

## LAMPIRAN

## Lampiran 1. Jurnal 1

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Potensi Antidiabetes pada Daun, Kulit Batang dan Biji Mahoni  
(*Swietenia macrophylla* King)

*Antidiabetic potential in the leaves, bark and seeds of Mahogany  
(Swietenia macrophylla King)*

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**Abstrak**---Diabetes melitus merupakan penyakit dimana terjadinya peningkatan kadar glukosa darah dalam tubuh yang melebihi batas normal. Dalam upaya mencari pengobatan dari bahan alam untuk diabetes dan salah satunya yang sudah digunakan dimasyarakat adalah biji mahoni. Tujuan penelitian ini adalah untuk mengetahui aktivitas antidiabetes ekstrak etanol daun, kulit batang dan biji mahoni (*Swietenia macrophylla* King) terhadap enzim  $\alpha$ -glukosidase secara in vitro. Bahan uji yang digunakan adalah kulit batang, daun dan biji mahoni (*Swietenia macrophylla* King) yang diperoleh dari pohon yang tumbuh di tepi jalan raya daerah Bogor, Jawa Barat. Pengujian aktivitas antidiabetes secara in vitro dilakukan dengan metode penghambatan kerja enzim  $\alpha$ -glukosidase dengan substrat p-nitrofenil- $\alpha$ -D-glukopiranosida. Serbuk simplisia daun, kulit batang dan biji mahoni (*Swietenia macrophylla* King) dimaserasi menggunakan etanol 96%. Penapisan golongan senyawa kimia pada serbuk dan ekstrak etanol daun dan kulit batang memperlihatkan adanya kandungan saponin, tanin, flavonoid dan steroid/triterpenoid, namun serbuk dan ekstrak etanol biji mengandung alkaloid, steroid/triterpenoid dan pada serbuknya juga terdapat saponin. Hasil penelitian menunjukkan bahwa ekstrak etanol dari daun, kulit batang dan biji mahoni mempunyai aktivitas antidiabetes terhadap enzim  $\alpha$ -glukosidase dengan nilai  $IC_{50}$  18,78  $\mu$ g/ml, 21,31  $\mu$ g/ml dan 1049,05  $\mu$ g/ml.

**Kata Kunci**---Diabetes Melitus, *Swietenia macrophylla* King,  $\alpha$ -Glukosidase

**Abstract**--- Diabetes mellitus is a disease where the increase in blood glucose levels in the body that exceeds normal limits. In an effort to find natural ingredients for the treatment of diabetes and one that has been used in the community are mahogany seeds. The purpose of this study was to determine the antidiabetic activity of the ethanol extract of leaves, bark and seeds of mahogany (*Swietenia macrophylla* King) against  $\alpha$ -glucosidase enzyme in vitro. The test material used is the bark, leaves and seeds of mahogany (*Swietenia macrophylla* King) obtained from trees growing on the edge of the highway area of Bogor, West Java. Testing of antidiabetic activity in vitro work done by the method of inhibition of  $\alpha$ -glucosidase enzyme with substrate p-nitrophenyl- $\alpha$ -D-glucopiranosida. Simplicia powder leaves, bark and seeds of mahogany (*Swietenia macrophylla* King) macerated using 96% ethanol. Screening class of chemical compounds in powder and ethanol extract of the leaves and bark showed saponins, tannins, flavonoids and steroids / triterpenoids, but the powder and ethanol extract seeds contain alkaloids, steroids / triterpenoids and the powder also contained saponins. The results showed that ethanol extracts of leaves, bark and seeds of mahogany have antidiabetic activity of the enzyme  $\alpha$ -glucosidase with  $IC_{50}$  value of 18.78  $\mu$ g / ml, 21.31  $\mu$ g / ml and 1049.05  $\mu$ g / ml.

**Keywords**---Diabetes Melitus, *Swietenia macrophylla* King,  $\alpha$ -Glukosidase

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### The $\alpha$ -Glucosidase Inhibitory Activity of Seed Extract of Mahogany (*Swietenia macrophylla* King.)

(Aktivitas Inhibisi  $\alpha$ -Glukosidase dari Ekstrak Biji Mahoni (*Swietenia macrophylla* King.))

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#### ABSTRACT

Diabetes mellitus is a chronic disorder that affects the metabolism of blood glucose inside the body. One of the alternative treatments is by using traditional medicine plants, which has the hypoglycemic effects. Mahogany seed is one of the traditional medicine plants that has been proven to be useful to treat diabetes and has been used for generations. The  $\alpha$ -glucosidase activity of the aqueous, 96% ethanolic, the ethyl acetate, and the hexane extracts of mahogany seeds were assayed by measuring *p*-nitrophenol from *p*-nitrophenyl- $\alpha$ -D-glucopyranoside (pNPG) on 400 nm. The percentage value of the inhibition for  $\alpha$ -glucosidase ranged from 6.36-56.77 %, with the 96 % ethanol extract showed the highest value and the hexane extract with the lowest value. Phytochemical screening revealed the presence of alkaloids, flavonoids, saponins and triterpenoid, which could be responsible for the bioactivities shown by the 96 % ethanolic and aqueous extract of *S. macrophylla*.

