• Review

Pharmacological effects and active phytoconstituents of *Swietenia mahagoni*: a review

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ABSTRACT: The usage of *Swietenia mahagoni*, a popular medicinal plant in India and some African countries, dates back to ancient times for its curative properties in diseases like malaria, diabetes, and diarrhea. It is also used as an anti-pyretic, bitter tonic and astringent. Its pharmacological activities are being widely explored. Although many important groups of phytochemicals have been identified and isolated from various parts of the plant, most of these researches have been focused on seeds. Toxicological studies have established the safety of many of these plant extracts, and found insignificant side effects. Here we present a comprehensive review of all the pharmacological effects and constituent phytochemicals of the plant.

KEYWORDS: *Swietenia*; plant extracts; medicine, oriental traditional; reviews

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1 Introduction

Plants have been used as medicine by a majority of cultures around the world. Currently these herbal medicines are being investigated as possible targets for drug development. During recent years, herbal medicine has begun to develop into a scientifically based system of healing. Due to demands from both the public and medical practitioners, studies leading to the scientific explanation of plant therapeutic capabilities are allowing this practice to gain increasing credibility and acceptance within the medical community. This review provides an introduction to the constituents and the therapeutic activities associated with *Swietenia mahagoni*.

*Swietenia mahagoni* Jacq. is a small, leafy, medium sized tree found in India and some African countries, but native to West Indies. Across the world, the plant is commonly called West Indies mahogany, caoba, caoba dominicana or acajou. It is one of the species of genus *Swietenia* which belongs to chinaberry family, Meliaceae. Other species in the group include *S. humilis*, *S. condolli* and *S. macrophylla*. The plant is normally a long lived, medium sized tree but it can reach very large sizes, depending on environmental conditions under which it grows. *S. mahagoni* was once the most sought-after cabinet wood in the world and continues to be famous for its wood, which is used in shipbuilding and furniture making. The species grows at a moderate rate. It is planted as an ornamental and managed in plantations and natural stands in dry and moist forests¹².

2 Ecological factors of the plant

*S. mahagoni*, one of several species referred to as mahogany, is indigenous to the southern region of Florida, the Bahamas, Cuba, Jamaica, and the island of Hispaniola. The species
is now planted as an ornamental and timber tree outside its natural range in several Caribbean islands, Hawaii, India, Sri Lanka, and Fiji. The species is reportedly best adapted to areas with annual precipitation, ranging from 760 mm to 1,780 mm\(^3\). The plant grows in variety of soil types but prefers habitats with moist and deep soils. The species range is restricted by cool, moist conditions and low-pH soils, particularly soils with high clay content.

3 Morphology

The plant attains a height of about 1,290 cm, with a crown diameter between 915 and 1,524 cm. The canopy is symmetrical with a regular outline and individuals all have a more or less identical crown form. The plant bears dark green-colored leaves that are alternate, and pinnately compound. The leaflet shape is lanceolate or ovate. The plant produces inconspicuous green flowers peri-annually. Fruits are a woody capsule, brown-colored with oval to pear shape, attaining a length of 8-16 cm, which does not attract wildlife. The branches of the tree droop as the tree grows (Figure 1).

4 Medicinal history

The parts of the plant have been used locally to treat many human ailments such as malaria, diabetes, diarrhea and hypertension. The fruit of the plant is used as a powerful anti-hyperglycemic drug. In some African countries the seed oil is used as an alternative body ointment therapy for a range of skin cuts, itches and wounds to ameliorate the healing process. A decoction of the bark is used to increase appetite, and treat anemia, diarrhea, dysentery, fever and toothache; it is also used as an energizer in cases of tuberculosis. A decoction of the leaf is used to treat nerve disorders, while an infusion of the seed relieves chest pain\(^3\). Mahogany seeds have potential in controlling amoebiasis, coughs and intestinal parasitism\(^5\).

