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Ethnomedicinal Uses, Phytochemistry and Pharmacology of Few Species of Genus *Atalantia* (Rutaceae): A Review

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Abstract: Synthetic drugs show major side effects, as well as the fact that they have been discovered to be extremely harmful to human assistance, many synthetic medications claimed to be used for treatment are of the least interest today. Therefore, herbal medicines have acquired prominence in recent decades. This review's primary objective is to give a complete overview of three distinct species of the Genus *Atalantia* mainly *Atalantia monophylla* (Roxb) DC, *Atalantia racemaosa* Wight, *Atalantia wightii* Tanaka. The Genus *Atalantia* belongs to Rutaceae family and there are 22 accepted species of which three species are selected because these are available in Western Ghat region of Maharashtra, these species have ethnopharmacological significance and many of their facets are still unexplored. The *Atalantia* genus is utilized in conventional medicine to treat a diverse array of ailments like fever, rheumatic pains, cough, allergy, swelling, and as a blood purifier, etc. The current work is a comprehensive analysis of the published literature on phytochemical and pharmacological reports of the above species of *Atalantia* genus in an effort to deliver comprehensive information and suggest future research avenues. Out of these three species, *Atalantia monophylla* has received the most research attention but the remaining two species are not much explored. The aim of this review is to discuss the potential application of these three species as herbal medicine. The plant characteristics, ethnobotanical uses, phytochemistry, and pharmacological activities are summarized as a guide for phytochemical and pharmacological investigations.

Keywords: Genus *Atalantia*; Traditional uses; Morphology; Phytochemistry; Pharmacology.

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1. INTRODUCTION

Phytochemicals are the bioactive compounds isolated from medicinal plants, also called plant-derived chemicals, reduce the risk of various chronic diseases. As most of the phytoconstituents have been identified until now but still numerous constituents need to be characterized. However, most of the affirmation suggests that the phytochemicals are more beneficial as compared to current therapy as phytoconstituents are potent in their action, and also, they are safe for use (1).

There are 22 accepted species in the *Atalantia* genus (Rutaceae), which are distributed in the Indian mainland, Andaman and Nicobar Island, Srilanka, Myanmar, Thailand, Peninsular Malaya, North and South Vietnam, Laos, Cambodia, south China, Sumatra, and Java (2). Three of these species are found in southern India such as *Atalantia monophylla* (Roxb.) DC, *Atalantia racemosa* Wight, *Atalantia wightii* Tanaka. Atalantia genus species are generally found in the areas like forest edges, roadsides, around the sides of streams, and at the periphery of water bodies having sufficient sunlight (3).

The plants of this genus have large spins and are tiny to medium-sized trees or shrubs resembling citrus fruits in general aspects. The plants bear white fragrant flowers and small globose fruits having the appearance of tiny greenish-yellow limes or oranges. Citrus pulp vesicles are stalked, whereas sessile pulp vesicles are distinct. Leaves are unifoliate similar to citrus but shows differences like more prominent, numerous lateral veins and veinlets which form reticulations between lateral veins (3, 4).

Due to the increasing importance of this species, its utilization as traditional herbal medicine to treat a variety of illnesses has increased (5). *Atalantia monophylla* (Roxb.) DC is mostly found in evergreen South Indian forests that means at an altitude of 600m. Its common name is "wild lemon." *Atalantia racemosa* Wight is known as Bombay Atalantia. It is usually encountered at elevations between 150 and 1000 meters in peninsular Sri Lanka and India's evergreen regions. Nilgiri atalantia is a common name of *Atalantia wightii* and is indigenous to Western Ghats Shola forests with an altitude of 100 and 1700 meters (4).

2. METHODOLOGY

A systematic review of published research and peer-reviewed journals was conducted for this study. The electronic versions of the reviewed literature were obtained from PubMed, Science Direct, Scopus, Google Scholar, Springer Link, Taylor, and Francis, and Web of Science Core Collection. Using a search engine such as Google, an additional search was conducted to locate further reports, documents, and botanical databases up to January 2023. The literature reported in the last 10 years was taken into account for information. The keywords used while searching were Genus *Atalantia*, Phytochemistry, Pharmacology, and Traditional uses. The reports were scrutinized for relevance and included in the review.

