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CURRENT REVIEW ON BIOTECHNOLOGICAL AND PHARMACOLOGICAL INVESTIGATIONS OF *SIMAROUBA GLAUCA*-AN OIL YIELDING PLANT

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ABSTRACT: *Simarouba glauca* is one of the important herbal drugs used against dysentery and has a long history in herbal medicine in many countries. The bark and leaf extract of *Simarouba* is well known for its different types of pharmacological properties such as hemostatic, antihelminthic, antiparasitic, antidysenteric, antipyretic and anti-cancerous. The bark is used to cure fever, malaria, stomach and bowel disorders, haemorrhages, amoebiasis as well as leaf, fruit pulp and seeds are possessing medicinal properties such as analgesic, antimicrobial, antiviral, astringent emmenagogue, stomachic tonic, and vermifuge. The crushed seeds are used as Antigo against snake bites. The crude drug contents and active principles such as glaucarubin, quassinoids, ailanthinone, benzoquinone, holacanthone, melamine, simaroubidin, simarolide, simarubin, simarubolide, sitosterol. These are mainly involved in the pharmacological activities of this plant. The present review summarizes pharmacological, biotechnological, ethnobotanical phytochemical aspects as well as nursery practices of this medicinal plant.

INTRODUCTION: *Simarouba* belongs to the family Simaroubaceae. It had also been known as paradise tree, Laxmi taru, Aceituno, a multipurpose tree that can grow well under a wide range of hostile ecological condition. Its origin is native to North America, now found in different regions of India.

Cultivation & Description: It was a medium sized tree generally attains a height about 20 m and trunk diameter approximately 50-80 cm and life about 70 years. It could grow under a wide range of agro-climatic conditions like warm, humid and tropical regions. Its cultivation depends upon rainfall distribution (around 400 mm), water holding capacity of the soil and sub-soil moisture.

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It was suited for temperature range 10-40 °C, the pH of the soil should be 5.5-8. It produces bright green leaves 20-50 cm length, yellow flowers and oval elongated purple colored fleshy fruits [1]. Its seeds contain about 40% kernel and kernels content 55-65% oil. The amount of oil would be 1000-2000 kg/ha/year for a plant spacing of 5 m × 5 m. It was used for industrial purposes in the manufacture of soaps, detergents, and lubricants, *etc*. The oil cake is rich in nitrogen (7.7 to 8.1%), phosphorus (1.07%) and potash (1.24%) could be used as valuable organic manure [2]. *Simarouba* was a rich source of fat having a melting point of about 290 °C.

Traditional Use: The major green energy components and their sources from *Simarouba* were biodiesel from seeds, ethanol from fruit pulps, biogas from fruit pulp, oil cake, leaf litter and thermal power from leaf litters, shell, unwanted branches, *etc*. Unlike fossil fuels, bio-diesel is a renewable source of energy, because it comes from biological sources like plants and animals which can be replenished by farming.

On the other hand, fossil fuels come from underground deposits of hydrocarbons which cannot be renewed. Biofuels have become a matter of global importance because of the need for alternative energy at a lower price and with less pollution [3]. *Simarouba glauca* is one of the important herbal drugs used against dysentery hence its bark is also known as dysentery bark. The bark and leaf extract of *Simarouba* is well known for its different types of pharmacological properties such as hemostatic, antihelminthic, antiparasitic, anti-dysenteric, and anticancerous. The bark is used to cure fever, malaria, stomach and bowel disorders.

Phytoconstituents:

Seed: In the *Simarouba glauca* seed Identification and estimation of different toxic and antinutritional factors in *Simarouba* meal is available, a systematic study was conducted by [4] and also observed that *Simarouba* Kernel contained fat in the range of 55-65 g/100g. Study of *Simarouba* from different sources has reported a range of protein values (45.6-56.8g/100g; average, 51.8g /100g) in their deoiled meal cake, have reported slightly higher protein content of 50g/100g in meal cake of *Simarouba*.

Protein content in the *Simarouba* Kernels was 18.2g/100g which increased to 47.7g/100g in a defatted meal of *Simarouba*. A meal of *Simarouba* contained residual fat of 1.1g/100g [5] Studies of indicated that deoiled meal of *S. glauca* is a rich source of protein (47.7g/100g) with high solubility (92%), *in-vitro* protein digestibility (88%) and amino acid-based computed nutritional indices.

Its seeds contain 50-65% oil that can be extracted by conventional methods. well grown tree yields 15-30 kg nutlets per year equivalent to 1-2 t oil per ha per year and about the same quantity and quality of oil cake, Each well grown tree yields 15-30 kg nutlets per year equivalent to 2.5-5 kg oil this amounts to 1-2 t oil per ha per year and about the same quantity of oil cake [6] scanty scientific literature available on *Simarouba*, mainly deals with composition and characteristics of its fat. [7]

S. glauca have afforded quassinoids and an alkaloid 8- hydroxyl canthin-6-one. And reported that the seeds contain 40% Kernels and the kernels contain 60% fat, which is edible a good source of fat for preparation of cocoa butter (CB) extender. The greenish yellow fat melts at 26.40C and has an iodine value of 52.6 and saponification value 190.5. It consists of about 30% of symmetrical monosaturated type triacylglycerols and appears to be a good source of fat for preparation of cocoa butter (CB) extender.

The odorless, greenish yellow fat melts at 26.4 °C, has an iodine value of 52.6 and a saponification value of 190.5, estimation of different toxic and antinutritional factors in *Simarouba* meal is available, systematic study was conducted and Fatty acid composition of *Simarouba* fat has been investigated by several researchers have reported slightly higher protein content of 50g/100g in meal cake of *Simarouba* and also considering the high fat content in the kernels and moderate iodine value and high content of oleic and stearic acids, the fat has good potential for use as edible fat. The odorless, greenish yellow fat melts at 26.4 °C and has an iodine value of 52.6 and saponification value 190.5, have reported oil content of *Simarouba* more than 60g/100g. [8, 9] have reported oil content of *Simarouba* more than 60g/100g.

And major components are oleic (52-54%), stearic (27-33%) and palmitic (11-12%). On the other hand during the study of *Simarouba* from different sources has reported a range of protein values (45.6-56.8g/100g; average, 51.8g/100g) in their deoiled meal cake. During the study of *Simarouba* from different sources has reported a range of protein values (45.6-56.8g/100g; average, 51.8g /100g) in their deoiled meal cake. Similarly, crude fiber content of *Simarouba* kernel (8.1g/100g) increased to 11.8g/100g in its deoiled meal. And major components are oleic, stearic and palmitic.

Further it has been reported that characteristics of the fat and fatty acid composition of Indian origin do not significantly differ from those reported from seeds of other countries, Fatty acid composition of *Simarouba* fat has been investigated by several researchers greenish yellow fat melts at 26.4 °C, has an iodine value of 52.6 and a saponification value of 190.5, considering the high fat content in the kernels and moderate iodine value and high content of oleic and stearic acids, the fat has good potential for use as edible fat or for blending with vanaspati or for use as cocoa butter (CB) substitute

or extender. *Simarouba glauca* is a rich source of fat having a melting point of about 29 °C and consisting of palmitic (12.5%) oleic (56%) and stearic (27%) as major fatty acids. It consists of about 30% of symmetrical monosaturated type triacylglycerols and appears to be a good source of fat for preparation of cocoa butter (CB) extender. They revealed that the stearic fraction obtained *from S. glauca* fat after removal of about 65% oleic fraction is suitable for use in chocolate products as CB extender.

FIG. 1: (A) SHOWS THE PURPLE COLOUR FRUIT, (B) SHOWS THE LEAVES ARRANGEMENT AND (C) SHOWS THE LEAVES, FLOWER, SEED AND THE YELLOWISH COLOUR FRUIT

Bark Constituents: *Simarouba* bark is obtained as long pieces from 4-12 cm wide and 2-5 mm thick, folded lengthwise, light flexible, tenacious, very fibrous, externally of a light brownish yellow color, rough warty and marked with transverse ridges, internally of a pale yellow. It is without odor and of a bitter taste (Remington and Wood, http://www. Henriette herbal.com/electric/usdisp/Simarouba.html 1918). [10] Isolated from *Simarouba* bark a bitter crystalline substance, simaroubin, to which he assigned a formula $C_{22}H_{30}O_9$. Some thirty years later [11], examined the crystalline constituents of the bark of *S. amara.*

They isolated simaroubin and confirmed the formula $C_{22}H_{30}O_9$ and another of undetermined composition were also obtained S. glauca afforded quassinoids and an alkaloid 8- hydroxyl canthin-6-one. Studies led to the isolation of crystalline compound from *S. glauca*, which has been designated glaucarubin [12]. It is resinous matter, a volatile oil having the odor of benzoin, malic acid, gallic acid in very minute proportion, an ammonical salt calcium malate and oxalate, some mineral salts, ferric oxide, silica, ulmin, and lignin. Remington and Wood, [http://www. Henriette sherbal.com/electric/usdisp/simarouba.html. 1918] noticed that *Simarouba* bark is used as a bitter and astringent in chronic dysentery.

