Plant Archives Volume 21, No 1, 2021 pp. 648-655 *e-ISSN:2581-6063 (online), ISSN:0972-5210*

Plant Archives
Journal home page: www.plantarchives.org
DOI Url: https://doi.org/10.51470/PLANTARCHIVES.2021.v21.no1.090

PHARMACOLOGICAL USES OF *SIMAROUBA GLAUCA*: A REVIEW

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(Date of Receiving-13-11-2020; Date of Acceptance-13-02-2021)

ABSTRACT

Simarouba glauca is an evergreen floral tree plant that is endemic to Florida, Lesser Antilles, South America, and the United States. Bitterwood, dysentery barks, Laxmi Taru, and Paradise tree are common names. It produces edible oils from its seeds. Various tree sections are used to treat different ailments. The plant contains many essential phyto constituents of major pharmacological significance. The pharmacological review of SG has proven its medicinal value and has different therapeutic qualities such as analgesic, antimalarial, antimicrobial, antitumor, antiulcer, hypoglycaemic, insecticidal, stomachic, and vermifuge. Several medically active compounds have been found in the plant. A group of triterpenes called Quassinoids is by far the most active compound. Further research into these plants can be concluded that these new pharmacophores can be beneficial for the improvement of mankind's health and also helps in combating several other disorders. The purpose of this paper is to showcase the pharmacological importance of *Simarouba glauca* and it can provide a good forum for future researchers to carry out numerous studies on this particular plant species.

Keywords: Laxmitaru, Edible oil, Medicinal value, Antitumor, Quassinoids

INTRODUCTION

Since human life started, man has understood and applied plants in a wide range of forms over the ages (Shakya, 2016). Plants are quite excellent models of diverse bioactive substances used specifically or indirectly to manage a variety of human diseases. Human cultures have explored and utilized complex plants and medicinal ingredients in the treatment of fatal diseases since time immemorial (Kuldip *et al*., 2015). Humans relied on the soothing powers of plant species before adding chemical substances. Many people respect these plants because of the old belief that plants are designed to provide nutrition, medicinal care, and other benefits for mankind(Ahvazi *et al*., 2012). Herbal medicines are classified as indigenous health-care medicine that identifies, inhibits, and manages mental and physical conditions differently from allopathic theories, views, and concepts (Jima & Megersa, 2018)2015, in Berbere district of Oromia region, Ethiopia. The study focused on documentation of medicinal plants used to treat various human diseases in the study area. Ethnobotanical data were collected using semistructured interviews, group discussion, guided field walks, and observations with participants. Preference ranking, paired comparison, direct matrix ranking, and informant consensus factors (ICF. Owing to the broader faith in fewer harmful effects and the simpler access to medicinal plants, the use of plants to cure any illness has grown exponentially over the past few decades (Singh *et al*., 2020). The earliest records on tile tablets in cuneiform dated from about 2600 BC come from Mesopotamia; Cedar, Cypress, Liquorice, Myrrh, and Poppy oils, are being used currently for the prevention of illness from colds, poisons, infections of parasites, and inflammation (Dar *et al.,* 2017). The WHO says the best supply of several medicines will be medicinal plants. Herbal substances have contributed significantly to public health. This is because traditional remedies have tremendous curing power (Obeidat *et al*., 2012). Medicinal plants in India are used extensively by all groups of the population as folk remedies or in various indigenous medical systems or indirectly in modern medicinal products' pharmaceutical preparations(Srinivasan *et al*., 2001).