3. RESULT AND DISCUSSION

These species are rich in phytochemicals which include several classes like alkaloids, steroids, flavonoids, tannins, terpenoids, saponins, coumarins, and phenolic compounds. These species contain triterpenes like friedelin, flavonoids like pyranoflavone, atalantaflavone, racemoflavone, and coumarins such as xanthyletin, xanthotoxin, luvangetin, racemosin, etc. These species mainly contain acridone alkaloids like cycloatalantaphylline-A, N-Methyl cyclo-atalantaphylline-A, N-Methylbuxifoliadine-E. It also contains caryophyllene, β- caryophyllene, caryophyllene oxide, D-limonene, decanal, β-phellandrene, eugenol, umbelliferone, rutarin, rutaretin, and furanocoumarins. The alkaloids possess several biological activities like inhibition of Epstein-Barr Virus, induction of human promyelocytic leukemia cell differentiation, and antiproliferative.

3.1. *Atalantia monophylla* Linn

Atalania monophylla contains essential oils in which methyl eugenol, elemicine, and sabinene are the major constituents. The root bark contains atalantin, stigmasterol, xanthyletin, sitosterol, tetratriterprnoid, and acridone alkaloids. The leaves contain friedelin and epifreidlanol.
The parts like leaves, roots, and fruits of this species are used medicinally. Traditional medicinal practitioners use leaves of *Atalantia monophylla* for treatment of glandular swelling, and rheumatoid arthritis. Decoction of leaves is used in skin problems and dysentery. Leaves and roots are used as blood purifiers. Oil from berries is used as a stimulant, anti-inflammatory, and in chronic rheumatism. The root is antiseptic, antispasmodic, and used in the treatment of snake bites. The leaf decoction is used in the treatment of cough, asthma, and bronchitis.

3.1.1. Ethnopharmacological activities of *Atalantia monophylla* Linn.
3.1.2. Chemical composition of *Atalantia monophylla* Linn
Atalantia monophylla root bark has been found to contain alkaloids and limonoids. Additionally, a terpenoid called atalatin was derived from acetone and is beneficial in treating rheumatism. Also other components like N-methylatalaphylline (IIb), N-methylbicycloatalaphylline IV, xanthyletin **(2)** were isolated. Atalaphylline **(1)** was recovered using pet. ether root extract (IIa) (22). Acridone alkaloids, cycloatalaphylline-A, N-methylcycloatalaphylline-A, and N-methyl buxifoliadine-E **(3)** were recovered from dichloromethane extract. It contains 8 types of known acridone alkaloids such as buxifoliadine-E, N-methylataphylline, atalaphylline, citrusinine–I **(4)**, N-methylatalaphyllin, yukocitrine, junosine, and two recognized coumarins as *Atalantia monophylla* auraptene and 7-O-geranyl scopoletin were isolated from acetone extract of roots, among them buxifoliadine –E shows potent anti-allergic property. 5-hydroxydictamnine and ß-sitosterol were extracted from *Atalantia monophylla* hardwood petroleum ether extract (23). Methanolic fruit extract contains hexadecanoic acid (**5**), brassicaterol (**6**), 3-bromocholest-5-ene, sinapinaldehyde, etc (52).

The bark from the roots of the *Atalantia monophylla* has been proven to include three different forms of limonoids, such as atalantolide, atalantin (24) and dehydroatalantin (25) (24). There seem to be further findings of two tetranotriterpenoids with biogenetically unique properties in root bark (25).

Table 1: Ethnopharmacological activities of *Atalantia monophylla* Linn.

Part Used	Treatment	Method of preparation	Treatment with dosage	References
Leaves, fruits	Rheumatic pain, Joint pain	Aqueous extract, Fruits juice	twice per day Externally applied	5
Leaves, fruits	Skin infection	Leaf extracts	Externally applied twice per day	13
Root	Cough with phlegm	Root decoction	One glass decoction per day for 2-3 days	14
Leaves	Rheumatic pains	Leaves decoction	One cup orally once a day	15
Leaves, Fruits	Chronic Rheumatic pain, Paralysis	Leaf oil	Apply twice per day for8–10 days	16
Fruits	Stimulant	Mature fresh fruit juice	1 glass once a day for a week	17
Leaves	Fever in adult	Leaf powder	About 10 g daily in the morning for a week	18
Leaves	Swelling and Joint pain	Aqueous extract of leaves	Used externally for applying 2 times a day for 5–8 days	19
Leaves	Fever, cough	Aqueous extract of leaves	Daily early morning 2 times for 2–3 days	20
Leaves, Fruits, bark	Coetaneous complaints, itch, Antispasmodic, Stimulant	A decoction of the leaves	Applied externally in apply 2 times 5–8 days	21

