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Research Article

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Isolation of Nontoxic Fraction from *Swietenia Mahagoni* Seed and its Hypoglycemic Activity in Normal and Diabetic Rats

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ABSTRACT

Swietenia mahagoni is a tropical ever-green hardwood timber species of Meliaceace family. In recent years increasing number of Bangladeshi people are using the Mahagoni seeds for the management of diabetes. The aim of the investigation was to evaluate the antidiabetic activity of Sm-SEF7 fraction of seeds from the plant Swietenia mahagoniinstreptozocin induced diabetic rats. Diabetes was induced by a single dose of intraperitoneal injection of streptozocin (90 mg/kg) in Long-Evans rats. Glibenclamide (5 mg/kg) was used as a standard antidiabetic agent. The result indicated that after oral ingestion of Swietenia mahagoni for 21 days in diabetic rat, a significant plasma glucose lowering effect (plasma glucose in mmol/l, Mean ± SD; 8.81 ± 1.22 vs. 3.57 ± 3.38, on the 1st day vs. 22nddays,p = .002) was improved. It also enhanced insulin releasing activity (plasma insulin in ng/ml, Mean ± SD: group 1 vs. group 3, 0.54 ± 0.13 vs. 0.93 ± 0.19; p=0.001) was significantly higher in the Sm-SEF7 treated type 2 rats (group 3) than in water treated control group (group 1). But there was no change in lipid level after 21 days fraction feeding on type 2 model rats. The results indicated that, nontoxic Sm-SEF7 fraction of Swietenia mahagoni seed possesses antidiabetic properties in type 2 diabetic model rats. It seems to act as an insulonomimetic and/or insulin sensitizing agent.

Keywords: Antidiabetic activity; Diabetes mellitus; Streptozocin; *Swietenia mahagoni*; Sm-SEF7 fraction

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INTRODUCTION

Diabetes mellitus (DM) is one of the common metabolic disorders with micro-and macro-vascular complications that results in significant morbidity and mortality considered as one of the five leading causes of death in the world [1,2]. It is a group of disorders characterized by circulating hyperglycemia resulting from either defect in insulin secretion or insulin action. According to the international diabetes federation (IDF), it was estimated that more than 382 million people throughout the world had diabetes in 2013. Its prevalence is increasing rapidly, particularly in developing countries, and is expected to rise to 552 million by 2030 [3]. According to the latest information of the World Health Organization (WHO), the global prevalence of diabetes in adult was 9% in 2014. In 2012 diabetes was the definite cause of 1.5 million deaths. More than 80% of diabetes deaths occur in low- and middle-income countries [4]. The clinical disclosure of hyperglycemia includes polydipsia, polyuria, fatigue, weight loss and polyphagia [5]. Untreated high blood sugar levels increase the risk of microvascular damage such as nephropathy, retinopathy and neuropathy. It is associated with significant morbidity, reduced life expectancy, increased risk of macro-vascular complications (stroke, ischemic heart disease and peripheral vascular disease), diminished quality of life and death [6]. Studies in various populations in Bangladesh have reported a prevalence of diabetes from 4% to 13% among adults with some variations by urban and rural setting [7,8]. This proportional increase in Bangladesh seemed relatively higher compared to other Asian countries [9].

Swietenia mahagoni (S. mahagoni), is one of the most significant plants of Meliaceae family. It is beautiful, lofty, evergreen, large native tree of tropical America, Mexico, South America, and India. Usually, this plant is 30-40 meters in height and 3-4 meters in girth [10]. It is used for furniture, fixtures, musical instrument [11]. The seeds of *S. mahagoni* have been reported for its anti-inflammatory, analgesic, antipyretic and anti-tumour activities [12]. Studies also reported that the seeds extracts also possess PPAR-γ agonistic [13], anti-microbial [14] and cytotoxic [15], anti-fungal [16], anti-ulcer [17] and PAF inhibition activities [18].
In Indonesia, India and now also in Bangladesh, *S. mahagoni* seed has folkloric reputation to cure diabetes [19]. There is no systematic work about the antidiabetic activity of *S. mahagoni* though there are very few information of this plant in this line [20,21]. So, this study was carried out to critically evaluate the antidiabetic effect of isolated nontoxic fraction of *Swietenia mahagoni* seeds instreptozocin induced diabetic rats.