**Keywords:**  $\alpha$ -Glucosidase, Diabetes mellitus, Phytochemical screening, *Swietenia macrophylla* King.

#### ABSTRAK

Diabetes melitus adalah suatu gangguan kronis yang khususnya menyangkut metabolisme glukosa di dalam tubuh. Salah satu alternatif penanggulangannya adalah dengan menggunakan tanaman obat tradisional yang mempunyai efek hipoglikemia. Biji mahoni merupakan salah satu tanaman obat tradisional yang terbukti dapat menanggulangi penyakit diabetes dan telah digunakan secara turun menurun. Ekstrak air, etanol 96 %, etil asetat dan heksan dari biji mahoni (*Swietenia macrophylla* King.) diperiksa aktivitas inhibisi  $\alpha$ -glukosidasenya dengan mengukur *p*-nitrofenol dari *p*-nitrofenil- $\alpha$ -D-glukopiranosida (pNPG) pada 400 nm. Nilai persen inhibisi untuk

## Lampiran 3. Jurnal 3

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### Alpha-Glucosidase Inhibition and Hypoglycemic Activities of *Swietenia mahagoni* Seed Extract

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Inhibition of  $\alpha$ -glucosidase and hypoglycemic activity are two effects commonly used to identify bioactive compounds with potential to treat diabetes. The objectives of this study were to analyse and compare the bioactive compounds and  $\alpha$ -glucosidase inhibitory effect of four different types of *Swietenia mahagoni* seed extract, and to analyse the hypoglycemic activity of the greatest inhibition of  $\alpha$ -glucosidase-extract in rats. The extracts were obtained using two different solvents (aqueous and ethanol) and two different methods: maceration and reflux methods. This resulted in four types of extract varying by solvent and extraction method. Testing of these extracts for  $\alpha$ -glucosidase inhibitory effect was carried out *in vitro* using spectrophotometer. Testing for hypoglycemic activity was carried out *in vivo* using rats. A total of 40 male *Sprague-Dawley* rats were divided into eight groups: (1) the negative control group, received an oral dose of aquadest only, (2) the positive control group, was given 90% sucrose orally without *S. mahagoni* seed extract, and five treated groups (3-7), were given 90% sucrose followed by the best extract-ethanolic *S. mahagoni* seed extract in doses of 100, 200, 300, 400, and 500 mg/kgBW, and (8) the acarbose group, was given 90% sucrose orally followed by acarbose. Glucose levels in each animal were measured at 0, 30, 60, 90, and 120 min after treatment. The results showed the greatest inhibition of  $\alpha$ -glucosidase in ethanolic extract, using maceration methods. This ethanolic-maceration *S. mahagoni* seed extract also showed hypoglycemic effects in hyperglycemic rats at dose from 100 to 500 mg/kgBW. Ethanolic extract of *S. mahagoni* seed, using maceration method, can be proposed as potential antidiabetic agent.

Keywords: *Swietenia mahagoni*,  $\alpha$ -glucosidase, hypoglycemia, ethanolic extract, antidiabetic

## Lampiran 4. Jurnal 4

### Studi Ekstrak Metanol Biji Mahoni (*Swietenia mahagoni*) terhadap SOD Serum Tikus Putih (*Rattus novergicus*) Pasca Induksi MLD-STZ

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#### ABSTRAK

Diabetes mellitus (DM) merupakan suatu gejala yang timbul pada seseorang dimana keadaan hiperglikemia (kadar gula yang tinggi) yang kronik dengan disertai berbagai kelainan metabolik akibat gangguan hormonal. Salah satu tumbuhan yang digunakan masyarakat untuk pengobatan DM adalah mahoni (*Swietenia mahagoni*). Bagian yang digunakan dari tumbuhan tersebut adalah bijinya. Namun mekanisme ekstrak metanol biji mahoni belum banyak diketahui. Pada penelitian ini menggunakan tikus model DM dengan induksi MLD-STZ. Tikus dikelompokkan dalam 5 kelompok, yaitu kelompok kontrol negatif, kontrol positif, dan kelompok DM dengan terapi 100, 250 dan 400 mg/KgBB. Metode yang digunakan dalam penelitian ini meliputi pengekstrakan biji mahoni, induksi DM dengan injeksi MLD-STZ secara intraperitoneal dan uji aktivitas SOD serum. Hasil penelitian menunjukkan bahwa nilai SOD serum yang didapatkan berdasarkan kelompok, yaitu 98,99; 61,12; 70,05; 79,29 dan 84,49 unit/ml. Pemberian terapi ekstrak metanol biji mahoni pada tikus model DM mampu menaikkan aktivitas SOD.

Kata Kunci : diabetes mellitus (DM), SOD (superoksida dismutase), STZ (streptozotocin)

#### ABSTRACT

Diabetes mellitus (DM) is a symptom that occurs in a person where the chronic hyperglycemia condition (high blood sugar level) with various metabolic abnormalities disorders accompanies by hormonal disorders. One of the plant used for treatment of DM is mahogany (*Swietenia mahagoni*). The part used of the plant is seed. But mechanism of methanol extract of mahogany seeds not widely known. On this research using a rat model DM by induction of MLD-STZ. Rats were grouped in 5 groups, which is the control negative, control positive, and DM group with therapy 100, 250, and 400 mg/KgWB. The methods used in this research include seed extraction, DM rats induced by injection MLD-STZ with intraperitoneal and activity SOD assay. The result showed that the value of serum SOD is 98,99; 61,12; 70,05; 79,29 dan 84,49 unit/ml. Therapy of methanol extract to DM type 1 rats model is able to raise the activity of SOD.