For the latter purpose, a decoction is prepared (1 in 20), often with an equal quantity of cinnamon bark.

Dose-1-2g (15-30 grains) [13]. investigated bioassay-guided phytochemicals of *S. glauca* stem extract, using the KB cell lines as a monitor, led to the isolation and identification of canthin-6-one(1), 2-methoxy canthin-6-one(2),9- methoxycanthin-6-one (3), 2 hydroxy canthin-6-one (4), melianodiol (7) and 14-deacytyleurylene (8) as cytotoxic principles together with two further canthin-6- one alkaloid derivatives. 4-5 dimethoxy canthin-6-one (5) and 4-5 dihydroxy canthin-6-one(6), two coumarins, scopoletriolein (9) and fraxidin(10) and two triglycerides, triolein(11) and trilinolein (12) as inactive constituents.

After their purification six canthin-6-one alkaloids (1-6), melianodiol (7), 14- deacetylleurylene (8), scopoletin(9), fraxidin (10), triolein (11) and trilinolein (12), isolated from twigs of *S. glauca* were tested for cytotoxicity against a panel of human cell lines. The main plant chemicals in Simarouba include - ailanthinone, benzoquinone, canthin, dehydro - glaucarubinone, glaucarubine, glaucarubolone, glaucarubinone, holacanthone, melianone, simaroubidin, simarolide, simarubin, simarubolide, sitosterol, and triucalla.

Anti-nutritional Factor: Identification and estimation of different toxic and anti-nutritional factors in *Simarouba* meal is available; the systematic study was conducted by [14]. They revealed after identification and estimation of toxic constituents that *Simarouba* meal required detoxification from saponin (0.95g/100g), alkaloid (1.01g/100g), phenolics (0.95g/100g) and phytic acid (0.73g/100g) before its usage potential could be utilized in feed/ food formulations.

To exploit the protein-rich (47.7g/100g) *Simarouba* meal in food/feed, have reported slightly higher protein content of 50g/100g in meal cake of *Simarouba*. Typical protein solubility profiles with similar solubility values were reported by [15, 16, 17] for rice bran, Jatropha and Karanja Proteins respectively. To identify different anti-nutritional factors in *Simarouba* meal related to quassine.

Studies indicated that of the methanolic extract of *Simarouba* meal gave purple mauve color with anisaldehyde in sulphuric acid, for the presence of saponins. They had purified saponins; the methanolic extract of *Simarouba* meal was passed through an ion exchange column, using di-ion HP_2O resin colorimetric determination indicated that *Simarouba* meal contained 3.7g/100g total saponins. They subjected Saponins from Simarouba meal to Lieberman-Burchard reaction, using acetic acid and sulphuric acid gave pink color. This indicated that the aglycone portion of saponin is the triterpenoid type. They speculated that saponins are amphiphilic compounds, in which sugars are linked to the nonpolar group (Sapogenin), which may be either a sterol or a triterpene.

Pharmacological and Clinical Aspects: Pancreatic cancer is one of the most lethal human malignancies. Nearly 100% of cases of pancreatic cancer carry mutations in KRas. P-21-activated kinases (PAKs) are activated by an act downstream of KRas. Glaucarubinone, a natural product first isolated from the seeds of the tree *Simarouba glauca*, was originally developed as an antimalarial drug and has more recently been recognized as an anticancer agent. This study aimed to determine whether glaucarubinone, alone or in combination with the front-line chemotherapeutic agent gemcitabine, would inhibit the growth of pancreatic cancer cells *in-vitro* or *in-vivo* and the mechanism involved.

The growth of the human pancreatic cancer cell lines PANC-1 and MiaPaCa-2 was measured by 3H-thymidine incorporation in vitro, and by volume as xenografts in SCID mice. The expression and activities of the two serine /threonine kinases PAK1 and PAK4, which are key regulators of cancer progression, were measured by Western blotting. Here, we report that glaucarubinone decreased proliferation and migration of pancreatic cancer cells *in-vitro*, and reduced their growth as xenografts *in-vivo*.

Treatment with glaucarubinone and gemcitabine reduced proliferation *in-vitro* and tumor growth *in-vivo* more than treatment with either glaucarubinone or gemcitabine alone. Treatment with glaucarubinone reduced PAK1 and PAK4 activities, which were further decreased by the combination of glaucarubinone and gemcitabine. These results indicate that glaucarubinone reduced pancreatic cancer cell growth at least in part *via* inhibition of pathways involving PAK1 and PAK4.

The synergistic inhibition by glaucarubinone and gemcitabine observed both *in-vitro* and *in-vivo* suggests that glaucarubinone may be a useful adjunct to current regimes of chemotherapy [18]. The tick *Rhipicephalus microplus* causes significant losses in livestock cattle and has developed increasing resistance to the primary acaricides that are used to treat these infections. The objective of this study was to identify new biomolecules or isolated substances showing acaricidal activity from plants. Larval packet tests were conducted to evaluate the effects of 11 species of plants and three isolated substances (betulinic acid, eugenol, and nerolidol) on *R. microplus*.

An adult female immersion test was performed with the substance that showed the highest larvicidal activity, which was evaluated for inhibition of reproduction. Tests using *Licania tomentosa, Hymenaea stigonocarpa, Hymenaea courbaril, Stryphnodendron obovatum, Jacaranda cuspidifolia, Jacaranda ulei, Struthanthus polyrhizus, Chrysobalanus icaco, Vernonia phosphorea, Duguetia furfuracea,* and *Simarouba versicolor* extracts as well as the isolated substance betulinic acid indicated lower acaricidal effects on *R. microplus* larvae.

The extract displaying the best larvicidal activity was the ethanolic extract from *L. tomentosa* at a concentration of 60%, resulting in a mortality rate of 40.3%. However, nerolidol and eugenol showed larvicidal activity, which was highest for eugenol. Nerolidol caused a 96.5% mortality rate in the R. microplus larvae at a high concentration of 30%, and eugenol caused 100% mortality at a concentration of 0.3%. In the adult immersion test, 5% eugenol was identified as a good biomolecule for controlling *R. microplus*, as demonstrated by its high acaricidal activity and inhibition of oviposition [19].

This study describes an outbreak of Simarouba versicolor intoxication in cattle from Mato Grosso do Sul, Brazil, and reproduces it experimentally. Clinical signs of the affected animals were a weakness, tremors, hind limbs incoordination, reluctance to move, sternal and lateral recumbency and death. The main necropsy findings, observed in the abomasum and segments of the small and large intestines, were diffuse redness and mucosal and serosal swelling. Histological examination revealed necrosis of lymphoid tissues and necrotizing enterocolitis.

One experiment was carried out using 3 male calves to test the toxicity of a single dose of *S. versicolor* leaves at 15 g/kg, 5 g/kg and 2.5 g/kg. Clinical signs necropsy findings and histological examination of calves receiving 15 g/kg and 5 g/kg leaves were similar to those of cattle from the intoxication outbreak. The calf fed 2.5 g/kg leaves developed clinical symptoms of poisoning and recovered naturally.

In a second experiment, two male calves received daily administration of *S. versicolor* leaves at 1.5 g/kg and 2.5 g/kg for 10 days. They developed clinical signs of intoxication within 24 h and recovered eight to nine days after the leaves were administered. These findings suggest that *S. versicolor* was responsible for the outbreak studied, although this plant does not have cumulative intoxication effects on cattle [20].

Ailanthus altissima (Mill.) Swingle, tree-of-heaven, is an invasive species native to Asia. It first was introduced into the United States in the 1700 s and now is distributed throughout much of North America. Mechanical and chemical controls are current suppression tactics; however, implementation is costly. A weevil, *E. brandti* (Harold), was identified in China and imported for quarantine testing in 2004 as a potential biological control agent.

Host specificity tests on adult feeding, larval development, and oviposition of this weevil were conducted from 2007 to 2011 on *A. altissima* and 29 non-target species. *Eucryptorrhynchus brandti* adults fed significantly more on *A. altissima* foliage when compared with all test species. The range of means for feeding on *A. altissima* was 32.5-106.5 mm (2)/ adult/ d. In no-choice tests, *Simarouba glauca* DC, *Leitneria floridana* Chapm, and Citrus limon (L.) Burm. F, had feeding rates of only 10, 49, and 10%, respectively, compared with the level of feeding on *A. altissima*.