EXPERIMENTAL SECTION

Plant Material

Swietenia mahagoni seeds were purchased from a local medicinal shop, Dhaka. The seeds were identified at the National Herbarium.

Extract Preparation

Swietenia mahagoni seeds were collected and white inner parts were separated from the brown peel of seed. The seeds were dried, ground and crushed to powder. The dried powder of *Swietenia mahagoni* seeds (3000 g) were extracted with 80% ethanol at room temperature for 3 days and then filtered and evaporate to concentrate by using rotary vacuum evaporator bellow 40°C. The extract was freeze dried. Then 50 g extract was dissolved in a small amount of water and applied to a sephalex LH-20 column (70 × 3.5 cm). The fractions were collected.

Acute Toxicity Study

After brine shrimp lethality assay it was found that Sm-SEF7 fraction was nontoxic (using National Cancer Institute protocol). As the LD50 was found to be more than 4000 mg/kg, so the dose 312.5 mg/(10 ml water)/kg body weight was selected.

Chemicals Used

All chemicals and drugs used were obtained commercially and of analytical grade. Streptozocin and Glibenclamide (Sigma-Aldrich Company, St. Louis, Missouri, USA) and all other chemicals, reagents and kits were purchased from the local market.

Experimental Animals

The experiments were carried out on Long-Evans rats (180-220 gm) of both sexes, bred at BIRDEM animal house and maintained at a constant room temperature of 22 ± 5°C with humidity of 40-70% and the natural 12 hours day-night cycle. The animals are housed in an air-conditioned animal room and fed on pellets and water. Fasted animal were deprived of food for at least twelve hours but allowed free access to plain water.

Induction of Type 2 Diabetes

Type 2 diabetes was induced by a single intraperitoneal injection of STZ at a dose of 90 mg/kg body weight. Experiments were carried out 3 months after STZ injection and rats having blood glucose level 8.5-12 mmol/l at fasting were taken as diabetic rat.

Experimental Design

In the experiment a total number of 18 rats were used. The rats were divided into 3 groups of six each.
Group 1: Type 2 diabetic control rats received only water.
Group 2: Type 2 diabetic control rats received standard drug glibenclamide at a dose of 5 mg/kg body weight.
Group 3: Type 2 diabetic rats were received Fraction Sm-SEF7 at a dose of 312.5 mg/10 ml water/kg body weight for 21 days orally.

At the end of the experiment rats were subjected to light ether anaesthesia then blood was collected from the retro-orbital venous plexus following the technique described by Coccheto and Bjornsson [22]. Blood glucose was determined by GOD–POD kit method. The change in body weight was observed once a week [23].
After 15 days, body weight was determined and the animals were sacrificed under theinfluence of anesthetic ether. The blood was collected by heart puncture. The blood sample withdrawn from the sacrificed animals was centrifuged at 3000 rpm for 15 min. [24]and was analyzed for lipid profiles [25] (Serum cholesterol, Serum triglyceride, HDL cholesterol).

Statistical Analysis

All the data are expressed as mean ± SD (Standard deviation). The differences between diabetic control and treatment group were evaluated by one-way analysis of variance (ANOVA), followed by Dunnett's test for multiple comparisons and the values of $P<0.05$ were considered as statistically significant.

RESULTS

Isolated Non- Toxic Fraction

From Brine Shrimp Lethality Assay it was found that Sm-SEF7 fraction of 80% ethanolic extract of *Swietenia mahagoni* seedwas non-toxic (Table 1).