Keyword: diabetes mellitus (DM), SOD (superoksida dismutase), STZ (streptozotocin)

## Lampiran 5. Jurnal 5

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### Research Article

## Antidiabetic Potentiality of the Aqueous-Methanolic Extract of Seed of *Swietenia mahagoni* (L.) Jacq. in Streptozotocin-Induced Diabetic Male Albino Rat: A Correlative and Evidence-Based Approach with Antioxidative and Antihyperlipidemic Activities

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Antidiabetic, antioxidative, and antihyperlipidemic activities of aqueous-methanolic (2:3) extract of *Swietenia mahagoni* (L.) Jacq. (family Meliaceae) seed studied in streptozotocin-induced diabetic rats. Feeding with seed extract (25 mg 0.25 mL distilled water<sup>-1</sup> 100 gm b.w.<sup>-1</sup> rat<sup>-1</sup> day<sup>-1</sup>) for 21 days to diabetic rat lowered the blood glucose level as well as the glycogen level in liver. Moreover, activities of antioxidant enzymes like catalase, peroxidase, and levels of the products of free radicals like conjugated diene and thiobarbituric acid reactive substances in liver, kidney, and skeletal muscles were corrected towards the control after this extract treatment in this model. Furthermore, the seed extract corrected the levels of serum urea, uric acid, creatinine, cholesterol, triglyceride, and lipoproteins towards the control level in this experimental diabetic model. The results indicated the potentiality of the extract of *S. mahagoni* seed for the correction of diabetes and its related complications like oxidative stress and hyperlipidemia. The extract may be a good candidate for developing a safety, tolerable, and promising nutraceutical treatment for the management of diabetes.



## Lampiran 6. Jurnal 6

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## ORIGINAL ARTICLE

# Antihyperglycemic and antioxidative effect of hydro - methanolic (2:3) extract of the seed of *Swietenia mahagoni* (L.) Jacq. in streptozotocin-induced diabetic male albino rat: An approach through pancreas

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## KEYWORDS

Carbohydrate  
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Pancreas;  
*Swietenia mahagoni*

**Abstract** The goal of this study was to investigate the effects of the hydro - methanolic (2:3) extract of the seed of *Swietenia mahagoni* (L.) Jacq. for the management of streptozotocin (STZ)-induced diabetes. Wistar rats were divided equally into four groups (n = 6): normal control, diabetes control, diabetes + extract treated, and diabetes + metformin treated. The extract (25 mg/100 g by weight) and metformin (2.5 mg/100 g by weight) were administered once a day, orally by gavages for 21 days at fasting condition. Hexokinase, glucose-6-phosphate dehydrogenase, and glucose-6-phosphatase activities were measured in hepatic tissue. Activities of catalase (CAT), peroxidase (Px), and superoxide dismutase (SOD), along with the quantity of thiobarbituric acid reactive substances (TBARS) and conjugated diene (CD) in hepatic and renal tissues, were assessed. Histoarchitecture of the pancreas and serum insulin level were also evaluated. Significant diminution in the activities of hepatic hexokinase and glucose-6-phosphate dehydrogenase along with elevation in glucose-6-phosphatase were noted in STZ-induced animals with diabetes in respect to control animals. Level of fasting blood glucose (FBG) was elevated in animals with diabetes. Activities of CAT, Px, and SOD were diminished significantly along with the elevation in TBARS and CD levels in animals with

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## Lampiran 7. Jurnal 7

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# The effects of the ethanolic extract of mahogany seeds (*Swietenia macrophylla* King) on the renal function of streptozotocin-induced diabetic rats

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## ABSTRACT

Diabetes-associated oxidative stress causes glomerular hypertrophy, decrease of glomerular filtration rate and inhibits cell proliferation that lead to the decrease of renal function as indicated by the increase of serum creatinine level and the presence of protein in urine. Mahogany seed (*Swietenia macrophylla* King) has been proven to have antidiabetic activity. This study was conducted to evaluate the effect of the ethanolic extract of mahogany seeds on the renal function of streptozotocin-induced diabetic rats. Six normal rats as control (Group I) and 24 diabetic rats were used in this study. The diabetic rats were randomized allocated into four groups with six rats in each group. Group II was considered as diabetic rats control and received aquadest. Group III-V were considered as extract administered diabetic group and received ethanolic extract of *S. macrophylla* seed for 21 days at a dose of 50, 100 and 200 mg/kg BW, respectively. Serum malondialdehyde (MDA), serum creatinine, and urine protein levels were monitored, before and after the ethanolic extract of *S. macrophylla* seed administration. Serum MDA, serum creatinine and urine protein levels of all rats after STZ induction (Group II-V) were significantly higher than without STZ induction ( $p < 0.05$ ). A significant decrease in the serum MDA and serum creatinine as well as urine protein levels were observed after the treatment with ethanolic extract of *S. macrophylla* seed compared to before treatment ( $p < 0.05$ ). In conclusion, the ethanolic extract of *S. macrophylla* seed is able to correct renal dysfunction of streptozotocin-induced diabetic rats.

