

Regeneration of pancreatic β -cells on streptozotocin induced diabetic rats under the effect of *Swietenia macrophylla* seeds

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Background: Diabetes mellitus is one of the major killers these days and has a profound effect in the quality of life. Despite considerable progress in the treatment of diabetes, search for newer drugs continues, especially from the natural resources. We have previously reported that the seed of the plant. *Swietenia macrophylla* is nontoxic. **Aim:** The current study was undertaken to investigate the effect of *Swietenia macrophylla* seeds on histopathological changes of pancreatic, hepatic and renal tissues, besides to observe its effect on the blood glucose level and lipid parameters in experimental diabetic rats. **Materials and Methods:** The Albino rat (Wister Strain) weighing 200-250 gm were divided into five groups of seven rats each and streptozotocin was used to induce diabetes except in the control group. The control group (I) and diabetic control group (II) received redistilled water. Group III and V diabetic rats were administered with aqueous extract of *Swietenia macrophylla* seeds (2 gm/kg body weight) daily for 30 days. Peptide was mixed with extract as adjuvant in the latter group (1:1, 2 gm/kg body weight/day for 30 days). Group IV diabetic rats were fed with aqueous extract of standard drug Metformin (10 mg/kg body weight). **Statistical Analysis:** Statistical analysis was done using Microsoft Excel, Office 2003 and SPSS 16 software. Values were expressed by mean \pm SD. *P* value <0.05, <0.01 were considered statistically significant. **Results:** The oral administration of extract alone and extract plus soya peptide to diabetic rats was found to possess significant hypoglycaemic as well as hypolipidemic activity. Histopathological changes include hypercellularity of islets tissue with increased hyperchromic nucleus in the same group. Increased density of islets in pancreatic tissue with higher percent of β cells and islets size in this group, in comparison to diabetic untreated group indicate regeneration of beta cells under the effect of *Swietenia macrophylla* seeds, without any significant change in hepatic and renal tissues. **Conclusion:** We conclude that the *Swietenia macrophylla* seeds have potentials for development into a therapeutic agent in diabetes mellitus.

Key words: Diabetes mellitus, histopathology, lipid profile, *Swietenia macrophylla* seeds

INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder that has profound effect in the quality of life in terms of physical health as well as social and psychological well-being. It is now a major killer worldwide. According to World Health Organization (WHO) the global population is in the midst of a diabetic epidemic, where the people of South East Asia and Western pacific region are specially having increased risk. Despite considerable progress in the treatment of diabetes by insulin and oral hypoglycaemic agents, search for newer drugs continues because the existing synthetic drugs have several limitations. The associated disadvantages with insulin

and oral hypo-glycaemia agents have lead to stimulation in the research for locating natural resources showing anti diabetic activity. The use of herbal medicines has been steadily increasing over the past decade. Several medicinal plants which have been traditionally used in the treatment of different disease including diabetes mellitus, cancer, liver disease and cardiac ailments^[1,2] etc., are now gaining attraction by researchers all over the world for scientific analysis. A considerable number of these plant based products are presently in use.^[3] *Swietenia macrophylla* which is commonly known as Mahogany in India, is one of them. It has been claimed to have antimalarial activity, antibabesial activity and anti diarrhoeal activity.^[4,5] A few studies have also documented its antioxidant property.^[6] We have earlier reported that the particular seed of this plant is nontoxic.^[7]

In the present study we wanted to observe the effect of this seed on the histopathological changes of different organs including liver, kidney and pancreas in streptozotocin induced Diabetic rats. Besides we also aimed to elucidate if it contains any hypoglycaemic and hypolipidemic property.

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MATERIALS AND METHODS

Plant

Seeds of *Swietenia macrophylla* were collected and authenticated by Botanical Survey of India. A voucher specimen (Ref.no.CNH/I-I/54/2009/Tech.II/154) was deposited at our laboratory for further reference.

Preparation of Extract

The seeds of *Swietenia macrophylla* were separated, washed, shed-dried at room temperature, powdered and sieved through 40 meshes. 200 mg powder was added to 1 ml of distilled water to make the solution.

