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A Review on Phytochemical Studies and Biological Activities of *Swietenia mahagoni*



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ABSTRACT

Since the beginning of the world civilization humans are depended on herbal medicine because of its health care and various disease treatment properties. Herbal drugs not only deals with disease but also prevent its complicity, however synthetic marketed drugs do not provide both characteristics at a same time. For the treatment of chronic diseases, long-term use of synthetic drugs has been identified. These causing drug resistance and several side effects. Though the natural herbs are not exhibit any severe adverse effects, so they are more safer and more effective choice to treat any type of ailment, other than synthetic medicines. In the world of so many herbal plants *Swietenia mahagoni* is a most important one. Different parts of this timber tree (leafs, seed, bark, fruit) has been traditionally used to treat many diseases. Limonoides are the main active compound in the *Swietenia* species. Alkaloids, tannins, phenols, flavonoids, saponins and glycosides are the phytochemicals that also found in this plant. For the presence of such vital phytochemicals, mahogany played a significant role as an ideal herbal drug. This paper will give a comprehensive overview about phytochemicals and pharmacological properties of *Swietenia mahagoni* plant.

INTRODUCTION:-

Swietenia mahagoni is a medium to large evergreen tree with 30-35 m of height, which belongs to Meliaceae family. Meliaceae (the mahogany) is a family of flowering plants that includes about 51 genera and 575 species of trees. *S. mahagoni* produced fragrant, yellow-green colour with less than 0.3 inches wide, small flowers. The plant is native to the Bahamas, Antilles, USA, Hispaniola, Jamaica, Haiti, Southern Florida, Cuba, and widely cultivated in India, Sri Lanka, Bangladesh, Indonesia, Philippines, Malaysia and China. Mahogany is an economically very valuable timber tree [2].

Diabetes is chronic, endocrine, metabolic condition that occurs due to the body either does not produce enough insulin or it resists insulin. Insulin is only one hormone that regulates the blood glucose level by using glucose for the sources of energy and store glucose as glycogen in the liver or as a fat in the tissue. Uncontrolled diabetes causes ischemic heart disease, stroke and also damages nerves, kidneys, eyes which lead to premature death of the patient. For the treatment of diabetes, doctors prescribed various synthetic oral antidiabetic drugs or Insulin injections. But this synthetic drug causes several adverse drug reactions like weakness, nausea, vomiting, weight gain of hyper-insulinemia, fatigue to lactic acidosis, diarrhoea, pancreatitis, etc. Since down of civilization plants has an important role in the treatment of diabetes. The Ethanolic/methanolic/petroleum/n-hexane/aqueous extracts of mahagonis's flower/leafs/bark or seed have anti-diabetic activity with no to relatively mild side effect than synthetic anti-diabetic agents [3].

Decoction of *S. mahagoni* bark has been tremendously used as febrifuge, so it uses as herbal antimalarial remedies. Various phytochemical studies proved that crude flower/bark extract and different parts of the plant having antioxidant and antimicrobial properties and also able to treat chronic disease like tuberculosis, hypertension and diabetes [1]. The seed extracts of mahogany inhibit Platelet Activation Factor induced platelet aggregation and used for treating eczema, rheumatic diseases, anorexia and maintain blood pressure [2], [4]. Whereas it's barks are used as antipyretic, astringent and tonic [5]. *S. mahagoni* also contain HIV protease inhibitory substance which is reported by Matsuse *et al.*, (1998).

Phytochemical study of *Swietenia mahagoni*:-

Mahogany family is characterized by synthesis of modified triterpenes known as limonoids, which having a 4,4,8-trimethyl-17-furanyl steroid skeleton [7]. Over 300 limonoids have been

isolated until now ^{[8], [9]} and they are more enormous in this special family than any other families. The special arrangements of subgroups and ring structures of limonoids provides various characteristics like insecticidal, insect antifeedant, insect growth regulation and medicinal activity to humans and animals.

