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Research Article

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Silibinin ameliorates hyperglycaemia, hyperlipidemia and prevent oxidative stress in streptozotocin induced diabetes in Sprague Dawley rats

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ABSTRACT

The global prevalence of diabetes is increasing at an alarming rate. The serious side effect of current pharmacotherapy limits its use in the general population, with increased dependence on herbal and polyherbal formulations. Thus the present study was undertaken to evaluate the anti-diabetic effect of silibinin, a bioflavonoid in streptozotocin induced diabetes in rats. Sprague Dawley rats (200-250 g) were randomly divided into six groups (n=6) and were treated orally for 28 days. Group I received 1% ($^{W}/_{V}$) CMC and was considered as normal control. Diabetic non-treated rats received STZ (55 mg/kg) i.p. Group III, IV and V received silibinin at dose of 20, 40 and 80 mg/kg respectively along with STZ. Group VI received standard treatment of glibenclamide. At the end of treatment the effect on body weight, blood glucose, HbA1c, insulin, lipid profile levels and glucose homeostasis indices were determined. Histopathological changes and oxidative stress parameters in the pancreas were investigated. Diabetic rats treated with silibinin at a dose of 40 mg/kg and 80mg/kg, significantly restored body weight, blood glucose, HbA1c, insulin, lipid profile levels and glucose homeostasis indices as compared to non-treated diabetic rats. Significant effect on the restoration of antioxidant defence such as decreased MDA concentration and increased GSH concentration as well as increased activities of SOD and CAT was also observed in diabetic rats treated with silibinin (40 and 80 mg/kg). Further a high dose of silibinin treated diabetic rats restore the normal histological structure of the pancreas. Thus it can be concluded that silibinin possesses a potent anti-diabetic activity and prevented oxidative stress-induced damage to the pancreas in diabetes.

Key words: Diabetes, Silibinin, Bioflavonoids, Streptozotocin, HbA1C

INTRODUCTION

Diabetes is a major lifestyle disorder characterised by impaired metabolism of carbohydrate, fat and protein. (1) Diabetes can be defined as a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. (2) According to the National Health and Nutrition Examination Survey, U.S. (NHANES 2005-2006) the prevalence of diabetes or pre-diabetes in adult American population accounts for more than 40 per cent, along with a prominently increased prevalence in Indian population which is assumed to reach 80 million by 2030. (3, 4) The current pharmacotherapy has several limitations owing to the associated side effects including hypoglycaemia with prolong use of sulphonylureas, weight loss and nausea associated with biguanides treatment, as well as cardiovascular complications associated with thiazolidinediones. (5) This generates an immediate need to consider herbal treatment for the effective management of diabetes along with optimum changes in the life style.

Herbal treatments are gaining major lime-light due to lesser side effects and cost effectiveness of the treatment. (6) Bioflavonoids comprise a group of phenolic secondary plant metabolites abundantly found in nature and have well

categorized structures as well as defined structure function-relationships. Bio-flavonoids are well-known for their multi-directional biological activities including anti-diabetic efficacy. (7) Silibinin (silybin), a natural occurring flavnone, is the active constituent of silymarin. Silibinin constitutes to about 50-70% of total constituents of silymarin. Milk thistle is the major source of Silibinin. It has been reported forvarious pharmacological actions like anti-oxidant, anti-inflammatory, adipogenesis, hepatoprotective, antibacterial, anticancer and protective effect on cardiovascular and central nervous system. (8- 10)

Streptozotocin, synthesized by *Streptomycete sachromogenes*is was used to induce both insulin-dependent and non-insulin-dependent diabetes mellitus owing to its cytotoxic effect on pancreatic cells (11). It is the most widely used animal model to evaluate the anti-diabetic effect of any synthetic or herbal moiety. Thus the present study was undertaken to evaluate the anti-diabetic activity of silibinin in streptozotocin induced diabetes model in rats.

MATERIALS AND METHODS

Drugs and Chemicals

Streptozotocin was purchased from Enzo Life Sciences (UK), Glibenclamide was obtained from Aventis Pharma (Mumbai, India) and silibinin was procured from Sigma Aldrich (Mumbai, India). The commercial diagnostic kits were obtained from Biolab (Mumbai, India), Crest systems (Goa, India) and Robonik (Navi Mumbai, India). All required chemicals were of laboratory grade obtained from local suppliers of Pune.