Thereafter the solution was centrifuged at 3000 rpm for 15 minutes. The supernatant was filtrated and collected. The pure extract of *Swietenia macrophylla* seeds was stored in glass vial sealed by air tight lid at 4-6°C.^[8]

Animal

The Albino rat (Wister Strain) weighing 200-250 gm were used in this study. The animals were housed in stainless-steel cages under conventional conditions (temperature $22 \pm 1^\circ\text{C}$; relative humidity $50 \pm 10\%$, natural light-dark cycle) and fed with standard laboratory diet and water *ad libitum*. The principle of laboratory animal's care^[9] and the instructions given by our institutional ethical committee were followed throughout the experiment.

Experimental Design

Streptozotocin is the mostly used agent for induction of diabetes mellitus. Rats were kept in fasting for 12 hrs before and after injection of streptozotocin as unfed animals were more susceptible for streptozotocin.^[10] The animals were randomly allocated into five experimental groups of seven rats each as given below:

- Group I and II: A control group and diabetic control group respectively, which received redistilled water.
- Group III: Diabetic rats, administered with aqueous extract of *Swietenia macrophylla* seeds (2 gm/kg body weight) daily for 30 days.
- Group IV: Diabetic rats, administered with aqueous extract of Metformin (10 mg/kg body weight) daily for 30 days. The standard drug metformin is being used for many years to treat diabetes. Metformin is approved as anti-diabetic drug by U.S. Food and Drug Administration.
- Group V: Diabetic rats, administered with aqueous extract of *Swietenia macrophylla* seeds (1 gm/kg) + peptide (1 gm/kg) daily for 30 days. Peptide was mixed with extract as it contains some adjuvant properties.^[11]

Biochemical study

After 30 days of treatment, blood samples were collected from tail veins in vials containing heparin, centrifuged and plasma separated. Plasma glucose, lipid and other parameters related to liver, kidney and pancreatic function tests were carried out in the Department of Biochemistry, Nilratan Sircar Medical College, Kolkata.

Urine was collected separately in glass metabolic cages for 24 hrs urine collection.

Concentrations of urea and creatinine in urine were also assessed.

Histological procedure

For histopathological study, the liver, kidney and pancreas were collected from sacrificed animals.^[12] On the last day of experiment the rats were anesthetized and liver; kidney and tail (Splenic part) of pancreas were removed and were kept in 10% formaldehyde. Tissue processing was carried out by autotechnicon and the prepared five-micron thickness sections were mounted on slide and stained with hematoxylin and eosin (H and E). The slides were examined using Leitz microscope and their photo-micrographs taken and examined.

Statistical Analysis

Statistical analysis have done using Microsoft excel, Office 2003. Values were expressed by mean \pm SD. *P* value <0.05 were considered statistically significant.

RESULTS

The results of bio-chemical investigations have been depicted in Table 1. Our results clearly showed there is significant reduction of plasma glucose, total cholesterol, triglyceride and LDL-cholesterol levels in the extract (Group III) as well as extract plus peptide (Group V) treated rat compared to the diabetic control group (Group II). HbA1c (5) though not statistically significant, also showed similar trend. HDL cholesterol level is significantly increased only in the Group V diabetic animals treated with extract plus peptide. Though Group IV diabetic rats treated with metformin also had similar hypoglycaemic and hypolipidemic effect compared to the diabetic control group (II), the SGPT level is significantly raised. A significant reduction in the urine creatinine level was observed in the extract treated group compared to the diabetic control. The histopathological study of pancreatic tissues exhibited regeneration of β - cells in the extract fed animals [Figure 1c] compared to the diabetic control [Figure 1b].

