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MINI REVIEW

Phytochemistry and Biological-Pharmacological Profile of *Aleurites moluccanus*: A Critical Review

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ABSTRACT

Background: Medicinal herbs are commonly used as fundamental ingredients in Asian countries. Our goal was to transcribe the ethno medicinal usage of *Aleurites moluccanus* and to highlight the stated pharmacological activity and composition.

Methods: Chemical composition and various pharmacological virtues of the different constituents of *Aleurites moluccanus* were obtained after an extensive survey from different scientific databases namely Elsevier, PubMed, Science Direct, Web of Science, Taylor and Francis, Google Scholar, Wiley On-line Library and ACS publications.

Results: *Aleurites moluccanus* are commonly used as a spice and flavoring element in cuisines, and their health advantages are well known. Perfumes contain them as well. Carbohydrates, proteins, minerals, lipids, essential oils, flavonoids, terpenoids, and carotenoids are among the chemical constituents of cardamom that have been identified through phytochemical investigations. Antioxidant, anti-diabetic, antibacterial, anticancer, gastroprotective, and insecticidal actions are only a few of the biological functions of the *A. moluccanus*. Further studies can be conducted to find out more about the pharmacological properties of the plant.

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Introduction

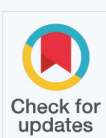
Plants have always played an important part in human medicine and wellness. Natural-based medications are progressively replacing synthetic drugs around the world. Different countries contribute to the worldwide market of medicinal plants by utilizing their capabilities, which include vegetation, climatic diversity, inexpensive energy, an adequate labor, and high-tech. Countries with high plant diversity and a wide variety of species like Indonesia and Malaysia have a long history of using medicinal plants in traditional medicine [1].

With about 300 genera and 8000 species, the Euphorbiaceae family is one of the largest groups of flowering plants, this family has a wide range

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of plants, from huge woody trees to simple weeds that grow prostrate on the ground. Many species in this family live in tropical climates and survive in the tropics, while others are rainforest trees and grasses [2].

Alternative medicine still uses several Euphorbiaceae plant mixtures, fresh latex, and teas. As an example, *Aleurites moluccanus* (L.) Willd, known for its healing properties to cure arthritis, asthma, bleeding, constipation, diarrhoea, dysentery, oedema, fever, gonorrhoea, headaches, haematochezia, haemorrhoids, rheumatism, ringworm, sores, sprue, swelling, and ulcers. Coughs, diarrhoea, chest pains, hernias, headaches, fever, ulcers and gonorrhoea, arthritis and other joint ailments were all treated with a decoction of the leaves [3-10].

Aleurites moluccanus (L.) Willd, is a Euphorbiaceae plant that is native to Indonesia, India, Malaysia, Polynesia, and the South Sea Islands. It has different nominations, including "Candlenut tree," "Kukui," and "Indian Walnut.", grows on roadsides, it was introduced in the first decades of the 20th century for its oil seeds, from which "tung oil" is obtained, and as an ornamental plant. *Aleurites moluccanus* produces spherical fruits with a thick, rough, hard shell that measure 5 cm in diameter or more. Each tree may generate 30-80 kg of nuts in a plantation [11].

However, the seeds are considered as dangerous when eaten [3]. Polyunsaturated molecules abound in the oil. The literature has already mentioned variations in the content of *A. moluccanus* oil. Walnut oil has been used topically to treat arthritis and other joint pains, according to reports [12,13].