The mean range of adult feeding by *E. brandti* on all other test species was <7% of feeding on *A. altissima* (0.0-3.3 ± 5.0 mm (2)/adult/d).

In the no-choice larval inoculation tests, larval development only occurred in two of 10 L. floridana seedlings compared with seven of 10 A. altissima seedlings. In the no-choice oviposition tests, oviposition and subsequent larval development did not occur in *L. floridiana*, whereas all seven *A. altissima* seedlings supported ovipositor and subsequent larval development. The weevil did not appear to be a threat to *L. floridana* or any other non-target species tested. Therefore, we conclude that *Eucryptorrhynchus brandti* is highly hosted specific to *A. altissimo* [21].

Dry skin is associated with a disturbed skin barrier and reduced formation of epidermal proteins and lipids. During recent years, skin-barrier-reinforcing properties of some botanical compounds have been described. Searching the PubMed database revealed 9 botanical extracts that specifically improve skin barrier and promote keratinocyte differentiation in vivo after topical application. The topical application of *Aloe vera* (leaf gel), *Betula alba* (birch bark extract), *Helianthus annuus* (sunflower oleodistillate), *Hypericum perforatum* (St. John's wort extract), *Lithospermum erythrorhizon* (root extract), *Piptadenia colubrina* (Angico-branco extract) and *Simarouba amara* (bitter wood extract) increased skin hydration, reduced the trans-epidermal water loss, or promoted keratinocyte differentiation in humans *in-vivo*.

The topical application of *Rubia cordifolia* root extract and rose oil obtained from *Rosa spp.* flowers stimulated keratinocyte differentiation in mouse models. The underlying mechanisms of these effects are discussed. It is concluded that some botanical compounds display skin-barrier-reinforcing properties that may be used in dermocosmetics for dry skin. However, more investigations on the mode of action and more vehicle-controlled studies are required [22].

Epidemiological evidence indicates that diets high in fruits and vegetables provide a measure of cancer chemoprevention due to phytochemical constituents. Natural products are a rich source of cancer chemotherapy drugs, and primarily target rapidly cycling tumor cells. Increasing evidence indicates that many cancers contain small populations of resistant, stem-like cells that can regenerate tumors following chemotherapy and radiation, and have been linked to the initiation of metastases.

Our goal is to discover natural product-based clinical or dietary interventions that selectively target cancer stem cells, inducing differentiation. We adapted an alkaline phosphatase (AP) stain to assay plant extracts for the capacity to induce differentiation in embryonic stem (ES) cells. AP is a characteristic marker of undifferentiated ES cells, and this represents a novel approach to screening medicinal plant extracts.

Following a survey of approximately 100 fractions obtained from 12 species of ethnomedically utilized plants, we found fractions from 3 species that induced differentiation, decreasing AP and transcript levels of pluripotency markers (Nanog, Oct-4, Rex-1). These fractions affected proliferation of murine ES, and human embryonal, prostate, and breast carcinoma cells in a dose-dependent manner. Several phytochemical constituents were isolated; the antioxidant phytochemicals ellagic acid and gallic acid were shown to affect the viability of cultured breast carcinoma cells [23].

We present an evaluation of the antiplasmodial and cytotoxic effects of four plants commonly used in Guatemalan folk medicine against malaria. Methanol extracts of *Simarouba glauca* D. C, *Sansevieria guineensis* Willd, *C. guatemalensis* Lotsy, and *Neurolaena lobata* (L.)R.Br. Significantly reduced parasitemias in *Plasmodium berghei*-infected mice.

Dichloromethane fractions were screened for their cytotoxicities on *Artemia salina* (brine shrimp) larvae, and 50% inhibitory concentrations were determined for *Plasmodium falciparum in-vitro* cultures. These extracts significantly inhibited both chloroquine-susceptible and -resistant strains of *P. falciparum* of all dichloromethane extracts, only the *S. glauca* cortex extract was considered to be toxic to nauplii of *A. saline* in the brine shrimp test[24].

An aqueous extract of *Simarouba amara* was studied for its activity on the differentiation of human skin keratinocytes. Submerged and air-exposed treated keratinocyte cultures displayed a more highly differentiated histoarchitecture, with

the presence of differentiated ultrastructural elements than untreated controls. Immuno-histochemistry of involucrin and activation of transglutaminase activity provided further evidence for the increase in corneocyte envelope formation observed ultrastructurally.

Lipid analysis of air-exposed cultures revealed an increase in cholesterol sulphate, cholesterol, and ceramide contents. After 4 weeks of treatment on the hemiface of volunteers, the capacitance and transepidermal water loss evaluation revealed the potential interest of this extract for improvement of skin hydration. Electron microscopic examination of the corneocyte envelope on tape strips confirmed its actions. Taken together these data demonstrated that an aqueous extract of *S. amara* increases human keratinocyte differentiation [25].

A microdilution technique for the assessment of in vitro activity against *Entamoeba histolytica* was devised and validated with metronidazole. The test was used to detect the antiamoebic activities of plant extracts prepared from the traditional remedies *Brucea javanica* fruits and *Simarouba amara* stems. The activity was associated with quassinoid - containing fractions. The 50% inhibitory concentrations for some quassinoids against amoebae were determined by using the microdilution method.

These concentrations ranged from 0.019 micrograms ml^{-1} for bruceantin, the most active quassinoid, to greater than 5 micrograms ml^{-1} for glaucarubol, the least active compound tested. These results are discussed regarding the known activities of these compounds against *Plasmodium falciparum*. Overall, the activities of the quassinoids against both protozoa are similar. The microdilution technique will be useful in the search for novel antiamoebic drugs [26]. Extracts prepared from *Simarouba amara* fruits collected in Panama are active against *Plasmodium falciparum in-vitro* and *Plasmodium berghei* in mice. Four active quassinoids have been identified as ailanthinone, 2'-acetylglaucarubinone, glaucarubinone, and holacanthone [27].

Genetic and Phytochemical Studies: A chemical investigation of the bark of *Simarouba amara*, collected in Barbados, resulted in the isolation of six new triterpenes (3-8), in addition to two known compounds, 3-oxatirucalla-7, 24-dien-23-ol (1) and niloticin (2). Compound 3 is a tirucallane triterpene, while compounds 4-7 are apotirucallane derivatives containing an epsilon-lactone in ring A. Compounds 6 and 7 were obtained as a mixture that could not be separated, while compound 8 is an octanorapotirucallane derivative that lacks the C(8) side chain. The structures of all compounds were determined by interpretation of physical data [28].

Activity-guided fractionation of a chloroform-soluble extract of *Simarouba glauca* twigs collected from a plot in southern Florida, and monitored with a human epidermoid (KB) tumor cell line, afforded six canthin-6-one type alkaloid derivatives, canthin-6-one (1), 2-methoxycanthin-6-one (2), 9-methoxycanthin-6-one (3), 2-hydroxycanthin-6-one (4), 4,5-dimethoxycanthin-6-one (5) and 4,5-dihydroxycanthin-6-one (6), a limonoid, melianodiol (7), an acyclic squalene-type triterpenoid, 14- deacetyleurylene (8), two coumarins, scopoletin (9) and fraxidin (10), and two triglycerides, triolein (11) and trilinolein (12). Among these isolates, compounds 1-4, 7 and 8 exhibited cytotoxic activity against several human cancer cell lines. 14-Deacetyleurylene (8) was selectively active against the Lu1 human lung cancer cell line but was inactive in an *in-vivo* hollow fiber assay using this same cell type [29].

Two male Labrador retrievers developed bleeding erosions/ulcerations involving the oral mucosa, mucocutaneous junctions of the lips, nose, prepuce, and anus, ulcerated nodules on the chin, and crusting lesions on the elbows, hocks and scrotum. One of the dogs was anorexic and depressed, had hematological abnormalities consistent with damage to the liver and signs of neurological disease. As these dogs had recently been exposed to bedding containing *Simarouba amara* shavings and because of the striking similarities of clinical signs to those described for horses, a probable diagnosis of wood poisoning was made. This assumption was supported by the clinical course as the healing of skin lesions occurred when the dogs were no longer exposed to the bedding [30].

From the roots, stems and fruits of *Simarouba versicolor* (Simaroubaceae) were isolated quassinoids (3, 5-7), triterpenoids (8-14), a mixture of steroids (15-17), the flavonoid kaempferol (18)

and the squalene derivative 11,14-diacetoxy-7,10; 15,18-diepoxy-6,19-dihydroxy-6, 7, 10, 11, 14, 15, 18, 19-octa hydro squalene (19). Spectral data were used for structural characterization [31]. Characterization of novel microsatellite loci isolated from the tropical dioecious tree *Simarouba amara* [32].

