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Review Article

A Systematic Review on the Hypoglycemic Potentials of Mahogany (*Swietenia* spp.) Seeds as Antioxidants in the Management of Gestational Diabetes Mellitus

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ABSTRACT

The prevalence of Gestational Diabetes Mellitus (GDM) has increased worldwide alongside an increase in the prevalence of type 2 diabetes mellitus (T2DM). Indonesia is endowed with a rich biodiversity and medicinal plants, including mahogany. Mahogany seeds contain flavonoids, saponins, and limonoids. Limonoid compounds have been shown to inhibit the production of reactive oxygen species (ROS) through the activation of antioxidant enzymes. This study focuses on a systematic review of the potential of the seeds of *Swietenia spp*. as an antioxidant in GDM. A systematic literature review of 13 scientific articles comprising 12 original research articles and 1 review article published within the last 7-8 years from various scientific databases was conducted. The original research articles were categorized into *in vivo* and *in vitro* studies with respect to the antioxidant activity of *Swietenia spp.* seeds. The systematic review provided a comprehensive understanding of the potential of mahogany seeds as an antioxidant and its role in the management of GDM.

Keywords: *Swietenia* spp., Antioxidant activity, Gestational Diabetes Mellitus, Oxidative Stress.

Introduction

Pregnancy is a physiological condition that is usually accompanied by oxidative stress and inflammation. In early pregnancy, intense oxidative stress can affect the process of implantation, foetal development and placental function. Distortion in the antioxidant defense mechanisms during pregnancy can result in various pregnancy-induced disorders including Gestational Diabetes Mellitus (GDM).[1] GDM is a condition where the body experiences glucose intolerance that occurs during pregnancy and progresses as the pregnancy advances.[2] Generally, this condition occurs around the second and third trimester of pregnancy.[3] Women with GDM have a higher risk of complications of pregnancy and stillbirth compared to normal pregnant women. Their children are also at risk of developing diabetes in the future.

GDM affects nearly 14% of the total pregnancies in the world, equivalent to 18-20 million births every year.[4] GDM prevalence has increased globally along with the increase in type 2 diabetes mellitus (T2DM) prevalence.[6] According to the center for disease control (CDC), 2-10% of pregnancies in the United States are influenced by gestational diabetes every year. A total of 21.3 million or the equivalent of 16.2% of live births in the world are associated with hyperglycemia in pregnancy where GDM causes 86.4%, while 6.2% are caused by type I diabetes or type II diabetes before pregnancy, and 7.4% are due to type I and II diabetes during pregnancy. Every year, GDM occurs in 7% of pregnancies in the world, including Indonesia which have up to 1.9 - 3.6% of cases of GDM.[2]

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Indonesia is a country with a rich biodiversity and medicinal plants, among which is mahogany or *Swietenia macrophylla* King, which belongs to the Meliaceae family (Figure 3). There are several reports on the uses of various parts of mahogany, including the seeds. Phytochemical studies of this species indicate that limonoids are the predominant compounds in mahogany seeds. However, phenolic compounds such as flavonoids, tannins, catechins, and epicatechins have also been widely reported. In Asia and South America, the leaves and seeds of the plant are used in the prevention and treatment of various diseases including diabetes and hypertension. Research has shown that the plant exhibits different biological properties including anti-inflammatory, antimutagenic, antitumor, and antioxidant activities.[7] Antioxidant compounds from *Swietenia* spp. seed have been shown to suppress reactive oxygen species (ROS) and oxidative stress, which can improve the insulin signaling pathway and increase the Insulin Receptor (IR) sensitivity.[8] Oxidative stress is a condition where the endogenous antioxidant defense system is overwhelmed due to ROS overproduction, which threatens cell survival. Oxidative stress increases the risk of complications of gestational diabetes. Cell structure damage can occur due to increased free radicals produced by the increased metabolic process during pregnancy. The placenta as a barrier between maternal and foetal blood circulation acts as a foetal protector from the dysfunctional process that occurs in the mother. One of the protective roles of the placenta is to provide antioxidant defense mechanism. Several types of antioxidant enzymes such as Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione peroxidase (GPx) are defensive mechanisms against damaging effects caused by oxidants like superoxide anion and hydrogen peroxide.[9] The potential of mahogany seeds as antioxidants has been widely studied. Therefore, the present study focuses on the review of previous scientific articles with the aim of showcasing the potential of mahogany plant as an alternative medicine for the prevention and management of certain diseases like gestational diabetes mellitus.

