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A Comprehensive Review on Medicinal Value and Pharmacological Profile of Simarouba Amara [Abul]

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Abstract

Simarouba amara is a tree species from the *Simaroubaceae family*, native to the rainforests, savannahs, and Caribbean regions of Central and South America. This study provides a comprehensive review of the medicinal and pharmacological profile of *S. amara.* The plant's leaves and bark have been traditionally used to treat various ailments, including malaria, diarrhea, and dysentery [1]. Phytochemical analysis reveals the presence of quassinoids, a class of triterpenes, which are responsible for the plant's therapeutic properties. Some of them are Ailanthinone, glaucarubinone, and holacanthone which are the principle biologically active phytochemical constituents present in *S. amara.* It possesses therapeutic qualities; Pharmacologically have been employed as an "anthelminthic, anticancer, anti-inflammatory, antiviral, anorectic, tonic, insecticide, antimalarial, antimicrobial, anti-amoebic, hepatoprotective, analgesic, antipyretic, antidiarrheal, anti-bacterial, gastroprotective, antileukemic, astringent, febrifuge and skin hydrator".

Keywords: *Simarouba amara*, Pharmacological activities, Phytochemical analysis, Medicinal value

1 Introduction

A type of tree found in the *Simaroubaceae* household, *Simarouba amara* is discovered in the savannahs additionally rainforests that of the Caribbean, Central and South America, as well as North America. One of the six species of *Simarouba*, it was initially characterized in French Guiana by Aubl. in 1775 [1]. *Simarouba amara* is a tree that grows in damp and rainy parts of the Amazon. The wood has both utilitarian and medicinal applications. Within Cuba, the bark and foliage are utilized as a potent digestive aid and to clear unwanted organisms. In Guatemala, it is a traditional treatment for various vector infections. As early as the 18th century, French explorers claimed that natives in Guyana utilized *Simarouba* bark to treat diarrhea [2].

1.1 Distribution

Simarouba amara is native to the tropical regions of Central and South America, including countries such as Brazil, Colombia, Costa Rica, Ecuador, French Guiana, Guyana, Panama, Peru, Suriname, Trinidad and Tobago, and Venezuela was shown in Fig. 1 [2].

Fig. 1: Geographic Distribution of *Simarouba amara*. The green shaded area represents the range of *S. amara*

Fig. 2: *S. amara* Plant Sections. A photograph of the whole *S. amara* plant, showcasing its various sections

The plant has also been introduced to other parts of the world, including the Caribbean, Africa, and Asia, where it has naturalized in some areas [3]. *S. amara* is commonly found in rainforests, savannahs, and along riverbanks, and is adapted to a variety of soil types and moisture levels [4].

1.2 Taxonomical Categories

Kingdom: Plantae

Group: Phytoplankton

Group: Angiosperms

Group: Eudicots

Group: Rosids

Order: Sapindales

Family: Simaroubaceae

Genus: Simarouba Aubl. 1775

Species: Simarouba amara (Abul)

Synonyms: *Quassia simarouba, Quasia simaruba, Zwigera amara, Quassia dioica O. Berg, Quassia officinalis Rich* [3].

Description & Habitat: *Simarouba amara* is a tree species that can grow up to 35 meters in height, with an estimated maximum age of 121 years. The trunk diameter can reach up to 125 cm. The leaves are complex, measuring up to 60 cm in length, with 4-5 cm long petioles and 9-16 leaflets per leaf. The leaflets are 12-45 mm wide and 2.5-11 cm long. The flowers are borne on a 30 cm long, heavily branched staminate panicle. The fruits are 17 mm long and range in color from bright green to dark purple-black and was presented in Fig. 2 [4].

2 Pharmacological Activities

Simarouba amara has demonstrated significant pharmacological activities, as highlighted in various studies. Its potential as an anti-inflammatory, antioxidant, and antidiarrheal agent underscores its value as a candidate for further research and development in the field of medicinal chemistry presented in Fig. 3.

Fig. 3: Therapeutics effects of *Simarouba amara* [Abul]

2.1 Anti-ameobic Activity

Simarouba amara has been traditionally used to treat amoebiasis, and its stem extracts have been shown to exhibit anti-ameobic activity against Entamoeba histolytica, with IC50 values ranging from 10-50 µg/mL [5]. The anti-ameobic activity of *S. amara* is attributed to the presence of quassinoids, which have been shown to inhibit the growth of E. histolytica trophozoites. The 50% inhibitory concentration (IC50) of metronidazole was 0.320 p.g ml^{-1}. The plant extract were prepared by using various solvents those are petroleum ether, methanol, aqueous, chloroform, butanol. *S. amara* stem petroleum and aqueous extract show little activity. Methanol has marked activity, chloroform and butanol extracts have effective activity [5].

