ORIGINAL ARTICLE

Investigation of lipid profile and occular oxidative stress of *Chloroxylon swietenia* on Streptozotocin-nicotinamide-induced diabetic rats

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Background: Diabetes mellitus is a chronic metabolic disorder, characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. **Aim:** This investigation was designed to study the antidiabetic effect of Ethanolic extract of *Chloroxylon swietenia* (EECS) in Streptozotocin-Nicotinamide-induced type-II diabetes in rats. **Materials and Methods:** The extract at doses of 250 and 500 mg/kg was given to the overnight-fasted Wistar albino rats for 14 days and the antidiabetic, lipid profile and ocular oxidative stress in Streptozotocin-Nicotinamide-induced diabetic rats were evaluated. The parameters studied were blood glucose, lipid profile [total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL)], serum enzymes such as serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT), antioxidant enzymes like catalase (CAT), thiobarbituric acid reactive substances (TBARS), glutathione (GSH), complete blood picture (RBC, haemoglobin, WBC), insulin and liver glycogen levels. The result of test drug was compared with diabetic control. Glibenclamide (10 mg/kg) was selected as standard hypoglycaemic drug. **Statistical Analysis:** Results were expressed as Mean ± SD. Dunnet's and one-way ANOVA test was used to compare the mean values of test groups and diabetic control. **Results:** Administration of EECS prior to glucose overload resulted significant attenuation in blood sugar level at 60 and 120 min in comparison to glucose control group. The antidiabetic activity of EECS showed significant ($P < 0.001$) reduction in blood glucose level at 250 mg/kg and 500 mg/kg dose levels at 14th day. EECS with (250 and 500 mg/kg) also decreased in serum SGOT, SGPT, TG, TC, VLDL-C, LDL-C, WBC and TBARS, in diabetic-induced rats. In addition EECS at (250 and 500 mg/kg) increased liver glycogen, insulin, complete blood picture RBC, haemoglobin, ocular oxidative enzymes CAT, GSH and body weight when compared with diabetic control. **Conclusion:** The results obtained from the present study revealed the potential anti-diabetic activity of Ethanolic extract of *Chloroxylon swietenia.*

Key words: Blood glucose, blood profile, *Chloroxylon swietenia,* diabetes mellitus, lipid profile, liver glycogen, ocular oxidative stress, serum insulin

INTRODUCTION

Diabetes mellitus is a metabolic disorder characterised by hyperglycaemia resulting from defective insulin secretion, resistance to insulin action or both.[1,2] It is a widespread disease, associated with chronic micro and macrovascular complications.[3] International diabetic federation (IDF) estimated the India leads in world around 4.1 crores diabetic patients in 2006 and by the year of 2025 it will rise to 7 crores.[4]

Chloroxylon swietenia belongs to family of Rutaceae. It is a medium-sized deciduous tree with a height of 900-1500 cm and 100-1200 cm girth with a spreading crown and clear bole up to 300 cm. It is commonly called like East Indian Satinwood in English, Bhirra in Hindi, Billudu in Telugu and Vaaimaram in Tamil. This plant is traditionally used for cuts, burns, wounds, rheumatism, optical infection, snakebites, etc.[5] Various extracts of this plant have been reported to possess antimicrobial activity,[6] antibacterial and antihelmintic,[7] hepatoprotective, antioxidant,[8] larvicidal,[9] anti-inflammatory,[10] analgesic,[11] and antifertility activity.[12]

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MATERIALS AND METHODS

Chemicals

Glibenclamide was obtained as a gift sample from Suzikem Drugs Pvt. Ltd., Hyderabad. Streptozotocin was purchased from Sigma Aldrich, Germany. Total cholesterol, triglycerides, HDL kits were purchased from CPC diagnostics Pvt. Ltd., Hyderabad. Antioxidant kits were purchased from Himedia Pvt Ltd., Mumbai.

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Whereas other biochemical kits were obtained from Span Diagnostic Ltd., India.

