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Full Length Article

Antidiabetic effect of *Chloroxylon swietenia* bark extracts on streptozotocin induced diabetic rats

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ABSTRACT

Diabetes has been increasing at an alarming rate around the world, and experts have relied on remedies from the utilization of ancient drugs that are essentially derived from plants. The present study aimed to evaluate the antidiabetic potential of *Chloroxylon swietenia* bark extracts on streptozotocin induced diabetic rats. Diabetes was induced in male albino Wistar rats by single intraperitoneal injection of streptozotocin (STZ) (50 mg/kg b.w.). The diabetic rats were administered orally with *C. swietenia* bark (CSB) methanolic (CSBMEt) and aqueous (CSBAEt) (250 mg/kg b.w.) extracts and glibenclamide (600 µg/kg b.w.) by intragastric intubation for 45 days. The result showed a heavy loss in weight, increase in blood glucose and glycosylated hemoglobin level, and decline in plasma insulin and total hemoglobin content. Furthermore, glucose-6-phosphatase and fructose-1,6-bis phosphatase were found to be increased whereas hexokinase and glycogen contents were decreased in STZ induced diabetic rats. CSBAEt, CSBMEt and glibenclamide treated diabetic rats showed moderate reduction in blood glucose and glycosylated hemoglobin levels; in addition, plasma insulin and hemoglobin levels were elevated. The altered activities of carbohydrate metabolizing enzymes and liver glycogen were improved remarkably. CSBMEt results were comparable to the standard drug glibenclamide. The present findings support the usage of the plant extracts for the traditional treatment of diabetes.

1. Introduction

Diabetes mellitus (DM) could be a bunch of metabolic disorders portrayed via hyperglycemia following imperfections in insulin emission, insulin activity, or both. The chronic hyperglycemia is identified with stretched pathology and damage, which distress multiple organs. It additionally incorporates a bigger chance of getting dyslipidemia, high blood pressure, and obesity (American Diabetes Association, 2011). The pathogenesis of insulin-dependent DM includes ecological reasons that may initiate immune system mechanisms on hereditarily defenseless people, prompting dynamic loss of pancreatic islet β-cell resulting in insulin deficiency (Harrison and Honeyman,

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1999; Gurudeeban et al., 2012). Non-insulin-dependent DM is related to impaired insulin secretion, obesity, insulin resistance, and hereditary disposition in individuals over 40 years of age (Zimmet et al., 1990). Streptozotocin could be an intense poison to the islets of Langerhans and causes extreme diabetes (Brenna et al., 2003). This condition is characterized by a noteworthy increment in serum glucose levels and a huge lessening in insulin discharge (Abdelmeguid et al., 2010). The surplus glucose within blood responds to hemoglobin (Hb) and frame glycosylated hemoglobin (HbA1c) (Koenig et al., 1976). Prior reports have demonstrated that insulin boosts property of glibenclamide and has thereby been accepted as qualified antidiabetic medication (Andrade Cetto et al., 2000).

The therapeutic management of polygenic disorder without feature impacts remains disputed. In light of the developing enthusiasm on assessing homegrown cures, these are seen to be less harmful and to possess insignificant feature impacts (Gupta et al., 2012). East Indian satinwood grows in dry deciduous forest, and is indigenous to Asian countries. It has been employed as a part of chimerical medicine (Venkataswam et al., 2010). This plant is conventionally used for cuts, burns, wounds, rheumatism, optical infection, snakebites, etc. (Kiran et al., 2008). Various extracts of *Chloroxylon swietenia* have been reported to possess antimicrobial activity (Vinatha and Estari, 2013), antibacterial and antihelminthic (Ranjith et al., 2011) hepatoprotective, antioxidant (Palani et al., 2010), larvicidal (Kiran et al., 2006), anti-inflammatory (Kumar et al., 2006), and analgesic (Senthilraja and Ramkumar, 2003) properties, and root bark consumed along with milk have been reported to treat impotence (Parrotta, 2001). Investigation of lipid profile and ocular oxidative stress of *C. swietenia* on Streptozotocin-nicotinamide-induced diabetic rats (Patchimatla et al., 2014) was studied in aerial parts. However STZ induced animal model on *C. swietenia* bark (CSB) extracts was not yet studied. The current study was intended to explore the antidiabetic activity of aqueous (CSBAEt) and methanolic extracts (CSBMEt) of *C. swietenia* bark (CSB) on STZ induced diabetic rats.

2. Materials and methods

2.1. *Chemicals*

STZ and glibenclamide was obtained from Sigma-Aldrich Company (Bangalore, India). The other experimental chemicals used were of analytical grade and were purchased from HiMedia (Mumbai, India).