2.2 Anti-bacterial Activity

The aqueous extract of *S. amara* bark has been shown to exhibit anti-bacterial activity against various bacterial strains, including *Escherichia coli, Staphylococcus aureus*, and *Pseudomonas aeruginosa*, with MIC values ranging from 100-500 µg/mL [6]. The anti-bacterial activity of *S. amara* is attributed to the presence of flavonoids, phenolic acids, and terpenoids. SAAE demonstrated its bactericidal properties by displaying an exact MBC/MIC ratio of "1." [6].

2.3 Anti-diarrheal Activity

Castor oil-induced diarrhea in mice: The aqueous extract of *S. amara* bark has been shown to exhibit anti-diarrheal activity in mice, reducing the frequency of diarrhea and increasing the latency period. The anti-diarrheal activity of *S. amara* is attributed to the presence of quassinoids, which have been shown to inhibit the release of prostaglandins and reduce intestinal motility. It was confirmed that SAAE exhibited efficacy dosages of 100, 200, and, and 300 mg/kg. Bark extract substantially ($p< 0.05$) decreased the amount of wet feces. Comparing extract from bark at 300 mg/kg to the reference medication loperamide (33.42%), the former 42.82% lessened the diarrhea caused by castor oil [6].

Gastrointestinal motility test: In this completed investigation, the effects of SAAE were substantially decreased in a dose-dependent manner on either charcoal meal movement or gastrointestinal motility ($p <0.05$). at 100, 200, 300 mg/kg b.w. 0.05). Bark extract has effectively inhibited the parasympathetic activity, hence reducing intestinal spasms and peristaltic movement with a 300 mg/kg dosage [6].

2.4 Anti-inflammatory Activity

SAAE on carrageenan induced peritonitis: Five groups of five mice each were created from the mice fasted overnight. Group 1 was given saline, 2nd group was given dexamethasone, and Groups 3, 4, 5 were given plant extract .After pre-treating the mice for one hour with SAAE, they received an intraperitoneal injection of carrageenan (0.25 mL; 1% carrageenan in 0.9% saline). SAAE's capacity to inhibit peritoneal cavity cell migration of PMNLs and nitrite effective in a way that is dose related. The data were displayed as One-way ANOVA and Mean ± SEM (n = 5) was used for analysis. *S. amara* is attributed to the presence of flavonoids, phenolic acids, and terpenoids, which have been shown to inhibit the production of pro-inflammatory cytokines and reduce oxidative stress [7].

2.5 Immunostimulatory Activity

SAAE on cyclophosphamide induced immuno-suppression: The aqueous extract of *S. amara* bark has been shown to exhibit immunostimulant activity, increasing the phagocytic activity of macrophages and enhancing the antibody titer in mice. Six groups of five mice each were formed after thirty mice had fasted for eighteen hours. For the first three days, group 1 was given saline (1 mL/100 g) 2, 3 ,4 ,5 & 6 groups were given cyclophosphamide. The immunosuppressed groups (3-4) were administered levamisole (50 milligram per kilogram) as a positive control, and SAAE (100, 200 & 300 mg/kg body weight, PO/day) to 4,5&6 correspondingly. The dosing was done from day four to day 15. On the sixteenth day, blood samples were collected and

examined. The immunostimulant activity of *S. amara* is attributed to the presence of quassinoids, which have been shown to stimulate the production of cytokines and activate immune cells [7].

2.6 Phagocytic Activity

SAAE of phagocytic activity (Carbon clearance test): The test were carried out using a modified version of the procedure. Group II was dosed with levamisole (50 milligram per kilogram), the positive control, whereas saline was given to group 1 (1 mL/100g body weight). SAAE 100, 200, and 300 milligram per kilogram body weight per os for III, IV, and V, sections respectively. On that 9th day, blood was promptly drawn from groups of all animals subsequently, an intravenous (tail vein) injection. The experiment was 3% gelatin (4 ml), saline (4 ml), and ink (3 ml) was administered. The phagocytic activity of *S. amara* is attributed to the presence of quassinoids, which have been shown to stimulate the production of cytokines and activate immune cells [7].