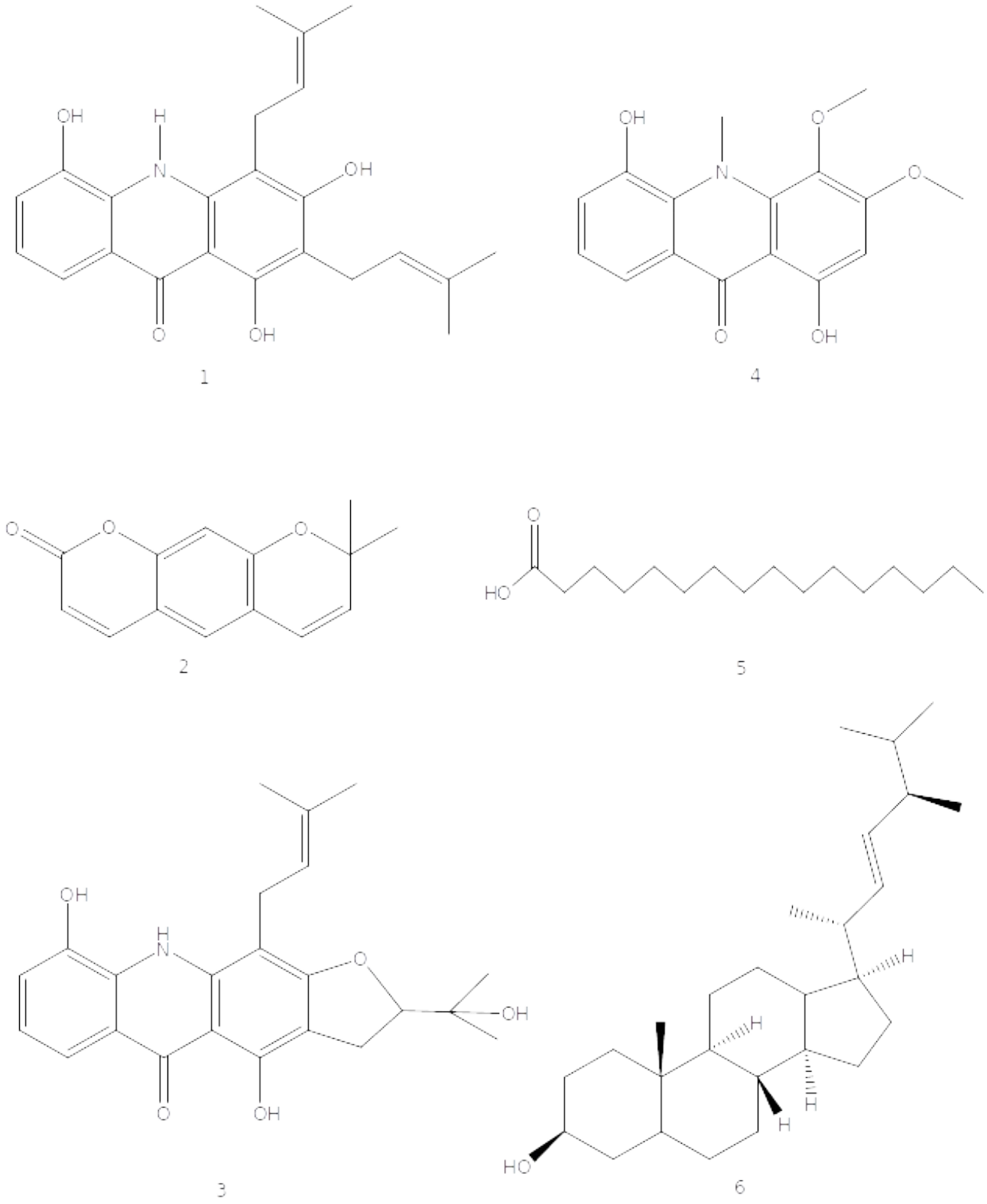


Figure 1: Structure of chemical moieties from *Atalantia monophylla* Linn.