2.2. *Plant material collection, processing, and preparation of extracts*

CSB placed in rue family was gathered amid December from Kalvarayan Hills Kallakurichi, Tamil Nadu, India. Dr. V. Chelladhurai (Research Officer – Botany Central Council for Research in Ayurveda and Siddha, Govt. of India) has given the taxonomic distinguishing proof. It was shade dried for a month, granulated in mechanical grinder and stuffed within airproof pack. CSB (300 g) was extracted with methanol (1 L) by soxhlet apparatus (72 h), and the mixture was dried (45 °C) in a rotary evaporator (Heidolph, Germany). The pounded bark (300 g) was soaked (3 days) in distilled water (1 L) in ambient temperature, subjected to periodic agitation and set aside using cotton attachment. Afterward, the bark was taken out with the use of Whatman filter paper (no. 1) and dehydrated at ambient temperature. The dried extracts were stored at 4 °C until further use.

2.3. *Experimental animals*

Grown-up adult male albino Wistar rats with body weight (b.w.) above 180 g at 8 to 10 weeks from conception were acquired from Madhavaram Veterinary Medical College, Chennai, Tamil Nadu, India. They have been housed at poly propylene confines and kept up in standard environment [12 h light and 12 h dark cycle, (25 ± 3)°C]. The rats were fed with standard rat pellet diet (Pranav Agro Industry Ltd, Maharashtra) and given water ad libitum and maintained at Central Animal House, RMMCH. All studies were conducted as per the National Institute of Health's Guide for the Care and Use of Laboratory Animals, and the study was endorsed by the Institutional Animal Ethical Committee of Rajah Muthiah Medical College and Hospital (Proposal No. 998, Reg. No. 160/1999/CPCSEA), Annamalai University, Tamil Nadu, India. Animals were adapted for 3 days in the research laboratory before start of the experiments.

2.4. *Experimental induction of diabetes*

Diabetes was prompted through single intraperitoneal injection of freshly prepared streptozotocin (STZ) (50 mg/ kg b.w.) in 0.1 M citrate buffer (pH = 4.5) to overnight starved rats (Gupta and Gupta, 2009). Diabetic rats were permitted to drink 20% glucose solution overnight to overcome the initial drug induced hypoglycemic death. The blood glucose level was measured after three days, and rats with glucose levels >250 mg/dL were considered as diabetic. At the time of induction, control rats were injected with 0.2 mL of vehicle (0.1 M citrate buffer, pH 4.5) alone.

2.5. *Experimental design*

In this experiment 30 rats (6 normal and 24 STZ diabetic existing rats) were used. They were separated into five groups of 6 rats each. The CSBMEt were dissolved in 2% CMC (Carboxyl methyl cellulose) in distilled water (Kumar et al., 2011), CSBAEt and glibenclamide 0.5 mL of 0.9% saline and administered orally (45 days).

Group I. Control rats (were given 0.5 mL of 0.9% saline orally for 45 days).
Group II. Diabetic group (STZ 50 mg/kg b.w.).
Group III. Diabetic rats were given CSBAEt (250 mg/kg b.w. dissolved in 0.5 mL of 0.9% saline) orally for 45 days.
Group IV. Diabetic rats were given CSBMEt (250 mg/kg b.w. dissolved in 0.5 mL of CMC) for 45 days.
Group V. Diabetic rats were given Glibenclamide (600 µg/kg b.w. dissolved in 0.5 mL of 0.9% of saline) for 45 days (Subash et al., 2007).

Toward the study's end (45 days), the animals were euthanized by ketamine (24 mg/kg/body) intramuscular injection and

sacrificed by cervical decapitation between 9:00 and 11:00 am to minimize diurnal variation. The blood was gathered. The liver was dissected and washed with ice-cold saline immediately to remove blood. Fresh/frozen liver (1 g) was slashed and homogenized in ice-cold sucrose (15 mL, 250 mM) with a Potter-Elvehjem homogenizer for 2 minutes, centrifuged at 10,000 rpm for 30 minutes, and the supernatant was gathered and utilized as the source for different biochemical estimation. The body weight of all the animals was recorded proceeding to the treatment and sacrifice.

2.6. *Biochemical analysis*

2.6.1. *Estimation of blood glucose*

Glucose level in plasma was determined by glucose oxidase/peroxidase method as described by Trinder (1969) using a reagent kit. In brief, to 0.01 mL of plasma, standard and distilled water (blank) into 3 test tubes, 1.0 mL of the enzyme was added, mixed and kept at 37 °C for 15 minutes. The color developed was read at 505 nm against reagent blank.

