

## Original Article

# Effect of Ethanolic Extract of *Swietenia mahagoni* Seeds on Experimentally Induced Diabetes Mellitus in Rats

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### Abstract

Diabetes mellitus is a heterogeneous group of syndromes characterized by an elevation of blood glucose caused by a relative or absolute deficiency of insulin. The incidence of diabetes is growing rapidly worldwide. Drug treatment for diabetes mellitus is expensive and carries risks for many adverse effects. Bangladesh is a rich emporium of medicinal plants useful in the treatment of diabetes. The study was performed to investigate the blood glucose lowering effect of *Swietenia mahagoni* seeds in experimentally induced diabetic rats. Twenty four healthy Long Evans Norwegian strain of rats were included in the study and divided into four groups (A, B, C and D) comprising 6 rats each. Diabetes was induced by alloxan (120 mg/kg body weight). Administration of ethanolic extract of *Swietenia mahagoni* seeds (group-B) produced no significant change in the blood glucose level as compared to control (group-A). Administration of ethanolic extract of *Swietenia mahagoni* seeds in group-D produced a significant reduction in blood glucose level as compared to diabetic control (group-C). Histological examination of pancreas showed destruction of beta cells in Islets of pancreas in group-C whereas retaining of islets and few degranulations of beta cells of pancreas found in group-D. These observations and results provide information that ethanolic extract of *Swietenia mahagoni* seeds has hypoglycaemic effect in experimentally induced diabetic rats which requires further investigation.

**Key words:** Diabetes mellitus, *Swietenia mahagoni*, Alloxan, Rat, Blood glucose.

### Introduction :

Diabetes mellitus is a metabolic disorder resulting in raised blood glucose (hyperglycaemia) from defects in insulin secretion; insulin action or both that arise from genetic as well as environmental factors. It is defined by documenting raised blood glucose in fasting state ( $\geq 7.0$  mmol/L) or 2 hours after an oral standard glucose drink ( $\geq 11.1$  mmol/L)<sup>1</sup>. The chronic hyperglycaemia is associated with long-term damage, dysfunction and failure

of various organs, especially the eyes, kidneys, liver, heart and blood vessels<sup>2</sup>. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030<sup>3</sup>.

Traditional medicine is fostered particularly in countries where scientific medicine is not accessible to large populations for economic reasons. Complementary and alternative medicine does not compete with the successful main stream of scientific medicine. Users of complementary and alternative medicine commonly have chronic conditions and have tried conventional medicine but found that it has not offered a satisfactory solution, or has caused adverse effects<sup>4</sup>. Bangladesh is a rich emporium of medicinal plants, some of which are used therapeutically in the treatment of various diseases by both traditional healers and local people. Many of them are highly efficacious and are internationally recognized as useful drugs<sup>5</sup>. Herbal medicines have several advantages such as fewer side-effects, better patient tolerance, relatively less expensive and well

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accepted due to a long history of use. The more important cause is that herbal medicines provide rational means for the treatment of many diseases that are obstinate and incurable in other systems of medicine<sup>6</sup>.

*Swietenia mahagoni* is one of the most significant plants of the family, Meliaceae. This plant has various types of medicinal values like antimalarial and antidiarrhoeal effects. The plant extracts have been accounted to possess antibacterial and antifungal activities. Limonoids obtained from *Swietenia mahagoni* have antifungal activity<sup>7</sup>. Study has clearly indicated the significant antidiabetic activity of *Catharanthus roseus* (Nayantara), *Azadirachta indica* (Neem) and *Allium sativum* (Garlic) and supports the traditional usage of the herbal preparations by Ayurvedic physicians for the therapy of diabetics<sup>8</sup>. The seed of *Swietenia mahagoni* is a natural agonist of peroxisome-proliferator activated receptor (PPAR $\gamma$ )<sup>9</sup>. The functions of these PPAR receptors after activation by drugs include an increase in lipid and cholesterol metabolism, adipocyte differentiation, and improvement in insulin sensitivity. It has been demonstrated that PPAR $\gamma$  is the receptor of the thiazolidinedione (TZD) class ligands. Among the TZD type antidiabetic drugs, Rosiglitazone and Troglitazone are potent adipocyte-differentiating agents, which activate ap-2 gene expression in a PPAR $\gamma$  - dependent manner<sup>9</sup>.

With this background information, in this study, attempt has been made to evaluate the hypoglycaemic effect of *Swietenia mahagoni* seeds in experimental diabetic rats. Alloxan has been chosen to induce diabetes mellitus in rat. Blood glucose level has been estimated to detect the extent of pancreatic damage. Pancreatic histology has also been performed to confirm the findings.

### Materials and Methods:

This experimental study was carried out at the Department of Pharmacology and Therapeutics, Dhaka Medical College (DMC), Dhaka, during the period July 2009 to June 2010. A total number of 24 Long Evans rats of either sex were used for the present study. The rats were fed normal diet and allowed to drink water ad libitum. The rats were divided into four groups (A, B, C and D). Each group consists of six rats.