Botanical Aspects

Aleurites moluccanus is 10-47 m tall, perennial, evergreen tree with an upper canopy. It's bark ranges in color from grey-brown to black. Along the stem and branches, leaves are placed alternately in a spiral pattern. The leaves are simple, whole, pubescent, petiolate, ovate-oblong or deltoid or shallowly 3-lobed, 24 cm long by 12 cm wide, with an acuminate apex and a rounded or slightly cordate base. The leaves are green above and a paler green. Younger trees, in particular, have larger, more deeply lobed leaves. Male and female flower parts appear in different flower clusters on the same tree, which bears flowers on axillary inflorescences. Flowers are 5-10 mm long and 5-8 mm wide, pale yellow or greenish white, with a prominent sepal whorl, pubescent elliptic spatulate

petals, unequal-length stamens, and a hairy ovary. A flaky, indehiscent, round to ovoid, 30-40 mm long, green or brown berry makes up the fruit. The 2.5 cm in diameter, hard, ridged, woody or stony-shelled seed is revealed when the outer skin rots away. A white, greasy, flaky kernel found inside the seed is made up of a thick endosperm surrounding a relatively tiny embryo [14-18] (Figure 1).

Chemical Composition

Alkaloids, polyphenols, steroids, flavonoids, tannins, coumarin, and triterpenoids, are components present, these compounds are responsible for the majority of the pharmacological activity [19-24].

Isolated Compounds

Various compounds have been isolated from the different parts of this plant included, n-hentriacontane, β -amyrin, α -amyrin, β -sitosterol, stigmasterol, and campesterol which were isolated by chromatography in the hexane and ethyl acetate fractions of the leaves. The compounds were more efficient than aspirin and paracetamol at preventing acetic acid-induced abdominal constriction [15,25]. Moluccanic acid, moluccanic acid 6,7-dehydromoluccanic acid and methyl ester, three novel 3,4-secopodocarpane-type trinorditerpenoids, were isolated from the twigs and leaves of *Aleurites moluccanus*, spectroscopic approaches, including 2D NMR research, were used to deduce their structures; these compounds were found to have cytotoxic activity against Raji cells (Burkitt's lymphoma) [26]. Liu HY, et al. [19] have succeeded in isolating four new podocarpane-type trinorditerpenes from twigs and leaves; (5 β ,10 α)-12,13 dihydroypodocarpa-8,11,13-trien-3-one, (3 α ,5 β ,10 α)-13 methoxyypodocarpa-8,11,13-triene-3,12-diol, (5 β ,10 α)-12-hydroxy-13-methoxyypodocarpa-8,11,13-trien-3-one, (5 β ,10 α)-13-hydroxy-12 methoxyypodocarpa-8,11,13-trien-3-one, 12-hydroxy-13-methylpodocarpa-8,11,13-trien-3 one, ent-3 α -hydroxypimara-8(14),15-dien-12-one, and ent-3 β ,14 α -hydroxypimara-7,9(11),15-triene-12-one and spruceanol were also isolated. Comprehensive spectroscopic analysis, including NMR and MS, were used to deduce their structures. A triterpene and a flavonoid C-Glycoside (swertisin and acetyl-aleuritic acid), were extracted from the leaves and barks, respectively, based on spectroscopic data. Swertisin was recently revealed to be an antibacterial agent [27]. Using UV-Vis spectrophotometer and NMR. Two compounds were isolated from the meth-