An investigation of the Guyana plant *Simarouba amara* Aubl. (Simaroubaceae) for antineoplastic quassinoids led to isolation and structural determination of the new quassinoids 2'-acetylglaucarubine (1a) and 13, 18-dehydroglaucarubinone. The previously known 2'-acetylglaucarubinone (3a) and glaucarubinone (3b) were also obtained. The new quassinoid 2 was found significantly to inhibit the growth of the murine lymphocytic leukemia [33]. The use of glaucarubin (a crystalline glycoside isolated from *Simarouba glauca*) in the treatment of human colonic amebiasis [34].

Antimicrobial and Insecticidal Actions: Ethanol extracts from six selected species from the Cerrado of the Central-Western region of Brazil, which are used in traditional medicine for the treatment of infectious diseases and other medical conditions, namely *Erythroxylum suberosum* St. Hil. (Erythroxylaceae), Hyptis crenata Pohl. ex Benth. (Lamiaceae), *Roupala brasiliensis* Klotz. (Proteaceae), *Simarouba versicolor* St. Hil. (Simaroubaceae), *Guazuma ulmifolia* Lam. (Sterculiaceae) and *Protium heptaphyllum* (Aubl.) March. (Burseraceae), as well as fractions resulting from the partition of these crude extracts, were screened *in-vitro* for their antifungal and antibacterial properties.

The broth microdilution assay assessed the antimicrobial activities against six control fungal strains, *Candida albicans*, *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. tropicalis*, and *Cryptococcus neoformans*, and five control Gram-positive and negative bacterial strains, *Escherichia coli, Enterococcus faecalis, Klebsiella pneumonia, Pseudomonas aeruginosa,* and *Staphylococcus aureus*.

Toxicity of the extracts and fractions against Artemia salina was also evaluated in this work. All plants investigated showed antimicrobial properties against at least one microorganism and two species were also significantly toxic to brine shrimp larvae. The results tend to support the traditional use of these plants for the treatment of respiratory and gastrointestinal disorders and skin diseases, opening the possibility of finding new antimicrobial agents from these natural sources. Among the species investigated, *Hyptis crenata*, *Erythroxylum suberosum,* and *Roupala brasiliensis* were considered the most promising candidates for developing future bioactivity-guided phytochemical investigations [35].

Natural products have long been providing important drug leads for infectious diseases. Leishmaniasis is a major health problem worldwide that affects millions of people, especially in developing nations. There is no immune-prophylaxis (vaccination) available for Leishmania infections, and conventional treatments are unsatisfactory; therefore, anti-leishmanial drugs are urgently needed.

In this work, 48 alcoholic extracts from 46 Cuban plants were evaluated by an *in-vitro* bioassay against Leishmania amazonensis. Furthermore, their toxicity was assayed against murine macrophage. The three most potent extracts against the amastigote stage of *Leishmania amazonensis* were from *Hura crepitans, Bambusa vulgaris*, and *Simarouba glauca* [36].

In the present study, an extensive *in-vitro* antimicrobial profiling was performed for three medicinal plants grown in Cuba, namely *Simarouba glauca, Melaleuca leucadendron,* and *Artemisia absinthium*. Ethanol extracts were tested for their antiprotozoal potential against *Trypanosoma brucei*, *Trypanosoma cruzi*, *Leishmania infantum* and *Plasmodium falciparum*. Antifungal activities were evaluated against *Microsporum canis* and *Candida albicans* whereas *Escherichia coli* and *Staphylococcus aureus* were used as test organisms for antibacterial activity. Cytotoxicity was assessed against human MRC-5 cells.

Only *M. leucadendron* extract showed selective activity against microorganisms tested. Although, *S. glauca* exhibited strong activity against all protozoa, it must be considered non-specific. The

value of an integrated evaluation of extracts with particular reference to selectivity is discussed [37].

Chagas' disease is chiefly transmitted by feces of hematophagous bugs (Triatominae) that ingested Trypanosoma cruzi from the blood of infected people or animals. Pyrethroids have been the main insecticides used against these insects. However, some populations of insects have shown significant levels of resistance to several pyrethroids, indicating the need for new insecticides for the control of triatomines. Insecticidal activity of 24 Cerrado plant extracts belonging to five species of four families was assayed on fourth instar nymphs of *Rhodnius milesi* Carcavallo, Rocha, Galvão & Jurberg (Hemiptera: Reduviidae), under laboratory conditions.

For the extract application on triatomines, 50 mg of the extract were topically applied in duplicate on dorsal tergites of ten insects. Insects topically treated with acetone, ethanol, as well as insects with no treatment were used as controls. Triatomines were observed over a 28-day period. Hexanic and ethanolic extracts of *Simarouba versicolor, Guarea kunthiana, Guarea guidonia* and *Talauma ovata* caused mortality between 20% and 95% of *R. milesi* in comparison with the controls, which showed no insect mortality. These preliminary data suggest that the ethanolic extract of the root bark of *S. versicolar* and the hexane extract of the root of *G. guidonia*, responsible for a 95% and 75% insect mortality, respectively, should be chemically investigated and monitored through biological assays in order to determine their insecticidal components, that could be used as a molecular model or as biorational compounds for use in insect control programmes [38].

A study was conducted to investigate the selective cleanup and determination of aflatoxin B1 (AfB1) from contaminated media. Composite adsorbents were formulated from calcium montmorillonite clay, which possesses a high affinity and enthalpy of adsorption for AfB1. Nanostructuring techniques were used to construct various formulations of the clay-based composite media. In AfB1 adsorption studies with prototypical affinity columns, these composites offered narrowly defined, reproducible capacity ranges. Composite recoveries of AfB1 from spiked grains exhibited linear trends that correlated well with the range of spike levels. Composite columns provided lower recoveries of AfB1 from naturally contaminated corn than did immunoaffinity columns; however, recoveries were consistent and purified extracts were free of interfering compounds, as determined by liquid chromatography with fluorescence detection [39].

Gastrointestinal disorders are important causes of morbidity in developing countries. Natural healing is the traditional way of treating these diseases in Guatemala. Ethnobotanical surveys and literature reviews showed that 385 plants from 95 families are used in Guatemala for the treatment of gastrointestinal disorders. The activity of 84 of the most commonly used plants was screened in vitro against five enterobacteria pathogenic to man (enteropathogenic *Escherichia coli, Salmonella enteritidis, Salmonella typhi, Shigella dysenteriae*, and *Shigella flexneri*). Results indicate that [34] (40.48%) plants inhibit one or more of the enterobacteria tested.

The most commonly inhibited bacterium was *S. typhi* (33.73%), and the most resistant was *E. coli* (7.35%). The plants of American origin which exhibited the best antibacterial activity were: *Byrsonima crassifolia, Diphysa robinioides, Gnaphalium stramineum, Guazuma ulmifolia, Psidium guajava, Sambucus mexicana, Simarouba glauca, Smilax lundelii, Spondias purpurea* and *Tagetes lucida*. These results indicate a scientific basis for use of these medicinal plants for attacking enterobacterial infections in man [40].

Against Cancer: A neurofibromatosis type 1 (NF1) based bioassay-guided phytochemical investigation on *Simarouba berteroana* led to the isolation of one new canthin-6-one-9-methoxy-5-O-β-D-glucopyranoside (1), seven known canthine alkaloids (2-8), two known quassinoids (9-10) and a known neo-lignan (11). The structures of all compounds were established by HRMS, 1D- and 2D-NMR analysis and comparison with previously reported data. Most of the compounds inhibited the proliferation of an Nf1- and p53-deficient mouse glioma cell line at non-cytotoxic concentrations [41].

The search for new anti-cancer drugs is one of the most prominent research areas of natural products. Numerous active compounds isolated from

Brazilian Cerrado plant species have been studied with promising results. To investigate the cytotoxic potential of 412 extracts from Brazilian Cerrado plants used in traditional medicine belonging to 21 families against tumor cell lines in culture. Maceration of 50 plant species resulted in 412 hexane, dichloromethane, ethanol and hydro-alcoholic extracts. The cytotoxicity of the extracts was tested against human colon carcinoma (HCT-8), melanoma (MDA-MB-435), and brain (SF-295) tumor cell lines, using the thiazolyl blue test (MTT) assay.

Bioassay-guided fractionation was performed for one active extract. Twenty-eight of the 412 tested extracts demonstrated a substantial antiproliferative effect, at least 85% inhibition of cell proliferation at 50 microg/mL against one or more cell lines. Those extracts are obtained from different parts of Anacardiaceae, Annonaceae, Apocynaceae, Clusiaceae, Flacourtiaceae, Sapindaceae, Sapotaceae, Simaroubaceae, and Zingiberaceae.