Experimental animals

Sprague Dawley rats of either sex (200-250 gm) were procured from National Institute of Biosciences, Pune. Rats were placed separately in polypropylene cages randomly with paddy husk as bedding. The animals were maintained under standard laboratory conditions at temperature 23 ± 2ºC with relative humidity 55 ± 10 % under 12 h light and 12 h dark cycle throughout the experiment. Animals had free access to water and standard laboratory feed ad libitum. All the experimental procedures and protocols used in this study were reviewed and approved (SCOP/IAEC/2011-12/33) by the Institutional Animal Ethics Committee of Sinhgad College of Pharmacy, Pune, constituted under Committee for Purpose of Control and Supervision of Experiments on Animals (CPCSEA) by Ministry of Environment and Forests, Government of India, New Delhi, India.

Experimental procedure

Diabetes was induced in overnight fasted rats by a single intraperitoneal injection of freshly prepared streptozotocin (STZ) at a dose of 55 mg/kg. STZ was dissolved in an ice cold citrate buffer (0.1M, pH 4.5). The rats were allowed to drink 5% glucose solution overnight after injection, to overcome streptozotocin-induced hypoglycemia. 48h after the STZ injection the blood glucose levels was estimated using commercial glucometer in an overnight fasted rats and the rats exhibiting fasting glucose levels more than 250 mg/dl were selected and used in this study. Ten days after the induction of diabetes, diabetic and age matched non diabetic rats were randomly assigned into six experimental groups (n=6) and were treated orally for 28 days.

Group I - Control rats- received 1% ($^{W}/_{V}$) CMC vehicle only.
Group II - Diabetic control rats- received 1% ($^{W}/_{V}$) CMC vehicle only.
Group III, IV and V - Diabetic rats treated with silibinin at 20, 40 & 80 mg/kg body weight respectively.
Group V- Diabetic rats treated with a standard drug, glibenclamide at 4 mg/kg body weight.

Body weight

The body weight of all animals was recorded on Day 1 (before dosing) and day 29th (24h after the last dose) using electronic weighing balance (Contech Instruments, India).

Biochemical estimations

At the end of treatment period (day 29), overnight fasted rats were weighed and sacrificed by cervical dislocation and blood was collected. Serum was separated by centrifugation at 3000 for 15 min. for the estimation of various biochemical parameters and hormone analyses.

Fasting blood glucose (FBG) levels was measured weekly *viz*., 0, 7th, 14th, 21st and 28th day (24h after the previous dose). The glucose levels were estimated by using commercial glucometer (Contour TS Bayer Healthcare, India).

Serum insulin levels were estimated using an enzyme-linked immunosorbent assay (ELISA). Glycosylated haemoglobin (HbA1c) was determined in whole blood by ion exchange resin method. (12) Total cholesterol (TC) (13), high density lipoprotein (HDL) (13), triglyceride (TG) (14) in separated serum was estimated by Chemstar

Biochemical Semi Autoanalyserusing commercial diagnostic kits. Low density lipoprotein (LDL) and very low density lipoprotein (VLDL) levels were calculated according to Friedwald's formula (15):
LDL in mg % = Total cholesterol − HDL-C – Triglycerides/5
VLDL in mg % = Triglycerides/5

HOMA indices
Insulin resistance index (HOMA-IR) and β-cell function (HOMA-β cell function) were calculated according to the Homeostatic model assessment (HOMA) (16)

Estimation of oxidative stress
At the end of experiment, rats were sacrificed and pancreas were excised, washed and weighed. Pancreas was homogenized in chilled 50mM phosphate buffer and centrifuged at 10000 rpm for 15 min at 4°C. The supernatant was used to determine the concentration of malondialdehyde (MDA) (17), reduced glutathione (GSH) (18), superoxide dismutase (SOD) (19) and Catalase (CAT) (20) activity. Protein concentrations of homogenates were also determined. (21)

Histopathological examination of Pancreas
At the end of experiment rats were sacrificed, pancreas were immediately harvested and fixed overnight in 10% formalin solution. The sections were embedded in paraffin and stained with Haematoxylin-Eosin (HE). HE stained sections were observed under light microscope (100 x) for morphological alterations.