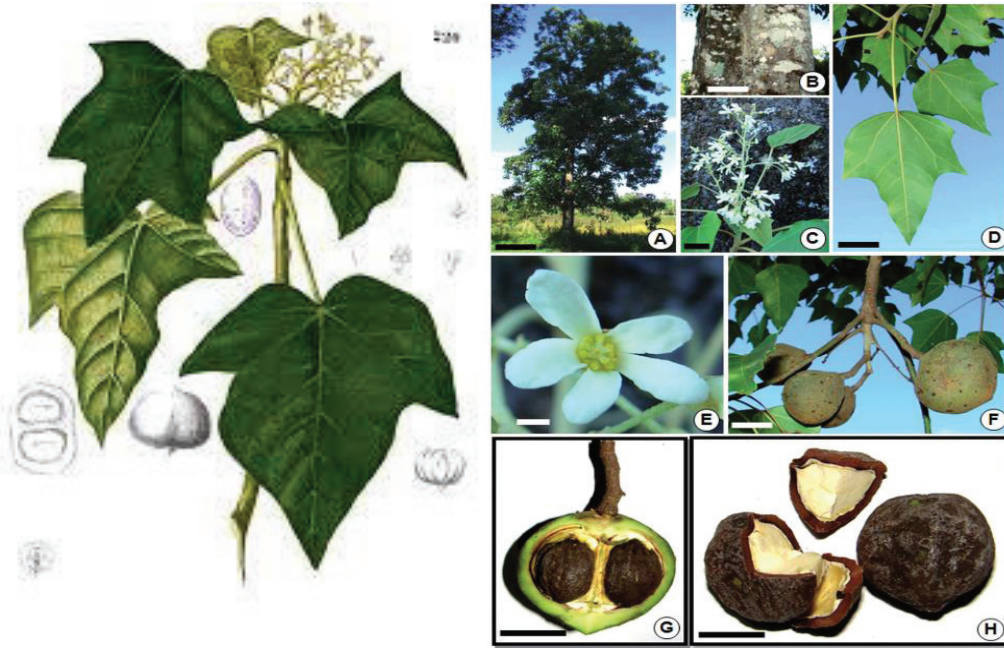


Figure 1 *Aleurites moluccanus*.

A). Adult specimen in Schwelm Park, Eldorado. **B).** Trunk. **C).** Flowering branch. **D).** Leaves. **E).** Flower. **F).** Fruit. **G).** Open fruit showing seeds. **H).** Seeds.

anolic extract from stem bark of *A. moluccanus*, the coumarin scopoletin and the pentacyclic triterpene 3-acetyl aleuritic [28]. The benzene extract of the heartwood of *A. moluccanus* yielded a novel phorbol diester, 13-O-myristyl-20-O-acetyl-12-deoxyphorbol. In addition hentriacontane, 6,7-dimethoxycoumarin (scoparone), 5,6,7-trimethoxycoumarin and β -sitostenone are being isolated this species [29]. Fatty acids 18:2 (43.8 mol%) and 18:3 (25.8 mol%) as well as delta-tocopherol were characterized by GC-MS in *A. moluccanus* seed oil [30]. 12-hydroxy-13-methoxy-8,11,13-podocarpatrien-3-one, spruceanol, and 3-acetylaleuritic acid were obtained by extensive 1D and 2D NMR spectroscopy from a dichloromethane extract of the bark of *Aleurites moluccanus* L. Willd [20]. Swertisine and 2'-O-rhamnosylswertisine, two flavonoids were separated from the ethyl acetate fraction of *Aleurites moluccanus* [31]. α -amyrenone, β -amyrenone, glutinol, α -amyrinewere and friedelenol also isolated from the plant in the dichloromethane fraction by gas chromatography [32] (Figure 2).

Pharmacological Properties

Antinociceptive activity

de Souza MM, et al. [33] examined the antinociceptive and anti-inflammatory properties of isolated compounds from *A. moluccanus* in

animal pain models. These compounds included acetyl aleuritic acid, atraric acid, spruceanol, (5,10)-12-hydroxy-13-méthoxy-8,11,13-podocarpatrien-3-one, and sonderianol. The hyperalgesia induced by carraghénine, PGE₂, cytokines, bradykinine, epinephrine, the complete Freund's adjuvant, and lipopolysaccharide were used to assess the antinociceptive and anti-inflammatory properties of the *A. moluccanus* egg extract. sonderianol. Up to 48 hours after receiving carraghénane, the (5,10)-12-hydroxy-13-méthoxy-8,11,13-podocarpatrien-3-one pur showed a beneficial effect, however the acetyl aleuritique acid was only effective for the first hour. Positive results were obtained from the production of hyperalgesia using the lipopolysaccharide and complete Freund's adjuvant models, These resulats support the antinociceptive and anti-inflammatory properties of *A. moluccanus* leaf extract. The effects were partially caused by the presence of (5,10), atraric acid, and acetyl acetate. -12-hydroxy-13-méthoxy-8,11,13-podocarpatrien-3-one [15,34,35].