2.7 T-Cell Population

SAAE on T-cell population [erythrocyte rosette assay]: Group 1 was given saline (1mL/100g body weight per os) whereas class 2 supplied levamisole (50 milligram per kilogram per day) as a positive control. SAAE (100, 200, and 300 milligram per kilogram.) was given to 3, 4 & 5 classes. On eleventh day, the mice in each group had their plasma separated. Mixture of 0.5% SRBC and 0.25 mL of plasma was equal, and it was incubated for 5 minutes at 37°C. After centrifuging the mixed mixture for five minutes at 1000 rpm, the supernatant was chilled for two hours at 4°C. The aqueous extract of *S. amara* bark has been shown to enhance the T-cell population in mice, suggesting its potential as an immunoadjuvant [7].

2.8 Antibody Titer

SAAE on humoral immune response (antibody titer): The 14-day study period involved dosing the animals. Group I was given saline (1mL/100g), whereas Group Ⅱ has given levamisole (50mg/kilogram) as a positive control. The SAAE doses for Groups III, IV, and V are 100, 200, and 300 mg/kg b.w., p.o. On day seven, mice had given an injection of 0.1 mL of SRBC (1×108). Following day 14, serum was isolated and utilized for antibody titration. In a dose-dependent way, SAAE raises the immunoglobulins and antibody titer against sheep red blood cells (SRBC). The antibody titer enhancement activity of *S. amara* is attributed to the presence of quassinoids [7].

2.9 Delayed Hypersensitivity

SAAE on delayed hypersensitivity test: Seven days were spent studying the experiment. Group II was dosed with levamisole (50 mg/kg), the control that is positive, whereas SG I was given salt (1 ml/100grams). SAAE was given to classes Ⅲ, Ⅳ, Ⅴ (100, 200, and 300 mg/kg).One day zero, animals received an injection of a volume of 0.1 ml of SRBc with 1×108 cells intraperitoneally. On 7th, day they were given a challenge of 0.05 mL. On the right hind paw, 2 x 108 SRBC. Opposing side paw, meantime, was given the same amount of salted water. SAAE's impact on delayed type hypersensitivity (DTH). SAAE causes delayed hypersensitivity to rise by stimulating TH cells [7].

2.10 Human Skin Keratinization

Effects of *Simarouba amara's* aqueous extract on Human keratinocyte development were investigated. Compared to untreated controls, keratinocyte cultures that were submerged . The lipid analysis of cultures exposed to air showed elevated levels of ceramide, cholesterol, and cholesterol sulphate. The examination of capacitance and transepidermal water loss on the hemiface of volunteers during a 4-week treatment period indicated that this extract may be useful for enhancing skin hydration. When combined, these findings showed that human keratinocyte development is enhanced by an aqueous extract of *S. amara* [8].

2.11 Anti-tumor Activity

Glyphosate-induced Toxicity: As a negative control, two planarians were placed in each of 3 petri plates along using spring water. The amount of 2% *S. amara* solution in 10 milliliters were added to three petri dishes, along with two planarians each dish for control. The two planarians and the 50 ppm glyphosate solution per petri dish were then added for carcinogen exposure, totaling 14 petri plates. As a therapy, 10 milliliter of a 2 percent *S. amara* solution was included in remaining seven petri dishes. For eight days following glyphosate exposure, we tracked the worms exposed to glyphosate in the *amara* extract and their survival rate. After 8 days, the worms exposed to glyphosate and their survival rate treated with *Simarouba amara* was 80%, which was considerably greater than the glyphosate-exposed worms treated with spring water, which had a survival rate of 0% [9].

2.12 Anti-oxidant Property

The oscillating Briggs-Rauscher reaction was utilized to look into the antioxidant actions of the *S.*

amara solution, 1 milliliter starch solution, 2 milliliters of purified water, 10 milliliters of 3% hydrogen peroxide (Walgreens), 10 milliliters of $CH_2[COOH]_2$ (0.3 M), and ten milliliters of acidic NaIO3 (0.2 M) were combined in a beaker. Three iterations of this procedure were carried out, along with an experiment in which the *S. amara* extract was replaced with one milliliter of purified H2O. Given that 2% it is known that green tea extract has antioxidant properties, twelve drops of the extract were utilized as a positive control. The aqueous extract of *S. amara* bark has been shown to exhibit anti-oxidant activity, scavenging free radicals and reducing oxidative stress. The anti-oxidant activity of *S. amara* is attributed to the presence of flavonoids, phenolic acids, and terpenoids [9].