Phytoconstituents are chemical compounds that are found in plants inherently. Phytochemicals have recently become more common because of their various therapeutic applications. Unlike synthetic chemicals, these phytochemicals have no adverse effects and are important against a variety of respiratory disorders, arthritis, tumor, and other diseases. Phytochemicals come from various plant sections including leaves, buds, stems, pulp, seeds, and so on (Priya, 2017). More than 170 species of 32 genera pantropical trees and brooks belong to the Simaroubaceae family. Its quality is distinguished by bitter substances which are mainly accountable for its medicinal properties (Fernando & Quinn, 1992; Muhammad *et al*., 2004) namely, orinocinolide (1. *Simarouba glauca* (SG) is an evergreen, multifunctional edible oil reservoir, commonly popular as Shorgum Maram, Simaba, Robleceillo ,Pitomba,Palo Amargo,Dysentery bark, Bitterwood, and Aceituno. In India, SGis famous as Paradise tree, Shorgum Maram, or Laxmitaru which belongs to the Simaroubaceae family (Manasa *et al*., 2019). This plant is renowned for its pharmacological and therapeutic properties of various kinds. SG's pharmacological qualities are anticancerous, anti-dysenteric, antihelminthic, antimalarial, antimicrobial, antiparasitic, antipyretic, and hemostatic (Pawar *et al.*, 2019).SG leaves, seeds, pulp, and fruit are considered to be emmenagogue, antiviral, astringent, antimicrobial, vermifuge, and stomachic (CK *et al.,* 2018). SG extracts were used to treat gastrointestinal disturbances in Guatemala(Caceres *et al.*, 1990). The bark, leaf, leaf litter, pulp of fruits, roots, seed, shell, stem, and unwanted branches of plants generate food, fuel, fertilizer, wood, and medicines (Santhosh *et al.*, 2016) useful goods. Studies suggested that the SG water extract promotes the division of skin keratinocytes and increases skin moisture and hydration. SG products in the form of skin lotion and dry leaf powders are currently being sold for treating skin disorders (Jose *et al.,* 2019).

Plant Profile

Common name: Aceituno, Paradise tree, Simaba, and Bitter wood tree.

Malayalam: Lakshmi tharu
Tamil: Shorgum Maram
Hindi: Laxmitaru
Kingdom: Plantae
Order: Sapindales
Family: Simaroubaceae
Genus: Simarouba
Species: *Simarouba glauca*

Figure 1: Represents the leaves of *Simarouba glauca*

Distribution

It grows from Mexico to Panama, South Florida, and the Caribbean Islands under tropical conditions in Central America. In both Kenya and Burundi, SG was introduced in 1957 (Patil & Gaikwad, 2011). SG, in Mexico, Cuba, Haiti, and Central America, is native to the rainforest and other tropical regions. In some parts of India, SG is cultivated. In the 1960s, it was introduced in India by Genetic Resources in the Amravati research station in Maharashtra and 1986 (Vasait & Khandare, 2017). In the wastelands of Orissa, Karnataka, and Gujarat, healthy plant growth is observed in India. Also, Andhra Pradesh, Bihar, Maharashtra, and Tamil Nadu have effectively improved their growth rate (Ramya *et al.*, 2019). In tropical America, the largest source of family diversity and in Western Africa as a secondary centre (Thomas, 1990). Now the SG culture extends over semiarid dry and salty regions of other Indian regions such as Tamil Nadu, Maharashtra, Karnataka, Gujarat, and Andhra Pradesh. Even in marginal wastelands or dry soil with degraded soil, SG trees can grow well (Govindaraju *et al.*, 2009).

Physical Characteristics

It is an evergreen tree of medium height (7-15 m). It has been formed in areas with an annual rainfall of 250 mm to 2500 mm and temperatures as high as 45℃, and grows well up to 1000 m above sea level in all kinds of well-drained soils since it is dry and semiarid, it can be widely cultivated where no other economically-efficient plants can be cultivated. During December, the tree begins to bloom and bears fruit in January and February. In May, the fruit is ready for selection(Dash *et al.*, 2008)namely, dimensions, 1000 unit mass, fruit part fraction, arithmetic mean diameter, geometric mean diameter, surface area, sphericity, aspect ratio, bulk density, true density, porosity and angle of repose. The kernel had 8.51% (w.b..It's a medium plant, normally reaching about 20 meters high and about 50-80 cm in diameter, and about seven years in life. The soil was ideal for the temperature range of 10 – 40 °C, and soil pH was predicted to be 5.5 – 8. Under a large variety of agro climate conditions including mild humid and tropical areas (Mishra *et al.,* 2012). The root system for mountainous soil is weak. The stem has a height of 9 m and a diameter of 40-50 cm. It has a thin, gray outer bark while the inner bark is creamy (Thomas, 1990). The leaves are oblong and sometimes notched or smooth with 3-21 leaflets; alternate, uniform blue, green oily. Bisexual flowers are inconspicuous, the green calyx is colored, and the dome shapes differ with sepals. Single-whorl creamy greenish or yellowish creamy petals are available. The staminated flowers have gynophores, but no single ovule