Statistical analysis
All the data were expressed as the mean ± S.E.M (n=6). Data were subjected to one-way analysis of variance (ANOVA) followed by the Tukey's multiple comparison test. $P<0.05$ was considered as minimum level of significance. Data was analysed using computerized GraphPadPrism version 5.0.

RESULTS

Body weight
The final body weight of non treated diabetic rats was significantly reduced as compared to the control ($P<0.001$). Diabetic rats treated with silibinin 40 and 80 mg/kg showed significant gain in body weight ($P<0.001$ and $P<0.001$; respectively) as compared to non treated diabetic rats. However, no significant change in body weight gain was observed with silibinin treatment at dose of 20 mg/kg. Further, diabetic rats treated with glibenclamide (4 mg/kg) produced significant restoration in the body weight ($P<0.001$). (Table 1)

Table 1: Effect of silibinin on body weight in streptozotocin induced diabetic rats

Treatment (mg/kg)	Body weight (g)	
	Initial	Final
Control	210.72± 5.22	238.44± 3.71
Diabetic	198.51± 4.28	173.50± 2.15[a]
Silibinin (20)	195.57± 4.25	208.24± 4.09
Silibinin (40)	197.17± 3.51	221.71± 5.03[#]
Silibinin (80)	198.45± 3.45	224.28± 3.35[#]
Glibencalmide (4)	201.75± 5.16	235.45± 4.66[#]

[a]P< 0.001 Vs Control. [#] P< 0.001Vs Diabetic

Biochemical estimations
Blood glucose levels
Figure 1 shows the effect of silibinin or glibenclamide treatment on diabetic rats fasting blood glucose levels (FBG). Our finding indicates, non-treated diabetic rats, fasting blood glucose levels was significantly higher than control rats at all the determined time intervals within 28 days. Silibinin treated diabetic rats at a dose of 20 mg/kg, produced significant decline in the blood glucose levels at day 7 ($P<0.05$), and it was further decreased at day 14^{th} ($P<0.05$), 21^{st} ($P<0.001$) and 28^{th} ($P<0.001$). However, silibinin treatment at a dose of 40 and 80 mg/kg showed highly significant effect at day 7 ($P<0.001$ and $P<0.001$; respectively) and it was further decreased at day 14^{th} ($P<0.001$ and $P<0.001$; respectively), 21^{st} ($P<0.001$ and $P<0.001$; respectively) and lowest on day 28^{th} ($P<0.001$ and $P<0.001$; respectively). Further, glibenclamide treated diabetic rats also showed significant decrease in the fasting blood glucose levels at all the determined time intervals.