Animals

Healthy Wistar albino rats of either sex weighing 150-200 g were used for the studies which were procured from Albino enter prices, Hyderabad. Housed individually in polypropylene cages, maintained under standard conditions (12 h light and 12 h dark cycle, 25 ± 2°C, 35-60% relative humidity), the animals were fed with standard rat pellet diet and water *ad libitum*. The Experiments were carried out after obtaining permission from Institutional Animal Ethical Committee (Approval number: 1047/ac/07/CPCSEA), Vaagdevi College of Pharmacy, Warangal and A.P.

Plant Material

The plant material *Chloroxylon swietenia* was collected from wastelands near Tekumatla village, Adilabad District, Andhra Pradesh, India, during the month of April 2013 and authenticated by Dr. E. Narasimha Murthy, Fellow of Indian Association of Angiosperm, Taxonomy, Department of Plant Sciences, School of Life Sciences, University of Hyderabad, Hyderabad.

Preparation of Plant Extract

The whole plant of *Chloroxylon swietenia* was shade dried and then powdered with a mechanical grinder to obtain a coarse powder. Equal quantity of powder was passed through 40-mesh sieve and extracted with ethanol (90% v/v) in Soxhlet apparatus at 60°C. The solvent was completely removed by rotary vacuum evaporator. The extract was freeze dried and stored in a vacuum desiccator.

Oral Glucose Tolerance Test

Oral glucose tolerance test (OGTT) was performed in non-diabetic Wistar albino rats. The overnight-fasted Wistar albino rats of either sex were randomly divided in to four groups of six each. The OGTT was performed in overnight-fasted normal rats. The first group served as vehicle control 1% sodium CMC (Na-CMC), second group served as standard, treaded with glibenclimde (10 mg/kg). The test drug was administered to third and fourth groups at the doses of 250 and 500 mg/kg, respectively. Vehicle, test drug and reference standard drug were given to the respective group of animals as per the body weight. After 30 min of drug administration glucose (2 g/kg) solution was administered to second, third and fourth groups orally by dissolving it in distilled water. Blood samples were collected at 0 min before the glucose load and 30, 60 and 90 min after the glucose load by retro-orbital vein plexus puncture under mild ether anaesthesia. The serum was separated and the glucose concentration was estimated by glucose oxidase-peroxidase (GOD-POD) method.[13]

Induction of Diabetes Mellitus

Non-insulin dependent diabetes mellitus (IDDM) was induced in overnight-fasted Wistar albino rats by a single intraperitonial (*i. p*) injection of 60 mg/kg Streptozotocin was dissolved in citrate buffer (pH 4.5), 15 min after the *i. p*, and administration of 120 mg/kg of Nicotinamide (*i. p*) was dissolved in normal saline. The fasting blood glucose levels were checked after 3 days. The rats with stable fasting blood glucose level above as > 126 mg/dl were used for the study. After induction of diabetes all the animals were kept in laboratory on normal diet.[14]

Experimental Design

Thirty Wistar albino rats were used in this study. The rats were randomised and divided into five groups of six animals each.

Group I : Vehicle control which received 1% Na CMC
Group II : Diabetic control
Group III: Diabetic + glibenclamide (10 mg/kg, *p. o*)
Group IV: Diabetic + EECS (250 mg/kg)
Group V : Diabetic + EECS (500 mg/kg).

Blood Collection

The blood samples were collected by retro-orbital plexus puncture of anaesthetised mice. Blood samples were collected at the time of grouping of animals (basal reading) and at 1st, 7th, and 14th day of treatment. Blood was centrifuged at 3500 r.p.m. for 20 min and serum was separated for biochemical estimation.

Estimation of Serum Glucose

The serum glucose was estimated by glucose oxidase-peroxidase (GOD-POD) method.[15]

Measurement of Body Weight Gain

Measure the body weight of all the selected animals during the 14 days experimental period.

Estimation of Lipid Profile

Serum total cholesterol and HDL were estimated by cholesterol oxidase-peroxidase (CHOD-POD) method[16] using commercially available kit. Serum triglyceride was estimated by glycerol phosphate oxidase-p-aminophenazone (GPO-PAP) method by the addition of enzyme present in reagent kit.[17] Serum VLDL and LDL concentrations were calculated according to Friedewald equation.[18]

VLDL = TG/5

LDL = TC–(HDL + VLDL)

Serum Glutamate Oxaloacetate Transaminase (SGOT), Serum Glutamate Pyruvate Transaminase (SGPT) estimated by modified IFCC method.[19] Glycogen content was determined as described by Morales.[20] Serum insulin levels

were estimated in Vijaya diagnostic center, Hanamkonda, A.P. Haematological parameters were determined using cell counter (Horiba, Vaagdevi College of pharmacy).