3.1.3. Pharmacological activities of *Atalantia monophylla* Linn

Table 2: Pharmacological activities are summarized in the following table.

Activity	Part Used	Treatment	Method of preparation	References
Larvicidal and antifeedant activity against *Earias vittella* fab	Hexane, chloroform, as well as ethylacetate extracts from leaves	Bhendi fruit borer method	Hexane extract exhibited great larvicidal and antifeedant activity.	26
Synthesis of new alkaloid-5-Hydroxydictamnine	Petroleum ether from the heartwood	The extracts were then chromatographed by eluting them with increasing amounts of polar solvents	The eluents collected from Benzene: chloroform shows β-sitosterol while chloroform: ethyl-acetate shows 5-Hydroxy-dictamnine	27
Ability to combat diabetes in alloxan-induced mice.	Methanolic bark extract	Levels of lipids, and sugar in serum were measured, including total cholesterol, triglycerides, HDL, LDL, and VLDL.	Methanolic bark extract showed potent antidiabetic activity	12
Investigation of ovicidal capacity	Leaves were extracted by using hexane, ethyl acetate, and chloroform.	Eggs of *Spodoptera litura* Fab treated with the extract.	The ovicidal property was shown by fractions of hexane extracts.	28
The pharmacognostic study, physicochemical evaluation, and phytochemical analysis	Leaves	Morphology, microscopy, leaf constants, total/acid insoluble/ water soluble ash, extractive values, preliminary screening, etc.	The standardization of the plant is aided by using this data.	29
Testing bioefficacy against *S. litura* Fab	Leaves were extracted by using chloroform, Hexane, and ethyl-acetate.	Anti-feedant, larvicidal, pupicidal activity	Potent action was shown by hexane extract. Out of 12 fractions of hexane extracts, 9th fraction showed maximum activity	30
Immuno-modulatory activity	Pet. ether, chloroform, and methanolic fractions of root ethanolic extracts	*E. coli*- induced abdominal sepsis, carbon clearance test, cell-mediated immune response, sheep erythrocyte agglutination test.	The methanolic fraction of ethanolic extract showed significant immunomodulatory activity.	31
Antioxidant, and antibacterial effect of oil	Essential oil from leaves	Hydro distillation and analysis of essential oil for its chemical composition, five different antioxidant methods, and antibacterial potential by using the broth dilution method	Oil had shown potent bioactive compounds and shows potent antibacterial and antioxidant activity.	32
In vitro antioxidant potential of ethanolic extracts from leaves	Ethanolic extract of leaves	DPPH-photometric assay, Iron-chelating Superoxide/, Hydroxyl/ Nitrous oxide radical scavenging, Ferric-ability power, and Total phenol/flavonoids/antioxidant content was used to assess antioxidant activity	Phenolic and flavonoids may act as the main antioxidants, and might serve as free radical inhibitors and thus possess antioxidant activity.	33

Anti-genotoxic and apoptotic activities	Oil from leaves	Prevention of DNA damage from H_2O_2 through anti-genotoxic characteristics (100 M) in 3T3-L1 cells and inhibition of growth of cervical cancer cells (HeLa)	The oil contains a promising natural compound that can be used to obstruct the growth of cancer cells and other dreadful ailments.	34
Toxic effects on *Sitophilus oryzae* and *Callosobruchus maculatus*	Oil from leaves	Toxicity was tested by methods like repellent activity, ovicidal activity, fecundity, and fumigation activity.	Oil showed good insecticidal, repellent, and ovicidal activity, also reduced Adult fecundity and emergence in test insects.	35
Free radical scavenging effect of stem and leaves	Pet ether, $CHcl_3$, CH_3H_6O, and CH_3OH extracts of stems and leaves.	DPPH, superoxide radical scavenging activity, phosphomolybdenum analysis, metal chelating, FRAP assay.	Methanolic extract of leaves and stems possess high antioxidant activity.	36
Phytochemical evaluation and anti-microbial activity	Ethanol, chloroform, and ethyl-acetate extract from leaves	3 Gram-positive and 6 Gram-negative bacteria were tested by the diffusion method	The potent activity was shown by the ethanolic extract.	37
A unique flavonoid in *A. monophylla* (Linn) DC leaves	Leaves are extracted by using hexane, ethyl acetate, and methanol.	*In vitro* cholinesterase and antioxidant activity.	Isolated atlantraflavon and eight known compounds show anticholinesterase and antioxidant activity.	38
Characterization and antibacterial evaluation of nanoparticles made from *A. monophylla* leaf extract.	Zinc oxide nanoparticles from methanolic leaf extract	Agar well diffusion method	Nanoparticles effectively destroyed bacteria and fungi more than plant extracts and conventional medications	39
Novel limonophyllines A–C that are poisonous to HepG2 and cholangiocarcinoma cell lines.	Hexane, ethyl acetate, and methanolic extracts of stem	All isolates were tested against KKU-M-156, Hep-G2, and cholangiocarcinoma cell lines.	All isolated compound structures were identified by spectroscopic analysis such as 1D and 2D NMR, IR, and mass spectrometry, and possess anticancer activity.	40
Anti-bacterial properties were studied on portions isolated from *C. guianensis* and *A. monophyla*	Ethanolic extract of leaves	Agar disc diffusion assay	Among the three fractions, fractions II and III showed the highest zone of inhibition	41
Extraction of Styrene from *Atalantia monophylla* seeds	Hexanes, ethyl acetate, and methanolic extracts from seeds	^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy	Atalantrenes A-D (1-4), four novel dimeric styrenes, was extracted from ethyl acetate, and structures were identified from spectroscopic analysis.	42