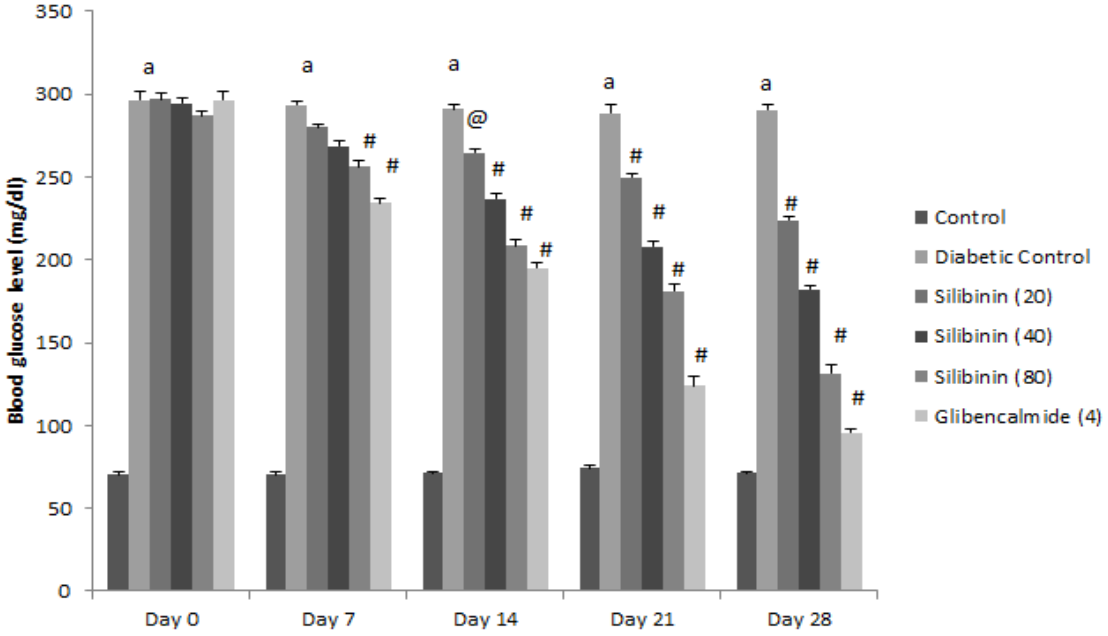

Figure 1: Effect of silibinin treatment on fasting blood glucose levels in streptozotocin induced diabetic rats
*[a]P< 0.001 Vs Control. [@] P< 0.05, * P< 0.01, [#] P< 0.001Vs Diabetic.*

Glycosylated Hemoglobin

Figure 2 shows a significant increase in glycosylated hemoglobin levels in the diabetic rats as compared to control rats (P<0.001). Diabetic rats treated with silibinin at a dose of 40 and 80 mg/kg/day showed significantly lower glycosylated hemoglobin (P<0.01 and P<0.001; respectively) as compared to diabetic rats. However, no significant effect was noted on glycosylated hemoglobin in diabetic rats treated silibinin 20 mg/kg. Glibenclamide treated diabetic rats showed significantly decreased glycosylated hemoglobin levels (P<0.001).

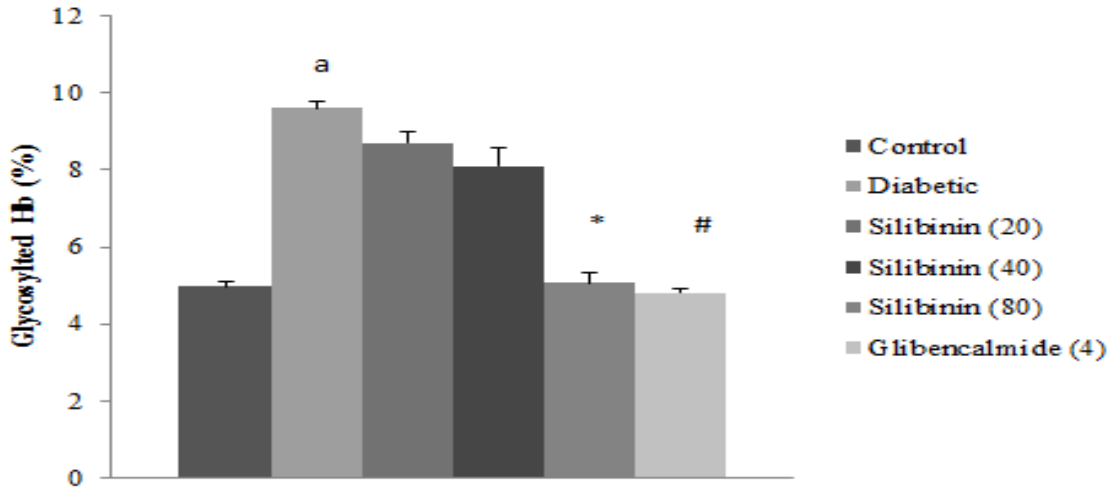

Figure 2: Effect of silibinin treatment on glycosylated haemoglobin in streptozotocin induced diabetic rats
*[a]P< 0.001 Vs Control. * P< 0.01, [#] P< 0.001Vs Diabetic.*

Lipid Profile

In the present investigation, we observed significantly increased levels of serum total cholesterol (P<0.001), triglyceride (P<0.001), LDL (P<0.001) and VLDL (P<0.001) as well as decreased HDL (P<0.001) in non-treated diabetic rats as compared to control rats. 28 days treatment of silibinin at a dose of 40 and 80 mg/kg in diabetic rats produced a significant decrease in the elevated levels of serum total cholesterol (P<0.001 and P<0.001; respectively), triglyceride (P<0.001 and P<0.001; respectively), LDL (P<0.001 and P<0.001; respectively) and VLDL (P<0.01 and P<0.001; respectively) ascompared to non-treated diabetic rats. However, high HDL level was observed only with80 mg/kg silibinin treated diabetic rats. Further significant decrease in total cholesterol and LDL levels was observed in silibinin (20 mg/kg) treated diabetic rats. Glibenclamide treatment (4 mg/kg) was also produced the significantly restore the altered lipid profile. (Table 2)