Method

The research used a systematic review of literature by identifying, assessing, and interpreting the potential of mahogany (*Swietenia* spp.) seeds as antioxidants in GDM. An extensive literature search was

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carried out, most of which was taken from central databases such as Science Direct, Pubmed, Google Scholar, MDPI, and NCBI using the keywords "*Swietenia* spp.", "Phytochemical", "Antioxidant activity", "ROS", "Malondialdehyde", “Catalase”, “SOD”, “Oxidative stress”, “Gestational Diabetes Mellitus”, and “Diabetes Mellitus”. Published articles for the last 7-8 years were reviewed. Inclusion criteria were articles relevant to the keywords and published within the last 7-8 years. Exclusion criteria were articles that do not contain the keywords and have been published earlier than the last 8 years. PICO (Patient/Population/Problem, Intervention, Comparison, and Outcome) analysis was carried out on all scientific articles that met the inclusion criteria as presented in Table 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) was used as a guide and instructions for the preparation of the systematic review. PRISMA is a flowchart that helps explain details supported by evidence in a transparent manner so that writers can easily understand. The PRISMA flowchart summary is presented in Figure 1.

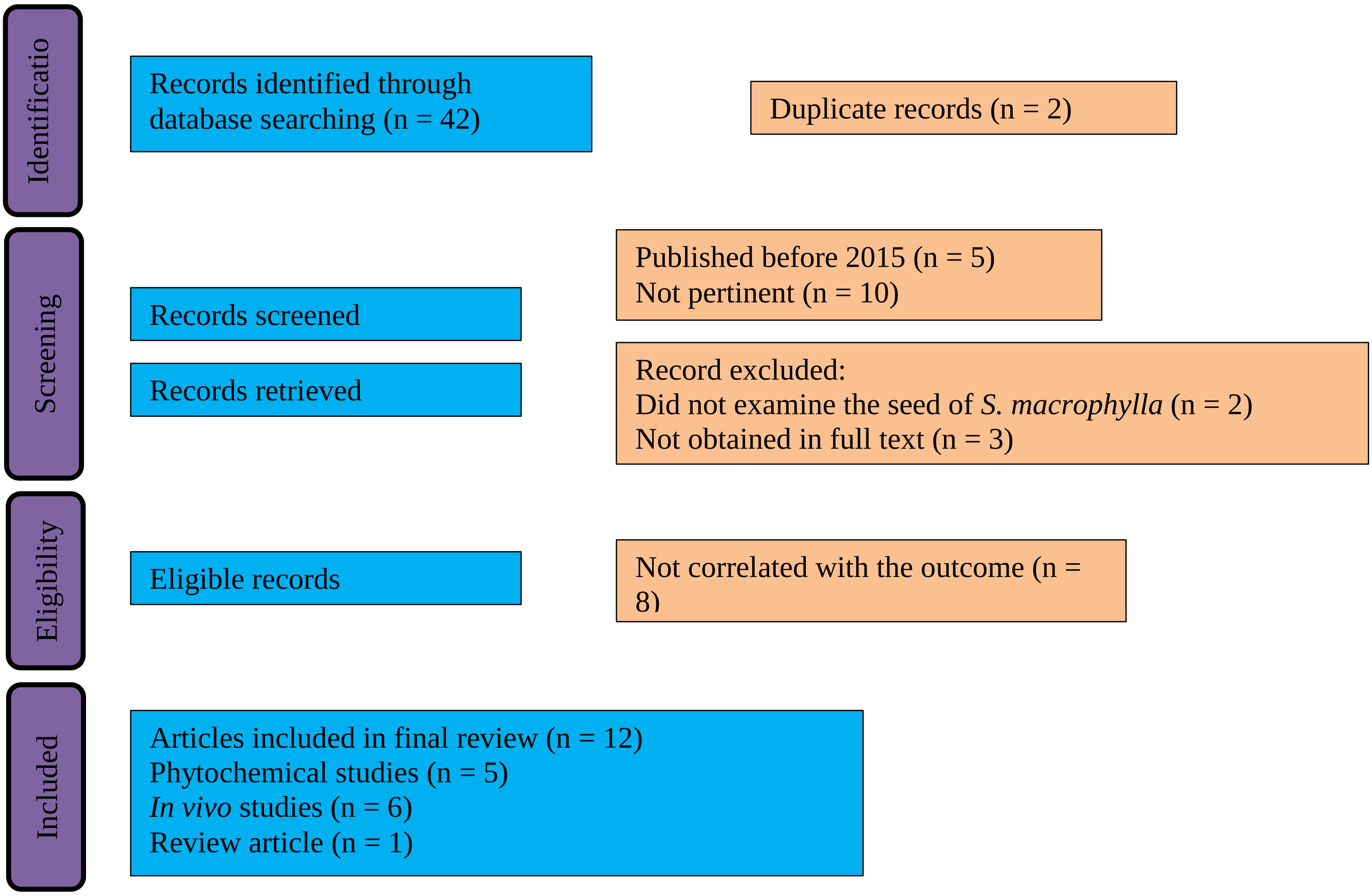

Figure 1: PRISMA flowchart.

Results and Discussion

From the results of the literature search, 29 articles matched the keywords, but several articles did not meet the inclusion and exclusion criteria. After careful scruitiny, 12 articles, both original articles and review articles were selected. The selected articles were subjected to PICO analysis as presented in Table 1.