3.2. *Atalantia racemosa* Wight & Arn

The leaves of *Atalantia racemosa* contains terpene, friedelin and four coumarins like xanthyletin, luvangetin, racemosin and xanthotoxin. It also contains umbelliferone, rutaretin, rutarin, pyranoflavones like atalantoflavone, racemoflavone.

Atalantia racemosa has been used traditionally in skin itching, snake bite, paralysis, and chronic

rheumatism. The leaves decoction is used treatment of bronchitis, asthma, and cough. The poultice of leaves is applied to wounds and the extract of leaves is used to treat eczema. The roots are used to combat dropsy.

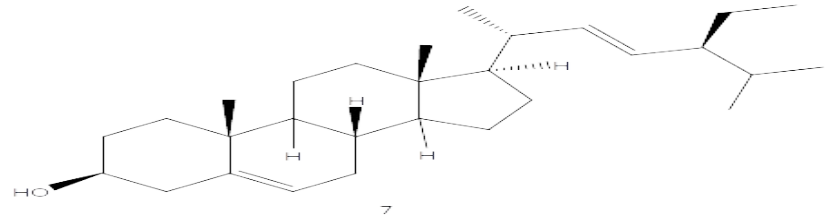
3.2.1. Ethnopharmacological activities of *Atalantia racemosa* Wt

Table 3: Ethnopharmacological activities of *Atalantia racemosa* Wt

Part Used	Treatment	Method of preparation	References
Leaves	Asthma, cough, bronchitis	Decoction	7
Leaves	Bronchitis	Chewed	7
Leaves, roots	Blood purifier	Decoction	7
Root	Allergy	Root paste	44
Leaves	Repeating fever	Leaves in boiled water for bath	44
Leaves	Acidity	Leaf juice	45
Fruit oil	Paralysis and Chronic Rheumatism	Oil from fruit	46

3.2.2. Chemical composition of *Atalantia racemosa* Wt

Atalantia racemosa was found to contain pyranocoumarins, atalantin **(24),** xanthyletin **(2)**, atalaphyllinine **(26)**, friedelin **(27)**, recemosin **(15)**, umbelliferone **(16)**, rutaretin, triterpene friedelin, xanthotoxin, etc. It also contains pyranoflavones like atalantoflavone **(17)**, racemoflavone. Other compounds present are stigmasterol **(7)**, campesterol **(8)**, β-sitosterol (**9**), n-Hexadecanoic acid **(5)**, eicosanoic acid (**10**) (2). Methanolic extract of the fruit contains heptafluorobutyrate (**11**), N-octadecanoic acid methyl ester (**12**), tetradecanoic acid (**13**), campesterol **(8**), stigmast-4-en-3-one **(14),** etc (52).