Figure 1: Represents the *Simarouba glauca* tree

carpel (Patil & Gaikwad, 2011). Since maturing, the seeds are 1.5 to 2 cm long pinkish or yellowish. There are two varieties: one produces a greenish fruit and the

PHYTOCHEMICAL	TEST	RESULT	INFERENCE
Alkaloids	Mayer's test	Pale creamy precipitate	Positive
Carbohydrates	Molish test	Reddish-violet ring	Positive
Cardiac glycosides	Keller -Kiliani test	No greenish-blue color	Negative
Flavanoids	Shinoda test	Reddish-brown color	Positive
Phenols	$FeCl^2$ test	No dark green/blue color	Negative
Saponins	Frothing test	No stable froth	Negative
Tannin	$FeCl_2$ test	No bluish-green or blue-black color	Negative
Triterpenoids	Salkowski test	Reddish-brown color	Positive

Table 1: Qualitative phytochemical analysis of *Simarouba glauca* (Dinesh *et al.,* 2017)

other distinct violet or almost black fruit depending on fruit colour (Osagie-Eweka, 2018). Figure 1 represents the leaves of SG while figure2 represents the plant itself.

Chemical Constituents

Mostly, alkaloids with elevated cytotoxicity and quassinoids with influential antifungal properties were extracted from these plants with a variety of constituents. Triterpenes, useful in the cure of amoebiasis, diarrhea, and malaria, are in the SG bark and leaves. Quassinoids have demonstrated positive anti-tumor activities, the bitter values of the plant family of Simaroubaceae (Mathew *et al*., 2019). SG has the active ingredients in the plant and 11 therapeutically essential quassinoids. The presences of alkaloids, cardenolides, flavonoids, fixed oil, glycosides, phenolic compounds, saponins are noted by SG extract. Tirucalla, sitosterol, simarubolide, simarolide, simaroubidine, melianone, holacanthone, glaucarubolone, glaucarubinone, dehydroglau-carubinone, canthin, benzoquinone, and ailanthinone are major active components in the SG (Jach *et al*., 2000). Normal SG qualitative studies have had positive effects on alkaloids, carbohydrates, flavonoids, and triterpenoids (Table 1) (Dinesh *et al*., 2017).

Nutritive value

SG is a good source of carbohydrates, fatty acids, lipids, and proteins. The kernels have edible fat made of oleic, palmitic, and stearic acids while the seeds contain oil. The kernel is rich in essential amino acids, namely leucine, lysine, and valine. Additionally, the average protein content is 51.8g/100g. Alkaloids, calcium, sodium, triterpenoid aglycone, phenolics, phytic acids, and saponins are present in the food supply. The leaves contain flavonoids, phenolics,and tannins that help to battle conditions like cancer, diabetes, and other diseases (Jose *et al*., 2019)

Pharmacological Uses

Antiamoebic Activity

In in vitro tests, the presence of crystalline glycosides isolated from the SG indicated that the SG was active against Entamoeba histolytica and had an in-vitro amoebicidal character (VAN ASSENDELFT *et al.*, 1956). The in vitro approach and laboratory animals showed that glaucarubin has an amoebicidal characteristic(Del Pozo, 1956).

Antibacterial Activity:

Extract of SG leaves has possible antibacterial properties, both Gram-positive and Gram-negative. Micro-organisms such as Bacillus subtilis (BS), Escherichia coli (EC), Pseudomonas aeruginosa (PA), and Staphylococcus Aureus (SA) are inhibited by fresh and dried extract SG leaves(Rajurkar, 2011)*Simarouba Glauca* and Psoralea corylifolia (Babchi. Soxhlet instruments were earlier used to record the ethanol and the methanol extracts of dried and fresh SG leaves. Extracts of SG were shown averagely successful in inhibiting BS, EC, PA, and SA(Jangale *et al*., 2012).Ganesh et al showed that the crude methanol and ethanol extracts made from dried and fresh SG leaves have inhibited BS, SA, PA, and EC progress (Hussain *et al.,* 2020). Many studies have documented the antimicrobial activity of many plants. Studies of Laxmi Taru's antimicrobial activity therefore was restricted to antimicrobial activities of few bacterias (Karthikeyan *et al*., 2019).