## ABSTRAK

Stres oksidatif akibat diabetes dapat menyebabkan hipertropi glomerulus, penurunan kecepatan filtrasi glomerulus dan penghambatan proliferasi sel yang berakibat terjadinya penurunan fungsi ginjal sebagaimana ditunjukkan dengan penurunan kreatinin serum dan adanya urin protein. Biji mahoni (*Swietenia macrophylla* King) terbukti mempunyai aktivitas antidiabetes. Penelitian ini dilakukan untuk mengkaji efek ekstrak etanol biji mahoni pada fungsi ginjal tikus diabetes yang diinduksi streptozotocin. Enam tikus normal sebagai kontrol (Kelompok I) dan 24 tikus diabetes digunakan dalam penelitian. Tikus diabetes dibagi menjadi 4 kelompok secara random dengan 6 ekor tikus masing-masing kelompok. Kelompok II sebagai kontrol tikus diabetes menerima air suling. Kelompok III-V sebagai

## Lampiran 8. Jurnal 8

### Studi Ekstrak Metanol Biji Mahoni terhadap MDA Serum Tikus Putih Pasca Induksi MLD-STZ

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#### ABSTRAK

Diabetes mellitus (DM) merupakan suatu penyakit gangguan metabolik yang ditandai oleh peningkatan kadar glukosa darah melebihi batas normal atau hiperglikemia. Salah satu tumbuhan yang dimanfaatkan masyarakat untuk pengobatan DM adalah tanaman mahoni (*Swietenia mahagoni*). Bagian tumbuhan yang digunakan untuk pengobatan penyakit ini adalah bijinya. Namun potensi dari ekstrak metanol biji mahoni belum banyak diketahui. Pada penelitian ini menggunakan tikus model DM dengan induksi MLD-STZ (*Multiple Low Dose-Streptozotocin*). Tikus dikelompokkan dalam 5 kelompok, yaitu kelompok kontrol negatif, kontrol positif, dan kelompok terapi 100, 250 dan 400 mg/KgBB yang sebelumnya telah diinduksi MLD-STZ. Metode yang digunakan dalam penelitian ini meliputi pembuatan tikus DM dengan injeksi MLD-STZ secara intraperitoneal, pemberian terapi ekstrak metanol biji mahoni secara oral, uji kadar MDA serum. Hasil penelitian menunjukkan bahwa kadar MDA (Malondialdehyde) serum yang didapatkan berdasarkan kelompok, yaitu 3,126; 10,245; 9,245; 7,203; 4,677 µg/ml. Dosis optimum untuk menurunkan kadar MDA adalah 400 mg/KgBB. Pemberian terapi ekstrak metanol biji mahoni mampu menurunkan kadar MDA serum tikus putih pasca induksi MLD-STZ.

Kata Kunci: diabetes mellitus, MDA, MLD-STZ, pankreas

#### ABSTRACT

Diabetes mellitus (DM) is a metabolic disorder characterized by elevated levels of blood glucose or hyperglycemia exceeds the normal limit. One of the plants that used the plant for the treatment of diabetes mellitus is mahogany (*Swietenia mahogany*). Parts of the plant are used for the treatment of this disease is seed. However, the potential of the methanol extract of mahogany seed has not been known. In this study, using a rat model of diabetes induced by MLD-STZ (*Multiple Low Dose*). Rats were grouped into 5 groups, namely the negative control group, positive control, and group therapy 100, 250 and 400 mg / KgBW previously MLD-STZ induced. The method used in this research are making DM mice with MLD-STZ injection in intraperitoneal, provide therapy mahogany seed methanol extract orally, serum MDA (Malondialdehyde) test. The results showed that serum MDA levels were obtained by the group, which is 3,126; 10,245; 9,245; 7,203; 4,677 µg / ml. The optimum dose pemberian therapy mahogany seed methanol extract to decrease MDA levels were 400 mg / KgBW.

Key words : diabetes mellitus, MDA, MLD-STZ, pancreas

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## Lampiran 9. Jurnal 9

### ***Effect of Methanolic Swietenia mahagoni Seed Extracts in Increasing Insulin Level, Decreasing TNF- $\alpha$ Expression and Repairing Pancreatic Tissue Damage on Diabetic Rat***

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#### **ABSTRAK**

*Diabetes mellitus* (DM) merupakan penyakit gangguan metabolisme yang ditandai dengan meningkatnya kadar glukosa darah (hiperglikemia) akibat gangguan sekresi insulin dan atau meningkatnya resistensi insulin. Terapi ekstrak metanol biji mahoni (*Swietenia mahagoni* Jacq) merupakan salah satu pengobatan alternatif penyakit DM. Penelitian ini dilakukan untuk membuktikan pengaruh pemberian terapi ekstrak metanol biji mahoni terhadap kadar insulin, ekspresi TNF- $\alpha$  dan perbaikan jaringan pankreas pada tikus hasil induksi *Multiple Low Dose-Streptozotocin* (MLD-STZ) dosis 20 mg/kgBB selama 5 hari berturut-turut. Tikus diukur kadar glukosa darah dengan menggunakan glukometer digital dan dinyatakan DM bila kadar glukosa darahnya  $\geq 300$  mg/dl. Penelitian ini menggunakan 25 ekor tikus putih (*Rattus norvegicus*) jantan galur wistar yang dibagi menjadi 5 kelompok yaitu kelompok 1 kontrol negatif, kelompok 2 kontrol positif, kelompok 3, 4 dan 5 tikus hasil induksi MLD-STZ serta masing-masing diberikan terapi ekstrak metanol biji mahoni dosis 100; 250 dan 400 mg/kgBB selama 7 hari. Hasil penelitian menunjukkan bahwa pemberian terapi ekstrak metanol biji mahoni dosis 100; 250 dan 400 mg/kgBB pada tikus hasil induksi MLD-STZ menunjukkan penurunan kadar glukosa darah berturut-turut sebesar 55,47%; 81,01% dan 73,63%, peningkatan kadar insulin sebesar 78,38%; 275,68% dan 145,95%, penurunan ekspresi TNF- $\alpha$  sebesar 30,34%; 67,28% dan 49,91%, serta perbaikan kerusakan jaringan pankreas pada penurunan derajat insulinitis ( $p < 0,05$ ). Berdasarkan penelitian ini dapat disimpulkan adanya pengaruh terapi ekstrak metanol biji mahoni terhadap kadar insulin, ekspresi TNF- $\alpha$  dan kerusakan jaringan pankreas tikus hasil induksi MLD-STZ. Pengaruh terapi tersebut optimal pada pemberian biji mahoni dosis 250 mg/kgBB.