Major Compounds of Swietenia macrophylla spp. *Seed*

Swietenia macrophylla seeds contain a lot of phytochemicals, but the main compounds are swietenine, swietenolide, and swietemahonin which belong to the Limonoid class (Figure 2). Swietenine is a natural tetranortriterpenoid isolated from *Swietenia macrophylla* seeds and is the main constituent of *Swietenia macrophylla* seeds. Swietenine has previously been reported to show anti-inflammatory and hypoglycemic effects. *Swietenia macrophylla* seeds have been used in folklore medicine to treat diabetes, hypertension, inflammation, and ulcers.[21–24] Limonoids originated from oxygenated tetracyclic triterpenes and side chains were modified into furan rings and the loss of four carbon atoms which were tetrarterpenoids.[25] Limonoids are known to trigger antioxidant enzymes which will suppress excessive ROS production.[8]

Phenols and flavonoids have been widely reported to have antioxidant activity in both *in vivo* and *in vitro* studies.[5] The results of a systematic review show that the phytochemical content of *S. macrophylla* seeds is mostly tannins, alkaloids, saponins, terpenoids, and stigmasterol.[10] A study on the determination of the phytochemical content of *S. macrophylla* seeds revealed a high concentration of phenolics (46.22 mg), flavonoids (26.12 mg), and tannins (9.23 mg).[7] Study on the phytochemical profile of *S. macrophylla* seeds has shown the presence of flavonoids, saponins, terpenoids, and alkaloids.[12] Similarly, the work of Kamaraj *et al*. (2021),[13] on the phytochemicals of *S. macrophylla* seeds, showed the presence of alkaloids, phenolics, flavonoids, tannins, saponins, steroids, and terpenoids. From these studies, it can be concluded that the major compounds in *S. macrophylla* seeds are alkaloids, flavonoids, tannins, and saponins.