2.6.2. *Qualitative determination of plasma insulin*

The plasma insulin was assayed by Enzyme Linked Immunosorbent Assay (ELISA) method using Boehringer-Mannheim kit (Andersen et al., 1993). In brief, 0.1 mL of plasma was injected into the plastic tubes coated with monoclonal anti-insulin antibodies. Phosphate buffer and anti-insulin POD conjugate was added to form anti-insulin antibody–POD conjugate. Substrate chromogen solution was then added to form indicators reaction. A set of standards were also treated in a similar manner. After the development of color the absorbance was read at 420 nm.

2.6.3. *Determination of hemoglobin*

Hemoglobin content in blood was determined by the cyanmethemoglobin method of Drabkin and Austin (1932). In brief, the reaction mixture in a volume of 5.02 mL contained 5 mL of Drabkin's reagent and 0.02 mL of blood. The reaction mixture was kept at room temperature for 5 min to ensure the completion of the reaction. The solution was read at 540 nm together with the standard solution of cyanmethemoglobin.

2.6.4. *Estimation of glycosylated hemoglobin (HbA1c)*

HbA1c in the blood was estimated by the method of Nayak and Pattabiraman (1981). The saline washed erythrocytes (0.5 mL) were lysed with 5.5 mL of water, mixed and incubated at 37 °C for 15 minutes. The contents were centrifuged and the supernatant was discarded, then 0.5 mL of saline was added, mixed and processed for estimation. To 0.02 mL of aliquot, 4 mL of oxalate hydrochloric solution was added and mixed. The contents were heated at 100 °C for 4 hours, cooled and precipitated with 2 mL of 40% TCA. The mixture was centrifuged and to 0.5 mL of supernatant, 0.05 mL of 80% phenol and 3.0 mL of concentrated H_2SO_4 were added. The color developed was read at 480 nm after 30 minutes.

2.6.5. *Estimation of liver glycogen*

Hepatic glycogen content was estimated by the method of Morales et al. (1973). A known amount of the tissue was subjected to alkali digestion in a boiling water bath for 20 minutes after addition of 5 mL of 30% potassium hydroxide. The tubes were cooled and 3.0 mL of absolute ethanol and a drop of ammonium acetate were added. The tubes were then placed in a freezer overnight to precipitate the glycogen. The precipitated glycogen was collected after centrifugation at 3000× *g* for 10 minutes. The precipitate was washed thrice with alcohol and dissolved in 3 mL of water. Aliquots were taken and 4 mL of anthrone reagent was added to the tubes kept in an ice bath, mixed and heated in a boiling water bath for 20 minutes. The green color developed was read at 640 nm. Working standard glucose and a blank were treated similarly.

2.6.6. *Assay of hepatic hexokinase (ec2.7.1.1)*

Hepatic hexokinase activity was assayed by the method of Brandstrup et al. (1957). The reaction mixture in a total volume of 5.3 mL contained the following: 1 mL of glucose solution, 0.5 mL of ATP solution, 0.1 mL of magnesium chloride solution, 0.4 mL of potassium dihydrogen phosphate, 0.4 mL of potassium chloride, 0.4 mL of sodium fluoride and 2.5 mL of Tris–HCl buffer (pH 8.0). The mixture was pre-incubated at 37 °C for 5 min. The reaction was initiated by the addition of 2 mL of tissue homogenate. 1 mL of the reaction mixture was immediately transferred to the tubes containing 1 mL of 10% TCA that was considered as zero time. A second aliquot was removed after 30 minutes incubation at 37 °C. The protein precipitate was removed by centrifugation and the residual glucose in the supernatant was estimated by the method of Trinder (1969).

2.6.7. *Activity of hepatic glucose-6-phosphatase (ec 3.1.3.9)*

Glucose-6-phosphatase was assayed by the method of Koida and Oda (1959). Incubation mixture contained 0.7 mL of citrate buffer, 0.3 mL of substrate, and 0.3 mL of tissue homogenate. The reaction mixture was incubated at 37 °C for 1 h. Addition of 1 mL of 10% TCA to the reaction tubes terminated the reaction of the enzyme. The suspension was centrifuged and the phosphorus content of the supernatant of tissue homogenate was estimated by the method of Fiske and Subbarow (1925). The supernatant was adjusted to known volume. To this 1 mL of ammonium molybdate was added followed by 0.4 mL of ANSA (amino napthol sulfonic acid). After 20 min the absorbance was read at 680 nm.