Complete dose-response curves were generated and IC_{50} values were calculated for these active extracts against four cell lines HCT-8, MDA-MB-435, SF-295 and HL-60 (leukemia), and their direct cytotoxic effects were determined. In summary, 14 extracts of 13 species showed toxicity in all tested tumor cell lines, with IC_{50} values ranging from 0.1 to 19.1 microg/mL. The strongest cytotoxic activity was found for the hexane extract of *Casearia sylvestris* var. lingua stem bark, with an IC_{50} of 0.1 microg/mL for HCT-8, 0.9 microg/mL for SF-295, 1.2 microg/mL for MDA-MB-435, and 1.3 microg/mL for HL-60, and *Simarouba versicolor* root bark, with an IC_{50} of 0.5 microg/mL for HCT-8, 0.7 microg/mL for SF-295, 1.5 microg/mL for MDA-MB-435, 1.1 microg/mL for HL-60. Bioassay-guided fractionation of the last extract led to the isolation of glaucarubinone, which showed pronounced activity against the four cell lines studied. Further studies of the active extracts are necessary for chemical characterization of the active compounds and more extensive biological evaluations [42]. beta-Sitosterol, epilupeo, amarolide-11-acetate, amarolide-2,11-diacetate, ailanthinone and glaucarubinone have been isolated from *S. versicolor*. The cytotoxic and antileukemic activities of extracts of this plant are due chiefly to glaucarubinone [43].

Commercial Applications and Aspects: The centesimal composition and the physical and chemical analyses of *Lentinus strigosus*, an edible mushroom occurring in the Brazilian Amazon and produced in alternative substrates based on wood and agroindustrial residues, were evaluated. For this purpose, the C, N, pH, soluble solids, water activity, protein, lipids, total fiber, ash, carbohydrate, and energy levels were determined. The substrates were formulated from *Simarouba amara* Aubl. ("marupá"), *Ochroma piramidale* Cav. Ex. Lam. ("pau-de-balsa") and A*nacardium giganteum* ("cajuí") sawdust and *Bactris gasipaes* Kunth ("pupunheira") stipe and *Saccharum officinarum* (sugar cane bagasse).

The results indicated that the nutritional composition of *L. strigosus* varied with the substrate of cultivation; the protein level found in mushrooms grown in the different substrates (18-21.5%) varied with the substrate and was considered high; the soluble solids present in the mushrooms could have a relation with complex B hydrosoluble vitamins. *L. strigosus* could be considered as important food owing to its nutritional characteristics such as high protein content, metabolizable carbohydrates and fibers, and low lipids and calories content [44].

In the context of multiple forest management, multipurpose tree species which provide both timber and non-timber forest products (NTFP), present particular challenges as the potential of conflicting use for either product may be high. One key aspect is that the magnitude of conflict of use can be location specific, thus adding complexity to policy development. This paper focuses on the extent to which the potential for conflict of use in multipurpose tree species varies across the Amazonian lowland forests shared by Peru, Bolivia, Colombia, Ecuador, and Venezuela, emphasizing the economic dimension of conflict.

Based on a review of the current normative and regulatory aspects of timber and NTFP extraction in the five countries, the paper also briefly discusses the opportunities and constraints for harmonization of timber and NTFP management of multipurpose species across the region.

It was found that about half of the 336 timber species reviewed across the five countries also have non-timber uses. Eleven timber species are multipurpose in all five countries: *Calophyllum brasiliense, Cedrela odorata, Ceiba pentandra, Clarisia racemosa, Ficus insipida, Jacaranda copaia, Schefflera morototoni, Simarouba amara,* and *Terminalia amazonia*. Seven other multipurpose species occurred only in either Venezuela (*Tabebuia impetiginosa, Spondias mombin, Pentaclethra macroloba, Copaifera Officinalis, Chlorophora tinctoria, Carapa guianensis*) or Ecuador (*Tabebuia chrysantha*).

Four multipurpose tree species presented the highest potential of conflict of use across the region: *Dipteryx odorata, Tabebuia serratifolia, Hymenaea courbaril* and *Myroxylon balsamum* yet these were not evenly distributed across all five countries. None of the five studied countries have specific legislation to promote sustainable use of any of the multipurpose species reported here and thus mitigate the potential conflict of use; nor documented management options for integration or else segregation of both their timber and NTFP values [45].

Seed dispersal and subsequent recruitment is the template on which forest regeneration takes place. Hence, considering the scale over which ecological processes occur is key for understanding the overall impact of various dispersal agents. To explore leafcutter ant (*Atta colombica*) dispersal effectiveness in space and time, seed movement and subsequent recruitment of a large-seeded predominately vertebrate-dispersed tree, *Simarouba amara* (Aubl. Simaroubaceae), was investigated on Barro Colorado Island, Panama.

At each of 218 reproductive-sized adults (≥20 cm diameter at breast height), presence or absence of a leafcutter ant colony was noted, with extensive checks for Atta activity taking place at or in close proximity to seed and seedling transects, which extended 4 cardinal directions for 30 m from each reproductive female tree (n= 74). Only at 2 *S. amara* trees were nests observed, and in these areas, a dense *Simarouba amara* seedling carpet was observed. Although, nearby nest and dump sites might increase local *S. amara* recruitment in the short term, mortality at these sites is complete or nearly so. Hence, the seed dispersal effectiveness by leafcutter ants appears to be ephemeral and likely contributes inconsequentially to the long-term recruitment and distribution patterns of the species. This finding highlights the importance of evaluating disperser effectiveness at the ecological environment [46]. To exploit the protein-rich (47.7 g/100g) *Simarouba* meal in food/feed, studies were conducted on its chemical composition with emphasis on protein characteristics and toxic constituents.

Simarouba meal contained high calcium (143 mg/100g) and sodium (79 mg/100g). Saponins with triterpenoid aglycone (3.7 g/100g), alkaloids (1.01 g/100g), phenolics (0.95 g/100g) and phytic acid (0.73 g/100g) were the major toxic constituents identified in *Simarouba* meal. TLC and HPLC results indicated that among different fractions of *Simarouba* saponins, one dominant fraction accounted for about 28%. Proteins of *Simarouba* recorded high in vitro digestibility (88%). SDS-PAGE revealed four major protein bands in molecular weight ranges of 20-24, 36-45 and 55-66 kDa.

Apart from, glutamic acid (23.43 g/100g protein) and arginine (10.75 g/100g protein), *Simarouba* protein contained high essential amino acids like leucine (7.76 g/100g protein), lysine (5.62 g/100g protein) and valine (6.12 g/100g protein). Among nutritional indices, *Simarouba* meal recorded a good EAA Index (75.02), C-PER (1.90) and PDCAAS (1.0-Adult group).

The importance of dispersal for the maintenance of biodiversity, while long-recognized, has remained unresolved. We used molecular markers to measure effective dispersal in a natural population of the vertebrate-dispersed Neotropical tree, *Simarouba amara* (Simaroubaceae) by comparing the distances between maternal parents and their offspring and comparing gene movement via seed and pollen in the 50 ha plot of the Barro Colorado Island forest, Central Panama. In all cases (parent-pair, mother-offspring, father-offspring, sib-sib) distances between related pairs were significantly greater than distances to nearest possible neighbours within each category. Long-distance seedling establishment was frequent: 74% of assigned seedlings established > 100 m from the

maternal parent [mean = 392 +/- 234.6 m (SD), range = 9.3-1000.5 m] and pollen-mediated gene flow was comparable to that of seed [mean = 345.0 +/- 157.7 m (SD), range 57.6-739.7 m]. For *S. amara* we found approximately a 10-fold difference between distances estimated by inverse modeling and mean seedling recruitment distances (39 m *vs.* 392 m). Our findings have important implications for future studies in forest demography and regeneration, with most seedlings establishing at distances far exceeding those demonstrated by negative density-dependent effects[47].

Simarouba amara (Simaroubaceae) is a vertebrate-dispersed, insect-pollinated Neotropical tree found in lowland moist forest from upper Mesoamerica to the Amazon basin. We assessed the spatial genetic structure of *S. amara* within the 50-ha Forest Dynamics Plot on Barro Colorado Island in the Republic of Panama. A total of 300 individuals were genotyped using five microsatellite loci, representing 100 individuals with a dbh>or=10 cm, 100 individuals of 1-10 cm dbh, and 100 individuals of <1 cm dbh.