Flavonoids and saponins are known to have antidiabetic activity.[14,18,30] Flavonoids protect the body from the damaging effect of free radicals and other pro-oxidants so they have the potential to prevent or reduce the risk of diabetes.[31] Meanwhile, saponin functions as an antidiabetic by lowering blood glucose levels, reducing MDA levels, and having strong hypoglycemic activity.[18]

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Table 1: Result of PICO analysis for the potential significance of *Swietenia* spp. as antioxidants

No.	Author, year	Population	Intervention	Comparison	Outcomes
1.	(Coello *et al*., 2020)[7]	Water extract of leaves and seeds of *Swietenia macrophylla* King	Determination of total phenolic content and evaluation of antioxidant activity of the aqueous extract of *Swietenia macrophylla* King seeds	Total phenolics, tannins, and flavonoids contents as well as antioxidant activity of extracts of seeds and leaves of mahogany	Total phenolics, tannins, and flavonoids contents were found higher in the leaf compared to the seeds. Observed antioxidant activity with the DPPH and FRAP methods
2.	(Sukardiman and Ervina, 2020)[10]	Journal-indexed and peer-reviewed *Swietenia* and *Swietenia* spp. from Scopus, PubMed, Medline, Google Scholar, and Research Gate with the keywords "*Swietenia*", "*Swietenia mahogany*", "diabetes", and "diabetic plants ".	Overview of systematic qualitative research (SR) was carried out by analyzing journal indexed and peer-reviewed on *Swietenia* and *Swietenia* spp. from various databases	Ethanol/methanol/water/ petroleum ether/n-hexane extract from seed or leaf of mahogany	Hypoglycemic mechanism of the ethanol/ methanol/water/petroleum ether/n-hexane extract of the seed/skin or leaf extract of mahogany was through reduction in blood glucose, restore heart and pancreatic β-cell function, blockade of epinephrine function, inhibition of α-amylase and β-glucosidase activity, antioxidant and antihyperlipidemic activity.
3.	(Bakar *et al*., 2020)[11]	Oil extract of *S. macrophylla* seeds	Analysis of antioxidants activity through 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) radical scavenging activity	Oil extract of *S. macrophylla* seeds using SE method	Seed extract of *S. macrophylla* at a concentration of 10 to 0.0001 mg/mL was not toxic with cell viability above 80%. Percentage of inhibition of α-amylase and α-glucosidase by *S. macrophylla* seed extract was 100.0 ± 0.3 % and 4.1 ± 2.0 %, respectively.
4.	(Handayani *et al*., 2019)[12]	Pure seed extract of mahogany at different concentrations of 20, 30, 40, 50, and 60 ppm	Determination of the antioxidant activity of the pure seed extract of mahogany using various methods.	There was no comparison group in this study	Purified seed extract of mahogany has antioxidant activity with IC_{50} of 33.86 ug/mL, and has potential for use as herbal medicine.
5.	(Kamaraj *et al*., 2021)[13]	Powdered seed extract of *Swietenia macrophylla*	Investigation of the antidiabetic effect of *Swietenia macrophylla* seeds and evaluation of *in vitro* antioxidant activity using DPPH, and *in silico* molecular docking	Results of preliminary phytochemical screening, *in vitro* antioxidant activity and *in silico* studies of *Swietenia macrophylla* seeds	*Swietenia macrophylla* seeds showed 56.0471% free radical scavenging activity compared with rutin. *In silico* studies using antidiabetic protein target, *Glutamine: fructose-6-phosphate amidotransferase* (GFAT) (PDB ID: 2ZJ3) showed interactions with *swietenine*, *swietenolide*, *β-sitosterol*, and *fukosterol*.
6.	(Shiming *et al*., 2021)[14]	78 mice (30 normal and 48 diabetics)	Normal mice were divided into five groups, diabetic mice were divided into 8 groups and were administered Swietenine at three different doses: 10, 20 and 40 mg/kg BW.	Control group (30 individual normal mice)	Swietenine (20 and 40 mg/kg BW) and metformin (50 mg/kg BW) have a significant effect in reducing the levels of glucose, cholesterol, triglycerides, LDL, urea, creatinine, alanine transaminase, alkaline phosphatase, aspartate transaminase, alanine transaminase, and malondialdehyde in serum.
7.	(Made Jawi *et al*., 2017)[15]	42 male Wistar rat at 3-4 months (175-225 g) divided into 7 groups	Hypertensive rat given mahogany seed water extract at 200 mg/day and 100 mg/day, ethanol extract of mahogany seeds at doses of 200 and 100 mg/day for 4 weeks	Control group (hypertensive rat)	There was a significant decrease in systolic blood pressure (SBP). SOD levels increase significantly in all treatment groups ($p < 0.05$). Ethanol extract of mahogany seed showed strong potential in increasing SOD and decreasing MDA and SBP levels.