There are various phytochemicals that found from *S. mahagoni* are, alkaloids, flavonoids, saponins, phenols, phospholipid, antraquinones, volatile oils, terpenoids, many long chain unsaturated acids and cardiac glycosides. This herbal plant contain approximately 45 limonoids, this are swiemahogins A and B, swietenolide, androbin, gendunin and phragmalin, swietenine dimeric triterpmahonienoid, 2-hydroxy-3-O-tigloylswietenolide, chlorogonic acid, triterpens and tetranortriterpenes^{[10], [11]}, 3,6-di-O-acetylswietenolide, 2- α -hydroxymexioanolide, swietenine acetate, 6-acetyl-3-tigloylswietenolide^{[12], [5]}.

According to Rahman *et al.*, (2009), Swietenolide and 2-hydroxy-3-O-tigloylswietenolide (limonoids) have been found from the methanolic extracts of *S. mahagoni* seed which have antimicrobial property. And the ether extract was isolated 28 tetranortriterpenoids ^[10]. Among those components 6-O-acetyl-swietenolide, swietemahonin A, D, E and G and 3-O-acetylswietenolide induced platelet aggregation activity by inhibiting platelet activating factor (PAF) ^[14]. Limonoids (81.91%), polyphenolics (4.26%), fatty acids (1.06%), steroids (4.26%), coumarin (1.06%), lignan (1.06%) and essential oils (6.38%) are the most phytochemicals that isolated from leaves, stembark, twig and seed of *S. macrophylla* ^[15]. Swietenia's bark content some phytochemical constituents such as alkaloids, flavonoids, phenolics and triterpenoids which having antidiabetic property ^{[16], [17]}. Falah *et al.* (2010), reported flavonoids have antioxidant activity.

Phytochemicals present in *S. mahagoni*:-

Parts of the plant	Phytochemicals	Reference
Leafs	Tetracyclic triterpene (cyclomahagenol)	[19]
	Melianone, swietenin, stigmasterol glucose, quercetin-3-O-L-rhamnoside and 3-O-rutinoside.	[20]
	Phragmaline limonoids swietephragmins A to I, 11-hydroxyswietephragmin B, and mexicanolide type limonoid 2-hydroxy-6-deacetoxy swietenine-6-O-acetyl-2-hydroxyswietenin, swietemahonin G and deacetylsecomahoganin, 7-deacetoxy-7-oxogedunin, methyl-6-hydroxyangoleosate.	[21], [22]
Seed	Tannins, alkaloids, terpenoids and saponins.	[23]
	Cardiac glycosides, anthraquinones	[24]
	6-Desoxyswietenine	[25]
	Secomahoganin, swietemahonolide, swietemahonin- F, B and C, 3-O-tiogloyl-6-O-acetylswietenolide, 6-acetoxygedunin.	[10]
	Protein, fats, carbohydrate and fatty acid of seed's oil [palmitic acid, linoleic acid, stearic acid, elaidic acid, ecosanoic acid, 2-furapentanoic acid]	[26]
Stem bark	Swietenialides – A to E, mexicanolide, 2-hydroxyswietenin	[27]
Twigs	Limonoids, swiemahogins A and B	[28]
Fruits	Swietmanis A to J, 2-hydroxy-3-O-benzoylproceranolide, andirobin-type limonoid, 8R-hydroxycarapin, khivorin, 2-hydroxyfissinolide, seneganolide A, 2-hydroxy-3-O-iosbutyrylproceranolide	[20]
Heart wood	Benzoate hedergenin, cyclo swietenol, cycloartenol, lupleol, β -sitosterol	[20]

Medical uses of *Swietenia* spp.:-

The herbal plant *Swietenia mahagoni* medicinally used as antipyretic, antihypertensive, antidiabetic, antimicrobial, antidiarrheal, anti-inflammatory, astringent, antimalarial, hepatoprotective, anticonvulsant, antiulcer, antioxidant, antifungal, antidepressant, anticancer, platelet aggregation inhibitors, anti-HIV, analgesic, antimutagenic, bitter tonic, immunomodulator and also used in neuropharmacology [30], [31], [32], [33], [5], [15].

Traditional uses of *Swietenia* spp.:-

Swietenia mahagoni has a very important role in the Ayurvedic system of India, Indonesia [11], Malaysia [33] and also some African countries. Almost all the parts of this plant have been used traditionally for the treatment of various human ailments.