Estimation of Oxidative Enzymes in Rat Eyes

After sacrificing the animals on 14th, eyes were removed and homogenate with 0.001M phosphate buffer (pH 7.4) and the resultant homogenate were centrifuged at 1000 rpm for 15 min and the supernatants were collected for the estimation of oxidative enzymes.[21-23] Antioxidant enzymes, such as Catalase (CAT), Thiobarbituric acid reactive substances (TBARS), and Glutathione (GSH), levels were determined according to the standard methods.[24-26]

Histopathological Studies

After sacrificing the animals on 14th day the pancreas were removed carefully from various groups of animals followed by washing thoroughly with cold saline and preserved in 10% formalin solution in buffered form. Blocks from tissues were routinely processed and embedded in paraffin. Thin sections were cut by using rotary microtome and stained with haematoxylin and eosin for histopathology evaluation.

Statistical Analysis

All the results were analyzed statistically using one-way analysis of variance followed by Dunnett's test. $P < 0.05$ is considered significant. All the results are expressed as mean ± SD for six animals in each group.

RESULTS

Oral Glucose Tolerance Test

He effects of EECS (250 and 500 mg/kg, *p.o*) on OGTT are summarised in Table 1. Maximum serum glucose level were found at 30 min in all groups after glucose load. In OGTT an increase followed by decreased in blood glucose levels was observed at 30 and 60 min respectively. The serum blood glucose levels were reduced significantly ($P < 0.01$) with 250 mg/kg of EECS at 120 min and 500 mg/kg of EECS were reduce the blood glucose significantly ($P < 0.001$) at 90 min when compared with glucose-loaded rats.

Streptozotocin-Nicotinamide-induced Diabetic Rats

Serum Glucose and Lipids

Table 2 summarises the serum glucose levels in all treated groups. There was a significant ($P < 0.001$) increase in blood glucose levels in a Streptozotocin-Nicotinamide-induced diabetic rats as compared with vehicle control rats [Table 2].

Table 3 illustrates the serum lipid levels in all treated groups. Serum levels of TC, TG, LDL and VLDL levels ($P < 0.001$) were higher, whereas HDL levels reduced in Streptozotocin-Nicotinamide- induced diabetic rats as compared with vehicle control rats [Table 3].

Effect of Ethanolic Extract of Chloroxylon Swietenia on Serum Glucose Level

EECS at 250 mg/kg showed significant ($P < 0.01$) reduction in blood glucose level on 7th day and more significantly ($P < 0.001$) on 14th day of treatment. Moreover, the most pronounced decrease in serum glucose was observed on Day 7 and 14 at a dose of 500 mg/kg. In addition, glibenclamide-treated rats also significantly ($P < 0.001$) decreased the serum glucose levels when compared with diabetic control rats.

Effect of Ethanolic Extract of Chloroxylon Swietenia on Serum Lipid Profile

Treatment of diabetic rats with EECS (250 and 500 mg/kg) showed significant ($P < 0.001$) reduction in elevated TG, TC, VLDL-C, LDL-C levels and simultaneously increase the HDL-C levels significantly ($P < 0.01$, $P < 0.001$) by the respective doses when compared with diabetic control. Moreover, glibenclamide-treated rats also significantly decreased the serum levels of TC, TG, LDL and VLDL and increased HDL level significantly ($P < 0.001$).