Table 2: Effect of Silibinin on lipid profile in streptozotocin diabetic rats

Groups	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Control	66.00 ± 1.65	46.16 ± 2.54	25.83 ± 1.07	28.08 ± 0.96	8.33 ± 0.49
Diabetic	144.54 ± 3.69[a]	98.00 ± 4.39[a]	16.33 ± 1.28[a]	107.00 ± 1.78[a]	20.50 ± 1.17[a]
Silibinin (20)	121.33 ± 7.32[@]	85.00 ± 3.04	16.83 ± 1.19	93.17 ± 4.12*	17.00 ± 1.18
Silibinin (40)	104.47 ± 5.60[#]	72.50 ± 5.29[#]	21.17 ± 1.19	67.17 ± 2.22[#]	14.50 ± 0.92[*]
Silibinin (80)	77.33 ±3.80[#]	60.33 ± 3.10[#]	23.67 ± 1.22*	42.83 ± 1.40[#]	11.50 ± 0.84[#]
Glibencalmide (4)	83.66 ± 4.98[#]	63.50 ± 4.63[#]	22.33 ± 0.76[@]	46.67 ± 1.66[@]	12.00 ± 0.86[#]

*[a]P< 0.001 Vs Control. [@] P< 0.05, * P< 0.01, [#] P< 0.001 Vs Diabetic*

Insulin Levels

Figure 3 shows the effect of silibinin or glibenclamide treatment in diabetic rats, serum insulin levels. We have noted significantly lower serum insulin levels in non treated diabetic rats as compared to control rats (P<0.001). Diabetic rats treated with silibinin for 28 days at a dose of 40 and 80 mg/kg significantly restored the serum insulin levels. However silibinin at a dose of 20 mg/kg could not produce significant rise in the serum insulin levels. Higher serum insulin level was also noted in glibenclamide treated diabetic rats as compared to diabetic rats.

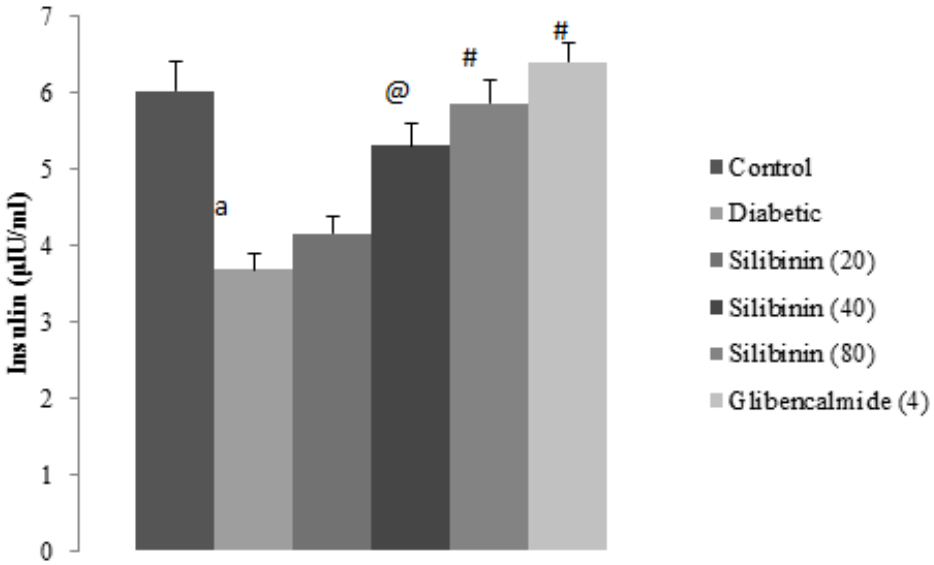

Figure 3: Effect of silibinin on insulin levels in streptozotocin induced diabetic rats