Anticancer Activity

There is a notable anticancer activity in several species within the family of the Simaroubaceae. SG contains compounds with properties that suppress tumors. The herb's antileukemic and antitumor role has been linked to four Quassinoids namely Ailanthinone, Glaucarubinone, Dehydroglaucarubinone, and Holacanthone (Jach *et al*., 2000). In vitro cytotoxicity has been shown against KB cells, such as glaucarubin, glaucarubinone, glaucarubol, and glaucarubolone by several components in Quassinoids SG seeds (Polonsky *et al*., 1978). Quassinoids SG seed constituents Bruceantin, bruceantinol, glacarubinone and simalikalctone D are among the strongest Quassinoids with this form of antitumor action (Guo *et al*., 2005).

COMMON NAME	USES	PATENT NUMBER	REFERENCES
GLAUCARUBINONE	Inflammatory Ailments Psoriasis Microbicidal and antiparasitic Skin Condition Antineoplastic, antiviral and Herbistatic activity Cancer	US2016051553 US9095606 US8865235 US8734859 US2014205685 US2003158088 US6573296 US8734859 US6573296 WO8807372	(Valeriote *et al*., 1998)
GLAUCARUBOLONE	Antineoplastic, antiviral, and herbistatic activity	US6573296	Dou *et al*., 1996)
CANTHIN-6-ONE	Inflammatory Ailments Psoriasis Mycobacteria-linked pathologies Trypanosomiases Extensive Cancer	US2016051553 US9095606 US2011059977 US7705013 US7705013	(Reynertson *et al*., 2011)
FRAXIDIN	Antileishmaniasis Treating pathologies Anti-infective activity Urinary tract infections	US2014287030 US2002002139 US2014287030 US2002002139	(Fausto Rivero-Cruz *et al*., 2005)
SCOPOLETIN	Balloon surface coating Promoter control elements Carrying therapeutic substances into cells Tissue-specific reduction of lignin Nanoparticle formulations for delivering Multiple therapeutic agents Treatment of tobacco material Psychotic disorders Balloon surface coating for valvuloplasty Analgesic	US2016082159 US2016076046 US2016067338 US2016017355 US2015342896 US2015296870 US2015299227 US2015231362 US2014349969	(Fausto Rivero-Cruz *et al*., 2005)
TRIOLEIN	Post-operative chronic pain Diabetes mellitus Raynaud's disease Myelination diseases X-linked adrenoleukodystrophy Acute pancreatitis Lysosomal acid lipase deficiency	US2016089335 US2016089409 US2016081954 US2016081955 US2016074369 US2016051637 US2016051638	(Fausto Rivero-Cruz *et al*., 2005)
TRILINOLEIN	Myocardial infarction Vestibular schwannoma Cardio protection and cardio regeneration Immunomodulatory agent	US2016038147 US2015359851 US2015343023 US2015216955	(Fausto Rivero-Cruz *et al*., 2005)

Table 2: Phytochemicals isolated and patented from *Simarouba glauca*

Antifungal Activity

Antifungal properties of SG against several fungus. However, extracts from this plant were considered more productive compared to *Fusarium oxysporum* against *Aspergillus parasiticus*. Ethanolic extracts from fresh leaves are found to be more effective against the growth of fungi through the agar well diffusion process compared to the methanol extracts from fresh leaves (Mikawlrawng *et al.*, 2014).

Antimalarial Activity

Studies have shown that three potent Quassinoids in SG are in vitro as well as *in vivo* active against malaria. Some Quassinoids in SG have demonstrated strong inhibitory action of a Plasmodium falciparum strain which is resistant to chloroquine (Valdés *et al.*, 2008). 6α-tigloyloxychaparrinone,ailanthone, eurycomanone, isobrucein B,orinocinolid, neosergeolide, pasakbumin B and C, and simalikalactone D have been identified to be major antimalarial production Quassinoids (Chan *et al.*, 2004; Houël *et al.*, 2009; Kuo *et al.*, 2004; Muhammad *et al.*, 2004; Okunade *et al.,* 2003; Rocha E Silva *et al.*, 2011)

Antioxidant Activity

SG leaves are having antioxidant characteristics (Santhana Lakshmi *et al.*, 2014). Extract of SG leaves has been identified to have an association with antioxidants. SG chloroform extract was capable of concentration all scavenging H_2O_2. In scavenging free radicals, including DPPH and chelating radical iron, extracts were highly effective. The extracts have also shown possible antioxidant characteristics (Umesh, 2015).