Table 2: Effect of EECS on fasting blood glucose in Streptozotocin-Nicotinamide induced diabetic rats

Group	Blood glucose (mg/dl)		
	1 day	7th day	14th day
Control	76.92±2.43	78.30±3.18	79.61±3.47
Diabetic control	260.64±5.78	267.82±3.05	270.73±3.64
Glibenclimide 10 mg/kg	254.73±2.89**	176.46±5.06***	112.02±3.12***
EECS 250 mg/kg	264.16±2.93	258.89±5.07**	180.08±3.21***
EECS 500 mg/kg	260.36±3.61	232.80±3.018***	141.59±2.97***

Data represents mean±S.D. (n=6). *P<0.05, ** P<0.01, *** P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test, EECS – Ethanolic extract of *Chloroxylon swietenia*

Table 1: Effect of EECS on oral glucose tolerance test

Group	Blood glucose (mg/dl)			
	0 min	30 min	60 min	120 min
Control	78.49±3.68	117.24±2.42	109.31±1.45	98.90± 1.88
Glibenclimide 10 mg/kg	76.74±2.14	110.46±2.89**	98.43±3.81***	81.26±1.44***
EECS 250 mg/kg	79.56±1.82	113.26±3.13	106.16±1.38	94.63±1.78**
EECS 250 mg/kg	75.10±2.44	112.76±2.46*	102.70±1.94***	88.47±1.79***

Data represents mean±S.D. (n=6). *P<0.05, ** P<0.01, *** P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test, EECS – Ethanolic extract of *Chloroxylon swietenia*

Table 3: Effect of EECS on serum lipid profile

Group	Lipid Levels (mg/dl)				
	TC	TG	HDL	LDL	VLDL
Control	73.05±5.27	76.25±5.71	37.03±4.18	20.66±2.05	15.87±1.79
Diabetic control	173.41±4.93	185.50±5.13	16.20±3.59	120.11±7.45	37.10±1.02
Glibenclimide 10 mg/kg	84.40±7.53***	87.70±7.38***	35.48±3.80***	31.37±3.68***	18.25±1.44***
EECS 250 mg/kg	116.46±3.95***	121.68±4.20***	23.60±1.79**	68.53±4.59***	24.33±0.84***
EECS 500 mg/kg	103.36±7.63***	101.88±7.68***	29.25±2.87***	53.74±7.48***	20.37±1.53***

Data represents mean±S.D. (n=6). *P<0.05, ** P<0.01, *** P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test, EECS – Ethanolic extract of *Chloroxylon swietenia*; TC – Total cholesterol; TG – Triglyceride; HDL – High-density lipoprotein; LDL – Low-density lipoprotein; VLDL – Very low-density lipoprotein

Effects of Ethanolic Extract of Chloroxylon Swietenia on Liver Enzymes Levels

Table 4 illustrate that biochemical parameters like SGOT, SGPT in the diabetic control group were significantly (P < 0.001) elevated when compared with the vehicle control group.

Treatment of diabetic rats with both doses (250 and 500 mg/kg) showed significantly (P < 0.01, P < 0.001) brought to the normal levels, respectively. The glibenclimide-treated rats also bring the liver enzymes significant (P < 0.001) to normal levels when compared with diabetic control.

Effects of Ethanolic Extract of Chloroxylon swietenia on Oxidative Enzymes

Table 5 represents the occular oxidative enzymes levels in all selected rats. The decreased levels of GSH should increase significantly with 250 and 500 mg/kg of EECS (P < 0.001) and the increased TBARS levels were decreased significantly (P < 0.01) with 500 mg/kg only. The catalase levels were significantly (P < 0.05, P < 0.001) increased by both doses, respectively.

Effects of Ethanolic Extract of Chloroxylon Swietenia on Serum Insulin and Liver Glycogen

The serum insulin and liver glycogen were significantly (P < 0.001) increased by EECS 500 mg/kg. Treatment with 250 mg/kg increases the serum insulin levels significantly (P < 0.001) and liver glycogen levels significantly (P < 0.01) increases when compared with diabetic control. The positive control glibenclimide increase significantly (P < 0.001) when compared with diabetic control [Table 6].

Effects of Ethanolic Extract of Chloroxylon Swietenia on Complete Blood Picture

Table 7 illustrate reduction of RBC, hemoglobin, platelets and elevation of WBC significantly (P < 0.001) diabetic rats. The EECS 500 mg/kg increase significantly RBC and haemoglobin (P < 0.05, P < 0.01) respectively and reduce the WBC significantly (P < 0.01). The EECS 250 mg/kg increase the haemoglobin significantly (P < 005) when compared with diabetic control.