In India decoction of *S. mahagoni* bark are traditionally used to treat diarrhoea, tuberculosis, fever, increasing appetite, anaemia, toothache [34]. The seeds are very useful against chest pain [35]. And in the west Bengal, Odisha the aqueous extract of *S. mahagoni* bark and seed is taken for the treatment of diabetes, psoriasis and also use as an antiseptic for wounds [36]. Its leaf and root used as emollient for bleeding [37].

In Indonesia the water decoction of *S. mahagoni* crushed seed has been used for maintaining blood glucose level and treating hypertension, constipation, rheumatism, menstrual pain, eczema fever and improving the fertility and the power of its dried crushed seed externally use as insect repellent [38], [10].

Kadota *et al.*, (1990) reported in Malaysia, the decoction of *swietenia macrophylla* crushed seed traditionally used for the treatment of various skin ailments and the raw seed are chewed for pain relieve and treating hypertension and diabetes like chronic diseases. The fruits of *S. macrophylla* have been use for manufacturing of healthcare products in industries due to its blood circulation maintaining and skin condition improving property. In Amazonian Bolivial mashed seed of *S. macrophylla* has been used as an abortion medicine and externally used for the treatment of leishmaniasis [30]. Guevara *et al.*, (1996) reviewed that the seeds have antitumor, anti-inflammatory and antimutagenicity activity.

Pharmacological Activities:-

1 Antidiabetic Activity:

Swietenia bark and seed are experimentally very useful for diabetic patients. In *In-vitro* antidiabetic study of Hajra *et al.*, (2011) was proved that ethanolic extract of *S. mahagoni* seed (EEMS) inhibited α -amylase. Moreover, when it's aqueous and ethanol extract was treated at 100-500 mg/kg Body Weight dose, it shows α -glucosidase inhibition and *in-vivo* hypoglycemic activities^[40]. Li *et al.*, (2005) reviewed, extract of *S. mahagoni* at 1g/kg B.W. dose have peroxisome proliferator-activated receptor (PPAR γ) agonists activity which nearly half of rosiglitazone on diabetic db/db mice.

Streptozotocin (STZ) and nicotinamide induced type 2 diabetic rats have been treated with methanol extract of *S. macrophylla* seed at a dose of 300 mg/kg B.W. for continuous 12 days, which shows reduction of fasting blood glucose level by 32.78%^[42]. Same dose of the extract also reduced the elevated level of total cholesterol in blood by 18.56% and triglyceride by 10.41% and increased the shorter glycogen level in liver by 46.27%^[42]. Dewanjee *et al.*, (2009) reported, oral administration of swietenine at a dose of 25 and 50 mg/kg B.W. for 5 days reduced fasting glucose level respectively by 47.34 mg/dL and 55.85 mg/dL. Treatment with swietenine has been importantly reduced the higher level of cholesterol and triglyceride and increase the liver glycogen level to the normal level in a dose dependent manner when compared with non-diabetic control group^[43]. STZ-induced type 2 diabetic rats have been treated with alcoholic seed extract in presence of glibenclamide as a reference, that gives a significant result of increasing level of serum insulin, haemoglobin, glycosylated haemoglobin. And the glycogen level in liver was elevated to the normal level which obtained with glibenclamide^[44]. Dutta *et al.*, (2013) reported, oral treatment with the aqueous extract of *S. macrophylla* King seeds (at 2 g/kg B.W.) on STZ-induced diabetic rats has been proved hypoglycaemic property with reduction of fasting blood glucose by 98.66 ± 9.26 mg/dL. The combination of herbal tea of *Andrographis paniculata* herbs and *S. mahagoni* seeds at 2:1 ratio has been given to alloxan diabetic mice for 7 days at the dose of 0.4 ml/20g B.W. and it observed highest blood glucose level reduction ($88.20 + 43.16$ mg/dl) compare to other ratios^[46]. Naveen and Urooj, 2015 had been tested the potency of aqueous extract of *S. mahagoni* leaf as antidiabetic remedies, by administering it orally to the diabetic rats for 45 days at 500 mg/kg B.W. dose. And it was founded that the extract reduces the fasting blood glucose level.