The 200 individuals in the two larger size classes were also genotyped with 155 AFLP loci. Spatial autocorrelation analysis using Moran's Index detected significant genotypic association at the smallest distance classes for 1-10 cm dbh (0-20 m) and >10 cm dbh (0-40 m) size categories. Significant spatial autocorrelations were detected over larger scales (0-140 m) in <1 cm dbh individuals. The relatively weak genetic structure of *S. amara*, in comparison to other recent studies, may be explained by pollen and seed dispersal over the 50 ha plot, overlapping seed shadows, and post recruitment mortality [48].

The idea of an inter-university project between the Universidad Central de Las Villas, Cuba and the University of Ghent, Belgium was conceived in order to improve the quality of the Cuban agriculture and to stimulate its independence from foreign chemical farm inputs, starting with an applied ethnobotanical investigation as basis for the development of sustainable agricultural practices. The project consists of three parts. The first, ethnobotanical part, subtends the two subsequent stages, *i.e*, the phytochemical and pharmacological stages. After ethnobotanical inventarization of plants with a possible phytotoxic or pesticide effect, these will be collected and taxonomically defined. Fresh vegetal material will be dried, and ground and this first crude extract (polar or apolar) will be tested for its activity *in-vitro* biological tests. When results are positive (presence of activity), this crude extract will be tested *in-vivo*, which could lead to immediate application in agriculture (short-term strategy). The long-term strategy will lead to the identification of chemical substances, responsible for the activity of the crude extract.

As highly sophisticated apparatus is needed for this last step (*i.e.,* identification of chemical compounds), this will be performed by the Department of Organic Chemistry, Faculty of Agricultural and Applied Biological Sciences of the University of Ghent. The project started in September 2000. Apart from all the (complicated) administrative steps to be undertaken for its successful execution, the ethnobotanical and phytochemical parts have already started. Ethnobotanical data were gathered given recollection of "traditional botanical knowledge," considering three main approaches: the use of plants in medicine, in Cuban religion (the famous "santería") and the use of allelopathic plants in agriculture.

Use of medicinal and religious plants is ubiquitous in Cuba. The concept of allelopathy, however, is much less known and applied. At this moment, and after preliminary screening and gathering of field data, in vitro germination tests are running, trying out extracts of tobacco (*Nicotiana tabacum*), banana (*Musa spp*.), sunflower (*Helianthus annuus*), *Simarouba glauca* and *S. laevis* (syn. Quassia, fam. Simaroubaceae) [49].

Phytoremediation: Removal of toxic Cr(VI) in aqueous medium was investigated using activated carbon adsorbents prepared from Simarouba glauca seed shells. The pH effect, Cr(VI) concentration, adsorbent dosage and contact period were studied in a batch experiment. The removal of Cr(VI) was in general most effective at pH range 2.0-4.0 and high Cr(VI) concentrations. Activated carbons are prepared at 80050 degrees C temperature. One is non-impregnated and the remaining three are

impregnated with zinc chloride in 1:1, 1:2, 1:3 ratio. Important characteristics of activated carbons are also investigated. The data for all the adsorbents fit well to the Freundlich adsorption isotherm. The removal of Cr(VI) is around 97% was observed with 1:2 impregnated activated carbon at pH 3.0 where as other adsorbents showed much lower activities [50].

Biotechnology: *S. glauca* (Simaroubaceae), a fast-growing multipurpose tree, grows even on marginal lands under water stress conditions. The absence of plant growth regulators/ cytokinins generally yielded better developmental responses for *S. glauca* [51]. *In-vitro* propagation of *Simarouba glauca* was reported by [52]. Of the four kinds of explants tested, only the shoot and nodal segments allowed somatic embryo induction and development.

They observed that frequency of somatic embryogenesis from callus cultures derived from immature cotyledon explants of *S. glauca* was highest on solid M.S. medium supplemented with 11.1µM benzyl adenine and 13.42µM NAA was highest on M.S. solid medium supplemented with 1.11 µM and 13.42 micro m benzyl adenine NAA while after transfer of the somatic embryos into maturation medium containing half-strength M.S. medium supplemented with 1.89 µM abscisic acid (ABA) and 2% (W/V) sucrose, 20-25% of embryos germinated within 20 days of culture with distinct cotyledon, hypocotyls and radical.

In-vitro shoot multiplication was achieved on MS medium containing 2.5 mg /l BA with 0.1 mg /l NAA and a maximum of 5.83 shoots was produced per nodal explants within 6 weeks of culture.

Elongated shoots were rooted on MS medium supplemented with 1.0 mg /l to 1.5 mg /l IBA. Studies of [53], observed that based on the peroxidase isozyme analysis at different intervals during the rooting process, the rizogenesis accompanied by the synthesis of certain proteins and enzymes indicated that the rooting occurred between the 12th and 15th day of culture on MS medium supplemented with 1.0 mg / l IBA while the percentage of rooting was the maximum (82.45%) on medium having 1.0 mg/l IBA rooting was inhibited on the devoid of IBA. The number of roots/shoot significantly varied with the different concentration of IBA. Roots produced in 1.0mg/l IBA were healthier than that produced in a higher concentration of IBA (1.5 mg/l to 2.0 mg/l). The media containing auxin stimulated the induction of rooting.

They achieved induction of rooting in micro shoots of *Simarouba glauca* L. within 12-15 days of culture on [54] medium supplemented with 1.0 mg /l IBA and 3% (W/V) sucrose. They noticed that there was no spontaneous rooting observed without the application of auxin while peroxides activity was the minimum at induction phase and maximum at the initiation and expression phase grown on medium containing 1.0mg / l IBA. They reported that rooting was associated with selective expression or repression of isoforms of peroxidase during induction, initiation and expression phase which indicates a key role of peroxidase in rooting of micro shoots of *S. glauca in-vitro*.

According to [55], enzymes which are known as metabolic markers change during development and differentiation. In the primary (induction) phase, four ethanolic bands (R_f=0.20, 0.28, 0.33 and 0.37) and anodic bands having RF values ranging from 0.62 to 0.64 were observed. After 3 days of culture on rooting, media three cathodic bands disappeared, and two anodic bands reappeared having R_f values 0.54 and 0.62. On the 6th and 9th day of culture, the appearance and disappearance of anodic and cathodic bands were noted. During initiation of rooting four cathodic bands (R_f=0.20, 0.28, 0.33 and 0.37) and two thick anodic bands (Rf=0.43, 0.48) became visible which might be additional multiple molecular forms of enzyme marker during rhizogenesis.

The number and intensity of anionic peroxidases continuously increased during the process of rhizogenesis. They determined the peroxidase activity in micro shoots on different treatments during the rooting process. They observed that activity became less apparent in micro shoots derived from the media without the growth regulator where as the peroxidase activity was also the minimum at the primary (inductive) phase and maximum at a secondary (imitative) phase in micro shoots grown on a medium having 1.0 mg/l IBA.

The minimum peroxidase activity was observed between the 0-day and the 9th day; maximum activity however, was noted between the 12th and 15th day. The results of [56], confirmed that during rhizogenesis, peroxidase activity was the minimum in the primary (inductive) phase and maximum at secondary (initiation) phase about auxin treatment. Tissues from five male plants, five female plants, and two andromonoecious plants were obtained from *Simarouba plantation* of the University of Agricultural Sciences, Bangalore was obtained by [57] *Simarouba* segregates into male, female and romonoecious during flowering.

Since, controlling is important. An attempt has been developing markers for a polygamodioecious character in *Simarouba*. They screened nine enzyme systems were screened with four different tissues, four extraction buffers, and four electrode buffers. They noticed that the use of Ferret extraction buffer containing ascorbic acid, Tris-Borate-EDTA electrode buffer and flower tissues, five enzyme systems gave good resolution and staining. They studied these enzyme systems using starch gel electrophoresis, and no polymorphism was detected.

To access variability, they analyzed plants using randomly amplified polymorphic DNA (RAPD). Out of one hundred and fifty decamer primers used. They selected seventeen decamer primers based on amplification polymorphism. They subjected the binary data obtained to cluster, 2D-PCA and 3D-PCA analysis, which showed five clusters. They speculated that t-test of two primers OPT-7 and OPW-3 could be used to differentiate between males and females. While one primer, OPS-6 gave a characteristics band only in 100% males and not in others. Studies of [58] initiated to determine useful sex-linked RAPD markers in *Simarouba*.

They have selected seventy 10-mer operon primers and used to generate consistent, clear amplification products ranging in size from 250 bp to 4.0 kbp. They observed that primer OPD-20 amplified a band of approx. 900 bp which was consistently present in all female individuals tested. Their results showed that RAPD analysis is an effective marker technology with which to develop sex-linked markers to enable the elimination of male seedlings. Conducted a glasshouse study to investigate the influence of the *Arbuscular mycorrhizal* (AM) fungus, *Glomus mosseae* and plant growth promoting rhizomicroorganisms (PGPRs). *Bacillus coagulans* and *Azotobacter chroococcum*, alone and in combination, on the growth and nutrition of *S.glauca*.