5 Constituent phytochemicals

The total ash content of bark, analyzed by extraction with various solvents, is reported to be 22.0%, containing sulphated ash (14.5%), and water soluble ash (1.4%), and the total acid insoluble ash is 0.6\%6\(^6\). The bark also contains tannin (15.0\%)\(^7\)\(^-\)\(^11\) with no presence of alkaloid principles. Cyclomahogenol, a new tetracyclic triterpene, has been identified in the leaves of the plant\(^12\). The methanolic and water extract of seeds showed the presence of tannins, alkaloids, saponins and terpenoids as main phytoconstituents\(^13\). The crude methanolic extract of seeds contains alkaloids, terpenoids, anthraquinones, cardiac glycosides, saponins, and volatile oils\(^13\). Two potent antimicrobial limonoids, swietenolide (Figure 2) and 2-hydroxy-3-O-tigloylswietenolide (Figure 3), have been isolated from the methanolic extracts of the seed, and the structures of the compounds have been confirmed using spectroscopic analysis\(^15\). When the ether extract of the seed was systematically separated, 28 tetranotriterpenoids related to swietenine and swietenolide were found. Among them, several new compounds, named swietemahonins A, D, E, and G and 3-O-acetyl-swietenolide and 6-O-acetyl-swietenolide were identified. These compounds have been shown to strongly inhibit platelet-activating factor (PAF)-induced platelet aggregation\(^16\). In the seeds, two tetranotriterpenoids, mahonin (Figure 4) and secomahoganin (Figure 5), were isolated. The structures of these compounds were determined through 2D-nuclear magnetic resonance techniques, \(^1\)H-\(^13\)C cosy, and \(^1\)H-\(^13\)C long range cosy. The possible biosynthetic pathways to the above compounds have also been proposed\(^17\). Also using spectroscopic methods, 11 new mexicanolide-type limonoids, swietmanins, 2-hydroxy-3-O-isobutyryl-proceranolide, 2-hydroxy-3-O-benzoylproceranolide, and a new andirobin-type limonoid, swietmanin J, together with 19 known compounds have been isolated from the fruits and their structures\(^18\).

Two novel limonoids, swiemahogins A (Figure 6) and B (Figure 7) have been isolated from the twigs and leaves. These are the first andirobin and phragmalin types of limonoids, in which the D-ring d-lactone is collapsed, and a rare c-lactone is fused to the C-ring at C-8 and C-14. Their structures have been elucidated by extensive spectroscopic means, and in the case of one, single-crystal X-ray diffraction\(^19\).

Figure 1 Images of the tree, fruit and leaves of *Swietenia mahagoni*
6 Pharmacological effects

6.1 Antimicrobial activity

*S. mahagony* has a potent antimicrobial activity on a variety of microorganisms, including pathogenic microorganisms. The various phytochemicals present in the plant are responsible for the observed antimicrobial activity. Most of the aerial parts of the plant have been shown to significantly inhibit the propagation of various microorganisms. A crude methanolic extract of the seed has been shown to inhibit growth of 5 Gram-positive and 9 Gram-negative bacteria. Further, the extract of the seed at a concentration of 1 mg/mL has been shown to inhibit growth of the fungus *Candida albicans*.[20] The methylene chloride and methanol extracts of the seed have been assayed for their inhibitory action on ten microbial species, of which four are pathogenic bacteria (*Escherichia coli, Staphylococcus aureus, Xanthomonas campestris* and *Bacillus subtilis*), one yeast, one fungi (*Candida albicans*) and five molds (*Pythium ultimum, Rhizoctonia solani, Sclerotium rolfsii, Aspergillus fumigatus* and *A. pytiumparasitica*). The methylene chloride extract inhibited growth of seven species, while the methanol extract was active only against *Rhizoctonia solani*.[21] The methanol extract of the seed also had an inhibitory effect on *Candida albicans* in both *in vivo* and *in vitro* assays. *In vitro* disc diffusion assays showed a minimum inhibitory concentration of the extract to be 12.5 mg/dL. The extract had a deleterious effect on cell structures of *C. albicans*, causing morphological change and death, as evidenced by electron microscope images of extract-treated fungi. Treatment of fungus-infected mice with seed extract reduced colony-forming units in the kidney and the blood when compared to positive control mice.[22] The oil extracted from the seed reduced growth rates of several diseases causing by bacterial (*Shigellady senterial, Salmonella typhi, and Staphylococcus aureus*) and fungal (*Macrophomina phascoloma, Alternaria alternata* and *Curvularia lunata*) pathogens.[23]