Compounds	Mechanism of action
Saponins	I. Enhance the expression level of GLUT4 transporter. II. Decrease insulin resistance and inhibits carbohydrates absorption. III. Prohibition of glycogen phosphorylases and glucose 6-phosphatase.
Flavonoids, sterols, terpenes	I. Protective regeneration of β cell function. II. Prohibition of glycogen phosphorylases and glucose 6-phosphatase. III. Inhibit lipid peroxidation and stimulate insulin secretion.
Berberine	I. Activation of AMPK. II. Inhibit lipid peroxidation and stimulate insulin secretion. III. Protective regeneration of β cell function.
Cathechin	I. Inhibit lipid peroxidation and stimulate insulin secretion. II. Activation of AMPK. III. Protective regeneration of β cell function. IV. Enhance the expression level of GLUT4 transporter.

GLUT4= Glucose transporter type 4; AMPK= 5' adenosine monophosphate-activated protein kinase

2 Antioxidant Activity:

During the metabolism, oxidation process made some free unstable molecules, that free radicals causes cell damage. Antioxidants are the chemical substance that protect cells from the damage by delayed or inhibit the oxidation of lipid or other molecules through inhibiting the initiation or propagation of oxidizing chain reactions. Phenolic compounds have a potent antioxidant activity due to its redox properties, which helps to neutralized the free radicals and destroy singlet and triplet oxygen or peroxides ^[48]. *S. mahagoni* contains phenolic phytochemicals like flavonoids and tannins ^[3].

Swietemacrophyllanin, catechin and epicatechin are the compounds (from polyphenols or flavan-3-ols class) that isolated from acetone extract of *S. macrophylla* bark when treats with n-hexane, diethyl ether and ethyl acetate. DPPH [1,1-diphenyl-2-picrylhydrazyl] free radical scavenging assay shows these compounds have antioxidant activity. This study proved

swietemacrophyllanin had a very potent antioxidant activity ($IC_{50} = 56 \mu\text{g/mL}$) than Trolox, which use as a reference ^[49]. When antioxidant activity of methanolic and aqueous extracts of *S. mahagoni* seeds had been studied by using DPPH and hydroxyl radical scavenging activities, it was obtained that the methanolic extract showed a powerful antioxidant outcome than the aqueous extract ^[50].

3 Anticancer Activity:

Cancer is a group of diseases characterized by uncontrolled division of abnormal cells that spread to distant parts of the body. Mainly malignant tumors are formed cancer. When the ethanol extract of *S. macrophylla* seeds and its hexane and methanol fractions have been tested using Epstein-Barr virus early-antigen (EBV_EA) activation, in the presence of 12-O-tetradecanoylphorbol-13-acetate as a tumor promoting agent, its significantly shows an antitumor-promoting effect ^[39]. The anticancer property of *S. mahagoni* seeds has been examined in Brine shrimp lethality bioassay, against the breast cancer T47D cell line ^[51]. A powerful anticancer activity of mahogany seeds was proved by this experiment, due to its fraction consisting of alkaloids, steroids and triterpenoids with an IC_{50} value of 49.12 ppm ^[51]. Moreover, its limonoids extract provide very potent cytotoxic action against the colon cancer cell line HCT-116, with an IC_{50} value of 55.87 $\mu\text{g/mL}$. And the limonoids did not provide any toxicity to the experimental mice ^[52]. The anticancer activity of the ethanol extract of mahogany crude seeds had been evaluating against some selected human cell lines (HCT116, KB, Ca Ski and MCF-7) by using MTT method.

4 Antimicrobial Activity:

Synthetic antimicrobial drugs are uses for the treatment of infectious diseases and often it causes drug resistance and also causes severe adverse drug reaction like hypersensitivity, immunosuppression and allergic reactions. Herbal plants are the very effective alternative of the antimicrobial drugs.