They noticed that Individual inoculation of these organisms significantly enhanced plant biomass, but biomass was significantly greater with inoculation of *G. mosseae* than with inoculation with coagulants further significantly enhanced plant biomass compared with all other treatments. This was also reflected in other parameters studied; plant height, no. of leaves and plant P-content. They also observed that the percent mycorrhizal colonization in the root and spore in the root zone soil were also highest in seedlings inoculated with both *Glomus* and *Bacillus coagulans*.

Ethnobotanical and Pharmaceutical Aspects: Online database on *Simarouba* created by Lele indicate the leaves and bark of *Simarouba* have long been used as a natural medicine in tropics. *Simarouba* was first imported into France from Guyana in 1713 as a remedy for dysentery. French explorers noticed that the indigenous Indian tribes in the Guyana rainforest used *Simarouba* bark as an effective treatment for malaria and dysentery.

Another indigenous tribe throughout the South uses bark for fevers, malaria, and dysentery as a hemostatic agent to stop bleeding and as a tonic. Further Lele [http: //www.svlele. com/Simarouba. htm. 2010] summarized the long history of *S. glauca* in herbal medicine in many other countries. In Cuba, where it is called gavilan, an infusion of the Leaves or bark is considered to be astringent and used as digestion and menstrual stimulant and an antiparasitic remedy.

It is taken internally for diarrhea, dysentery, malaria, and colitis. It is used externally for wounds and sores. In Belize, the tree is called negrito or dysentery bark. There the bark (and occasionally the root) is boiled in water to yield a powerful astringent and tonic used to wash skin sores and to treat dysentery, diarrhea, stomach and bowel disorders, hemorrhages and internal bleeding. In Brazil, it is employed much the same way against

fever, malaria, diarrhea, dysentery, intestinal parasites indigestion and anemia.

In Brazilian herbal medicine, *Simarouba* bark has long been the most highly recommended (and most effective) natural remedy against chronic and acute dysentery. Bark and leaf of *Simarouba* contain triterpenes useful in curing amoebiasis, diarrhea, and malaria. Joshi and Joshi speculated that the chemicals present in leaf, fruit, pulp, and seed of *Simarouba glauca* are known to possess the medicinal properties such as analgesic, antimicrobial, antiviral, astringent, emmenagogue, stomachic, tonic, vermifuge.

Simarouba extract is used for reducing patchy skin pigmentation (US Patent Issued on October 14, 1997). *Simarouba* is subject of one US Patent, whereby its water extract was found to increase skin keratinocyte differentiation and to improve skin hydration and moisturization [59]. The seeds extracted in alcohol are used against snake bites. An infusion of the bark is used against malaria, rheumatism, shingles, and fever. [www.tropilab. com/Simarouba.html]

Similar properties have been described in other Latin American [60], the antiprotozoal [61] the quassinoids, glaucarubin along with glaucarubinone and glaucarubol from the seeds of *S. glauca* showed promising activity against *Plasmodial falciparum* in culture and antibacterial. [62] Activities and reported that the extract of *S. glauca* had been used in Guatemala for the treatment of gastrointestinal disorders. Studies of [63], revealed a strong inhibitory activity against all protozoa rested, but without selectivity.

Also, Cuban folk medicine information also shows several other medicinal uses for these plants, including antihelminthic, anti-dysenteric and antipyretic action. They are useful in curing amoebiasis, gastritis, ulcers in alimentary systems, chikungunya and malaria. A febrifuge made by extracting the astringent juice of bark used as a remedy for diarrhea. Panhwar [http: //farzanapanhwar.blogspot.com/2007/08/simarouba - galauca – a – new – forest – plant - in. html. 2007]. [64] reported that the extract of *S. glauca* had been used in Guatemala for the treatment of gastrointestinal disorders [65]. Isolated glaucarubin, a crystalline glycoside from *S. glauca* and found to have amebicidal properties *in-vitro* and in experimental animal amebiasis were evaluated in the treatment of human infection.

They observed that cure rate was in the order of 70 percent following treatment by mouth for 10 days with daily doses of 5 mg/kg (maximum daily dose 300 mg) with exception of vomiting in 2 patients and a transitory decrease in leucocyte count in another; the drug was well tolerated in 113 patients. *Simarouba glauca* contains glaucarubin having antiamoebic property [66 67, 68, 69].

Franssen studied the antiplasmodial and cytotoxic effects of four plants commonly used in Guatemalan folk medicine against malaria. They noticed that the Methanol extracts of *S. glauca* DC. *Sansevieria guineensis* Willd, *C. guatemalensis* Lotsy and *Neurolaena lobata* (L) R.Br. significantly reduced parasitemias in *Plasmodium bergheri* infected mice. They screened dichloromethane fractions for their cytotoxicities on *Artemia salina* (brine shrimp) larvae and 50% inhibitory concentrations were determined for *Plasmodium falciparum in-vitro* cultures. They concluded that both chloroquine susceptible and resistant strains of *P. falciparum* were significantly inhibited by these extracts of all dichloromethane extracts, only the *S. glauca* cortex extract was considered to be toxic to nauplii of *A. salina* in the brine shrimp test.

The quassinoids, glaucarubin along with glaucarubinone and glaucarubol from the seeds of *S. glauca* showed promising activity against *Plasmodial falciparum* in culture [70]. Glaucarubin was shown to have amoebicidal properties by both an *in-vitro* method and experimental animals [71, 72, 73]. Isolated alkaloids with high toxicity and quassinoids with antimalarial and cytotoxic characteristics from *Simarouba*. The antiplasmodial and cytotoxic properties of quassinoids are both linked to protein synthesis inhibition [74], and it is likely that parasite, and host cell ribosomes are too similar to allow for the development of selective inhibitors [75].

Because some quassinoids have shown greater selectivity against P. falciparum than against cellular lines, chemical derivation has attracted

much attention as supplying potential leads for drug design [76]. Based on eurycomanone structure, a monoacylated derivative with reduced toxicity and potent inhibitory activity of chloroquine-resistant P. falciparum strain was synthesized by [77]. The results of [78] strongly supported the view that the *S. glauca* extract should not become a priority for further follow-up, because all the observed activities are considered as nonspecific.

They also noticed that the activity obtained against *Microsporum canis* (IC_{50}= 2 µg /ml) was likely to be related to non-specificity. Ethanolic extracts of three plants were used in Cuba as antipyretic and as antimalarial (*Simarouba glauca*, *Melaleuca leucadendron*, and *Artemisia absinthium*) were found active *in-vitro* against *Plasmodium falciparum* and marginally active *in-vivo* against *Plasmodium berghel* [79] *S. glauca* shows acridal activity [80, 81]. Several quassinoids from *S. glauca* seed have exhibited cytotoxic activity *in-vitro* against KB cells (human oral epidermoid carcinoma), including glaucarubin, glaucarubinone, glaucarubol and glaucarubolone [82], the seeds of *S. glauca* have afforded quassinoids and an alkaloid 8- hydroxyl canthin-6-one.

The esters of glaucarubolone, ailanthinone and glaucarubinone, exhibited significant activity *in-vivo* in the P388 lymphocytic leukemia model [83, 84]. The soluble chloroform extract of *S. glauca* exhibited significant cytotoxicity against several human cancer cell lines [85, 86]. Quassinoids a class of chemicals commonly found in members of family Simaroubaceae are toxic to brine shrimp [87], strongly antiplasmodial [88] and strongly toxic to mice [89] for this type of the compound, toxicity in the brine shrimp test (BST) is often used as a tool for biologically guided fractionation of extracts.

Quassinoids led to isolation and structural determination of the new quassinoids 2-acetylglaucarubine and 13, 18- dehydro glaucarubinone. The previously known 2- acetyl glaucarubinone and glaucarubinone were also obtained. The new quassinoid 2 was found significantly to inhibit the growth of murine lymphocytic leukemia. The polar fractions 3, 5 and6 are devoid of the quassinoids listed above (33 r), but they contain other more polar quassinoids including quassinoid glycosides [90].

One of the nonglycosides from the polar fractions, bruceine D, had antiamoebic activity comparable to that of bruceines B and C, whereas the glucoside, yadanzioside F, was much less active. The antiamoebic activity of the polar fractions is thus presumably due to the presence of polar quassinoids. However, the position of methyleneoxy bridge does not seem to affect biological activity significantly. Quassinoids of both types have antimalarial [91] and antileukemic [92] activities.