2.13 Anti-malarial and Mosquitocidal

For a whole day, pupae or larvae of 25 *A. stephensi* were inoculated with the appropriate 500, 400, 300, 200, or 100 ppm of *S. amara* oil concentration within a beaker. Every measured focus was given 0.5 mg of larval diet. Five tests were conducted on each concentration across all instars *S. amara* oil's LC_{50} against *A. stephensi* larvae and pupae in a mosquitocidal bioassay was 230.126 parts per million for larvae 1, 267.032 ppm for larvae 2, 301.825 ppm for larva 3, 356.880 ppm for larva 4, and 435.900 ppm for larva. The LC_{50} values for *A. stephensi's* 50% adult mortality in adulticidal assays were 332.375 ppm. Our research overall indicated that *S. amara* oil would be a good option for creating bioformulated insecticides that are effective against *A. stephensi*, the malarial vector [10, 13].

2.14 Hepatoprotective Activity

This study's goal is to investigate the hepato-protective effects of stem bark extract from *S. amara* on CCl4-induced liver injury on rats. Using high performance liquid chromatography, SAAE was assessed. Six groups each group consists of six animals were created from the animals. Teams One vehicle was given corn oil, two controls were given CCl4, 3, 4, 5, and 6 were pretreated for ten days straight with Legalon® 50 mg/kg . and SAAE at dosages of 100, 250, and 500 milligram per kilogram. On the eleventh day, 2 milliliter per kilogram of a 20% carbon tetra chloride solution was used to cause hepatotoxicity. At all doses, the SAAE decreased the concentrations of lipid peroxidation & liver indicators. As a result, SAAE enhanced the liver's capacity for regeneration and repair while also preventing oxidative damage [11].

2.15 Acute and Subacute toxicity

This study assessed the acute and sub acute toxicities of stem bark extract (SAAE) from *S. amara* in rats and mice, correspondingly. One oral dosage of 2.0 grams per kilogram of plant extract was administered (n = 5/group/sex) for the acute toxicity test, and for the sub acute, doses of 0.5, 1.0, and 0.25 g/kg/day (n = 12/group/sex, according to os.) were employed for thirty days in a row. Plant extract wasn't result in death or clinically evident toxicity during the acute toxicity. In conclusion, the greatest dose of SAAE administered sub acutely raises the possibility of long-term harm [12].

3 Green Synthesis of Silver Nano-Particles

30g of raw, unripe fruit are ground up and screened through First-rate Whatman filter paper in 100ml that of Millipore distilled water. A 250 ml beaker wrapped with aluminum foil containing 1 mM of 100 ml silver nitrate solution was maintained in a magnetic stirrer. 10 ml drop by drop of fruit extract was added to the $AgNo_3$ solution. while being vigorously stirred. The extract was added dropwise to the $AgNO_3$ solution while being vigorously stirred. Upon four hours of nonstop stirring, the color shifted from pale yellow to dark brown. ώ max was recorded and the creation of AgNPs was confirmed by 350–700 nm UV/visible spectra [14].

4 Phytochemical Analysis

For thousands of years, people have used medicinal plants as a source of medication. The seed oil of *Simarouba amara* has been found to contain triterpenoids, alkaloids, flavonoids, phenols, tannins, and steroids, among other biologically active ingredients [10]. Several compounds, including coumarins, anthraquinones, flavonoids, triterpenes, alkaloids, steroids, and other metabolites, have been isolated from *S. amara,* and their structures have been elucidated [16]. Querulosides such as $C_{25}H_{34}0_{10}$, $C_{22}H_{28}0_9$, and 13-Dehydrochaparrinone, are present in *S. amara* and are believed to be responsible for the plant's medicinal properties. These compounds have been shown to exhibit antimalarial, antiprotozoal, anti-ameobic, and even lethal effects against cancerous and leukemic cells [16].

Six novel triterpenes were isolated from *Simarouba amara* bark collected in Barbados using a chemical analysis, and two previously identified substances, $C_{30}H_{48}O_3$ and 23-Hydroxy-5α-tirucalla-7. Compounds 4 through 7 are derivatives of

apotirucallanes with ring A contains an ε-lactone, while compound 3 is a tirucallane triterpene. Compound 8 is a derivative of octanorapotirucallane without the C8 side chain, whereas compounds 6 and 7 were obtained as an inseparable combination. [17].

Table 1: Pharmacological activities of *Simarouba amara* [Abul.]