Another study conducted by Cesca TG, et al. [35] which aims to develop an effective drug for topical use in the treatment of pain and that from inflammation and wound healing, containing 0.5 and 1.0% of standardized dry extract of *A. moluccanus*, the phytomedicine is composed of

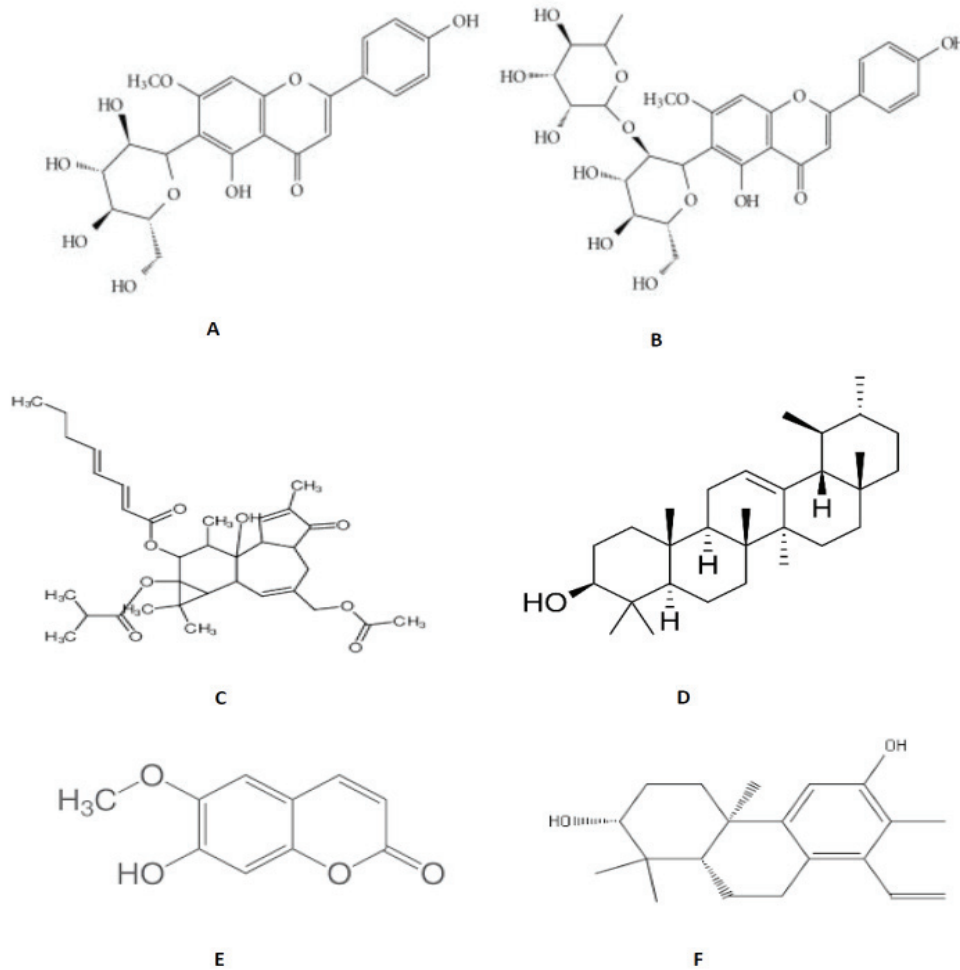


Figure 1 *Aleurites moluccana*.

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two flavonoids isolated from *A. moluccana* namely 2*-O-rhamnosylswertisin (I) and swertisin (II), , The phytomedicine was analyzed in the model of ear edema induced by croton oil in mice, in the healing process, using the excisional wound model in rats, and to prevent mechanical sensitization after plantar incision in rats in the postoperative pain model, The phytomedicine reduced ear edema by 37.675.7% and 64.876.2%, for 0.5 and 1.0% dry extract, respectively. The formulation also accelerated the healing process by up to 50.874.1% and 46.074.0% for 0.5 and 1.0% extract, respectively, and both amounts were able to prevent the development of mechanical sensitization after plantar incision in rats.