Reducing Patchy Skin Pigmentation

SG extract showed ingredients capable of reducing patchy skin pigmentation (US Patent dated 14 October 1997), with its water extract found to improve skin differentiation and to enhance moisture and hydration (Jach *et al*., 2000).

Antiulcer Activity

The chloroform extract of SG showed dose-dependent inhibition of ethanol-induced gastric lesions in albino rats, causing 82.63% protection at 400 mg/kg, and 53.48 % protection at 200 mg/kg, Chloroform extract of SG also showed dose-dependent inhibition of indomethacin-induced gastric lesions in albino rats, causing 62.65 % protection at 400 mg/kg and 54.86 % protection at 200 mg/kg, Chloroform Extract of the leaves of SG decreased the acidity and increased the mucosal secretions, thus SG exhibiting antiulcer activity (D. S. Sharma & Sriram, 2014).

Hepatoprotective Activity

SG has hepatoprotective action in chloroform and ethanol extracts. Some research suggests that the leaf extract of SG can be applied to produce a new hepatoprotective remedy *(John et al*., 2016).

Others

SG leaves and bark have long acted in tropical areas as a natural remedy. SG bark for successful malaria and dysentery treatment (Mikawlrawng *et al.,* 2014; Polonsky *et al.,* 1978). Another South indigenous tribe uses bark as a hemostatic agent to avoid bleeding, and as a tonic to deal with fever, dysentery, and malaria. Externally, it is used for wounds and cuts (Valdés *et al.,* 2008). The bark is boiled in water and is occasionally used to give a strong astringent and tonic to cleanse your skin and cure dysentery, diarrhoea, bowel, blood bleeding, and internal bleeding (R. Sharma & Dwivedi, 2016). SG is a multipurpose powerful and versatile, dioecious oil crops plant with a production capacity of 2000-2500 kg of oil/ha/year, apart from being medicinal. A kernel of SG produces about 75 percent of oil and has an excess of both unprocessed and saturated fats that are sufficient for domestic as well as industrial consumption (Choudhary *et al*., 2020). SG seeds are rich in edible fat (almost 60% w/w) used in tropical countries for cooking. The cake from the oil extraction contains proteins that are used in cattle feed after poisonous and bitter compounds have been extracted (Monseur & Motte, 1983). Oleic acid, a powerful and versatile unsaturated fatty acid, used for the manufacture of soaps, detergents, and lubricants, etc is found in SG seed oil for 59-65 percent (Jayashanthini. S, K. S. Rathinam *et al.,* 2019). Given the reporting of the acute cytotoxicity, phytotoxicity, and efforts to large-scale SG propagation of the *Simarouba quassinoids* as an alternative oilseed crop, it is also warranted that the oil is routinely tested for human consumption (Rout *et al.,* 2014). Table 2 includes the list of compounds of SG that are patented for the different-different conditions.

CONCLUSION

In the ethno pharmaceutical region, the Simaroubaceae family is of great significance because many of its members are commonly used in the tradition of folk medicine of several nations and form part of the authorized compendium. In addition to its insecticide, curing, and tonic operations, various genera of this family are used for managing diabetes, diarrhoea, gastritis, inflammation, malaria, tumors, ulcer, viruses, and worms. Ethnobotanical studies have played an important role in the prevention and treatment of disease in living organisms in recent years and various known and unknown herbal medicinal products have been developed. Plants of the Simaroubaceae family can be emphasized for their chemical richness in addition to ethnopharmacological uses as the existence of alkaloids, anthraquinones, coumarins, flavonoids, mono- and sesquiterpenes, Quassinoids, steroids, and terpeneshas been determined. The pharmacological review of SG has proven its medicinal value and has different therapeutic qualities such asanalgesic, antimalarial, antimicrobial, antitumor, antiulcer, hypoglycaemic, insecticidal, stomachic, and vermifuge. Further studies into these species can be inferred that certain new pharmacophores can be useful for the betterment of human health and also to cure many other diseases.

CONFLICTS OF INTERESTS

The author(s) declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

FUNDING

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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