Sl. No	Extract type	Parts used	Pharmacological activities	References
1	Aqueous	Stem	Antiameobic activity	5
2	Aqueous	Bark	Antibacterial activity	6
3	Aqueous	Bark	Antidiarrheal activity	6
4	Aqueous	Bark	Antiinflammatory activity	7
5	Aqueous	Bark	Immunostimulant activity	7
6	Aqueous	Bark	Phagocytic activity	7
7	Aqueous	Bark	T-Cell population	7
8	Aqueous	Bark	Antibody titer	7
9	Aqueous	Bark	Delayed Hypersensitivity	7
10	Aqueous	Bark	Human skin keratinisation	8
11	Aqueous	Bark	Anti Tumour activity	9
12	Aqueous	Bark	Antioxidant activity	9
13	Aqueous	Seeds	Antimalarial & Mosquitocidal	10
14	Aqueous	Stem Bark	Hepatoprotective activity	11
15	Aqueous	Bark	Treat Acute & sub acute toxicity	12

C, H, O, and triterpene 2. With its OH-band depletion, its infrared spectrum (CHClr) displays wavelengths of 1710 and 1730 cm^{-1}. The proton's RMN spectrum consists of two resonances and the following structural elements: the isopropylidène group = CMe, the methyl group = cmq, the -CH-CHO group, and two final X-type rotons 016 = CH-CI+. These olefinic protons' dp and positions as well as the attraction of their signals are consistent with their location in C-24 and C-7. The two double liaisons found in Compound 2 are essentially equivalent to those seen in C&O-3, A' triterpenoides [18]. The conclusions of the mass spectrometry reveal the composition of the lateral chain and, in particular, the localization of the aldehyde function at C-20. [18]. Utilizing a gradient elution and phenyl column, a practical and trustworthy high performance liquid chromatography using a reversed phase approach was created for the identification of eight significant Quassinoids, such as $C_{20}H_{26}O_8$, paraine, Simalikahemiacetal A, Nigakilactone D, holacanthone [$C_{22}H_{28}O_9$], $C_{25}H_{34}O_{10}$, and 15-SENECIOYL-CHEMBL557693. For these chemicals, the technique produced well-resolved peaks with good linearity and responsiveness in the 25–1000 nano gram range [19].

Table 2: Phytochemical constituents of *Simarouba amara* [Abul.]

Sl. no	Chemical constituents of *Simarouba amara*	Type
1	C25H34010	Querulosides
2	C22H2809	Querulosides
3	13-Dehydrochaparrinone	Querulosides
4	C30H48O3	Triterpenes
5	23-Hydroxy-5α-tirucalla-7	Triterpenes
6	ε-lactone	Triterpenes
7	C20H26O8	Triterpenes
8	Paraine, Simalikahemiacetal A	Quassinoids
9	Nigakilactone D	Quassinoids
10	Holacanthone [C22H28O9]	Quassinoids
11	15-SENECIOYL-CHEMBL557693	Quassinoids

4.1 Gas chromatography - mass spectrometry analysis

The GC-MS analysis of *S. amara* Oil from seeds was conducted utilizing the Clarus 680 system from Perkin-Elmer. Pure helium gas served as the carrier gas, flowing continuously at a rate of one milliliter per minute. For GC-MS spectrum detection, a high energy of 70 eV of ionization, a 0.2 sec scan period, and pieces having a mass to charge ratio between 40 and 600 were employed in the electron ionization energy method. One liter of injection was used, along with the injector's heat was maintained at 250° centigrade. Temperature of the oven in columns was adjusted to 50 °C in light of three min, reached 280 °C after rising at a pace of 10 °C per minute. After that, it has risen to 300° centigrade for ten min. By contrasting the mass, peak height, peak area, and retention time (min) comparing the test materials' spectral patterns to those in the spectrum database.

Results: Seven peaks were visible in the *S. amara* oil GC-MS chromatogram, which was recognized as the bioactive compounds through comparison of their mass spectrum fragmentation patterns. The results of the *S. amara* oil showed 7 compounds. Similarly, this product contains 33.55% palmitic acid, 100% linoleic acid, 21.72% caffeine, and 14.49% vitamin E, 21.96% stearic acid. *C. sinensis* seed oil according to GC-MS analysis. Pharmacokinetic testing

revealed higher plasma concentrations in every member of the fasted group [10].

5 Conclusion

Since manufactured medicine has harmful side effects, natural products of therapeutic ingredients have been more popular and useful in developing nations throughout the past ten years. Research and study on medicinal plants may yield numerous practical solutions for the treatment and alleviation of human suffering. The extract from *Simarouba amara*'s bark and leaves is well known for its several therapeutic uses, which include treating both infectious and non-infectious illnesses like malaria, diarrhea, fever, and intestinal parasites. Potential antimicrobial, antibacterial, antioxidant, anti-malarial, antimicrobial, anti-amoebic, hepatoprotective, anti-inflammatory, analgesic, and anti-cancer effects are displayed by the leaf extract of this medicinal plant. Future researchers may find it useful to conduct additional research on this plant in order to create some innovative and promising medicinal formulations.

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