It was found that the ethanolic, chloroform, aqueous and petroleum ether extracts of *S. macrophylla* leaves have antifungal activity against *Trichophyton mentogrophytes*, *Aspergillus niger*, *Candida* spp. and *Aspergillus favus* and also have antibacterial property against methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Bacillus subtilis* ^[53]. The antibacterial effect of the volatile oils extracted of *S. macrophylla* seeds has been obtained against *Salmonella typhimurium* ^[54]. Chiranjib *et al.*, (2011) was reported that the aqueous extracts of *S. mahagoni* leafs have antimicrobial activity

against pathogenic microorganisms and the methanolic extract was very effective against *K. pneumoniae*, *Aspergillus niger*, *B. subtilis*, *Candida albicans* and *E. coli*. The radial growth technique has been proved that ten limonoids from mahogany plant have antifungal attribute. Deacetoxy-7-oxogedunin at a concentration of 1500 mg/L inhibit the growth of *Botrytis cinerea* by 60.8% and in the same experiment, at 1000 mg/L concentration swietenine provide 57.5% and 3-O-acetylswietenolide at 1500 mg/L concentration provide 63.1% [56]. The conventional agar disc diffusion assay confirmed 2-Hydroxy-3-O-tigloylswietenolide and swietenolide acts against eight multiple-drug-resistant bacterial strains. 2-hydroxy-3-O-isobutyrylproceranolide and 2-hydroxyfissinolide are the limonoids that found in *S. mahagoni*, can exhibit action against *Micrococcus luteus* ATCC 9341 with the MIC values of 50 and 12.5 µg/mL respectively, this phenomenon was obtained from broth dilution technique where Ofloxacin used as a reference [57]. But there are 30 more limonoids from *S. mahagoni* which inactive in *in-vitro* antimicrobial study against 11 microorganisms (seven bacteria and four fungi).

5 Anti-Inflammatory Activity:

Anti-Inflammatory activity is a property of a chemical substance that able to reduce inflammation or swelling. Anti-Inflammatory agents also make up about half of analgesics.

It was proved by an experiment, that 3,6-O, O-diacetylswietenolide, swietemahonin E, 3-O-tigloylswietenolide, methyl 3β-tigloyloxy-2-hydroxy-8α, 30α-epoxy-1-oxomeliacate, 6-O-Acetyl-3'-demethylswietephragmin E, 6-O-acetylswietemahonin G and 3-O-tigloyl-6-O-acetylswietenolide have formyl-L-methionyl-L-leucyl-L-phenylalanine (fMLP)-induced superoxide anion generation inhibitory activity with 27.6 – 48.7 µM, IC₅₀ value. In this experiment ibuprofen had been using as reference and it was founded superoxide dismutase inhibit the reduction of ferricytochrome c. 6-O-acetylswietemahonin G was very effective against superoxide generation [58]. On the other hand, swietemacrophin and humilinolide F had been showing moderate activity with respectively 45.44 and 27.13 µg/mL, IC₅₀ values [59].

6 Anti-PAF Activity:

In *in-vitro* study of rabbit platelets Ekimoto *et al.*, (1991) has been founded swietemahonins A, D, E, and G, 3-O-acetylswietenolide and 6-O-acetylswietenolide, strongly inhibit PAF-induced aggregation. And in the same study it also reviewed that swietemahonin E reduced PAF-induced mortality in mice.

CONCLUSION:-

In *Swietenia's* Meliaceae family *Swietenia mahagoni* is one of the most potent phytomedicine that act as very effective antidiabetic agent which makes this herbal plant a best alternative of synthetic marketed antidiabetic medicine.

The methanolic/ethanolic/aqueous/petroleum/hexane extract of its seed/bark/leaves are able to treat hyperglycemia by restoring liver and β -cells islet function, blocking epinephrine function, reducing blood glucose level, inhibiting of α -amylase and β -glucosidase mechanism. This plant is a rich source of various vital phytochemicals like saponins, alkaloids, flavonoids (swietemacrophyllanin, catechin and epichatechin), tannins, triterpenoids, limonoids (swietemahonins, secmahoganin, swietmanins, swiemahogins, swietenolide, swietenine, 2-hydroxy-3-O-isobutyrylproceranolide, 2-hydroxyfissinolide, etc.) which not only deals with diabetes but also deals with so many diseases such as bacteria/fungus infection, hypertension, malaria, cancer, HIV, depression, etc. *S. mahagoni* is a very important plant in ayurvedic medicinal world. Based on the obtainable data, this paper has been summarizing various types of limonoids and their bioactive properties like antimicrobial, anti-inflammatory, antifeedant, hypoglycemic, antioxidative, insecticidal, anti-PAF, antihyperalgesic and antitumor. In spite of all this medicinal importances, *S. mahagoni* still mainly utilized as timber wood in various parts of the world.

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