Table 4: Effect of EECS on Liver enzymes levels

Group	SGPT (IU/L)	SGOT (IU/L)
Control	46.56±4.09	38.23±3.21
Diabetic control	80.35±1.81	75.47±3.58
Glibenclimide 10 mg/kg	52.85±3.25***	43.98±4.14***
EECS 250 mg/kg	72.92±3.43**	67.64±4.04**
EECS 500 mg/kg	62.98±3.50***	72.92±3.43***

Data represents mean±S.D. (n=6). *P<0.05, ** P<0.01, *** P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test, EECS – Ethanolic extract of *Chloroxylon swietenia*; SGPT – Serum glutamate pyruvate transaminase; SGOT – Serum glutamate oxaloacetate transaminase

Table 5: Effects of Ethanolic extract of *Chloroxylon swietenia* on oxidative enzymes

Group	Dose (mg/kg)	TBARS (nmols/g)	Catalase (U/m)	GSH (nmols/mg)
Control	1% Na CMC	7.81±1.63	50.66±3.65	36.10±1.25
Diabetic control	-	11.33±1.40	18.44±4.55	6.38±1.34
Glibenclamide	10	8.18±1.09***	45.11±4.03***	25.49±1.53***
EECS	250	10.59±1.34	24.55±3.89*	11.67±1.42***
EECS	500	8.55±0.60**	31.22±3.89***	18.61±1.09***

Data represents mean±S.D. (n=6). *P<0.05, **P<0.01, ***P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test. EECS – Ethanolic extract of *Chloroxylon swietenia*

Table 6: Effects of Ethanolic extract of *Chloroxylon swietenia* on serum insulin and liver glycogen

Group	Dose (mg/kg)	Serum insulin (µU/mol)	Liver glycogen (mg/g)
Control	1% Na CMC	138.60±1.62	12.45±0.58
Diabetic control	-	65.98±1.47	7.53±0.62
Glibenclamide	10	118.50±1.70***	12.23±0.56***
EECS	250	83.41±1.72***	8.71±0.33**
EECS	500	109.03±1.63***	10.06±0.67***

Data represents mean±S.D. (n=6). *P<0.05, **P<0.01, ***P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test. EECS – Ethanolic extract of *Chloroxylon swietenia*

Effects of Ethanolic Extract of Chloroxylon Swietenia on Body Weights

Table 8 illustrate the body weight changes in selected rats. Vehicle control animals were found to be stable in their body weight but diabetic rats showed significant reduction in body weight during 14 days. Streptozotocin causes reduction in the body weight, which was significantly reversed in both test fractions after14 days of treatment. EECS at 250 and 500 mg/kg significant (P < 0.001) increases in body weight when compared with diabetic control. The

glibenclamide is also significantly ($P < 0.001$) increase the body weight.

Histopathological Studies of Pancreas

Figure 1 represents the histopathological study of EECS on pancreas. (a) Control (b) Disease control (c) Glibenclamide 10 mg/kg (d) EECS (250 mg/kg) (e) EECS (500 mg/kg)

(A) Pancreas of normal group showing normal pancreatic acini and islets of langerhans (β cells) with normal cellularity.

(B) Pancreas of diabetic control group showing degeneration of pancreatic cells. There is damage to islets of langerhans cells.

(C) Pancreas of glibenclamide 10 mg/kg group showing mild degeneration of pancreatic cells. Cellular population of islets of langerhans is normal.

(D,E) Pancreas of EECS 250 and 500 mg/kg groups respectively showing mild to moderate degeneration of pancreatic cells. Cellular population of islets of langerhans is near to normal.

Table 7: Effects of Ethanolic extract of *Chloroxylon swietenia* on blood profile

Group	Dose (mg/kg)	Haemoglobin (g/dl)	RBC× 10^6/µl	WBC× 10^3/µl
Control	1% Na CMC	15.93±0.68	8.37±0.56	7.66±0.40
Diabetic control	-	8.03±0.88	4.40±0.99	13.10±0.79
Glibenclamide	10	13.66±1.33***	6.06±0.92**	9.83±0.48***
EECS	250	10.01±1.44*	4.93±0.46	12.26±0.45
EECS	500	10.86±1.38**	5.55±0.62*	11.56±0.95**

Data represents mean±S.D. (n=6). *P<0.05, **P<0.01, ***P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test. EECS – Ethanolic extract of *Chloroxylon swietenia*

