ORIGINAL ARTICLE

Hypoglycemic effect of *Swietenia macrophylla* seeds against type II diabetes

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The antidiabetic effect of *Swietenia macrophylla* seeds was evaluated in Streptozotocin and Nicotinamide induced type II diabetic rats. Methanol extract of *Swietenia macrophylla* seeds was administered orally at doses of 150 and 300 mg/kg body weight for 12 consecutive days. Fasting blood sugar (FBG) was estimated on overnight fasted rats on day 1, 5 and 12 days. Lipid profiles, liver glycogen levels and changes in body weight were also measured. The extract was found more effective at the dose of 300 mg/kg body weight and it lowered FBG levels was statistically significant $P < 0.01$ (32.78%) in diabetic rats at day 12. Extract at the same dose also significantly reduced $P < 0.01$ the elevated level of serum total cholesterol (18.56%) and triglyceride (10.41%), and increased $P < 0.01$ (46.27%) the reduced liver glycogen level. Though statistically non-significant the extract at both the doses was found to improve the body weight of diabetic rats. The observation concludes that the methanol extract of seeds of *Swietenia macrophylla* has hypoglycemic as well as hypolipidemic effect.

Key words: *Swietenia macrophylla,* Streptozotocin, Nicotinamide, type II diabetes

INTRODUCTION

Before the introduction of insulin in 1922, the treatment of diabetes mellitus relied on dietary measures which included the use of traditional plant therapies. Many traditional plants were successfully used for the treatment of diabetes.[1-3] Though the active principles of various classes of chemical compounds have been isolated from plants, some remain to be identified.[4] The World Health Organization has recommended that traditional plant treatments for diabetes warrant further evaluation.[5] An antidiabetic agent could exert a beneficial effect in the diabetic situation by enhancing insulin secretion and or by improving/mimicking insulin action.[6] Nowadays, the use of complementary and alternative medicine and especially the consumption of botanicals have been increasing rapidly worldwide, mostly because of the supposedly less frequent side-effects when compared to modern western medicine.[7]

Swietenia macrophylla is a folk-medicinal tree known as mahogany. The powdered seed in empty stomach is successfully employed for the treatment of diabetes in east Midnapore, India. The effectiveness of seed extract was scientifically evaluated in type I model.[8] An attempt has been taken to investigate the antidiabetic activity of methanol extract of *Swietenia macrophylla* seed on type II model.

MATERIALS AND METHODS

Plant Material

The seeds of the plant *Swietenia macrophylla* (Family: Meliaceae) were collected in the month of December 2005 from the district of Midnapore (East), West Bengal, India. The plant was taxonomically identified and authenticated by Botanical Survey of India (Ref. No. CNH/1(64)/2005-Tech.II/697), Sibpur, India. The seeds of *Swietenia macrophylla* were separated, washed, shed-dried at room temperature, powdered and sieved through 40 meshes. The powder was preserved in an air-tight container for further use. A voucher specimen deposited in our herbarium for further use.

Preparation of Extract

The shed-dried powdered seeds (1200g) were exhaustively extracted with (40-60°C) petroleum ether followed by 90% methanol using a soxhlet apparatus.[14] It was then concentrated, dried *in vacuo* (yield 15%) and the residue stored in a desiccators for further use. As methanol is a solvent takes almost all the phytoconstituents to the extract it was selected as the solvent for extraction.

Preliminary Phytochemical Screening

The qualitative phytochemical screening[9,10] revealed the presence of triterpenoids.

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Antidiabetic Studies

Standard drugs

Streptozotocin (STZ) used for the induction of diabetes was procured from SRL, India. Nicotinamide and other reagents used in the experiments were of analytical grade from Ranbaxy Chemicals, Mumbai, India and Glibenclamide (Daonil™, Hoechst, India) tablets were procured from local market.

Animals

Wistar albino rats (150-200 g) of either sex were selected for the experiment. The animals were kept under standard conditions of 12:12 h light and dark cycle in polypropylene cages and fed with standard laboratory diet and water *ad libitum*. The animals were acclimatized to laboratory condition for seven days before commencement of experiment. All studies were carried out using six rats in each group. The Animal Ethical Committee, Jadavpur University reviewed the entire animal protocols prior to conducting the experiments.