**Kata Kunci:** Ekstrak metanol biji mahoni, ekspresi TNF- $\alpha$ , insulin, kerusakan jaringan pankreas, MLD-STZ

#### **ABSTRACT**

*Diabetes Mellitus* (DM) is a disease with metabolism disorder signed by increasing of glucose blood (hyperglycemia), caused by disorder of insulin secretion and or increasing of insulin resistance. Therapy of Methanolic *Swietenia mahagoni* Seed Extracts is an alternative treatment for DM. The objective of this research is to prove the effect of extract of *Swietenia mahagoni* Jacq to increasing of insulin, decreasing Tumor Necrosis Factor (TNF- $\alpha$ ) expression and repair pancreatic tissue damage of rat result *Multiple Low Dose-Streptozotocin* (MLD-STZ) induced dose of 20 mg/kg weight for 5 days successively. Blood glucose of rat was measured using digital glucometer and categorized as DM if it is  $\geq 300$  mg/dL. This research used 25 wistar strain white rat (*Rattus norvegicus*). Which were classified into 5 groups, they are one group of negative control, one group of positive control, and three groups of MLD-STZ induced given treatment of Methanolic *Swietenia mahagoni* Seed Extracts with dose of 100, 250 and 400 mg/kg weight for 7 days. The result showed that treatment of Methanolic *Swietenia mahagoni* Seed Extracts with dose of 100, 250 and 400 mg/kgBW decreased blood glucose 55,47%; 81,01% and 73,63% successively, increased insulin as 78,38%; 275,68% and 145,95%, decreased TNF- $\alpha$  expression as 30,34%; 67,28% and 49,91%, and improved damage of pancreas tissue from decreasing in the degree of insulinitis ( $p < 0.05$ ). There was a protective effect of methanolic *Swietenia mahagoni* seed extract to insulin secretion, TNF- $\alpha$  expression and damage of rat pancreas tissue MLD-STZ induced. The therapeutic effect was optimal at dose of 250 mg/kgBW.

**Keywords:** Damage of pancreas tissue, insulin, MLD-STZ, *swietenia mahagoni* seed extract, TNF- $\alpha$  expression

## Lampiran 10. Jurnal 10

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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 Meliaceae 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 mahagoni* in streptozocin 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  $\pm$  SD;  $8.81 \pm 1.22$  vs.  $3.57 \pm 3.38$ , on the 1<sup>st</sup> day vs. 22<sup>nd</sup> days,  $p = .002$ ) was improved. It also enhanced insulin releasing activity (plasma insulin in ng/ml, Mean  $\pm$  SD; group 1 vs. group 3,  $0.54 \pm 0.13$  vs.  $0.93 \pm 0.19$ ;  $p = 0.001$ ) 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 insulinomimetic and/or insulin sensitizing agent.

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

## Lampiran 11. Jurnal 11



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**ANTIDIABETIC ACTIVITY OF DRY EXTRACTS OF SWIETENIA MAHAGONI SEEDS IN ALLOXAN-INDUCED DIABETIC BALB/C**
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**ABSTRACT**
**Objective:** The present study was carried out to evaluate the antidiabetic activity of dry extracts of Swietenia mahagoni seeds

**Methods:** Antidiabetic was induced experimentally by a single intraperitoneal administration of 3,8 mg/20 g body weight of Alloxan-monohydrate in each male mice. Three days after alloxan administration, blood glucose level was measured using a glucometer. Mice with blood glucose levels above 200 mg/dL were considered diabetic and were used in this study. Then the mice were randomly divided into five experimental groups of six mice each. First group as positive control (Glibenclamide 0,06 mg/20 g body weight). Second group as negative control (CMC-Na 0.5%). Samples were given by oral route at three dosage levels (10mg / 20g, 20mg / 20g and 40mg /

 20g body weight). After treatment finished, blood sampling was done by sterilizing the tail with alcohol and then nipping the tail at the start of the experiment and this was repeated after 2nd, 4th, 6th and 24th h. **Results:** Oral administration of dry extracts of Swietenia mahagoni seeds at doses of 10, 20 and 40 mg/20g body weight demonstrated antidiabetic activity in a dose independent manner comparable to that demonstrated by glibenclamide at 3 mg/kg body weight from two second to the twenty-fourth hour. **Conclusion:** From the studies it is concluded that, dry extract of Swietenia mahagoni seeds is suitable to prepare formulation for treatment of diabetic.