The alcoholic and aqueous extracts of the leaf, stem/bark and root have inhibitory effects on *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Proteus vulgaris* and *Bacillus subtilis*. The efficiency of inhibition is comparable to benzyl penicillin and ampicillin.[24] Swietenolide and 2-hydroxy-3-O-tigloylswietenolide, two limnoids from the seed, have potent growth-inhibitory efficiency against eight multiple-drug-resistant bacterial strains (clinical isolates) including four Gram-positive (Group A haemolytic *Streptococcus aureus, Staphylococcus* aureus
aureus, Streptococcus pneumoniae and Haemophilus influenzae) and four Gram-negative (Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, and Salmonella paratyphi) bacteria. 2-Hydroxy-3-O-tigloylswietenolide has, overall, more potent activity than swietenolide. The most potent activity of swietenolide is against Haemophilus influenzae, Salmonella typhi, and Salmonella paratyphi, and 2-hydroxy-3-O-tigloylswietenolide is most active against Streptococcus pneumoniae, Salmonella typhi, and Salmonella paratyphi. Both the compounds are least effective against Klebsiella pneumoniae.

6.2 Anti-inflammatory effect

The methanolic extract of S. mahagoni seed has an ameliorating effect on paw edema induced by carrageenan and arachidonic acid, acetic acid-induced writhing, ear inflammation induced by croton oil, cotton pellet-induced granuloma and Freund’s adjuvant-induced polyarthritis in rats. The extract significantly reduced the acetic acid-induced writhing in rats; the writhing reducing effect was superior to the standard ibuprofen. Carrageenan-induced paw edema was reduced by 56.8% and 68.0% in rats treated with doses of 50 and 100 mg/kg extract, respectively. Croton oil-induced ear inflammation was reduced by 7.35% at 50 mg/kg dose and 47.06% at 100 mg/kg. Polyarthritis induced by Freund’s adjuvant was reduced by 53.79%, which was more than the positive control, ibuprofen. Cotton pellet-induced granuloma was reduced by 28.29% at 50 mg/kg and by 42.86% at a dose of 100 mg/kg; the effect of the extract was far more than the standard drug ibuprofen (14.29%). The extract also significantly increased the intraperitoneal count of white blood cells and macrophages.

Although there are many studies which indicate effective anti-inflammatory activity of S. mahagoni in animal models, the mechanism of action has yet to be explored. Future studies that measure the mRNA expression of inflammatory marker genes (e.g., cyclooxygenase and nitric oxide synthase) and expression of other inflammatory markers (e.g., interleukin (IL)-1β, IL-6, monocyte chemotactic protein-1, tumor necrosis factors-α and C-reactive protein) will be helpful in elucidating the precise mechanism of action.

6.3 Hepatoprotective effect

The petroleum and 80% aqueous methanol extracts of S. mahagoni bark showed a hepatoprotective effect against paracetamol-induced hepatic damage in male Wistar rats. Treatment with S. mahagoni bark extract significantly reduced the alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and serum bilirubin levels, suggesting the hepatoprotective effect. Histopathology revealed that the liver cells in the extract-treated group were indistinguishable from liver cells of healthy rats. The extract also significantly reduced the thiobarbituric acid-reactive substances, when compared to the paracetamol-treated group. Bark extract was also reported to increase the reduced glutathione level in the liver. The above findings indicate that the hepatoprotective efficacy of the bark extract may be mediated through the modulation of lipid peroxidation and the augmentation of endogenous enzymatic and non-enzymatic antioxidant defense systems. To determine safety for human use, acute toxicity tests were carried out on Swiss albino mice; the dose at which 50% of recipients died (LD50), for orally administered bark extract, was 200 mg/kg.