Oral Glucose Tolerance Test

The oral glucose tolerance test (OGTT)[11] was performed in overnight fasted (18h) normal rats. Rats divided into three groups (n = 6) were orally administered distilled water and *S. macrophylla* methanol extract (MESM) (200 and 300 mg/kg), respectively. Glucose (2 g/kg) was fed orally, 30 min prior to the administration of extracts. Blood was withdrawn from the tail vein and the glucose level was estimated by using the glucose estimation kit obtained from Jhonson and Jhonson, Mumbai.[12]

Antihyperglycemic Studies

Induction of type II diabetes mellitus or non-insulin dependent diabetes mellitus (NIDDM) was induced in overnight fasted adult Wistar strain albino rats of both sex weighing 150– 200 g, by a single intraperitoneal (i.p) injection of 65 mg/kg STZ in citrate buffer (pH 4.5), 15 min after the i.p administration of 110 mg/kg of nicotinamide in normal saline (Pellegrino *et al.*, 1998). Hyperglycemia was confirmed by the elevated glucose levels in plasma, determined at 72h and then on day seven after injection. The rats found with permanent NIDDM (FBG > 200 mg/dl) were used for the antidiabetic study.

Experimental Design

Animals were divided into four groups of six rats each. Group I animals were treated with vehicle while Group II and III animals were treated with MESM extract at 200 and 300 mg/kg body weight, respectively. Group IV animals were treated with glibenclamide 0.25 mg/kg.[13] The extracts were administered for 12 days from the day of induction. Fasting blood sugar was estimated on overnight fasted rats on day one, five and 12 days. Lipid profiles, liver glycogen levels[14] and changes in body weight were measured after the animals were sacrificed on day 12 by decapitation.

Statistical Analysis

All results are expressed as the mean ± SEM. The results were analyzed for statistical significance by one–way analysis of variance (ANOVA) followed by Dunnett's test using computerized Graph Pad InStat version 3.05, Graph pad software, U.S.A.

RESULTS

In OGTT, the extract, at the second hour, showed significant reduction in plasma glucose level indicated in Table 1. The effect of methanol extract of *Swietenia macrophylla* (MESM) on fasting blood glucose (FBG) levels of STZ induced animals are presented in [Table 2]. The difference between the experimental and control rats in lowering the FBG levels was statistically significant ($P < 0.01$) at both the selected doses and comparable to that of standard drug glibenclamide. The extract, at 300 mg/kg oral dose, was found to be most effective with maximum reduction of FBG of 32.78% on day 12. As compared to the diabetic control rats, the significant differences were observed in serum lipid profiles, liver glycogen levels.

Serum total cholesterol and triglyceride level were significantly elevated in diabetic group in comparison to control. Supplementation of this extract for 12 days significantly reduced the level [Table 3].

There is an elevation in levels of hepatic glycogen in type II-diabetic rats, after *S. macrophylla* treatment. Whether in standard group an increased level of liver glycogen also observed in Table 3.

Significant changes between initial and final body weights were observed in all the extract and standard treated groups [Table 4].

Table 1: Effect of methanol extract of *Swietenia macrophylla* seed on oral glucose tolerance test

Group	Treatment	Plasma glucose concentration (mg/dl)		
		0 min.	60 min.	120 min.
I	Normal control	76.25 ± 0.69	97 ± 0.91	99 ± 0.81
II	Normal + MESM 200 mg/kg	78.75 ± 0.85	91.25 ± 0.85	83.25 ± 0.47
III	Normal + MESM 300 mg/kg	77.25 ± 0.75	83 ± 0.4	77.25 ± 0.85

Table 2: Effect of methanol extract of *Swietenia macrophylla* seed on oral fasting plasma glucose level in rats

Group	Treatment	Plasma glucose concentration (mg/dl)		
		Ist day	5th day	12th day
I	Normal control	76.25 ± 0.62	76 ± 0.91	75.75 ± 0.47
II	Diabetic control	169.25 ± 3.59	178.75 ± 2.65	210.25 ± 2.05
III	Diabetic + MESM 200 mg/kg	162.75 ± 3.96	142.75 ± 2.56**(12.28%)	132.75 ± 2.56**(18.43%)
IV	Diabetic + MESM 300 mg/kg	183.75 ± 2.52	151.25 ± 3.25**(17.68%)	123.5 ± 2.21**(32.78%)
V	Diabetic + Glibenclamide 0.25 mg/kg	190.75 ± 1.93	161.5 ± 3.30**(15.53%)	113.5 ± 1.55**(40.49%)