2.6.8. *Assay of fructose-1,6-bisphosphatase activity (ec3.1.3.11)*

Fructose-1, 6-bisphosphatase activity was measured by the method of Gancedo and Gancedo (1971). The assay mixture in a final volume of 2 mL contained 1.2 mL of Tris-HCl buffer (0.1M, pH 7.0), 0.1 mL of substrate (0.05M), 0.25 mL of magnesium chloride (0.1M), 0.1 mL of potassium chloride (0.1M), 0.25 mL of EDTA (Ethylene diamine tetra acetic acid) (0.001M) and 0.1 mL of liver homogenate. The incubation was carried out at 37 °C for 15 minutes. The reaction was terminated by adding 1 mL of 10% TCA. The suspension was centrifuged and the supernatant was used for phosphorus determination by the method of Fiske and Subbarow (1925). The supernatant was adjusted to known volume. To this 1 mL of ammonium molybdate was added followed by 0.4 mL of ANSA. After 20 min the absorbance was read at 680 nm.

2.7. Histopathological studies

The liver tissues of the tested rats were fixed in 10% formaldehyde, dried out in an evaluated arrangement of ethanol and embedded in paraffin. Liver sections (5 µm thick) were acquired utilizing rotary microtome, and afterward rehydrated. Sections were then stained by hematoxylin-eosin (H&E) (Kehar and Wahi, 1967) and viewed under the light microscope and shot by photomicrography.

2.8. Statistical analysis

All values were expressed as mean ± SD. The statistical significance was evaluated by one-way analysis of variance (ANOVA) using SPSS and the Duncan's Multiple Range Test (DMRT). A value of $p < 0.05$ was considered to indicate a significant difference between groups.

3. Result

Changes in body weight (Fig. 1), blood glucose (15, 30 and 45 days) (Fig. 2), plasma insulin (Fig. 3), Hb (Fig. 4), and HbA1c in normal and experimental rats are presented (Fig. 5).

A vast reduction in the body weight was seen in STZ prompted untreated diabetic control rats when compared with normal rats. Significant increment in the body weight of diabetic rats treated with CSBMEt, CSBAEt and glibenclamide were observed when compared to diabetic control rats. Blood glucose of the diabetic rats was higher than the normal rats. Significant increase in insulin was observed at the end of the treatment period and decrease in blood glucose level was observed from the 15th day of treatment in diabetic rats treated with CSBMEt, CSBAEt and glibenclamide. Decreased Hb and increased HbA1C were observed in diabetic control rats, and these values were improved significantly upon treatment with the CSBMEt, CSBAEt and glibenclamide on STZ induced diabetic rats. CSBMEt and glibenclamide treatment results on the diabetic rats were comparative.

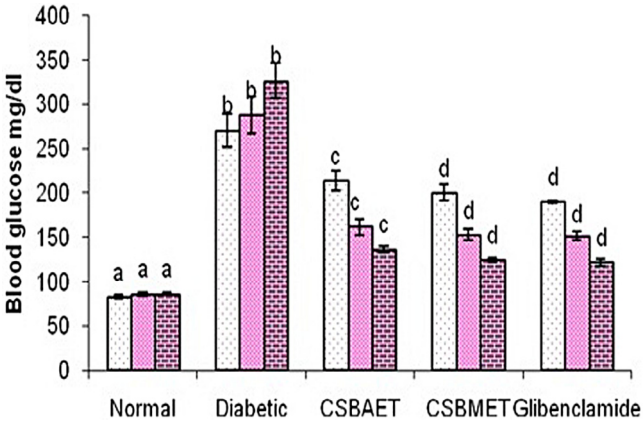

Fig. 2 – Effect of CSB extracts on blood glucose level of normal and experimental rats. Values are expressed as Mean ± SD (n = 6 rats in each group). Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT). [b]$p < 0.05$ as compared with normal rats[a]. [c]$p < 0.05$ as compared with diabetic control[b]. [d]$p < 0.05$ as compared with diabetic control[b]. CSBAEt – *Chloroxylon swietenia* bark aqueous extract (250 mg/kg). CSBMEt – *C. swietenia* bark methanol extract (250 mg/kg).