### EXPERIMENT DESIGN:

#### Experiment-1:

This part of experiment comprised of 12 rats which were divided into 2 groups, each having 6 rats (Group-A and Group-B). All the rats were fasted overnight before collection of blood. Group-A (Control group) received standard rat food for 14 days. Fasting blood glucose (FBS) level was estimated on day 1 and day 15 of the experiment. Group-B received ethanolic extract of *Swietenia mahagoni* seeds 1000 mg/kg orally along with standard rat food for 14 days. FBS level was estimated on day 1 and day 15 of the experiment. On day 15 the rats were sacrificed and pancreas was preserved in 10% formalin for histological study.

#### Experiment-2:

This part of experiment comprised of 12 rats which were divided into 2 groups, each having 6 rats (Group-C and Group-D). All the rats were fasted overnight before collection of blood. Group-C (Diabetic control group) was given alloxan 120 mg/kg intraperitoneally for induction of diabetes on day 1. Then the rats were given standard rat food. FBS level was estimated on day 1 (before alloxan), on day 4 and on day 15. Group-D was given alloxan 120 mg/kg intraperitoneally on day 1. Then the rats were given standard rat food. After 3 days ethanolic extract of *Swietenia mahagoni* seeds (1000mg/kg) was given orally along with standard food for 10 days. FBS level was estimated on day 1 (before alloxan), on day 4 and on day 15. On day 15 the rats were sacrificed and pancreas was preserved in 10% formalin for histological study.

### Observations and Results:

#### Effect of EESM (ethanolic extract of *Swietenia mahagoni*) seeds on blood glucose level in non-diabetic rats:

In group-A, blood glucose levels (mean  $\pm$  SD) were  $5.80 \pm 0.52$  mmol/L and  $5.80 \pm 0.46$  mmol/L on day 1 and day 15 respectively. Percentage change was 2.31%. In group-B, blood glucose levels (mean  $\pm$  SD) were  $5.50 \pm 0.39$  mmol/L and  $5.60 \pm 0.46$  mmol/L on day 1 and day 15 respectively. Percentage change was 2.17%. Unpaired t test was done between group A and group B. The change was not significant statistically ( $p > 0.05$ ) (Table I).

**Table I:** Effect of EESM (ethanolic extract of *Swietenia mahagoni*) seeds on blood glucose level in non-diabetic rats.

Group	FBG (mmol/L) on day 1 (Mean $\pm$ SD)	FBG (mmol/L) on day 15 (Mean $\pm$ SD)	Percent Change
A (n=6)	$5.80 \pm 0.52$	$5.80 \pm 0.46$	+ 2.31%
B (n=6)	$5.50 \pm 0.39$	$5.60 \pm 0.46^{NS}$	+ 2.17%

**Effect of alloxan on blood glucose level of group C and D rats on day 4:**

In group-C, blood glucose levels (mean  $\pm$  SD) were  $5.50 \pm 0.64$  mmol/L and  $15.00 \pm 3.38$  mmol/L on day 1 and day 4 respectively. Percentage change was 173.90%. In group-D, blood glucose levels (mean  $\pm$  SD) were  $5.80 \pm 0.64$  mmol/L and  $15.05 \pm 3.45$  mmol/L on day 1 and day 4 respectively. Percentage change was 162.63%. Unpaired t test was done between group-C and group-D on day 4. The change was not significant statistically ( $p > 0.05$ ) (Table II).

**Table II: Effect of alloxan on blood glucose level of group C and D rats on day 4**

Group	FBG (mmol/L) on day 1 (before alloxan) (Mean $\pm$ SD)	FBG (mmol/L) on day 4 (after alloxan) (Mean $\pm$ SD)	Percent Change
C (n=6)	$5.50 \pm 0.64$	$15.00 \pm 3.38$	+ 173.90%
D (n=6)	$5.80 \pm 0.64$	$15.05 \pm 3.45^{ns}$	+ 162.63%

ns = not significant

**Effect of EESM (ethanolic extract of *Swietenia mahagoni*) seeds on blood glucose level in diabetic rats:**

In group-C, blood glucose levels (mean  $\pm$  SD) were  $5.50 \pm 0.64$  mmol/L and  $16.00 \pm 2.83$  mmol/L on day 1 and day 15 respectively. Percentage change was 192.37%. In group-D, blood glucose levels (mean  $\pm$  SD) were  $5.80 \pm 0.64$  mmol/L and  $8.03 \pm 2.04$  mmol/L on day 1 and day 15 respectively. Percentage change was 41.50%. Unpaired t test was done between group-C and group-D. The difference was statistically significant ( $p < 0.001$ ) (Table III).

**Table III: Effect of EESM (ethanolic extract of *Swietenia mahagoni*) seeds on blood glucose level in diabetic rats.**

Group	FBG (mmol/L) on day 1 (Mean $\pm$ SD)	FBG (mmol/L) on day 15 (Mean $\pm$ SD)	Percent Change
C (n=6)	$5.50 \pm 0.64$	$16.00 \pm 2.83$	+ 192.37%
D (n=6)	$5.80 \pm 0.64$	$8.03 \pm 2.04^{***}$	+ 41.50%

\*\*\* = significant at  $P < 0.001$ .