*[a]P< 0.001 Vs Control. [@] P< 0.05, * P< 0.01, [#] P< 0.001Vs Diabetic*

HOMA-IR and HOMA-β cell function

A significantly higher HOMA-IR index (P<0.001) and lower HOMA-β cell functioning index (P<0.001) was observed in diabetic rats as compared to control rats. Diabetic rats treated with silibinin at a dose of 80 mg/kg resulted in significant decrease in the HOMA-IR index (P<0.01) as well as higher HOMA-β cell functioning index (P< 0.001) as compared to the non-treated diabetic rats. Glibenclamide treatment was also produced significant effect onhigher HOMA-IR index (P<0.001) and lower HOMA β-cell functioning index (P<0.001). However treatment with silibinin at a dose of 20 mg/kg and 40 mg/kg could not produced statistically significant effect on HOMA indices. (Table 3)

Table3: Effect of silibinin on *HOMA-IR and HOMA-β cell function* in streptozotocin induced diabetic rats

Groups	HOMA-IR	HOMA-β cell functioning
Control	1.06 ± 0.07	119.11 ± 9.28
Diabetic	2.60 ± 0.15[a]	5.94 ± 0.39[a]
Silibinin (20)	2.30 ± 0.14	9.31 ± 0.39
Silibinin (40)	2.31 ± 0.14	15.51 ± 0.87
Silibinin (80)	1.70 ± 0.08*	31.41 ± 2.33[#]
Glibencalmide (4)	1.51 ± 0.07[#]	71.40 ± 3.76[#]

*Mean ±S.E.M (n=6). [a]P< 0.001 **Vs** Control. [@] P< 0.05, * P< 0.01, [#] P< 0.001**Vs** Diabetic*

Oxidative Stress

Our finding indicates, significantly higher pancreatic MDA concentration (P<0.001) and lower GSH levels in diabetic rats as compared to control rats. Silibinin treated diabetic rats at all dose levels *i.e.*, 20, 40 and 80 mg/kg

(P<0.01, P<0.001 and P<0.001, respectively) significantly decrease the concentration of MDA. However increased GSH levels was noted in diabetic rats treated with silibinin at a dose of 40 and 80 mg/kg ((P<0.05 and P<0.001, respectively) as compared to non treated diabetic rats. Glibenclamide treatment also produced significant effect on altered MDA and GSH levels. Further, we have observed significantly decreased activity of SOD and CAT in non treated diabetic rats (P<0.001 and P<0.01, respectively) as compared to control rats. Silibinin (40 and 80 mg/kg) treated diabetic rats observed significantly higher SOD and CAT activity as compared to diabetic rats. Glibenclamide administration produced significant effect on oxidative stress parameters. However, diabetic rats treated with silibinin at dose of 20 mg/kg could not produce significant effect on GSH levels as well as SOD and CAT activities. (Table 4)

Table 4: Effect of silibinin on oxidative stress parameters in streptozotocin induced diabetic rats

Groups	MDA (nmol/mg of protein)	GSH (ng/mg of protein)	SOD (U/mg of protein)	CAT (U/mg of protein)
Control	7.39± 0.24	42.17±1.30	32.67 ± 1.43	21.08 ±1.75
Diabetic	12.53±0.62[a]	28.67±1.62[a]	23.50±1.23[a]	13.33± 1.02[b]
Silibinin (20)	9.65± 0.59*	33.50± 1.62	23.50± 1.56	16.17± 0.86
Silibinin (40)	7.92±0.43[#]	37.17± 1.92[*]	30.03± 0.92*	18.50± 1.92[*]
Silibinin (80)	6.96±0.45[#]	40.17±1.13[#]	32.17±1.01[#]	20.83± 1.02[*]
Glibencalmide (4)	9.54±0.54[*]	38.33±1.47[*]	31.50±0.95[#]	20.50± 0.84[*]

*[a]P< 0.001, [b]P< 0.01 Vs Control. [@]P< 0.05, * P< 0.01, [#]P< 0.001Vs Diabetic.*

Histopathological examination of pancreas

Normal appearance of Islets of Langerhans and acinar cells were seen in control rats. Destruction of the Islets, blood-filled interlobular duct and disorganized acinar cells were observed in diabetic rats. Milder histopathological alterations were seen in silibinin (80 mg/kg)and glibenclamide (4 mg/kg) treatments in diabetic rats. (Figure 4)