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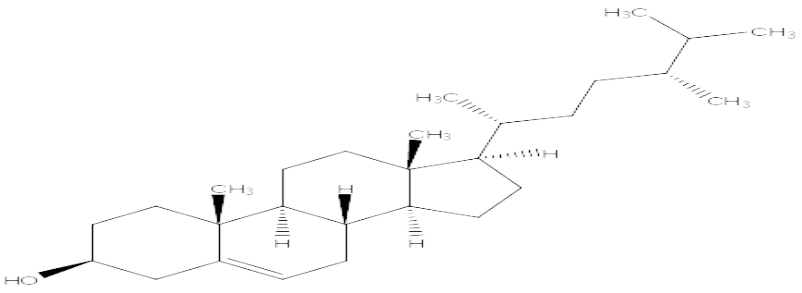

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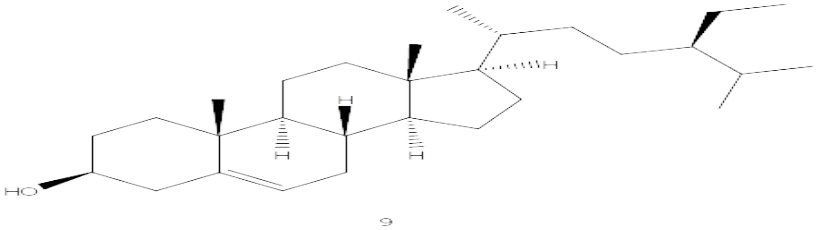

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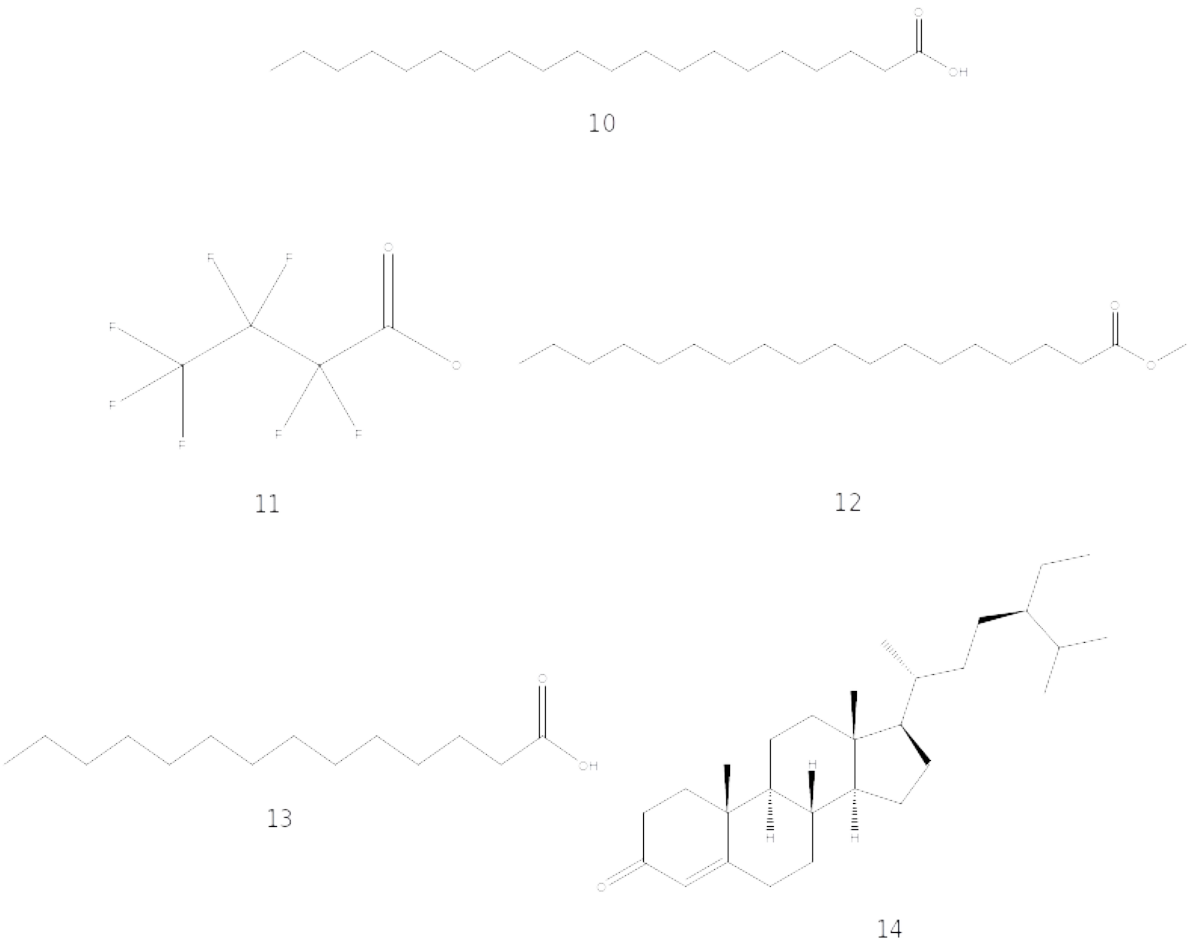