**Effect of EESM (ethanolic extract of *Swietenia mahagoni*) seeds on pancreatic islets of Langerhans:**

In group-A the islet of pancreas and the beta cells in islet are clearly seen. Acinar and islet components are clearly separated from each other. In group-B (received ethanolic extract of *Swietenia mahagoni* seeds 1000 mg/kg body weight and normal rat food orally for 14 days). The acinar and islet components are clearly separated and the overall feature is almost similar to group-A. In group-C the islet of pancreas is destroyed and dilated ducts are filled with secretory product. Complete beta cell degranulation is seen. In group-D the islets configuration is retained and beta cells are partially degranulated. The islets of pancreas are increased in size.

**Discussion:**

The present study was carried out to evaluate the effect of ethanolic extract of *Swietenia mahagoni* seeds on experimentally induced diabetes mellitus in rats. The blood glucose lowering effect of *Swietenia mahagoni* seeds was tested in non-diabetic and experimentally induced diabetic rats. The ethanolic extract of *Swietenia mahagoni* seeds was given for 14 days in non-diabetic and for 10 days in alloxan induced diabetic rats. In addition, histological studies of rat pancreas following administration of ethanolic extract of *Swietenia mahagoni* seeds and alloxan were also done. In the present study, diabetes was induced by alloxan. The dose and route of administration of alloxan monohydrate was selected from Andrade et al<sup>10</sup> and Kim et al<sup>11</sup> respectively. The blood glucose levels in animals were measured 72 hours after administration of alloxan which was done according to experiment of Etuk EU et al<sup>12</sup>. In this study, intraperitoneal administration of single dose of alloxan (120mg/kg), increased blood glucose level significantly. Similar observations were reported by number of researchers. Ghosh et al<sup>13</sup> observed the condition of diabetes after 24 hours of intravenous injection of sterile, freshly prepared 1% alloxan monohydrate solution at a dose of 40mg/kg in albino rats. In the present study, the rise in blood glucose level in experimental diabetic rats was also very high. The dose of *Swietenia mahagoni* (1000 mg/kg body weight), used in this study was selected in keeping conformity with the dose used in different research work by Li DD et al<sup>9</sup>. The duration (15 days) of study was selected according to Bokaeian et al<sup>14</sup>.

There was no significant change ( $p > 0.05$ ) in the mean value of blood glucose level of non-diabetic rats treated with EESM (ethanolic extract of *Swietenia mahagoni*) seeds as compared with normal control. It may be concluded that *Swietenia mahagoni* seeds have no effect on lowering the blood glucose level in non-diabetic rats. Decrease in the mean value of blood glucose level was observed in the experimental diabetic group when treated with EESM (ethanolic extract of *Swietenia mahagoni*) seeds at a dose of 1000 mg/kg and these changes were significant ( $p < 0.001$ ). Therefore, the findings of this study are in well agreement with the findings of other researcher Li DD et al<sup>9</sup>. It may be concluded that *Swietenia mahagoni* seeds have hypoglycaemic effect in experimentally induced diabetic rats.

The histology of the islets and the beta cells of pancreas were observed in non-diabetic, diabetic and *Swietenia mahagoni* treated diabetic rats. This was done in addition to the research of Li DD et al<sup>9</sup> and to confirm the findings. In non-diabetic group, the islet of Pancreas and the beta cells in islet were clearly seen. Acinar and

islet components were clearly separated from each other. The destruction of islets, filling of dilated ducts with secretory product and complete degranulation of beta cell were seen in Alloxan treated diabetic group. The islets configuration was retained and beta cells were partially degranulated in *Swietenia mahagoni* treated diabetic group. Maiti et al<sup>15</sup> isolated the hypoglycaemic phytoconstituent named Swietenine from seeds of a related species *Swietenia macrophylla* and the effect was comparable to that of human insulin.

The active constituent of *Swietenia mahagoni* that might be responsible for hypoglycaemic activity is yet to be isolated. The exact mechanism of ethanolic extract of *Swietenia mahagoni* in reducing blood glucose level is not well understood. The scientists of China claimed that the hypoglycaemic activity of *Swietenia mahagoni* is mediated by agonistic activity to PPAR $\gamma$  receptor which after activation improves insulin sensitivity. It was observed that the EESM (ethanolic extract of *Swietenia mahagoni*) seeds have hypoglycaemic effect in Alloxan treated diabetic rats but has no effect on blood glucose level in non-diabetic rats. The result suggested that the ethanolic extract of *Swietenia mahagoni* seeds may be a useful hypoglycaemic agent in the treatment of diabetes mellitus. It is recommended that further studies regarding pharmacokinetics, pharmacodynamics, toxicology and posology of extract of *Swietenia mahagoni* seeds should be undertaken to develop it as a useful antidiabetic agent for human.

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