**KEYWORDS:** Diabetes mellitus, Antidiabetic activity, Swietenia mahagoni seeds dry extract, alloxan.

## Lampiran 12. Jurnal 12

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### Comparative study of the effect of ethanolic extract of *Swietenia mahagoni* seeds with rosiglitazone on experimentally induced diabetes mellitus in rats

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#### Abstract

The study was performed to compare the blood glucose lowering effect of *Swietenia mahagoni* seeds with an oral antidiabetic drug, rosiglitazone in experimentally induced diabetic rats. Twentyfour 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. Group A (control group) received standard rat food for 14 days. Diabetes was induced by a single intraperitoneal administration of alloxan 120mg/kg body weight in Group B, C and D. Group B was given standard food for 10 days and considered as diabetic control. Group C and D were treated with ethanolic extract of *Swietenia mahagoni* seeds 1000mg/kg and rosiglitazone 10mg/kg orally respectively. Administration of ethanolic extract of *Swietenia mahagoni* seeds in group C and rosiglitazone in group D produced a significant reduction in blood glucose level as compared to diabetic control (group B). Histological examination of pancreas showed destruction of beta cells in Islets of pancreas in group B whereas retaining of islets and few degranulations of beta cells of pancreas found in group C and group D. The observations and results of the present study provide information that ethanolic extract of *Swietenia mahagoni* seeds has hypoglycaemic effect in experimentally induced diabetic rats which requires further investigation.

#### 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 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* (Neyantara), *Azadirachta Indica* (Neem) and *Allium sativum* (Garlic) and supports the traditional



## Lampiran 13. Jurnal 13

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### Antihiperlikemik Kombinasi Minyak Biji Mahoni (*Swietenia mahogani* (L.) Jacq)-Glibenklamid pada Tikus Diinduksi Aloksan

### (Antihyperglycemic Combination of Mahogany Seed Oil (*Swietenia mahogani*(L.) Jacq)-Glibenklamid in Alloxan-Induced Rats)

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Diterima 25 November 2016, Disetujui 20 Januari 2017

**Abstrak:** Diabetes mellitus (DM) adalah suatu gangguan kronis metabolisme glukosa di dalam tubuh. Biji mahoni (*Swietenia mahogani* (L.) Jacq) dilaporkan mengandung senyawa flavonoid, alkaloid dan saponin yang dapat digunakan sebagai terapi diabetes mellitus. Penelitian ini bertujuan untuk mengetahui efek antihiperlikemik kombinasi minyak biji mahoni-glibenklamid pada tikus putih jantan yang dibuat hiperlikemik dengan induksi aloksan. Penyarian minyak biji mahoni dilakukan dengan menggunakan alat pres hidrolik dengan tekanan 100 psi. Penelitian ini menggunakan tikus jantan galur wistar yang berumur 2-3 bulan sebanyak 35 ekor tikus dan dibagi dalam 7 kelompok: kelompok 1 (kontrol normal) diberi *aquadest* dan kelompok 2-7 diinduksi aloksan intraperitoneal 140 mg/kg BB sebanyak 2 kali. Kelompok 2 (kontrol negatif) diberikan CMC 0,5%, kelompok 3 diberi glibenklamid 0,09 mg/200 g BB, kelompok 4 diberi minyak biji mahoni 2 mL/200 g BB, kelompok 5, 6, dan 7 diberi kombinasi minyak biji mahoni dengan glibenklamid dengan masing-masing perbandingan (75%:25%, 50%:50%, 75%:25%). Pemberian sediaan uji sebanyak 1 kali sehari selama 12 hari dan pengukuran kadar glukosa darah dilakukan pada hari ke 3, 6, 9, dan 12. Data yang diperoleh dianalisis dengan ANOVA satu jalan (signifikan  $p < 0,05$ ). Hasil yang diperoleh yaitu kombinasi minyak biji mahoni-glibenklamid dapat memberikan pengaruh terhadap penurunan kadar glukosa darah tikus putih jantan yang diinduksi aloksan, kelompok kombinasi minyak biji mahoni-glibenklamid memiliki aktivitas yang setara dalam menurunkan kadar glukosa darah dengan obat kimia tunggal glibenklamid. Minyak biji mahoni berpotensi sebagai antidiabetes.

**Kata Kunci:** *Swietenia*, biji mahoni, glibenklamid, aloksan, antihiperlikemia.

**Abstract:** Diabetes mellitus (DM) is a chronic disorder metabolism of glucose in the body. Mahogany seeds (*Swietenia mahogani* (L.) Jacq.) reportedly contains flavonoids, alkaloids and saponins which can be used as therapy of diabetes mellitus. This study aimed to determine the effects of antihyperglycemic combination of mahogany seed oil-glibenclamide in male rats hyperglycemic by alloxan induction. The mahogany seed oil liquefaction processed by using hydrolic pressed instrument 100 psi pressure. This study using Wistar strain male rats aged 2-3 months as many as 35 heads which were divided into 7 groups: group I (normal control) with distilled water added, while the II-VII group with alloxan induced intraperitoneal 140 mg/kg body weight two times. Group II as a negative control was added 0.5% CMC, group III was added glibenclamide 0.09 mg/200 g BB, IV groups oiled mahogany seeds 2 mL/200 g BW, group V, VI, and VII were added a combination of mahogany seed oil glibenclamide with each ratio (75%: 25%, 50%: 50%, 75%: 25%). The distribution of the test preparation 1 times a day for 12 days and blood glucose measurement performed on days 3, 6, 9, and 12. Data has been analyzed by oneway ANOVA (significant  $p < 0.05$ ). The results obtained the combination of mahogany seed oil-glibenclamide provides effect to reduction in blood glucose levels induced male rats alloxan, the combination group mahoni-glibenclamide seed oil have equal activity in lowering blood glucose levels with a single chemical drug glibenclamide. Mahogany seed oil is potentially antidiabetic.