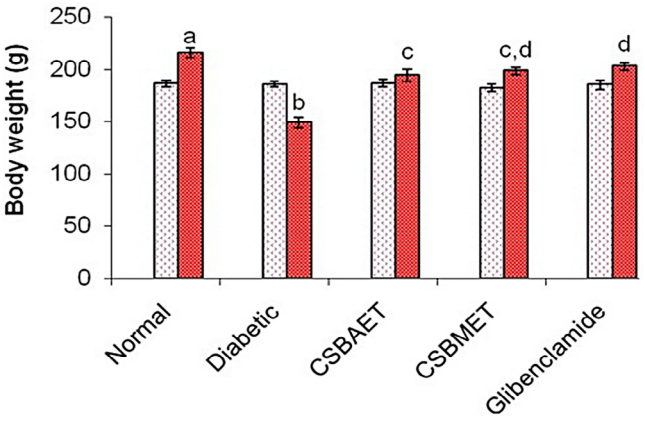

Fig. 1 – Effect of CSB extracts on body weight in normal and experimental rats. Values are expressed as Mean ± SD (n = 6 rats in each group). Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT). [b]$p < 0.05$ as compared with normal rats[a]. [c]$p < 0.05$ as compared with diabetic control[b]. [d]$p < 0.05$ as compared with diabetic control[b]. CSBAEt – *Chloroxylon swietenia* bark aqueous extract (250 mg/kg). CSBMEt – *C. swietenia* bark methanol extract (250 mg/kg).

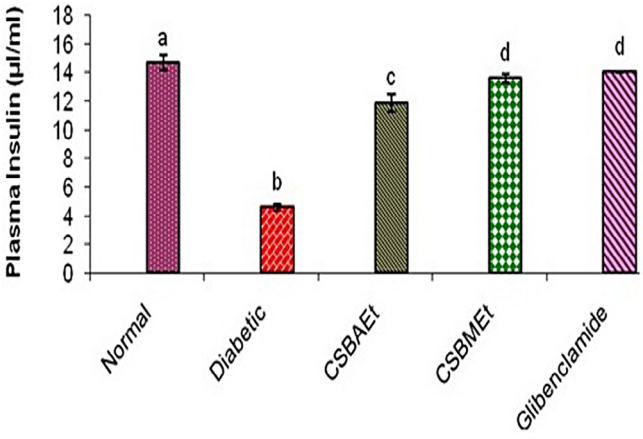

Fig. 3 – Effect of CSB extracts on Plasma Insulin levels in normal and experimental rats. Values are expressed as Mean ± SD (n = 6 rats in each group). Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT). [b]$p < 0.05$ as compared with normal rats[a]. [c]$p < 0.05$ as compared with diabetic control[b]. [d]$p < 0.05$ as compared with diabetic control[b]. CSBAEt – *Chloroxylon swietenia* bark aqueous extract (250 mg/kg). CSBMEt – *C. swietenia* bark methanol extract (250 mg/kg).

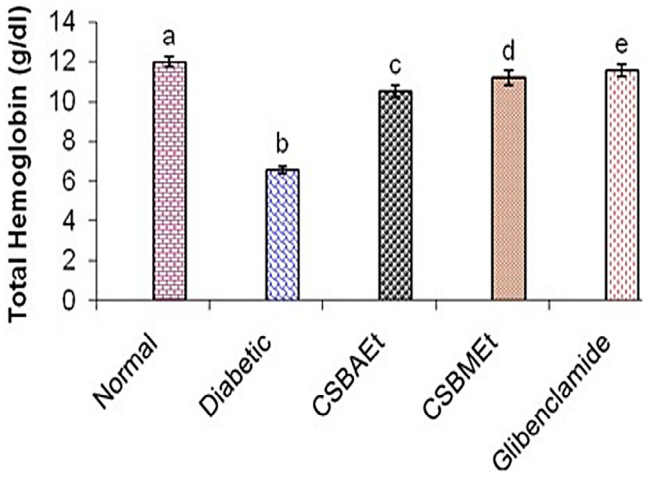

Fig. 4 – Effect of CSB extracts on total hemoglobin level of normal and experimental rats. Values are expressed as Mean ± SD (n = 6 rats in each group). Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT). $^{b}p < 0.05$ as compared with normal rats^{a}. $^{c}p < 0.05$ as compared with diabetic control^{b}. $^{d}p < 0.05$ as compared with diabetic control^{b}. $^{e}p < 0.05$ as compared with diabetic control^{b}. CSBAEt – *Chloroxylon swietenia* bark aqueous extract (250 mg/kg). CSBMEt – *C. swietenia* bark methanol extract (250 mg/kg).

Significant elevation of glucose-6-phosphatase, fructose-1,6-bisphophatase and declined hexokinase activity was found in STZ instigated diabetic rats when compared with normal rats. However, the treated groups had a tendency to convey these values to normal. Liver glycogen was diminished in STZ induced diabetic rats. CSBMEt, CSBAEt and glibenclamide significantly increased the liver glycogen levels (Table 1) in STZ induced diabetic rats.

Fig. 6 shows the histopathological consequences of normal and experimental rat liver. Extensive vacuolization degenerated nuclei was observed in STZ induced diabetic rat liver (B) when compared to normal rats (A), while diabetic rats treated with CSBAEt (C) and CSBMEt (D) group indicated improved histopathology of the liver as compared to the diabetic control group rats. Glibenclamide (E) treated group rats showed liver histopathology similar to the normal control rats.