8.	(Assaduzzaman *et al*., 2020)[16]	n-hexane, ethanol seed extract of *Swietenia mahagoni (Linn.)*	Evaluation of antioxidant activity by DPPH free radical scavenging effect.	There was no comparison group in this study	Results show that Mahagony seeds can be used as source natural antioxidant compounds that can be used to prevent the development of various oxidative stress-related diseases.
9.	(Mak *et al*., 2023)[17]	30 mice divided into 3 groups of 10 mice each consisting of group D which is diabetic, group S which is diabetic and treated with extract, and group N which is non-diabetic and not treated.	Mice were given a high-fat diet followed by injection of streptozotocin. Liver cholesterol, triglycerides, and lipids were increased, and this was reversed with oral administration of 80 mg/kg body weight of swietenine on alternate days for eight weeks.	Control group divided into 2 groups (diabetic control and cohort normal control) where each the group contains 10 mice.	Swietenine displayed antioxidant defense mechanism by upregulation of Nrf2, NQO-1, and HO- 1 levels. Swietenine showed beneficial effect in diabetes-induced NAFLD through inhibition of lipogenesis and activating Nrf2.
10.	(Muthmainah *et al*., 2019)[18]	36 male Wistar rats were divided into six groups (Normal control, DM rats, DM + glibenclamide, DM + extract 10 mice, DM + extract 20 mice, and DM + extract 40 mice.	Streptozotocin-induced diabetic rats administered nicotinamide, mahogany seed extract and glibenclamide for 21 days. Then glucose and MDA levels were measured after 7, 14, and 21 days of treatment.	Control group (normal rats and DM rats)	Average glucose and MDA levels were lower in the treatment groups compared to DM group (diabetic control). Average glucose level in the DM + extract group was significantly different from the normal control group, but MDA levels did not show any significant difference.
11.	(Hammam *et al*., 2020)[19]	Male albino rats were divided into 7 groups: (1) negative control, (2) positive control, (3) methanol extract, (4) acetone extract, (5) water extract, (6) oil extract, and (7) glibenclamide	Blood samples were collected from the eye plexus under diethyl ether anesthesia. Heparin was added as anticoagulants and then centrifuged at 3000 rpm for 20 minutes.	Negative control and control positive	Treatment with extracts and oils of mahogany seeds significantly lower glucose levels, and also significantly decrease GOT, GPT, ALP, urea, creatinine and malondialdehyde levels compared to the diabetic group.
12.	(Basy *et al*., 2015)[20]	Six normal rats as control and 24 STZ-induced diabetic rats.	Ethanol extract of *S. macrophylla* King starting from the 4th day and continued for the next 21 days. Blood glucose, creatinine serum, MDA, and urine protein were measured.	Control group (normal rats and diabetic rats)	STZ-induced diabetic rats (groups II-V), MDA levels, creatinine serum, and protein urine were higher compared to the normal control group ($P < 0.05$). There was a significant decrease in MDA and serum creatinine after treatment with *S. macrophylla* seed ethanol extract ($p < 0.05$).

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In vitro and In vivo Studies on the Antioxidant Activity of S. macrophylla Seed

The percentage of DPPH radical scavenging activity was higher in *S. macrophylla* seed oil extracted by supercritical carbon dioxide (SC-CO_2) than that obtained from Soxhlet extraction (SE). The values were 45.95 ± 0.30%, and 34.68 ± 0.20%, respectively.[11] *S. macrophylla* seed extract exhibited high antioxidant activity with an IC_{50} value for DPPH radical scavenging activity of 50 µg/mL. Similar results were obtained for *S. macrophylla* powder extract which gave a high free radical scavenging activity with percentage scavenging activity of 56.0471%. The results indicate that *S. macrophylla* powder extract has strong potential as natural antioxidants.[13]