The water extract of S. mahagoni leaves showed hepatoprotective efficacy in rats with chronic alcohol-induced liver damage. In the study, animals were divided into 4 groups. The first group (negative control) received increasing concentration of alcohol (10% ethanol for 1 week, 20% for another 2 weeks and 30% for remaining 9 weeks). The second group was used as control, receiving no alcohol. Groups 3 and 4 received 250 and 500 mg/kg, respectively, of extract after they received their dose of alcohol. After 12 weeks, animals from each group were sacrificed and markers of liver function (activity of ALT, AST and ALP and total bilirubin) were measured in the serum. In addition, pentobarbitone-induced sleeping time was determined. At all doses, the extract significantly reduced the serum activity of ALT, AST, and ALP and significantly reduced serum levels of bilirubin compared to the negative control that received only alcohol. The duration of pentobarbital-induced hypnosis was also significantly shortened. The histopathological result showed significant protection in the extract-treated groups compared to the negative control group.

6.4 Antidiarrheal activity

The ethanolic, methanolic and aqueous extracts of S. mahagoni seed show antidiarrheal activity in castor oil-induced diarrhea as well as in charcoal-induced gastrointestinal motility in Wistar albino rats. The ethanolic, methanolic and aqueous extracts of seeds at various concentrations (50, 100, 200 and 300 mg/kg) were used in this study. Among the three solvent extracts, the ethanolic extract showed the most potent antidiarrheal activity, as evidenced by reduction in the rate of defecation and improved consistency of faeces. Treatment with the extract produced a profound decrease in intestinal transit and significantly inhibited castor oil-induced enteropooling compared to standard drugs diphenoxylate (50 mg/kg) and atropine sulfate (2.5 mg/kg). The delayed onset of diarrhea, inhibition of castor oil-induced enteropooling and the suppressed propulsive movement all support the traditional claim that S. mahagoni functions as an antidiarrheal drug in the Indian system of medicine without any side effects.

6.5 Antioxidant effect

Studies have reported that the seed of S. mahagoni possesses...
antioxidant activity. The methanol extract of the seed was shown to be a potent antioxidant in various in vitro assays (i.e., xanthine oxidase assay, hydrogen peroxide-scavenging activity, ferric-reducing antioxidant power (FRAP) assay and 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) assay). The methanol extract inhibited superoxide formation with a value of 47.2%, which was less than standard drug allopurinol (87.51%). Hydrogen peroxide-scavenging activity of the extract was found to be 49.5, which was comparable to standard drug ascorbic acid (51.1). The seed extract had FRAP activity of 0.728 mmol Fe++/g, which was higher than the FRAP activity of ascorbic acid (0.405). The extract showed a DPPH-scavenging activity of 23.29% at 1 mg/mL concentration, this value was less than that of ascorbic acid[29].

6.6 Gastroprotective effect

The ethanol extract from the seed of the S. mahagoni has shown gastroprotective activity against ethanol-induced gastric mucosal injury in rats. Six groups of rats were orally fed with carboxymethyl cellulose, omeprazole (standard drug, 20 mg/kg) or seed extract (50, 100, 200 and 400 mg/kg) one hour before oral administration of absolute ethanol (to generate gastric mucosal injury). The carboxymethyl cellulose group exhibited severe mucosal injury, whereas pre-treatment with plant extract provided significant protection of gastric mucosa in rats. The carboxymethyl cellulose group showed severe damage to gastric mucosa (edema and leucocyte infiltration of sub-mucosa) compared to the plant extract-treated group, which showed gastric protection as evidenced by histological observations. The authors also carried out similar studies using ethanol extract of mahogany leaf. The leaf extract significantly reduced the mucosal injury and increased the mucus secretion when compared to the control group; the effect was similar to standard drug omeprazole. The extract, in addition, reduced the edema and leucocyte infiltration into the sub-mucosal layer[30].