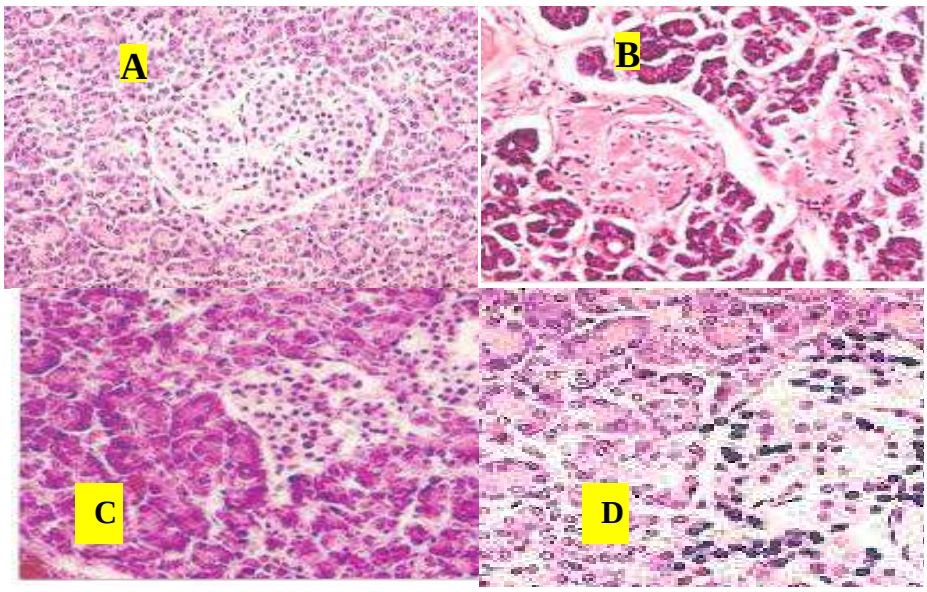

Figure 4: Histological section of pancreas stained with H&E A) Normal rats, B) Diabetic rats, C) Silibinin (80 mg/kg), D) Glibenclamide (4 mg/kg)

DISCUSSION

The effective management of diabetes and other associated diseases focuses on appropriate changes in the lifestyle, considering that sedentary habits, lack of exercise and improper diet are the major contributors towards the development of the same. Even though lifestyle modifications are considered to manage diabetes, pharmacotherapy is still necessary to achieve required glucose concentrations. (22, 23) Herbal and polyherbal formulations are gaining importance in the management of the various diseases and disorders, owing to lesser side effects as compared to the current pharmacotherapy. (24)

Flavonoids are natural products which are consumed in large amounts in the daily diet. Most recent researchers have focused on the health aspects of various categories of flavonoids for humans. (25, 26)Silibinin (silybin), a natural occurring flavnone, is the active constituent of silymarin. It occurs as a diastereoisomeric blend of Silibinin A and

Silibinin B which contributes to the numerous pharmacological activities.(27, 28)Thus, the present study was undertaken to evaluate the anti-diabetic effect of silibinin in streptozotocin induced diabetes in experimental rats.

Diabetes mellitus is a metabolic disorder, occurring due to either insulin deficiency or absolute absence of insulin in the body leading to reduced ability of cells to utilise glucose. Thus, a considerable shift in substrate utilization for energy maintenance causes a dependence on fat and protein sources. Further breakdown of fats and proteins contributes to body weight loss in a diabetic person. Further an elevated rate of glycogenolysis and possibly gluconeogenesis leads to an overall increase in glucose production from a non-carbohydrate source, thus contributing towards depletion of fats and protein stores. (29)In the present study a significant decrease in body weight was observed in non-treated diabetic rat as compared to control. Silibinin is reported to inhibit gluconeogenesis and formation of glucose from non-carbohydrate source by down-regulating associated genes such as Forkhead box O1, phosphoenolpyruvatecarboxykinase and glucose-6-phosphatase. (30) Thus it maintains body weight by restoring the fats and protein source and produces a significant increase in the body weight.

Streptozotocin induces cytotoxicity in the pancreatic cells and thus is considered as a potent moiety to induce diabetes and prolonged hyperglycaemia in rats. (11) A Significant increase in fasting blood glucose was reported in non-treated diabetic rat which isin agreement with previous reports. (31). 28 days of silibinin treatment maintained the target blood glucose concentration owing to the inhibitory effect of silibinin on both hepatic glucose-6-phosphatase and gluconeogenesis. (32) Glibenclamide being widely used for effective management of diabetes also significantly reduced the blood glucose levels.