Antihypercholesterolaemic activity

In rats with Triton W-1339-induced hypercholesterolaemia and on a hyperlipemic diet,

methanol extract of the leaves of *A. moluccana* (300 mg/kg, body weight) lowered serum lipids (total cholesterol, LDL- and HDL-cholesterol and triglycerides) and body weight. The findings revealed that this natural extract's ability to lower cholesterol was caused by its ability to reduce intestinal lipid absorption and inhibit hepatic cholesterol production [36].

Cytotoxicity activity

Four novel trinorditerpenenes of the podocarpane class (5 b, 10 a) Dihydroxy-12,13-podocarpa-8,11,13-trien-3-one, (5 b, 10 a) 12H-13M-Podocarpa-8,11,13-trien-3-one, (5 b, 10 a) 13-hydroxy-12-methoxypodocarpa-8,11,13-trien-3-one and (3 a,5 b,10 a)-13-methoxypodocarpa-8,11,13-triene-3,12-diol were isolated from the twigs and leaves of *A.*

moluccanus, along with four other known diterpenes: spruceanol.

All compounds were tested for cytotoxicity, with the exception of 3 α ,5 β ,10 α)-13-methoxypodocarpa-8,11,13-triene-3,12-diol, and 13-O-myristyl-20-O-acetyl-12-deoxyphorbol showed only modest inhibitory action against Raji cells, with an IC₅₀ value of 4.24 mg/ml [37].

Anti-inflammatory activity

A. moluccanus dried leaf extract (AMME) was discovered to have antiinflammatory and antipyretic properties. Pre-treatment with the methanol extract (100–300 mg/kg, p.o.) significantly and dose-dependently avoided an increase in the volume of paw oedema. Similar to diclofenac (20 mg/kg, orally), a peak effect was seen at 300 mg/kg. Rats' body temperatures significantly decreased when given a 300 mg/kg dosage of the methanol extract from *Aleurites moluccana* [35,38–40].

Other Uses

There have been reports of Pacific Islanders, including Fijians, Hawaiians, and Tahitians, tattooing with caustic fruit wall juice and burned nuts. As soap and shampoo, Tongans used kernels that had been ground into a paste. The nuts have been made into toys like tops and marbles. As fish bait, the crushed kernels have been combined with various additives. The shells are used to create earrings and other costume jewelry because they can be polished to a high sheen. In Hawaii, Leis have traditionally been made from the nuts, flowers, and leaves' outer shells. After the new rice was dried in Malaysia, the nut was employed in social ceremonies together with an iron nail and cockle shells [15,41]. When bathing a baby with a fever in Malaysia, candle nuts, bryophyllum leaves, cockle shells, and iron nails were added to the water.

The wood can be used to make paper pulp, light furniture, small boats, canoes, small utensils, fuel wood, and matches. For the Hawaiian holiday of Makahiki, a wooden carving in the shape of a pig's head is set up on an altar [37,42]. Recent laboratory tests using the Formosan termite (*Coptotermes formosanus*) revealed that yellowpine wood treated with kukui oil (*Aleurites moluccanus*) was resistant to termite damage when the wood contained > 27% kukui oil by weight. Findings also showed that the oil operated more as a feeding inhibitor than as a toxin.

Conclusion

In order to emphasize the potential of this species as a viable source of new therapeutic candidates, this review highlighted a few notable chemical and biological publications on *A. moluccanus*. Being part of traditional knowledge among many tribes worldwide, this plant has been widely used in folk medicine since ancient times, according to a number of scientific discoveries. However, by employing various techniques to isolate more chemicals from *A. moluccana*, the research of secondary metabolites could be expanded. Additionally, the scant pharmacological data show that the biological activities have not been evaluated clinically. As a result, our work highlights the significant potential for conducting additional research and development in the revitalization of this species as a source of innovative therapeutic candidates.

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