**Represents statistical significance when compared with diabetic control ($P < 0.01$).

Table 3: Effect of methanol extract of *Swietenia macrophylla* seed on serum lipid profiles and liver glycogen in rat

Group	Treatment	Cholesterol (mg/dl)	Triglyceride (mg/dl)	Liver glycogen (mg/g)
I	Normal control	50.59 ± 0.38	84.14 ± 0.48	9.27 ± 0.01
II	Diabetic control	67.45 ± 0.83	96.03 ± 0.64	4.4 ± 0.03
III	Diabetic + MESM 200 mg/kg	60.47 ± 0.64*(10.34%)	88.49 ± 0.19*(7.85%)	7.91 ± 0.01**(44.37%)
IV	Diabetic + MESM 300 mg/kg	54.93 ± 0.28**(18.56%)	86.03 ± 0.03**(10.41%)	8.19 ± 0.01**(46.27%)
V	Diabetic + Glibenclamide 0.25 mg/kg	42.51 ± 0.24**(36.97%)	76.41 ± 0.19**(20.43%)	9.48 ± 0.01**(53.58%)

Unit of glycogen in mg/g multiplied by 10. *$P < 0.05$ when compared with diabetic control, **$P < 0.01$ when compared with diabetic control.

Table 4: Effect of methanol extract of *Swietenia macrophylla* seed on change in body weight in rats

Group	Treatment	Initial (g)	Final (g)
I	Normal control	157 ± 2.59	158.5 ± 1.55
II	Diabetic control	170.5 ± 2.59	143.25 ± 3.49
III	Diabetic + MESM 200 mg/kg	175.25 ± 1.70	184.25 ± 2.65
IV	Diabetic + MESM 300 mg/kg	163.75 ± 1.75	176.5 ± 1.84
V	Diabetic + Glibenclamide 0.25 mg/kg	172.5 ± 1.7	190.75 ± 1.91

DISCUSSION

The antidiabetic activity of the folk medicinal plant *Swietenia macrophylla* was brought to light by our previous research report.[8] The seed of this plant (methanol extract) is active against both aloxan and streptozotocin induced diabetic rats. In glucose loaded normal rats, hypoglycemia was observed at 120 min on administration of the MESM [Table 1]. This justified the efficacy of the extract to control elevated blood sugar levels. Maintenance of blood sugar levels in normal and diabetic rats were observed throughout the period of study.

The single high dose of streptozotocin (STZ) injection can produce type 1 diabetes by destroying the β-cells of the pancreas[15] in adult rats but when STZ injected in mild dose in rats develop type II diabetes in the adult age.[16] A new animal model of type II diabetes has been produced by combination of STZ and nicotinamide administration in adult rats.[17,18] Nicotinamide has antioxidant property, exerts protective effect on the cytotoxic action of STZ by scavenging free radicals and causes only minor damage to pancreatic β-cell mass producing type II diabetes.[19]

Fasting blood glucose level in diabetic rats is an important basal parameter for monitoring diabetes[16] and it has shown that the MESM causes the antidiabetic effect by reducing the Fasting blood glucose level. The significant decrease in the levels of fasting blood glucose in diabetic rats treated with the MESM [Table 2] may be by stimulation of the residual pancreatic mechanism, probably by increasing peripheral utilization of glucose.[20]

Diabetes is associated with hyperlipidemia.[21] The serum total cholesterol and triglyceride have been decreased significantly in type II diabetic rats after the extract supplementation [Table 3]. This effect may be due to low activity of cholesterol biosynthesis enzymes and or low level of lipolysis which are under the control of insulin.[22]

Increase in liver glycogen can be brought about by an increased in glycogenesis and or inhibited glucogenolysis. Excessive hepatic glycogenolysis and gluconeogenesis associated with decreased utilization of glucose by tissues is the fundamental mechanism underlying hyperglycemia in the diabetic state.[23] This may be due to the lack of or resistance to insulin, which is essential to trigger the activation of glycogen synthase systems.[24] The significant increase of liver glycogen levels in the extract treated diabetic animals [Table 3] may be because of the reactivation of the glycogen synthase systems.

Qualitative phytochemical assay indicated the presence of triterpenoids in the methanol extract. Thus triterpenoids may serve as potential hypoglycemic agent in this extract. Now our aim is to isolate lead triterpenoid molecule to be useful against diabetes.

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