**Keywords:** *Swietenia*, seed oil, glibenclamide, alloxan, antihyperglycemic.

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## Lampiran 14. Jurnal 14

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### Research Article



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## Antidiabetic Activity of *Swietenia mahagoni* Seed Powder in Alloxan Induced Diabetic Mice

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### ABSTRACT:

*Swietenia mahagoni* (Meliaceae) is an evergreen hard wood timber species widely distributed in India and has ethno medicinal uses in malaria, diabetes, anemia, diarrhoea, fever, and dysentery. In this present study antidiabetic effect of *Swietenia mahagoni* seeds were evaluated in alloxan induced diabetic mice. Blood and urine Glucose levels, food and water consumptions and histopathological studies were determined. In diabetic mice, *Swietenia mahagoni* seeds significantly reduced the elevated blood glucose level by 43.92% at 500mg/kg and 42.47% at 250mg/kg compared to vehicle treated diabetic mice, without increase in urine glucose, food and water intake. The experimental data indicated that *Swietenia mahagoni* demonstrated significant antidiabetic action in alloxan induced diabetic mice and could be a potential orally active drug for diabetes mellitus.

**KEYWORDS:** Antidiabetic, Indian Mahogany, Alloxan, diabetic mice, *Swietenia*.

### INTRODUCTION:

*Swietenia mahagoni* is an evergreen hard wood timber species of the family Meliaceae. The fruit is a large greenish brown capsule, splitting into 5 parts revealing flat and long winged, light brown seeds. Its wood is red brown in colour with seeds 4-5 cm long, compressed, crested and extended into a wing at the attachment end. The bark extracts are used as an astringent for wounds. Seed extracts are used to cure malaria, anemia, diarrhea, fever, dysentery and as depurative<sup>1</sup>. The leaves contain several limonoids; seven phragmalin limonoids of swietephagmins A-G as well two other different types of 2-hydroxy-3-O-tigloylswietenolide and deacetyl secmahoganin<sup>2</sup>. Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, glucosuria, polydipsia, polyphagia, weight loss, hyperlipidemia, retinopathy, neuropathy and peripheral vascular insufficiency. Diabetes is a disease condition where the pancreas does not produce enough insulin to process glucose or insulin receptors are not working properly<sup>3</sup>. Management of diabetes with agents devoid of any side effects is still a challenge to the medical system<sup>4</sup>. Hence search for a drug, which is cost effective, more potent, and without side effect is being pursued in several laboratories. Herbal remedies have become a major component of human health care as they have no or less side effects. Many herbs and plant products have been shown to have antihyperglycemic action. In the present work, antidiabetic activity of *S. mahagoni* seed were studied on alloxan induced diabetic mice.

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## Evaluation of plasma H<sub>2</sub>S levels and H<sub>2</sub>S synthesis in streptozotocin induced Type-2 diabetes—an experimental study based on *Swietenia macrophylla* seeds

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## PEER REVIEW

## Peer reviewer

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## Comments

Over all the paper is very informative and gives very scientific information, which makes us to rethink about the relationship of H<sub>2</sub>S and diabetes mellitus.

Details on Page S486

## ABSTRACT

**Objective:** To evaluate the plasma H<sub>2</sub>S levels and H<sub>2</sub>S synthesis activity in streptozotocin induced type 2 diabetes rats compared to the healthy controls and also to observe the effect of the aqueous extract of *Swietenia macrophylla* (*S. macrophylla*) seeds on the experimental groups.

**Methods:** Seeds of *S. macrophylla* were separated, washed, shed-dried and finally extract was prepared. Thirty two wistar rats were selected for the experimental study. Streptozotocin was used for the induction of diabetes. H<sub>2</sub>S concentration in plasma was measured. H<sub>2</sub>S synthesizing activity in plasma was measured. Statistical analysis have done using Microsoft excel, Office 2003. Values were expressed by mean±SD. *P*<0.05 were considered statistically significant.

**Results:** Fasting blood glucose level (7.74±0.02) mmol/L was significantly increased in diabetic rats. The glucose levels are significantly lowered in the rats treated with metformin (5.48±0.03) mmol/L as well as with aqueous extract of *S. macrophylla* seeds (3.72±0.04) mmol/L. The HbA1c percentages in different groups of study subjects also indicate similar trends. Our study shows both the plasma H<sub>2</sub>S levels (22.07±0.73) mmol/L and plasma H<sub>2</sub>S synthesis activity (0.411±0.005 mmol/100 g) are significantly reduced in the streptozotocin induced diabetic rats.

**Conclusions:** Although considering a small sample size, it can conclude that the fasting blood glucose levels are inversely related to plasma H<sub>2</sub>S levels as well as H<sub>2</sub>S synthesis activity in plasma and the extract of *S. macrophylla* is associated with increased plasma H<sub>2</sub>S levels with effective lowering of blood glucose in streptozotocin induced diabetic rats.