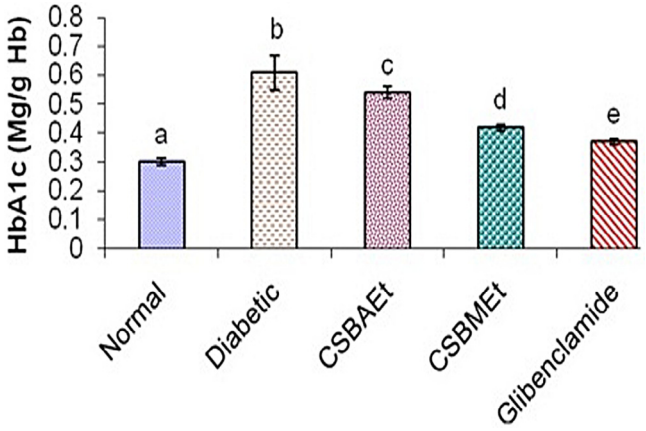

Fig. 5 – Effect of CSB extracts on glycosylated hemoglobin level on normal and experimental rats. Values are expressed as Mean ± SD (n = 6 rats in each group). Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT). $^{b}p < 0.05$ as compared with normal rats^{a}. $^{c}p < 0.05$ as compared with diabetic control^{b}. $^{d}p < 0.05$ as compared with diabetic control^{b}. $^{e}p < 0.05$ as compared with diabetic control^{b}. CSBAEt – *Chloroxylon swietenia* bark aqueous extract (250 mg/kg). CSBMEt – *C. swietenia* bark methanol extract (250 mg/kg).

4. Discussion

In this study, STZ (50 mg/kg b.w.) was utilized as diabetogenic operator to prompt the diabetes in albino Wistar rats. Heavy loss in body weight was observed in STZ induced diabetic rats. Minimum dosage of STZ was normally utilized to incite type I diabetes (Sithole, 2009). STZ partly destroys the beta cells bringing about inadequate insulin discharge, creating type 2 diabetes (Gomes et al., 2001). It is the generally used animal model for the diabetic study (Weir et al., 1981). Diminishing body weight in diabetic rats plainly affirms a corruption of basic proteins because of diabetes (Rajkumar and Govindarajulu, 1991). The deficit in body weight noticed in STZ instigated diabetic control rats may be due to muscle squandering (Swanston-Flatt et al., 1990; Chatterjee and Shinde, 2002). Oral administration of CSBAEt, CSBMEt and glibenclamide results in weight gain in STZ induced diabetic rats.

In DM, insulin is not or inadequately incorporated, creating hyperglycemia, which leads to change in glucose synthesis. A previous report proposes that to facilitate normal plasma insulin plays a vital role in keeping up the glucose equilibrium through upgrading glycolysis (Shimazu, 1987). Similarly decreased insulin and increased glucose level were observed in STZ induced diabetic rats; oral administration of CSBAEt, CSBMEt and glibenclamide results in recovery of blood glucose and plasma insulin significantly. Acute toxicity studies revealed the non-toxic nature of CSBMEt and CSBAEt at high concentrations. CSB extracts had a tendency to lower the blood glucose level over a period of 15 days' treatment in STZ induced diabetic rats (Jayaprasad et al., 2015b). In light of the outcomes it can now be proposed that hoisted pancreatic insulin discharge might improve glucose use through fringe tissues of diabetic rats by upgrading glucose uptake or else via hindering hepatic gluconeogenesis in addition to diminished blood glucose concentrations (Sundaram et al., 2014; Tanko et al., 2008). The conceivable component by which extracts intervene in their antidiabetic impacts could be by potentiation of pancreatic discharge of insulin from existing b-cells of islets, as shown by the huge increment in the level of insulin in the extract treated rats (Ramkumar et al., 2011).

HbA1c concentrations are a helpful and solid tool for the appraisal of glycemic control in diabetics as suggested by the International Diabetes Federation (Consensus Committee, 2007). Our study likewise bolsters the past study that HbA1c levels was hoisted in addition to exhausted total hemoglobin levels

Table 1 – Effect of CSB extracts on carbohydrate metabolic enzymes and liver glycogen of normal and experimental rat liver.