6.7 Depressant, anticonvulsant and neuropharmacological activity

The methanol extract of S. mahagoni bark also showed depressant (sleep-potentiating) and anticonvulsant effects in male Swiss albino mice. The extract significantly increased pentobarbital-induced shortened sleeping time in a dose-dependent manner. The anticonvulsant effect of the extract at the doses of 25 and 50 mg/kg was examined against seizures induced by pentylentetrazole (80 mg/kg) and strychnine (2.5 mg/kg). In these experiments the extract significantly delayed the onset of seizures and also antagonized these seizures in a dose-dependent manner. The effects of the extract were comparable to the reference drug diazepam (2.0 mg/kg)[31].

The ethanol extract of S. mahagoni seed has shown antinociceptive potency and neurodepressive effect. Antinociceptive activity was tested using the model of acetic acid-induced writhing in mice at oral doses of 300 and 600 mg/kg. The extract showed a significant writhing inhibition in mice, which was comparable to the standard drug diclofenac sodium. Neurodepressive activity was studied using the pentobarbital-induced hypnosis effects on exploratory behavior, such as open field test, hole cross test and hole board test. Treatment with leaf extract significantly increased pentobarbital-induced hypnosis and decreased the exploratory behavior of the mice, indicating its depressant activity on central nervous system[32].

The results of in vivo experiments indicated the scope to carry out in vitro antidepressant assays such as expression and inhibition of monoamino-oxidase (A and B) and acetyl choline esterase, as well as neurotransmitter uptake inhibition studies on serotonin, norepinephrine, dopamine, and 5-hydroxytryptamine receptors.

6.8 Antidiabetic effect

Aqueous-methanol extract of S. mahagoni seed has been reported to exhibit hypoglycemic and antihyperlipidemic potency in streptozotocin-induced diabetic rats. Oral feeding of the extract to diabetic rats for 21 d lowered the blood glucose level and improved liver glycogen content. Furthermore, treatment with the seed extract normalized the levels of serum urea, uric acid, creatinine, cholesterol, triglyceride and lipoproteins. In addition, the extract increased the activity of antioxidant enzymes and reduced the oxidative stress in liver, kidney and skeletal muscles[33].

The ethanolic extract of S. mahagoni seed inhibited α-amylase to an extent of 70.33% at a concentration of 200 μg/mL[34]. Seed extract acted as an antagonist to the peroxisome proliferator-activated receptor γ in both the yeast two-hybrid system and diabetic mice. The activity was comparable to that of standard drug rosiglitazone[35].

Based on the in vivo antidiabetic potency, in vitro antihyperglycemic assays (i.e., glucose-6-phosphatase inhibition, glucose uptake in muscle and adipocytes, insulin secretion from the β-cells of pancreas, glycogen synthase activity, glycogen phosphatase activity) should be explored. Refining the mechanistic understanding of S. mahagoni seed extract bioactivity may help to develop a natural drug for diabetes.

6.9 Anti-HIV effect

Methanol extract of mahogany bark is reported to exhibit anti-HIV-1 activity by inhibiting a key enzyme, HIV protease, which is required by the virus to replicate in host cells. Bark extract also suppressed the formation of syncytdia in co-cultures of human acute lymphoblastic leukemia cell line (MOLT-4) and MOLT-4/HIV-1 cells[36].

6.10 Immunomodulatory effect

The methanolic extract of seeds enhanced the immune efficiency, as assessed by neutrophil adhesion, phagocytic index by carbon clearance, hemagglutinating antibody
cytotoxicity of the extract at high concentration. The LD6, 12, and 24 h, respectively. The bioassay showed moderate the number of dead larvae in each bottle was counted after with different concentrations of the extract. Subsequently, where matured nauplii (\textit{Chironomus}) were incubated has been assessed using a brain shrimp lethality assay, significant 6.12 Cytotoxicity and acute oral toxicity