Table 1: Toxicity of different extract of *Swietenia mahagoni* seed

Name of extract	LD50 at 24 h (mg/ml)	LD50 at 48 h (mg/ml)
Sm-W	1.019×10^{-6}	0.087×10^{-6}
Sm-E	0.18×10^{-6}	0.02×10^{-6}
Sm-M	0.06×10^{-6}	All Shrimp dead (Too much toxic)
Sm-C	0.01×10^{-6}	Too much toxic
Sm-SEF7	No toxicity was found	No toxicity was found

Sm-W= Water extract, Sm-E=Ethanol extract, Sm-M=Methanol extract, Sm-C=Chloroform extract and Sm-SEF7=Fraction isolated from LH20 column

Effect on Body Weight of Type 2 Diabetic Model Rats

The effect of *Swietenia mahagoni* seed extract (Sm-SEF7) on body weight of type 2 diabetic model rats was observed during 21 days study period. Body weight of each rat was taken at 7 days interval. No significant change was found in body weight in any group after 21 days chronic study (Table 2 and Figure 1).

Table 2: Effect of Swietenia mahagoni seed extract (Sm-SEF7) on body weight of type 2 diabetic model rats

Group	BW_0 day (g)	BW_7 day (g)	BW_14 day (g)	BW_22 day (g)
Group 1(n=6)	192 ± 21	185 ± 28	188 ± 14	190 ± 29
Group 2 (n=6)	182 ± 13	189 ± 25	183 ± 32	182 ± 7
Group 3(n=6)	202 ± 7	193 ± 19	200 ± 18	198 ± 20

BW= Body Weight. Results are expressed as Mean ± Standard Deviation (SD). n = Number of Rats

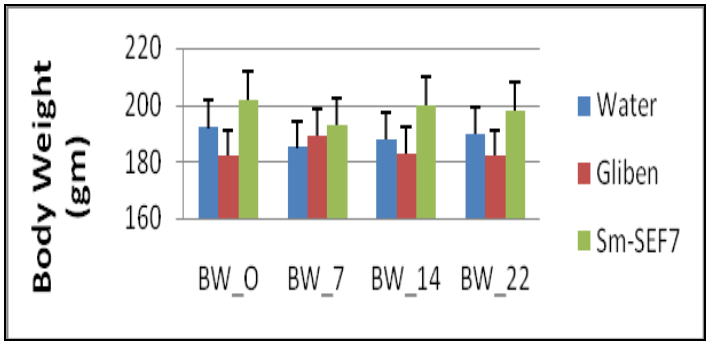

Figure 1: Effect of *Swietenia mahagoni* seed extract (Sm-SEF7) on body weight of type 2 diabetic model rats

Acute Hypoglycemic Effect on Type 2 Diabetic Model Rats

The acute hypoglycemic effect of *Swietenia mahagoni* seed extract (Sm-SEF7) on type 2 diabetic model rats was observed at 0, 30 and 75 min after oral glucose load. A significant plasma glucose lowering effect was observed

between water control and Sm-SEF7 feed group as compared to the glibenclamide treated group (Table 3 and Figure 2).

Table 3: Acute effect of *Swietenia mahagoni* seed fraction (Sm-SEF7) on plasma glucose levels (M ± SD) of type 2 diabetic model rats when the extract was fed simultaneous with glucose load

	Plasma Glucose (mmol/l)			
Group	**Min 0**	**Min 30**	**Min 75**	**Iobv**
Group 1 (n=6)	7.99 ± 1.05	15.02 ± 2.43	15.80 ± 2.01	7.81 ± 1.93
Group 2 (n=6)	8.81 ± 1.22	16.60 ± 1.97	12.38 ± 3.53^{b*}	3.57 ± 3.38^{b**}
Group 3 (n=6)	7.62 ± 1.20	14.72 ± 4.67	13.39 ± 2.75^{a**}	4.19 ± 1.86^{a**}

ANOVA was done as the test of significance; 'a' means significant difference between group 1 and group 2; 'b' means significant difference between group 1 and group 3; $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$; iobv (sum of the increments over the basal value)