Parameters	Normal	Diabetic control	CSBAEt	CSBMEt	Glibenclamide
Hexokinase	4.02 ± 0.03[a]	1.46 ± 0.05[b]	3.59 ± 0.05[c]	3.89 ± 0.07[d]	3.92 ± 0.01[d]
Glu-6-phosphatase	7.65 ± 0.05[a]	18.43 ± 0.07[b]	9.65 ± 0.04[c]	8.73 ± 0.04[d]	8.66 ± 0.04[d]
Fru-1-6-bis phosphatase	4.87 ± 0.04[a]	10.35 ± 0.02[b]	5.16 ± 0.05[c]	4.48 ± 0.04[d]	4.89 ± 0.04[d]
Glycogen	15.89 ± 0.06[a]	7.99 ± 0.08[b]	13.66 ± 0.05[c]	15.32 ± 0.06[d]	15.65 ± 0.05[d]

Values are expressed as Mean ± SD for six rats (n = 6 rats in each group).
Glu-6-phosphatase – nmoles of Pi liberated / min/ mg protein; Fru-1-6-bis phosphatase – nmoles of Pi liberated / min/ mg protein; Hexokinase – nmoles of glucose phosphorylated/min/g protein; Glycogen –mg per gm tissue; Free Fatty Acid –mg per gm in wet tissue.
Statistical significance was evaluated by one-way analysis of variance (ANOVA) and the Duncan's Multiple Range Test (DMRT).
[b] $p < 0.05$ as compared with normal rats[a].
[c] $p < 0.05$ as compared with diabetic control[b].
[d] $p < 0.05$ as compared with diabetic control[b].
CSBAEt – *Chloroxylon swietenia* bark aqueous extract (250 mg/kg).
CSBMEt – *Chloroxylon swietenia* bark methanol extract (250 mg/kg).

in diabetic control rats. Treatment groups (CSBAEt, CSBMEt and glibenclamide) of diabetic rats unquestionably decrease the level of HbA1c and increased the total hemoglobin level. This may be a direct result of the initiation of glycogen production framework of the extract. A noteworthy decrease of HbA1c showed the ability of the extract in the control of diabetes (Shirwaikar et al., 2005). Similar results were observed by previous researchers who found that *Plectranthus esculenthus* restored the blood glucose, Hb and HbA1c levels in STZ induced diabetic rats (Eleazu et al., 2014).

Liver plays a critical part in glucose balance in diabetic condition (Nordlie et al., 1999). Diminished glycolysis, hindered glycogenesis and expanded gluconeogenesis are a progressive part of glucose synthesis in diabetic liver (Baquer et al., 1998). Hexokinase first enzyme in glycolysis (Tara and Teitell, 2014) joins transformation of glucose to G6P in addition to vitality (Kumar et al., 2014). Decreased movement of hexokinase prompts weakened oxidation of glucose by means of glycolysis, bringing about diabetic state and diminished adenosine triphosphate generation (Ramachandran and Saravanan, 2013).