Administration of Swietenine to diabetic rats at doses of 20 and 40 mg/kg reduced the levels of malondialdehyde (MDA) from 6.913 nmol/µL, and 5.080 nmol/µL. When combined with metformin, Swietenine at doses of 20 and 40 mg/kg boost metformin effects in reducing MDA levels. As for the Total Antioxidant Capacity (TAC), administration of Swietenine increased TAC levels from 237.6 nmol/µL to 175.2 nmol/µL at 20 mg/kg dose, and from 237.6 nmol/µL to 208.4 nmol/µL at 40 mg/kg dose.[14] The average initial serum MDA level was between 1.00 ± 0.11 to 1.13 ± 0.16 mmmol/L in all groups. After 4 weeks, MDA levels increased significantly, but ethanol extract of mahogany seeds at a dose of 200 mg/kg reduced the increase in MDA level. Similarly, at dose of 200 mg/kg, the ethanol extract of *S. macrophylla* seeds reduce SOD levels in all treatment groups ($p < 0.05$).[15]

S. macrophylla seed antioxidant activity with that of ascorbic acid and butylated hydroxytoluene (BHT) was tested at various concentrations (30 - 1000 µg/mL). LC_{50} values were measured at concentrations of 140 µg/mL, 160 µg/mL, and 180 µg/mL for ethanol, n-hexane, and water extracts. The LC_{50} values were 78-79 µg/mL, 90 µg/mL, and 88-89 µg/mL for the ethanol extract n-hexane, and aqueous, respectively. Among all the samples, the ethanol extract showed the lowest LC_{50} value.[16] The MDA levels in the normal and hyperglycemic rats were 14.58 mg/dL and 16.87 mg/dL, respectively. After administration of methanol extract, acetone extract, water extract, and *S. macrophylla* oil, MDA levels were 15.45 mg/dL, 16.22 mg/dL, 15.78 mg/dL, and 15.79 mg/dl, respectively. As for catalase (CAT), in normal and hyperglycemic rats, the catalase level which initially were 509 IU/L and 539.2 IU/L, respectively became 527 IU/L, 507.6 IU/L, 503 IU/L, and 522 IU/L after the same treatment protocols.[19] In a study of the antioxidant and antihyperlipidemic effects of *S. macrophylla* in diabetic rats, the extract of *S. macrophylla* significantly reduced blood glucose levels in the rats after 45 days of treatment with an optimal dose of 100 mg/kg. The activities of SOD, catalase, and glutathione peroxidase were significantly increased in rats treated with *S. macrophylla* seed extract.[32]

The NRF2 transcription factor is the main regulator of adaptive response to oxidative stress which plays an important role in reducing NAFLD. One of NRF2 transcription target is NADPH quinone oxidoreductase 1 (NQO-1) and heme oxygenase 1 (HO-1) which play a role in the antioxidant response and ward off oxidative stress. An *in vitro* study using qPCR analysis and immunohistochemistry to determine the expression of genes and proteins Nrf2, NQO-1, and HO-1 resulted in mRNA levels in diabetic rats of 1.80 ± 0.48, 3.94 ± 0.74, and 1.85 ± 0.12, respectively. After Swietenine treatment at 80 mg/kg body weight, the mRNA levels were 4.19 ± 0.40, 3.87 ± 0.39, and 3.82 ± 1.01, respectively. Whereas in the immunohistochemistry study, the levels of Nrf2, NQO-1, and HO-1 were 2.53 ± 0.03, 1.59 ± 0.01, and 1.82 ± 0.02, respectively.[17]

After 21 days of treatment with *S. macrophylla* seed extract, the average glucose and MDA levels in each of the following treatment groups: (DM + glibenclamide, DM + mahogany seed extract 10 mg/kg BW, DM + mahogany seed extract 20 mg/kg BW, and DM + mahogany seed extract 40 mg/kg BW) were significantly decrease over time. On day 0, the average serum MDA level in all groups increases by greater than 2 nmol/mL, except in the normal control group. The average level of serum MDA in the DM group treated with mahogany seed extract decreased significantly from day 0 to day 21.[18] In STZ-induced diabetic rats, treatment with *S. macrophylla* seed ethanol extract at 50, 100, and 200 mg/kg for 4 days and 25 days, MDA levels were significantly lower compared to the control group.[20]