Glycosylated haemoglobin (HbA1C) is an important biomarker used for surveillance of glycemic control in diabetes. Moreover, it is used to evaluate the risk of developing micro- and macrovascular complications and to assess the cumulative damage due to hyperglycemia and glycooxidation in diabetes. (33, 34) Aldehyde group of glucosemoiety combines non- enzymatically with the amino-terminal valine of the β -chain of haemoglobin to form Glycatedhemoglobin (GHb). (35) Significantly increased levels of in HbA1C was observed in non-treated diabetic rats owing to prolonged hyperglycemia as compared to control. Silibinin at dose of 40mg/kg and 80mg/kg produced a significantly lower HbA1C level. Glibenclamide treatment also significantly lowered glycosylated haemoglobin level. (36)

Uncontrolled hyperglycaemia majorly affects the lipid metabolism. (37) In the present investigations significant increase in serum levels of total cholesterol, triglyceride, LDL and VLDL as well as decreased HDL levels was observed in non-treated diabetic rats which may be due to altered metabolism of triglyceride rich lipoproteins and insulin resistance which contributes to the development of diabetic dyslipidaemia. (38) In comparison with non-treated diabetic rats, silibinin treatment (40mg/kg and 80mg/kg) significantly decreased the serum levels of total cholesterol, triglyceride, LDL and VLDL while increased serum HDL levels. Silibinin is reported to induce thermoregulation improving metabolic homeostasis by modulates adipocytes lipid metabolism, inducing thermogenesis and promoting a brown remodeling of white adipose tissue. (39) Glibenclamide treatment also produced a significant alteration in the lipid profile in comparison with diabetic non-treated rats.(40)

Hyperinsulinemia, insulin resistance, and impairment of glucose-stimulated insulin release are intertwined biologically. (41) Lack of insulin availability or resistance leads to impaired uptake of glucose and contributes to prolonged hyperglycemia. Further, basal hyperinsulinemia perpetuates insulin resistance by a wide range of mechanisms. Literature suggests that silibinin inhibits IRS-1/PI3K/Akt pathway and thus improves insulin resistance in mouse C2C12 myoblast cell line (42) The present study suggests that silibinin (40mg/kg and 80 mg/kg) showed improved insulin levels, thus suggesting increased insulin secretion or decreased insulin resistance. Glibenclamide treated rats showed a significant increase in insulin levels as compared to diabetic non-treated rats in agreement of previous reports. (43)

The degree of insulin resistance (IR) and beta-cell dysfunction is measured using homeostatic model assessment (HOMA). Higher HOMA-IR values indicate Insulin Resistance, and lower HOMA-B values indicates greater beta-cell dysfunction. (16) Oral treatment of Silibinin is reported to improve insulin function by decreasing HOMA-IR index in rat model. (44)Higher concentration of insulin and HOMA-β cell functioning as well as lower HOMA-IR was observed in the diabetic rats treated with silibinin (40 and 80 mg/kg), suggesting this bioflavonoid might possess insulin secretogogue property.

Diabetes associated complications are majorly observed as a result of increased oxidative stress. (45). Damaged antioxidant defence mechanism along with abnormally high levels of reactive oxygen species (ROS) in the pancreas affect insulin secretion and action.(46)Diabetic non-treated rats showed a significant effect on antioxidant system. Highly significant effect on the restoration of antioxidant defence such as decreased MDA concentration and

increased GSH concentration as well as elevated activities of SOD and CAT was observed in the diabetic rats treated with silibinin (40 and 80 mg/kg), owing to thepotent antioxidant property possessed by the bioflavonoid. (47) A remarkable alteration in the morphology of beta cells of islets of pancreas is observed in diabetic condition. (48) In the present investigation destruction of the islets, blood-filled interlobular duct and disorganized acinar cells were observed diabetic rats. The high dose treatment of silibinin (80mg/kg) was found to restore the structural abnormalities of pancreas induced due to diabetes.

CONCLUSION

In conclusion, 28 days oral administration of silibinin at dose of 40mg/kg and 80mg/kg significantly restored body weight, biochemical parameters, histological alterations and oxidative parameters. Thus it suggests silibinin possesses as potential anti-diabetic and antioxidant action.

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