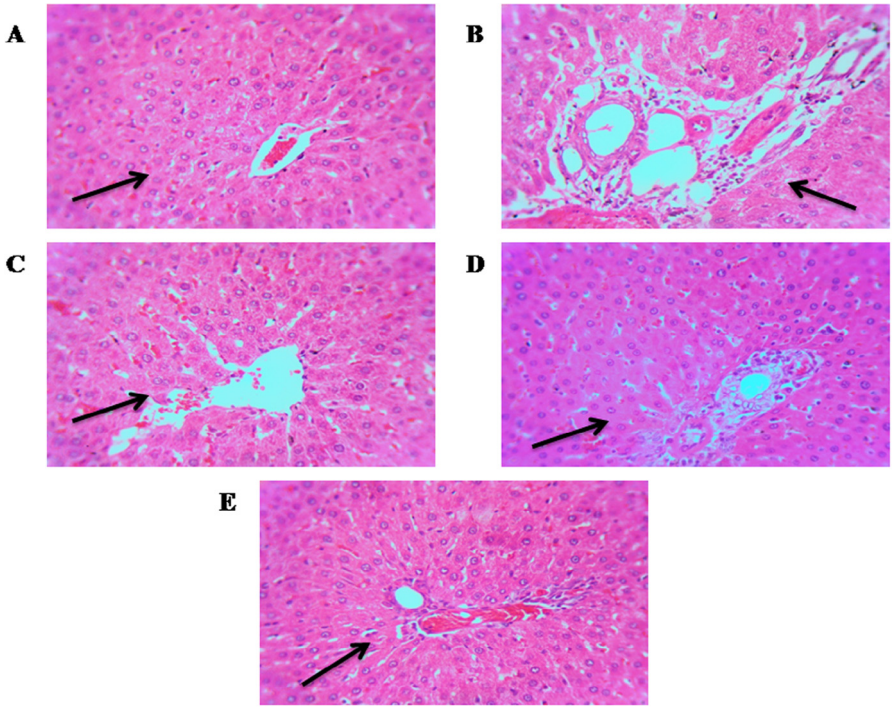

Fig. 6 – Histopathology. Figure shows the photomicrographs of H and E staining of liver tissues of control and Experimental rats. (A) Normal rat liver shows normal hepatocytes. (B) Diabetic rat liver shows disappearance of nuclei with extensive vacuolization. (C) Diabetic rats treated with CSBAEt show the regeneration of nuclei with minimal vacuolization. (D) CSBMEt shows the regeneration of nuclei. (E) Diabetic rats treated with glibenclamide significantly attenuated hepatocytes.

Diminished level of insulin in the STZ impelled diabetic animals at last prompts the impedance in the activity of hexokinase, since lack of insulin is a sign of diabetes (Postic et al., 2001). Diminished hexokinase level was found in diabetic rats though; CSBMEt, CSBAEt and glibenclamide expanded the action of hexokinase. Results acquired may be due to the increased level of insulin.

Insulin directs the exercises of carbohydrate metabolic enzymes and gluconeogenic enzymes such as G6P and F1,6BP (Prasath and Subramanian, 2011). Enhanced hepatic glucose production and impaired hepatic glucose utilization in STZ prompted diabetic rats might be mediated by dysregulation of hepatic G6P activity (Alemzadeh et al., 2002). In the present study increased gluconeogenic enzymes were observed in STZ induced diabetic rats. Hepatic glucose production is increased in a diabetic state and has been found to be directly associated with the impaired suppression of G6P and F1,6BP. The activity of G6P is stimulated by cAMP (Schmoll et al., 1999) and inhibited via insulin (Gardner et al., 1993). Reduced endogenous glucose production may play a central role in maintaining glucose homeostasis and implicates insulin in the gluconeogenic flux (Balamurugan et al., 2015). Action of these gluconeogenic enzyme increments in the liver of diabetic rats could be due to insulin deficiency (Baquer et al., 1998; Kavishankar and Lakshmidevi, 2014). Diabetic rats administered with CSBMEt, CSBAEt and glibenclamide modified the levels of G6P and F1,6BP to near normal, which may be due to higher insulin emission.

Glucose is stored as glycogen in intracellular regions (Kalaivanan and Pugalendi, 2011) and serves as a tissue reserve for the body's glucose needs. The transformation of glucose to glycogen relies on the existence of insulin; insulin arouses glycogen synthesis by means of animating glycogen level and hindering glycogen phosphorylase (Stalmans et al., 1991; Bhandari et al., 2013). DM disables the typical limit of liver to incorporate glycogen. Synthase phosphatase incites glycogen synthase achieving glycogenesis (Prabu et al., 2012). In this study, diabetic rats exhibited a significant reduction in liver glycogen content. Diabetic rats treated with CSBMEt, CSBAET and glibenclamide appropriated liver glycogen levels to normal. The activity of glycogen synthase is controlled by diminished cell glycogen content, hormone signaling, sub-cell limitation, focusing of phosphatase and allosteric initiation by G6P (Parker et al., 2004). The flawed glycogen concentration of the diabetic condition was in part rectified by the extract (Arokiyaraj et al., 2011).

Natural antioxidant agents fundamentally originate from plants in the form of secondary metabolites (Marjorie, 1996). The presence of different types of phytochemicals like alkaloids, coumarins, flavonoids and steroids could be responsible for the antidiabetic activities (Sharma, 2012). Previously we have reported that CSB extracts (CSBMEt and CSBAEt) possess the presence of various phyto constituents such as tannins, steroid, glycosides, phenolic compounds, anthroquinones and flavonoids, and especially total phenol and flavonoid contents seem to be high and both extracts showed their own strong *in vitro* free radical scavenging activity (Jayaprasad and Sharavanan, 2015a). CSBMEt and CSBAEt are capable of restoring the tissue glycoprotein components in STZ induced diabetic rats (Jayaprasad et al., 2015c). Thus the antidiabetic effect of *C. swietenia* bark methanol and aqueous extracts might be due to these phytochemical constituents.

5. Conclusion

According to our findings, the *C. swietenia* bark methanol and aqueous extracts have proved to possess antidiabetic activity in STZ induced diabetic rats, which might be due to increase in plasma insulin levels, and this would be responsible for the restoration of carbohydrate metabolizing enzymes and liver glycogen. Results of CSBMEt are more effective and comparable to the standard drug glibenclamide. Further research on the molecular mechanism and the isolation of the compound responsible for this effect may lead to a new antidiabetogenic agent.

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