Table 8: Effects of Ethanolic extract of *Chloroxylon swietenia* on body weights

Groups	Dose (mg/kg)	Initial weight (gm)	Final weight (gm)
Control	1% Na CMC	212.50±19.68	241.60±11.25
Diabetic control	-	171.60±10.32	149.10±7.35
Glibenclamide	10	175.00±11.83	200.80±12***
EECS	250	174.10±9.70	180.80±10.68***
EECS	500	172.50±9.35	190.80±9.17***

Data represents mean±S.D. (n=6). *P<0.05, **P<0.01, ***P<0.001, Significant compared to diabetic control analyzed by one-way ANOVA followed by Dunnett's test. EECS – Ethanolic extract of *Chloroxylon swietenia*

DISCUSSION

Diabetes Mellitus is mainly characterised by hyperglycaemia and often associated with hyperlipidemia due to lack of insulin secretion or insulin resistance. The hyperglycaemia mainly involved due to overproduction and decreased utilisation of glucose.[27]

Non-insulin-dependent diabetes mellitus (Type II DM) occurs predominantly and affects major population, i.e., 90% of diabetic patients.[28] Streptozotocin selectively causes damage of insulin producing pancreatic β-cells of rats. This in turn induces diabetic condition that mimics the type II diabetes of human[29] and also produces raised levels of cholesterol triglycerides and liver enzymes. Therefore in order to know the effects of test drug, levels of blood glucose, and serum biochemical parameters were checked at specific time interval after drug administration.

The induction of diabetes is confirmed by elevated levels of fasting blood glucose levels in selected rats. The present study was focused to explore the antidiabetic activity of EECS. The results of present study indicate that decreasing fating blood glucose levels achieved by multiple dose study in different groups in sub acute studies indicates the effectiveness of extract in Streptozotocin - Nicotinamide

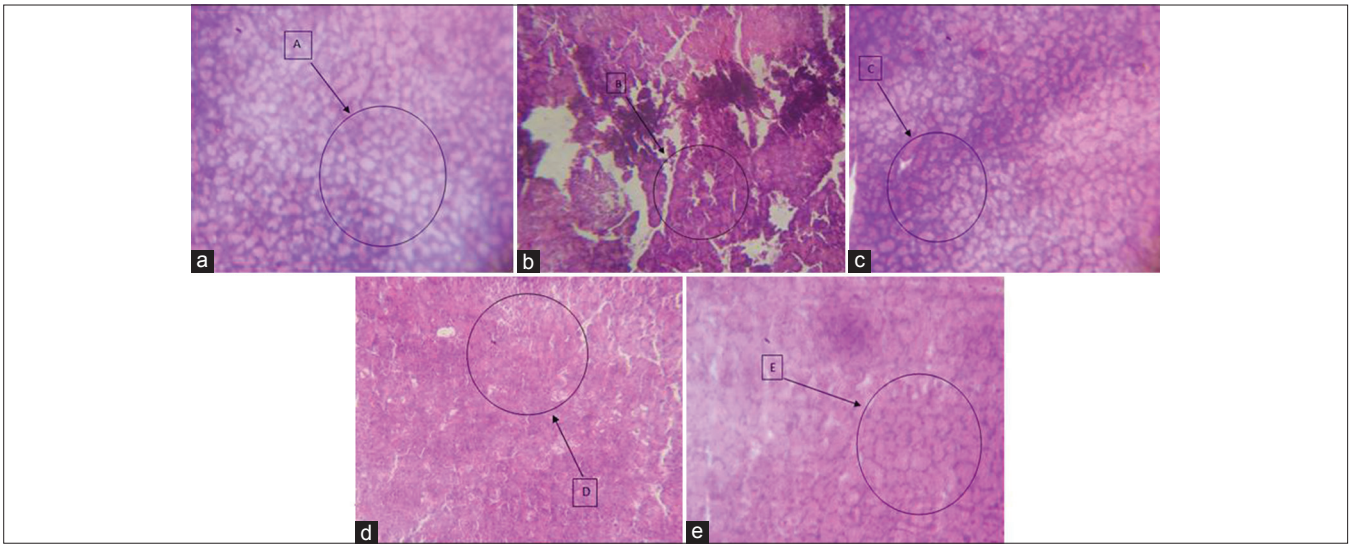

Figure 1: Histopathological studies of pancreas

induced diabetic rats. Considering this, EECS was administered daily for 14 days, the period which may be produced a significant reduction in all the diabetic markers, and this effect was more potent as compared to acute dosing.[30]