Other species of *Swietenia* are also reported to have good antioxidant properties. The study of Asmara *et al*. (2023) reported that the antioxidant activity of mahogany seed oil (*S. humilis* Zucc.) obtained through ultrasound-assisted extraction (UAE) produced a higher antioxidant capacity (IC_{50} = 25.29 mg/mL).[33] Findings from the study of Lina *et al.* (2016)[34] has reported that the species *S. macrophylla, S. mahagoni, and S. humilis* have significant antioxidant activity and contain quite large amounts of phenolic and flavonoid compounds. Of the three species, *S. macrophylla* was the most effective in terms of the total antioxidant ability.[34] Apart from Swietenine, tetranortriperpenoid was also identified as a hypoglycemic ingredient whose effect is comparable to human insulin. Swietenine at 50 mg/kg p.o. has been proven by *in vivo* tests on streptozotocin-nicotiamide-induced T2DM rats to reduce fasting blood glucose levels by 39.91% on the 28th day of treatment.[35]

Association Between Oxidative Stress, ROS, and GDM

GDM is a complication of pregnancy where glucose intolerance occurs during pregnancy. In pregnancy, the antioxidant defense mechanism is disrupted such that the amount of free radicals become excessively high leading to increased levels of some markers of oxidative stress. Some studies have reported that one of the causes of foetal growth retardation is oxidative stress. Oxidative stress in GDM can cause vascular and pancreatic damage.[18] Reactive oxygen species (ROS) are agents that are often implicated in various disease pathogenesis, one of which is diabetes. With the presence of ROS in diabetes mellitus and GDM, there needs to be a balance between oxidation and antioxidants so that the normal physiological system is maintained.[36] ROS are defined as free radicals and non-radical derivatives of oxygen which include superoxide anion (O^{2-}), hydroxyl radical (OH), and hydrogen peroxide (H_2O_2). Pregnancy with hyperglycemic condition are associated with oxidative stress.[37]

Oxidative stress occurs due to an imbalance between cellular oxidants and antioxidants resulting in redox and/or molecular damage. Antioxidants are needed to maintain homeostasis. Enzymatic antioxidants such as SOD and catalase are needed as the body's first line antioxidant defense mechanism.[19] Hyperglycemia and GDM arising from oxidative stress causes changes in the main transcription factor leading to modification of gene expression, exacerbate insulin resistance, and increase DNA and chromosome damage.[1]

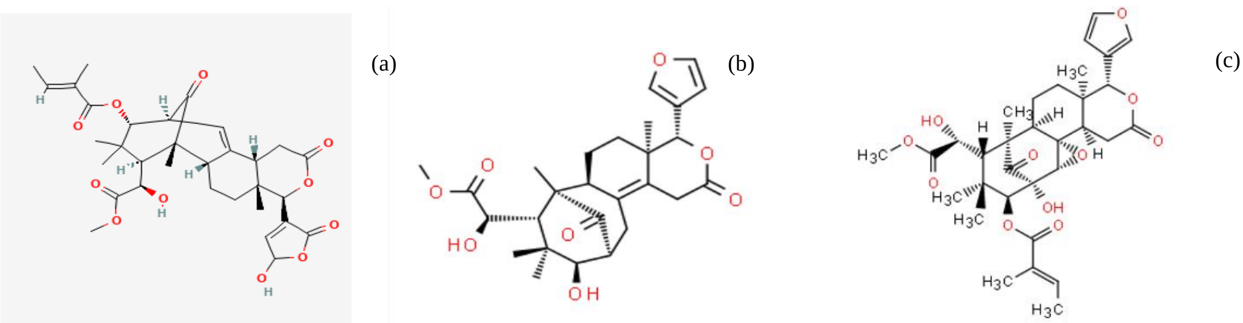

Figure 2: Structure of Limonoids from *Swietenia macrophylla* (a) swietenine,[26] (b) swietenolide,[27] (c) swietemahonin G.[28]