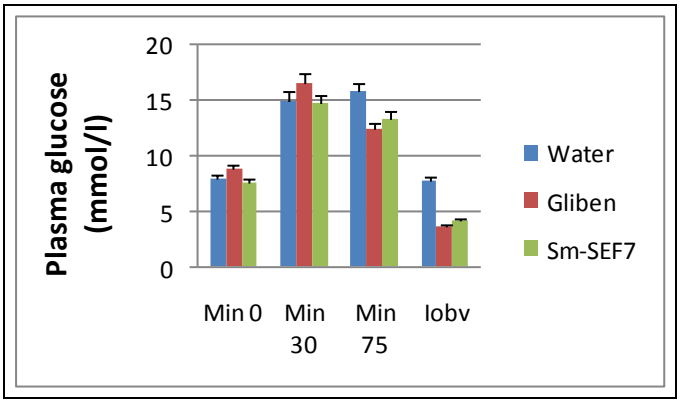

Figure 2: Acute effect of *Swietenia mahagoni* seed fraction (Sm-SEF7) on plasma glucose levels (M ± SD) of type 2 diabetic model rats when the extract was fed simultaneous with glucose load

Chronic Effect on Glycemic Status of Type 2 Model Rats

After 21days of consecutive feeding Sm-SEF7 fraction, the type 2 diabetic rats were sacrificed on the 22nd day, showed a significant reduction in the fasting plasma glucose level in type 2 diabetic rats (Table 4 and Figure 3).

Table 4: Chronic effect of *Swietenia mahagoni* seed fraction (Sm-SEF7) on glycemic status of type 2 diabetic model rats on 22nd day

Group	**Plasma Glucose (mmol/l)**	
	0 day	**22nd day**
Group 1 (n=6)	7.99	7.99
Group 2 (n=6)	8.81	5.02**
Group 3 (n=6)	7.62	4.91**

Results are expressed as Mean ± Standard Deviation (SD). n = Number of Rats

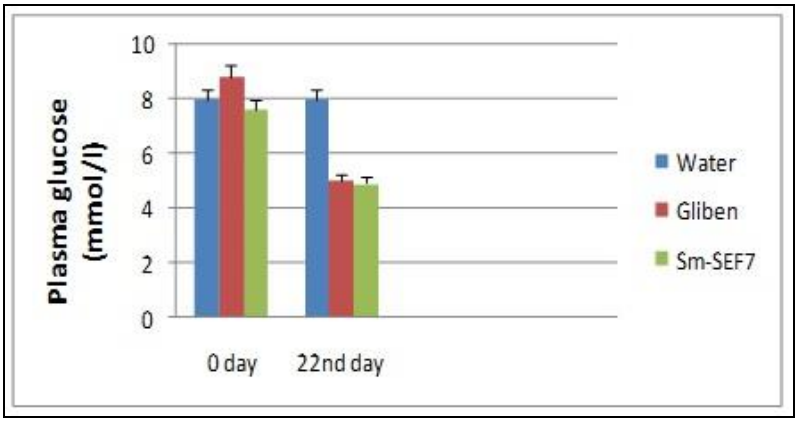

Figure 3: Chronic effect of *Swietenia mahagoni* seed fraction (Sm-SEF7) on glycemic status of type 2 diabetic model rats on 22nd day

Chronic Effect on Plasma Insulin of Type 2 Model Rats

After 21days of consecutive feeding Sm-SEF7 fraction, the fasting plasma insulin was significantly higher in group 3 rats (Sm-SEF7 feeding group) as compared to group 1 (water control) (Table 5 and Figure 4).

Table 5: Chronic effect of *Swietenia mahagoni* seed fraction (Sm-SEF7) on plasma insulin of type 2 diabetic model rats on 22nd day

Group	Plasma insulin (ng/ml)	
	0 day	22nd day
Group 1 (n=6)	0.54	0.54
Group 2 (n=6)	0.63	1.24***
Group 3 (n=6)	0.62	0.89**

Results are expressed as Mean ± Standard Deviation (SD). n = Number of rats

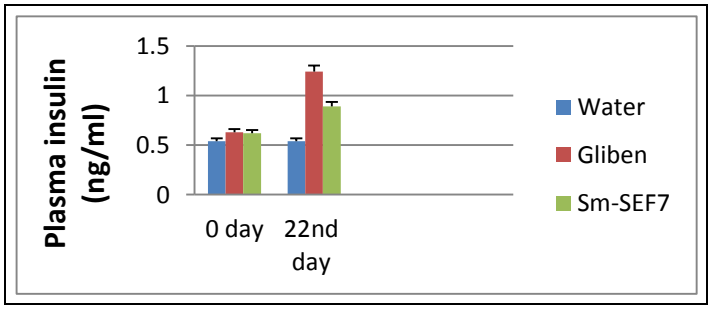

Figure 4: Chronic effect of *Swietenia mahagoni* seed fraction (Sm-SEF7) on plasma insulin of type 2 diabetic model rats on 22nd day