Physiological Studies: Effect of growth regulators on four-month stored seeds of *S. glauca* (*Quassia Simarouba*) was studied by Radhakrishnan and Renganayaki, to improve germination and vigor potential. They have treated the seeds with 2 concentrations of IAA, IBA andGA3 (200 and400ppm), they noticed that the beneficial effect of IAA at 200 ppm over the rest with 36.33 % germination as against 11.67 % in control 38 days after sowing. They reported that the improvement of vigor by IAA at 200 ppm was 4 fold higher than the control. The root length and root biomass were increased significantly by GA3 treatment. According to [93], pretreatment is not necessary since it does not have any dormancy.

The germination of normal seeds takes 20-30 days. However, the scarification hastens it at least 10- 12 days earlier than normal. Scarification is done by soaking seeds in cold water overnight or hot water (20 minutes or partial breaking of seed coat). The seeds are germinated in the sand at fluctuating 35-45 °C and12 h light and other dark condition [94]. Speculated that such uncoupling between stomatal closure and bulk leaf water status suggests that the pressure-volume relation for guard cells is different to that of the bulk leaf, or that guard cells are somewhat hydraulically isolated from the rest of the leaf.

These conclusions are supported by evidence for the coordination between stomata where bulk leaf conditions remain unchanged. Ninety-five[95] noticed that the leaf cells lose turgor at a water potential which induced 99% stomatal closure. Thus in species *S. glauca* most of the stomatal response to leaf water potential (ψL) occurs as mesophyll cell turgor declines The major benefit of this would be protection of upstream xylem; a realistic motivation

considering that the petiole xylem in *S. glauca* is only slightly more resistant to cavitations than the leaf and may be more difficult to repair.

According to [96] mechanisms aside, it remains to explain the advantage to leaves in producing a vascular system that is vulnerable to cavitation during the normal daily function. They speculated that in the case of *S. glauca* probably lies in the relationship between the guard cell environment and the evaporative environment. The high hydraulic conductivity of *S. glauca* leaves means that the guard cell water potential is likely to be dominated by the water potential of the upstream xylem and soil.

One of the evergreen species *Simarouba glauca* produced relatively short-lived leaves that maintained high hydraulic conductance year round by periodic flushing. As a result, even large changes in the evaporative environment of the leaf will impact minimally on the water potential of the guard cells, and this may impede the responsiveness of stomata to changes in evaporation flux. It is possible then that a reversible loss of hydraulic conductivity in the leaf may be an adaptive means of amplifying the evaporative demand signal to the stomata to expedite a stomatal response [97].

Compared light environment, leaf physiological characteristics, and growth for forest grown samplings of three species of tropical trees with known life histories. They tested the species included *Lecythis ampla*, a species tolerant of understorey conditions, *Pithecellobium elegans*, a species found in relatively bright sites and *S. amara*, a fast growing, light demanding species. They noticed that concerning similar light regimes the species differed markedly in leaf area and gas exchange. Leaf areas of *Lecythis* samplings were five and ten-fold greater than *Simarouba* and *Pithecellobium* samplings, respectively. Light-saturated leaf photosynthesis and leaf dark respiration rates of *Lecythis* were about half those of *Simarouba* while rates of *Pithecellobium* were intermediate. They concluded that Lecythis had the highest leaf photosynthesis at understorey diffuse light with the strongest correlations between sapling performances and diffuse light. [98] measured CO_2 efflux from stems of 2 tropical wet forest trees, both found in the canopy, but with very different growth habits.

The species were *S. amara* a fast growing species associated with gaps in old growth forest and abundant in secondary forest and *Minquartia guianesis*, a slow-growing species tolerant to low light conditions in old growth forest. They reported that per unit of bole surface, CO_2 efflux averaged 1.24μ mol/m-2s-1 for *Simarouba* and 0.83μ mol/m-2s-1 for *Minquartia* CO_2 efflux was highly correlated with annual wood production (r^2=0.65), but only weekly correlated with stem diameter (r^2=0.22). CO_2 efflux from stems of two wet forest trees varied seven fold but was only related to stem diameter.

Their results showed that partitioning CO_2 efflux into the functional components of construction and maintenance respiration can explain much of the variability in CO_2 efflux from stems of wet forest trees. CO_2 efflux was highly correlated with annual wood production, and estimated maintenance respiration was linearly related to sapwood volume.

Phytochemical Constituents (Seed): In the previous work the seeds of *S. glauca* have afforded quassinoids [99], and an alkaloid 8- hydroxyl canthin-6-one. In earlier studies, [100] have reported oil content of *Simarouba* more than 60g/100g.Whereas Severan observed that *Simarouba* kernel contained fat in the range of 55-65g/100g. Protein content in the *Simarouba* kernels was 18.2g/100g which increased to 47.7g/100g in a defatted meal of *Simarouba*. A meal of *Simarouba* contained residual fat of 1.1g/100g. Its seeds contain 50-65% oil that can be extracted by conventional methods. Jeyarani and Reddy reported that the seeds contain 40% kernels and the kernels contain 60% fat, which is edible.

The odorless, greenish yellow fat melts at 26.4 °C, has an iodine value of 52.6 and a saponification value of 190.5, Further it has been reported that characteristics of the fat and fatty acid composition of Indian origin do not significantly differ from those reported from seeds of other countries considering the high-fat content in the kernels and moderate iodine value and high content of oleic and stearic acids, the fat has good potential for use as

edible fat or for blending with vanaspati or for use as cocoa butter (CB) substitute or extender.

Simarouba glauca is a rich source of fat having a melting point of about 29 °C and consisting of palmitic (12.5%) oleic (56%) and stearic (27%) as major fatty acids. They revealed that the stearic fraction obtained *from S. glauca* fat after removal of about 65% oleic fraction is suitable for use in chocolate products as CB extender. And during the study of *Simarouba* from different sources has reported a range of protein values (45.6 56.8g/ 100g; average, 51.8g /100g) in their deoiled meal cake. Conducted studies on its chemical composition with emphasis on protein characteristics and toxic constituents.

They noticed that *Simarouba* meal contained high calcium (143mg/100g) and sodium (79mg/100g) while saponins with triterpenoid aglycone (3.7g/ 100g), alkaloids (1.01g/100g), phenolics (0.95g/ 100g) and phytic acid (0.73g/100g) as the major toxic constituents identified in *Simarouba* meal. Their results of TLC and HPLC studies indicated that among different fractions of *Simarouba* saponins, one dominant fraction accounted for about 28% proteins of *Simarouba* recorded high *in-vitro* digestibility (88%).

While, SDS-PAGE studies revealed four major protein bands in molecular weight ranges of 20-24, 36-45, and 55-66 k Da. They observed that apart from glutamic acid (23.43g/100g protein) and arginine (10.75g/100g protein), *Simarouba* protein contained high essential amino acids like leucine (7.76g/100g protein), lysine (5.62g/100g protein) and valine (6.12g/100g protein).

Finally, they concluded that among nutritional indices, *Simarouba* meal recorded a good EAA Index (75.02), C-PER (1.90) and PDCAAS (1.0 Adult group). Amino acid composition of *Simarouba* meal, along with that of reference Soy protein is given in Table result of amino acid analysis indicated that glutamic acid (23.43g/100g protein), arginine (10.75g/100g protein) and aspartic acid (10.50g/100g protein) are the major amino acids in *Simarouba* meal, which is typical of oilseed proteins. Among essential amino acids, *Simarouba* meal contained greater levels of leucine (7.76g/100g protein), lysine (5.62g/100g protein) and valine (5.62g/100g protein), when compared with FAO/WHO recommended reference soy protein *Simarouba* meal was found to be deficient in sulphur containing amino acids, methionine, and cysteine.

Simarouba glauca is a wonderful plant having an enormous range of different activities. In this article have to assembled almost all information related to different research activity of the plant. Same types of reviews have been published on *Tribulus terrestris* [101], *Oxalis corniculata* [102], *Solanum nigrum* [103], *Cuscuta reflexa* [104], and *Acorus calamus* [105]. Which became popular articles for further investigations on particular medicinal herbs.

CONCLUSION: This review will help to researchers & scholars to go deep in this area as plant indicate the vast range of phytochemical related to origin so it can be suggested the further work can be done on *Simarouba glauca* which is collected from a different season and agro-climatic zone. It is assumed that research will be able to find out more suitable and specific drug plant having a particular activity in specific season. Some scientist needs this data and concepts to re-research on the present scientific plant. It can contribute to medical and pharmaceutical practices. There are still many more activities waiting for screening the drug from *Simarouba glauca.*

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