The petroleum ether and methanol extracts of \textit{S. mahagoni} leaves both showed insect repellent and larvicidal activity against mosquito \textit{Culex quinquefasciatus} (Cx. \textit{quinquefasciatus}) in a laboratory bioassay. The extracts were applied to mosquito larvae of all stages at various concentrations. The extract led to cent percent mortality in the 2nd instar larvae at a concentration of 50 ppm. Exposure to the extract also caused significant mortality in the 1st, 3rd and 4th instar larvae. The extracts showed 100% repellent power for up to 135 min. No mosquito bites were observed during the repellent period. The safety of the extracts was assayed using larvae of \textit{Gambusia affinis}, tadpole of \textit{Bufo} and \textit{Chironomus}. The extracts did not cause mortality in these larvae at any of the tested concentrations\cite{38}. Along with the larvicidal and insect repellent activity, the acetone, methanol and water extracts of the leaf showed anti-feedant property against the red flour beetle, \textit{Tribolium castaneum} Herbst. The toxic effect of the extract on the beetle was significant\cite{39}.

6.11 Insect repellent and larvicidal effect

The petroleum ether and methanol extracts of \textit{S. mahagoni} leaves both showed insect repellent and larvicidal activity against mosquito \textit{Culex quinquefasciatus} (Cx. \textit{quinquefasciatus}) in a laboratory bioassay. The extracts were applied to mosquito larvae of all stages at various concentrations. The extract led to cent percent mortality in the 2nd instar larvae at a concentration of 50 ppm. Exposure to the extract also caused significant mortality in the 1st, 3rd and 4th instar larvae. The extracts showed 100% repellent power for up to 135 min. No mosquito bites were observed during the repellent period. The safety of the extracts was assayed using larvae of \textit{Gambusia affinis}, tadpole of \textit{Bufo} and \textit{Chironomus}. The extracts did not cause mortality in these larvae at any of the tested concentrations\cite{38}. Along with the larvicidal and insect repellent activity, the acetone, methanol and water extracts of the leaf showed anti-feedant property against the red flour beetle, \textit{Tribolium castaneum} Herbst. The toxic effect of the extract on the beetle was significant\cite{39}.

6.12 Cytotoxicity and acute oral toxicity

The safety of the methanol extract of \textit{S. mahagoni} seed has been assessed using a brain shrimp lethality assay, where matured nauplii (\textit{Artemia salina}) were incubated with different concentrations of the extract. Subsequently, the number of dead larvae in each bottle was counted after 6, 12, and 24 h, respectively. The bioassay showed moderate cytotoxicity of the extract at high concentration. The LD50 after 24 h of exposure was 0.68 mg/mL. An acute oral toxicity study was carried out \textit{in vivo} in mice. The mice were orally fed with 25, 200, 2,000, and 5,000 mg/kg of seed extract and monitored for changes in clinical signs such as weakness or aggressiveness, food refusal, loss of weight, diarrhea, discharge from eyes and ears, and noisy breathing, and the number of deaths in group was monitored carefully. After 14 d, the animals were sacrificed and the vital organs were observed for macroscopic and histological changes. The LD50 for acute oral toxicity of the seed extract in mice was found to be greater than 5,000 mg/kg, indicating the relative non-toxicity of the sample\cite{39}.

7 Conclusions

\textit{S. mahagoni} is a medicinal plant that is being extensively investigated for its various therapeutic values. The present review combines most of the lab and clinical data on the plant and proposes some \textit{in vitro} studies, which will guide researchers in further study. The presence of novel phytochemicals, such as limnoids and triterpinoids, reflects the potential pharmacological value of the plant. Based on pharmacological activities in animal models, there is a scope to design \textit{in vitro} assays that explore the mechanism of action. While qualitative analysis of phytochemicals has been the focus of previous studies, there is still a great need for quantitative evaluation and characterization of the phytochemicals in all the parts of the plant. The identification and isolation of the individual phytochemicals responsible for the healing effects may help to design drugs with potent healing activity as well as negligible side effects. Although most of the claims about the efficacy of \textit{S. mahagoni} by traditional medicine have been scientifically verified, much of the work is restricted to only a few areas, namely, diabetes, malaria and hypertension. Nevertheless, the available scientific data on \textit{S. mahagoni} confirms its usage in traditional medicine.

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9 Competing interests

The authors declare that they have no competing interests.

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