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The Role of Antioxidants in the Development of Gestational Diabetes Mellitus

One of the roles of the placenta is protection against biochemical changes such as distortion in antioxidant defense. Enzymatic and non-enzymatic antioxidants modify oxidative stress conditions in placental tissue, maternal and fetal plasma. The use of antioxidants has been shown to decrease the insulin dose needed to control blood sugar in GDM. One of the causes of GDM is insulin resistance during pregnancy. Insulin resistance generally occurs in the second trimester and reaches its peak in the third trimester. This situation occurs due to diabetogenic hormone secretion such as Human Placental Lactogen (HPL), growth hormone, cortisol, progesterone, and prolactin. These hormones cause a decrease in insulin sensitivity so that glucose utilization is limited and gluconeogenesis increases so that glucose is transferred to the foetus which has the potential for macrosomia.[38] One study concluded that the use of antioxidants during pregnancy can reduce the risk of premature babies and reduce the risk of respiratory distress syndrome (RDS) in babies. In general, total serum antioxidant defense status in GDM mothers and macrosomic infants is lower compared to normal pregnant women. This shows that there is a relationship between GDM and macrosomia with the downregulation of antioxidant status. From these results, antioxidants can reverse oxidative stress in GDM women and infants.[9]

The placenta of women with GDM showed 8-isoprostane secretion twice as high as normal pregnancy placenta. This is possibly due to high antioxidants in the placenta which accumulate in mild oxidative stress condition that occurs during pregnancy.[39] Antioxidant supplementation has a positive effect including ROS scavenging and damage repair. Various studies have proven that an increase in antioxidant levels can reduce ROS in women with recurrent abortion caused by high ROS. GDM also triggers oxidative stress in the foetus, so the intake of antioxidants during pregnancy is an important way of preventing GDM and maintaining maternal and fetal health.[40]

In a cross-sectional study on pregnant women, a flavonoid intake at 31.75 mg/day was less likely to cause obesity in pregnant women when compared to a lower intake of flavonoids. Flavonoids have the ability to maintain pancreatic β-cell function and insulin sensitivity. Flavonoids can also reduce hyperglycemia by inhibiting pancreatic lipase activity.[41] However, the intake of flavonoids during pregnancy can also be harmful if consumed in excess, including impaired foetal development and impaired absorption and metabolism of nutrients. Consumption of flavonoids and their derivatives (flavanol, naringenin, etc.) at a dose of 718 mg/day has been shown to have a lower risk of developing GDM in pregnant women. In addition, flavonoids can significantly increase insulin sensitivity in pregnant women which is associated with the NF-κβ, Akt, and MAPK Erk1/2 pathways.[42]

Polyphenols are the main contributors to antioxidants that allow phenols to donate electrons or hydrogen atoms to neutralize free radicals. Phenol also reduces the rate of oxidation by preventing the formation of ROS and deactivating ROS. Another action of polyphenols is to induce antioxidant enzymes such as catalase, SOD, and glutathione.[43] Some studies have reported the ability of polyphenols to modulate cellular homeostasis and affect AMP-activated protein kinase. Polyphenol intake, especially flavonoids during pregnancy can reduce the risk of GDM. Polyphenols are also reported as useful in reducing GDM symptoms.[44]

Conclusion

This systematic review provides a comprehensive understanding of the potential of mahogany seeds as an antioxidant and its role in the management of GDM. Literature review from various studies have proven that mahogany seeds have the potential as medicinal plants that have high antioxidant activity that can inhibit ROS production in GDM conditions. Antioxidant roles in the control of GDM can be explained from both the maternal and neonatal perspective. From the maternal perspective, antioxidants produced by mahogany seeds reduce ROS production in GDM mothers thereby minimizing cell and tissue damage. Meanwhile, from the neonatal perspective, antioxidants reduce the risk of macrosomic births and reduce the risk of premature newborns that need to be cared for in the neonatal intensive care unit (NICU).

Figure 3: *Swietenia* capsule showing the internal arrangement of the seeds.[29]

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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