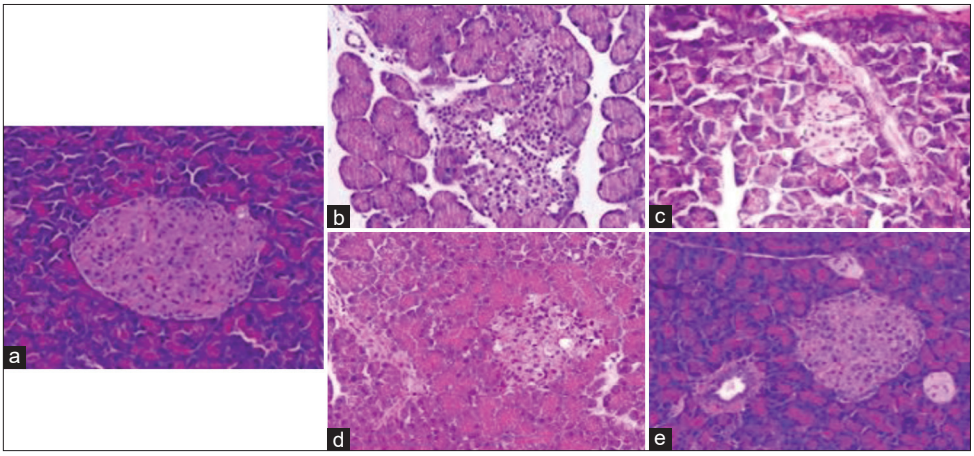

Figure 3: Effect of treatment with polyherbal formulation for 28 days on cellular damage in pancreas of control and experimental groups of rats. a=Normal control (normal acini with islets of *β*-cells), b=Diabetic control (atrophic acini and reduction of *β*-cell size; shows degreased islets), c=Glibenclamide (markedly normal regenerated and preserved cells; with marked proliferated and regenerated *β*-cells), d=PHF 200 mg/kg (shows hyperplastic condition; with marked increased proliferation of (hyperplastic) *β*-cells), e=PHF 400 mg/kg (shows pancreas with acini and normal islets. *β*-cell regeneration and markedly normal regenerated and preserved cells; with marked proliferated and regenerated β-cells)

and coronary heart disease which are the secondary complications of diabetes [27]. Our results specify that treatment with PHF and glibenclamide administered to diabetic control rats group reduced TC, LDL cholesterol, VLDL cholesterol, and lowed serum levels of HDL cholesterol. Thus, PHF at the dose of 400 mg/kg could have a potential to reduce long-term cardiovascular complications in diabetic conditions.

In STZ-NC-induced diabetic rats, the liver was necrotized. An increase in the activities of AST, ALT, and ALP in plasma might be mostly due to the leakage of these enzymes from the liver cytosol into the blood stream which gives an indication of the hepatotoxic effect of STZ [28]. Hence, our study was also focused to know the protective activity of PHF against hepatic and renal damage caused by diabetes. Treatment of the diabetic control rat group with PHF and glibenclamide reduced the activity of these enzymes when compared to the diabetic control rat group and consequently alleviated liver damage caused by STZ-NC-induced diabetes rats. Significant reductions in the activities of these enzymes in PHF-treated diabetic rats indicated the hepatoprotective role in preventing diabetic complications.

Histopathology of the pancreas in normal control rat group showed normal pancreatic parenchyma cells and islet cell (Fig. 3a). STZ-NC-induced diabetic rats result in degenerative changed in the islets of Langerhans of the pancreas (Fig. 3b) due to moderate hyperplasia of islet cells with severe congestion in the pancreatic parenchyma and mild infiltration of inflammatory cells, nitric oxide production, and free radical generation, leading to a total lack or deprived insulin production and chronic hyperglycemia [29]. The islet is considerably reduced and shrunken, there is the destruction of some β-cells with central hyalinization with pyknotic nuclei and the number of cells is lower [30]. Treatment with PHF and glibenclamide restored the activity of the islets of Langerhans (Fig. 3c-e).

CONCLUSION

The novel polyherbal preparation supplemented in the present study exhibited antidiabetic effect parallel effect to that of glibenclamide and reversal of deteriorated liver marker enzymes and lipid profile of type 2 diabetic rats. Clinical trials employing such novel herbal preparations would be of great interest and beneficial to disease management and human welfare at large.

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AUTHORS' CONTRIBUTIONS

All authors were contributed to the idea, design the study, draft the article, review the data, and edit the article.

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