## KEYWORDS

Hydrogen sulphide, Streptozotocin, Diabetes, *Swietenia macrophylla* seed

## Lampiran 16. Jurnal 16

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## ORIGINAL ARTICLE

## Antidiabetic and antioxidant effect of *Swietenia macrophylla* seeds in experimental type 2 diabetic rats

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Runu Chakraborty · Piyasa Banerjee · Debasish Maji ·  
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**Abstract** The detrimental effects of diabetic complications are mainly mediated through oxidative stress. Despite considerable progress in the treatment of diabetes by insulin and oral hypoglycemic agents, search for newer drugs continue. Many studies have been carried out in search of a suitable plant drug that would be effective in diabetes mellitus. The present investigation was undertaken to evaluate the effect of aqueous extract of *Swietenia macrophylla* seeds on blood glucose levels and oxidative stress in streptozotocin induced type 2 diabetic rats. The Albino rat (Wistar Strain) weighing 200–250 g were divided into five groups of six 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 g / kg body weight/ day for 30 days). Group IV diabetic rats were fed with aqueous extract of established drug Metformin (10 mg/kg body weight). The oral administration of extract alone (2 g / kg body) and extract plus soya peptide (1:1, 2 g / kg body weight) per day for 30 days to diabetic rats was found to possess significant hypoglycemic activity. The antioxidant activity in the blood of *Swietenia macrophylla* seeds extract-treated

diabetic rats and aqueous extract of *Swietenia macrophylla* seeds, estimated by modified FORD test and expressed as Torlox equivalents also revealed significant antioxidant activity. The present study demonstrates that the aqueous extract of *Swietenia macrophylla* seeds have substantial anti-diabetic and antioxidant properties. An extensive population based study is required in this direction, to establish this natural product as a therapeutic agent for diabetes mellitus.

**Keywords** *Swietenia macrophylla* seeds · Antidiabetic · Antioxidant activity · Type 2 diabetes · Free Oxygen Radical Defence (FORD)

### 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. The detrimental effects of diabetic complications are mainly mediated through oxidative stress [1]. Diabetes is associated with increased production of the reactive oxygen species (ROS), with or without impaired antioxidant defence system, which results in oxidative damage [2–5]. Mechanisms by which increased oxidative stress causes diabetic complications are partly known, which includes activation of transcription factors and formation of advanced glycosylated end products (AGEs), and protein kinase C [1]. The resulting oxidative stress enhances lipid peroxidation [6]. Despite considerable progress in the treatment of diabetes by insulin and oral hypoglycemic agents, search for newer drugs continue because of several limitations of the existing synthetic drugs [7, 8]. The associated disadvantages with insulin and oral hypo-glycemic agents have stimulated research for

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## Lampiran 17. Jurnal 17

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### UJI AKTIVITAS SEDIAAN TEH BIJI MAHONI ( *Swietenia mahagoni* ) UNTUK MENURUNKAN KADAR GLUKKOSA DAN AKTIVITAS PEROKSIDASI LIPID PADA TIKUS DIABETES MILLITUS TIPE 2

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#### ABSTRACT

Penelitian ini bertujuan untuk mengetahui pengaruh pemberian the biji mahoni ( *Swietenia mahagoni* ) terhadap kadar MDA tikus diabetes melitus tipe 2 yang diinduksi aloksan. Dengan menggunakan metode desain control group pre-test-post-test dan menggunakan 15 tikus yang dibagi dalam 5 kelompok yaitu kelompok I kelompok negatif, kelompokII kelompok kontrol positif, kelompokIII teh biji mahoni 5 gram/kgBB, kelompok IV teh biji mahoni 10 gram/kgBB dan kelompok V teh biji mahoni 15 gram/kgBB. Perlakuan dilakukan selama 14 hari..Pada penelitian ini menunjukan bahwa kadar glukosa darah berpengaruh terhadap kenaikan kadar MDA. Pada pemberian dosis teh 15 gram/kgBB menunjukan nilai signifikan terhadap penurunan kadar glukosa darah  $P = 0,000 < (\alpha 0,05)$  dan kadar MDA darah  $P = 0,000 < (\alpha 0,05)$  dan dapat disimpulkan bahwa Teh biji mahoni ( *Swietenia mahagoni* ) memiliki pengaruh terhadap penurunan kadar MDA tikus diabetes melitus tipe 2 yang diinduksi aloksan, dengan dosis 15 gram/kg BB yang merupakan dosis optimal dalam menurunkan kadar Glukosa dan Kadar MDA

#### ABSTRACT

This research aimed to know the effect of mahagony seeds ( *Swieteniamahagoni* ) tea of MDA levels induced type 2 diabetes mellitus alloxan. By using the control group design method, post-test and by using 15 rats divided into 5 groups, namely group I negative group, group II control Alloxan induction, group III tea mahagony seeds 5 gram/kgBB, group IV tea mahagony seeds 10 gram/kgBB and group V mahagony seeds 15 gram/kgBB. The treatment was carried out for 14 days. In this research showed that the level of blood glucose affects increase of MDA levels. At 15 gram/kgBBof tea dosage presentationshowed a significant value on decreasing blood glucose levels  $P = 0,000 < (\alpha 0,05)$  and blood MDA levels  $P = 0,000 < (\alpha 0,05)$  and it can be concluded that mahagony seed tea ( *Swieteniamahagoni* ) had an effect on decreasing levels of rat MDA type 2 diabetes mellitus induced by alloxan, with a dose of 15 grams /kgBB which is the optimal dose in reducing blood Glucose and MDA levels.

**Keywords :** Type 2 Diabetes Mellitus, MDA, Mahogany Seeds Tea, Alloxan