The EECS significantly decreased the serum glucose levels in glucose loaded rats, and this information could be recognised to the potentiation of the insulin effect on blood glucose by increasing the pancreatic secretion of insulin from β-cells or its release from bound insulin Results on the insulin release from pancreas directly indicate that the antidiabetic activity of EECS may be through the release of insulin from the pancreas.

The elevated levels of blood glucose are accompanied with the increases in TC, TG, VLDL and LDL and fall of HDL levels. Considerable research has been shown that abnormal lipid metabolism is an important predictor for diabetes mellitus.[31] The administration of EECS showed a significant reduction in serum levels of TC, LDL, TG and VLDL, whereas a significant elevation in HDL levels. Elevated levels of serum biomarker enzymes such as SGOT, SGPT was observed in diabetic rats indicating impaired liver function, which is evidently due to hepatocellular necrosis. The elevated levels of transaminase activities produce diabetic complications such as increased gluconeogenesis and ketogenesis.[32,33] The 14 day treatment with extract restored all the above mentioned hepatic biochemical parameters towards the normal levels.

The administration of EECS to diabetic rats showed significant decrease in the levels of blood glucose and an increase in serum insulin levels. The decreases seen in hepatic glycogen content in diabetes are probably due to lack of insulin in the diabetic state which results in the inactivation of glycogen synthase systems. The significant increase in the glycogen levels of the extract-treated diabetic animals may be because of the reactivation of glycogen synthase system. The progress of diabetes is mainly associated with the close relationship between the increased free radicals and decreased antioxidant potential. Increased thiobarbituric acid reactive substances (TBARS) are index of enhanced lipid peroxidation in diabetes, which may be due to enhanced production or decreased destruction of reactive oxygen species.[14] The increased lipid peroxidation in the tissues of diabetic animals may be due to the observed remarkable increase in the concentration of TBARS and MDA as a main mediator of lipid peroxidation in the tissues.[34] Present study showed that administration of EECS and glibenclamide inhibit the production of lipid peroxides. This indicates the antilipidperoxidative potential of EECS. Catalase involves in the reduction of hydrogen peroxide and detoxification of high hydrogen peroxide concentrations.[34] Treatment with EECS for 14 days significantly augmented the activity of catalase in diabetic rats which could be attributed to the strong antioxidant property of EECS. Glutathione plays an important role in the endogenous non-enzymatic antioxidant system. It primarily acts as a reducing agent and detoxifies hydrogen peroxide in the presence of the enzyme glutathione peroxidase.[35] The depleted GSH may be due to reduction in GSH synthesis or degradation of GSH by oxidative stress in Streptozotocin-induced hyperglycaemic rats.[36] EECS treatment significantly elevated GSH levels towards normal in diabetic rats.

Streptozotocin-induced diabetes is characterised by severe loss in body weight. This may be due to increased muscle wasting and loss of tissue proteins. In this study a significant weight loss was observed in the Streptozotocin-induced diabetic control rats. The EECS-treated rats showed significant recovery in body weight gain when compared with diabetic control rats. This might be due to regulating muscle wasting and improvement in insulin secretion as well as glycaemic control by EECS. The extract had a positive effect on the haemopoietic system of the rats. It increased the red cell, haemoglobin concentration, and significantly decreases total white cell.

CONCLUSIONS

In the present study the administration of Ethanolic extract of *Chloroxylon swietenia* to Streptozotocin-Nicotinamide-induced diabetic rats showed permanent reduction in blood glucose level, normalisation of various serum biochemical parameters such as lipid profile and serum liver enzymes compared with diabetic control and also significant modulation of antioxidant enzymes (TBARS, CAT and GSH), insulin and liver glycogen in EECS-treated rats when compared with diabetic control. Therefore, it can be concluded that Ethanolic extract of *Chloroxylon swietenia* remarkably effective against induced Streptozotocin-Nicotinamide diabetes in Wistar rats.

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