Figure 2: Structure of chemical moieties from *Atalantia racemosa* Wight & Arn

3.2.3. Pharmacological activities of *Atalantia racemosa* Wt

Table 4: Pharmacological activities are summarized in the following table.

Activity	Part Used	Treatment	Method of preparation	References
Comparison of three *Atalantia* species for volatile oil composition	Leaves	GC-MS analysis	*A monophylla* mostly contains ether compounds while Sesquiterpenes are the significant component in both *A racemosa* and *A wightii*.	47
Examination of three different species of *Atalantia* genus for their larvicidal efficacy and essential oil content.	Oil obtained from leaves by distillation	The larvicidal activity was tested on mosquito vectors like *A. aegypti, A. stephensi,* and *C. quinquefasciatus* and GC-MS analysis.	The larvicidal activity was shown by all species and GC-MS analysis shows that *A monophylla, A racemosa,* and *A wightii* contain 27, 65, and 64 compounds respectively.	48
Ability to combat diabetes in alloxan-induced mice.	Methanolic bark extract	Levels of lipid, sugar in serum were measured, including total cholesterol, triglycerides, HDL, LDL,	Methanolic bark extract showed potent antidiabetic activity	12

		and VLDL.		
Antioxidant potential and isolation of bio-active compounds by GCMS	Methanolic fruit extracts	DPPH and Phospho-molybdenum method	In DPPH method *Atalantia monophylla* and in the phospho-molybdenum method all extracts showed significant activity.	2
In vitro antioxidant and antimicrobial potential	Leaf extracts	*In vtrio* assays such as DPPH, hydroxy radical scavenging, ABTS radical cation, phosphomolybdenum, and ferric reducing power assay and well diffusion	Possess a powerful source of antioxidants that can combat a variety of free radicals.	49
Evaluated several medicinal plants for anti-microbial properties	Methanol, ethyl acetate, and acetone extracts from leaves	Agar well diffusion method	All extracts were found to be significant against bacteria and fungi.	50
Qualitative analysis of compounds of selected medicinal plants	Acetone, ethyl-acetate, methanol, and water extracts	Phytochemical screening	Quinoline derivatives, coumarins, phenolic compounds, flavonoids, tannins, catechins, alkaloids, terpenoids, and saponins are prevalent in these plants	51
Antioxidant, a-glucosidase, and Alpha-amylase inhibitory properties	Different crude solvent extracts of leaves.	Antioxidant activity by radical activities of scavenging of DPPH and ABTS methods. Antidiabetic by using the alpha-amylase and alpha-glucosidase inhibition assay.	Potent antioxidant, α-amylase, and α-glucosidase inhibitory activities were shown by *A. racemosa* extracts.	52
Investigation of the morpho-anatomical characteristics	Roots, stems, and leaves	Morphological and microscopical analysis	Characteristics clearly distinguish it from other adulterant taxa in terms of anatomy	43
Phytochemical analysis and anti-bacterial effect	Chloroform, acetone, methanol, and aqueous extracts	Agar plate well diffusion method against four different bacterial strains namely *Bacillus subtillis, Staphylococcus, Escherichia,* and *Klebsiella.*	Methanolic extract gave more positive results than the other extracts.	53
Anatomy of the leaf.	Leaf	Sectioning and Photomicrographs	Anatomical findings show the presence of different structures in the midrib and lamina portions, which help in the authentication of plant.	54

3.3. *Atalantia wightii* Tanaka

Atalantia wightii is used to shock the fish during fishing activity (57). Coumarins like umbelliferone and geranyl umbelliferon were revealed to exist in *Atalantia wightii.* Also, a few triterpenes like lupeol, lupenone, and epi-friedelinol were proven to occur in *Atalantia wightii* (58).