DISCUSSION

Diabetes is becoming the third 'killer' disease of mankind,

Table 1: Biochemical study in the experimental rats

Parameters	Group I (Normal control)	Group II (Diabetic control)	Group III (Diabetic rats with extract)	Group IV (Diabetic rats with meformin)	Group V (Diabetic rats with extract plus peptide)
Plasmaglucoase level (mg/dl)	72.73 \pm 4	139.33 \pm 9.04	98.66 \pm 9.26 ^b	67 \pm 9.23 ^b	87.33 \pm 5.04 ^b
HbA1c (%)	5.5 \pm 1.2	5.7 \pm 1.04	5.0 \pm 1.11	4.9 \pm 0.9	5.0 \pm 0.8
Plasma total cholesterol (mg/dl)	64.47 \pm 3.4	103.28 \pm 8.3	64.42 \pm 3.3 ^a	61.65 \pm 4.40	58.85 \pm 7.5 ^b
Plasma triglyceride (mg/dl)	60 \pm 2.58	93 \pm 10.64	58.85 \pm 4.41 ^b	64.14 \pm 8.19	58.85 \pm 4.87 ^b
Plasma LDL (mg/dl)	20.71 \pm 2.13	34.28 \pm 7.8	22.57 \pm 5.3 ^b	19.71 \pm 1.11	21.57 \pm 4.27
Plasma HDL (mg/dl)	50.14 \pm 11.99	37.14 \pm 5.8 ^a	35.42 \pm 6.60 ^b	39.14 \pm 8.47	49.57 \pm 7.95
Plasma lypase (U/L)	43.85 \pm 7.08	44.14 \pm 11.81	48.28 \pm 3.30	52.28 \pm 2.9	50.42 \pm 3.99
Plasma amylase (U/L)	38.14 \pm 10.62	35 \pm 5.7	27.57 \pm 4.9 ^a	34 \pm 12.49	27.42 \pm 4.15 ^a
SGOT (U/L)	42.22 \pm 3.59	46.83 \pm 4.79	42.66 \pm 1.96	46.66 \pm 9.24	47.33 \pm 4.84
SGPT (U/L)	38.91 \pm 3.20	42.16 \pm 3.86	34.16 \pm 2.85 ^a	41 \pm 4.97	39.83 \pm 3.76
Urea (mg/dl)	22.95 \pm 2.43	24.45 \pm 3.4	19.56 \pm 1.4	20.05 \pm 2.11	21.0 \pm 2
Creatinine (mg/dl)	0.5 \pm 0.09	0.7 \pm 0.07	0.4 \pm 0.02	0.67 \pm 0.01	0.6 \pm 0.012
Urine urea (gm/L)	11.21 \pm 1.62	17.25 \pm 4.34 ^b	10.85 \pm 1.34	11.14 \pm 1.86	11.85 \pm 2.47
Urine creatinine (gm/L)	0.77 \pm 0.25	1.3 \pm 0.23 ^b	0.64 \pm 0.06	0.70 \pm 0.12	0.99 \pm 0.33

Paired two tail student's T test was done. Values are expressed as mean \pm SD. Indicate the level of significance in comparison to the healthy controls (Group I). ^aP< 0.05; ^bP<0.01; *Plasma LDL=Low Density Lipoprotein; Plasma HDL= High Density Lipoprotein; SGOT/AST=Serum Glutamic Oxaloacetic Transaminase; SGPT/ALT = Serum Glutamic Pyruvic Transaminase