Chronic Effect on Fasting Plasma Lipid of Type 2 Model Rats

After 21 days Sm-SEF7 treatment the cholesterol and triglyceride level were decreased in group 3 than in group 1 but the differences was not significant. Other two parameters HDL-cholesterol and LDL-cholesterol did not show any difference among any group (Table 6).

Table 6: Plasma lipid in group 1, group 2 and group 3 (Sm-SEF7 treated type 2 diabetic model rats)

Parameters	Groups		
	Group 1 (n=6)	Group 2 (n=6)	Group 3 (n=6)
Cholesterol (mg/dl)	76.83 ± 10.98	61.5 ± 9.25	66.50 ± 8.73
Triglyceride (mg/dl)	81.50 ± 17.56	69.67 ± 6.20	75.83 ± 20.88
HDL (mg/dl)	44.73 ± 9.25	45.73 ± 4.22	39.02 ± 7.19
LDL (mg/dl)	15.79 ± 9.71	13.79 ± 8.17	12.31 ± 6.25

DISCUSSION

In the allopathic medicinal systems Management of diabetes is still a challenge. Though, various types of oral anti-hyperglycemic agents and insulin are available for the treatment of diabetes mellitus but these synthetic agents are also having more side effects [26]. In the present study the antidiabetic activity of 80% Ethanolic extract of Sm-SEF7Fraction of *Swietenia mahagoni seeds* was evaluated in Streptozocin induced diabetic rats. The nontoxic fraction was isolated by extraction of *Swietenia mahagoni* seed with aqueous 80% ethanol and passing through the LH column. Due to lower toxicity and higher β-cell specificity relative to other diabetogens Streptozocin was chosen to induce diabetes in the present study. From this research work it was found that 80% Ethanolic extract of Sm-SEF7Fraction of *Swietenia mahagoni* seeds produced no significant change in body weight in any group of diabetic rats after 21 days chronic study (Table 2 and Figure 1).

It also found that acute hypoglycemic effect of 80% Ethanolic extract of Sm-SEF7Fraction of *Swietenia mahagoni* seed was significant at 75 min interval. A significant plasma glucose lowering effect (p value <0.001) was observed between group 1 and group 3 (plasma glucose level, mmol/l, M ± SD, 13.39 ± 2.75 in Sm-SEF7 fed group or group 3 vs. 15.80 ± 2.01 in water control group 1) at 75 min interval. Plasma glucose was also significantly lowered in glibenclamide treated group (group 2) than diabetic control group (group 1) at 75 min interval (Table 3 and Figure 2). The 80% Ethanolic extract of Sm-SEF7Fraction of *Swietenia mahagoni* seeds also showed chronic hypoglycemic effect by significantly reducing the fasting plasma glucose level in type 2 diabetic rats after 21 days of consecutive feeding of Sm-SEF7 fraction (Tables 4 and 5). From this study it also decided that Sm-SEF7 fraction also significantly increase the plasma insulin in type 2 diabetic rats after 21 days (Figures 3 and 4).

It also included that from the present study it was found that cholesterol and triglyceride level was decreased in Sm-SEF7 treated rat (group 3) than in diabetic control rat (group 1). But the differences were not significant. Other two parameters HDL-cholesterol and LDL-cholesterol did not show any difference among any group (Table 6).

CONCLUSION

From the findings and above discussion it may be concluded that, the fraction Sm-SEF7 of *Swietenia mahagoni* seed has no toxicity. It possesses antidiabetic properties in type 2 diabetic model rats. It seems to act as an insulinomimetic and/or insulin sensitizing agent. Therefore, the fraction Sm-SEF7 of *Swietenia mahagoni* seed may be useful in the treatment of type 2 diabetes.

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