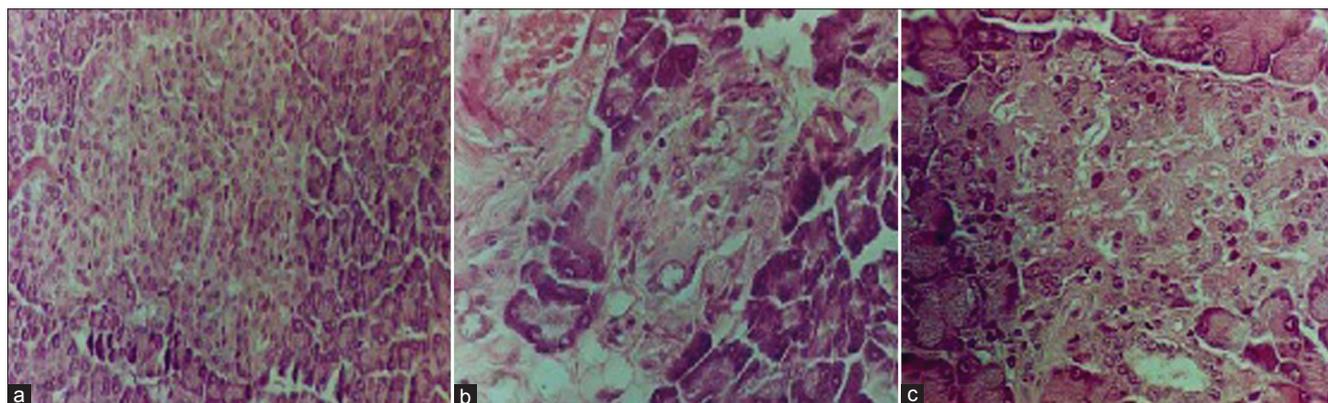


Figure 1: Histopathological pictures (H and E stain) of pancreas: (a) Pancreas of normal healthy control (GR I) rat; (b) Pancreas of Diabetic Control (GR II) rat; (c) Pancreas of diabetic rat treated with extract of *Swietenia macrophylla* seeds (GR III)

after cancer and cardiovascular diseases, because of its high prevalence, morbidity and mortality.^[13] The oral hypoglycaemic agents currently in use have characteristic profiles sometimes with serious long term side effects^[14] and drug resistance. However medicinal plants used in diabetes claimed to have comparatively less toxic effect besides its economic advantage. *Swietenia macrophylla* seeds have also some medicinal properties as reported earlier. In our previous study we demonstrated that the seeds were nontoxic.^[8] The present study also showed no change in the liver of and kidney tissues of the rats under the effect of these seed extract as well as there was no abnormality in the biochemical parameters related to those organ function [Table 1]. There were no significant changes also in the pancreatic function tests. But the histopathological study of pancreatic tissues exhibited regeneration of β - cells in the extract fed animals [Figure 1c] compared to the diabetic control [Figure 1b]. Figure 1a shows histopathology of pancreatic tissue of healthy control animals. The effect of consumed extract of

the seeds on percent of β -cells in islets of pancreas in different experimental groups has been given in Figure 2.

This study also revealed that the extract of the seeds had significant hypoglycaemic effect and hypolipidemic activity as depicted in Table 1. After 30 days of treatment with extract, the plasma glucose level was adequately controlled in the Group III and V experimental animals when compared to the diabetic control (Group II). The Group III and Group V animals, which were treated with extract and extract plus peptide had significantly reduced plasma total cholesterol, triglyceride as well as LDL cholesterol levels, compared to diabetic control (Group II) animals. HDL level was increased only in case of the animal treated with extract plus peptide (Group V). This may be due to effect of peptide as an adjuvant. In our study the Group IV diabetic rat treated with metformin, a standard drug used in diabetes, exert similar effect compared to the extract. But increased SGPT levels in

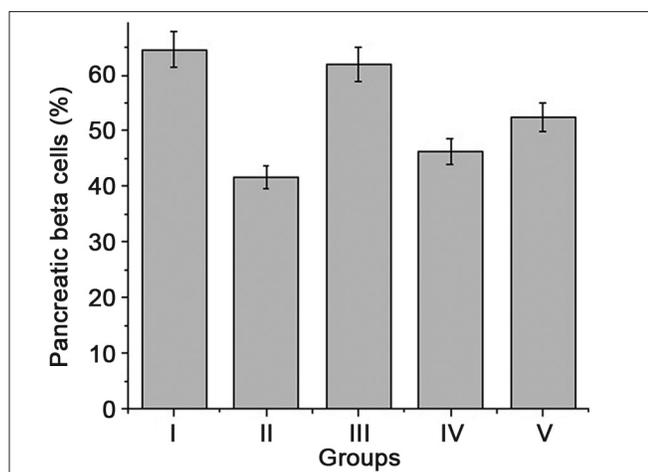


Figure 2: Effect of consumed extract of seeds on percent of β cells in each islet

those animals indicate some form of hepatotoxicity. Similar studies with other plant products in the diabetic models, reported earlier had demonstrated hypoglycaemic^[15] and also hypolipidemic effects. Our study for the first time revealed several beneficial effects of this seed-extract on diabetic model, especially with the regeneration of pancreatic β -cells.^[8]

CONCLUSION

Tough our study had limited sample size, our observations elucidated that the extract of *Swietenia macrophylla* had not only hypoglycaemic and hypolipidemic effect on experimental diabetic rats but it also helped to regenerate the pancreatic β -cells. We conclude that the *Swietenia macrophylla* seeds have potentials for development into a therapeutic agent for diabetes mellitus. Further large scale study with different active components of the extract is needed in this direction.

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