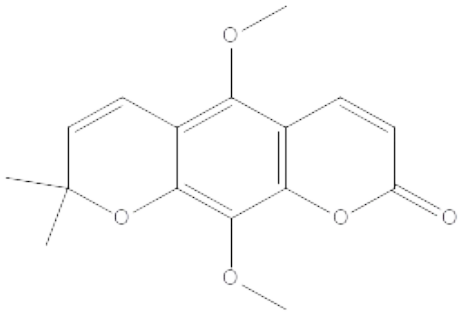
3.3.1. Ethnopharmacological activities of *Atalantia wightii* Tanaka

Table 5: Ethnopharmacological activities of *Atalantia wightii* Tanaka

Part Used	Treatment	Method of preparation	References
Fruits	Rheumatism	Oil from fruit	2
Fruits	Edible purpose	Pickle	2

3.3.2. Chemical composition of *Atalantia wightii* Tanaka

Atalantia wightii was found to contain umbelliferone **(16),** atalantin **(24)**, dehydroatalantin **(25)**, hexadecenoic acid methyl ester **(5)**, heptadecoinoic acid methyl ester **(23)**, racemosin (**15**), umbelliferone (**16**), atlantoflavone (**17**), undecanoic acid methyl ester (**18**), etc (2). Methanolic extract of the fruit contains 1,1 dichloro-2-dodecanol (**19**), Methyl 10-undecenoate (**20**), heptadecanoic acid (**21**), Phthalic acid **(22)**, ditridecyl ester, stigmasterol (**7**), β-sitosterol **(9)**, etc (52).



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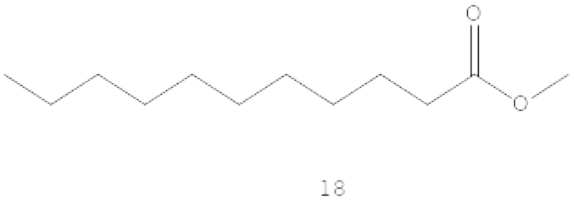

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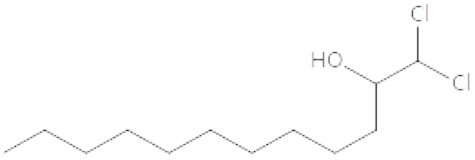

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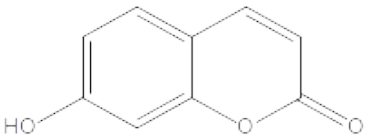

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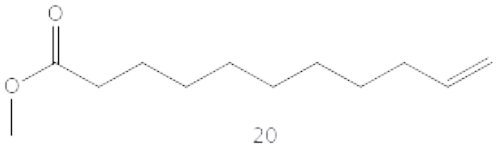

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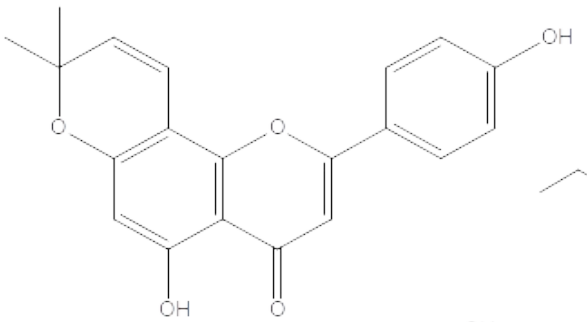

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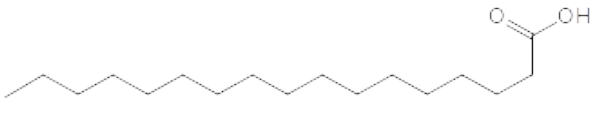

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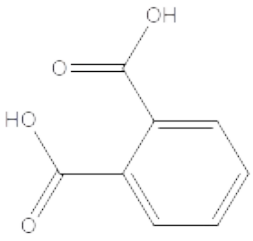

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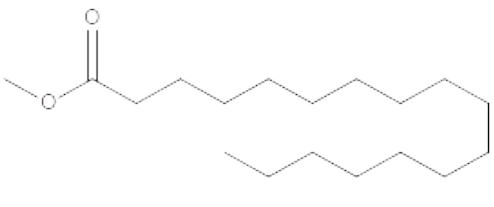

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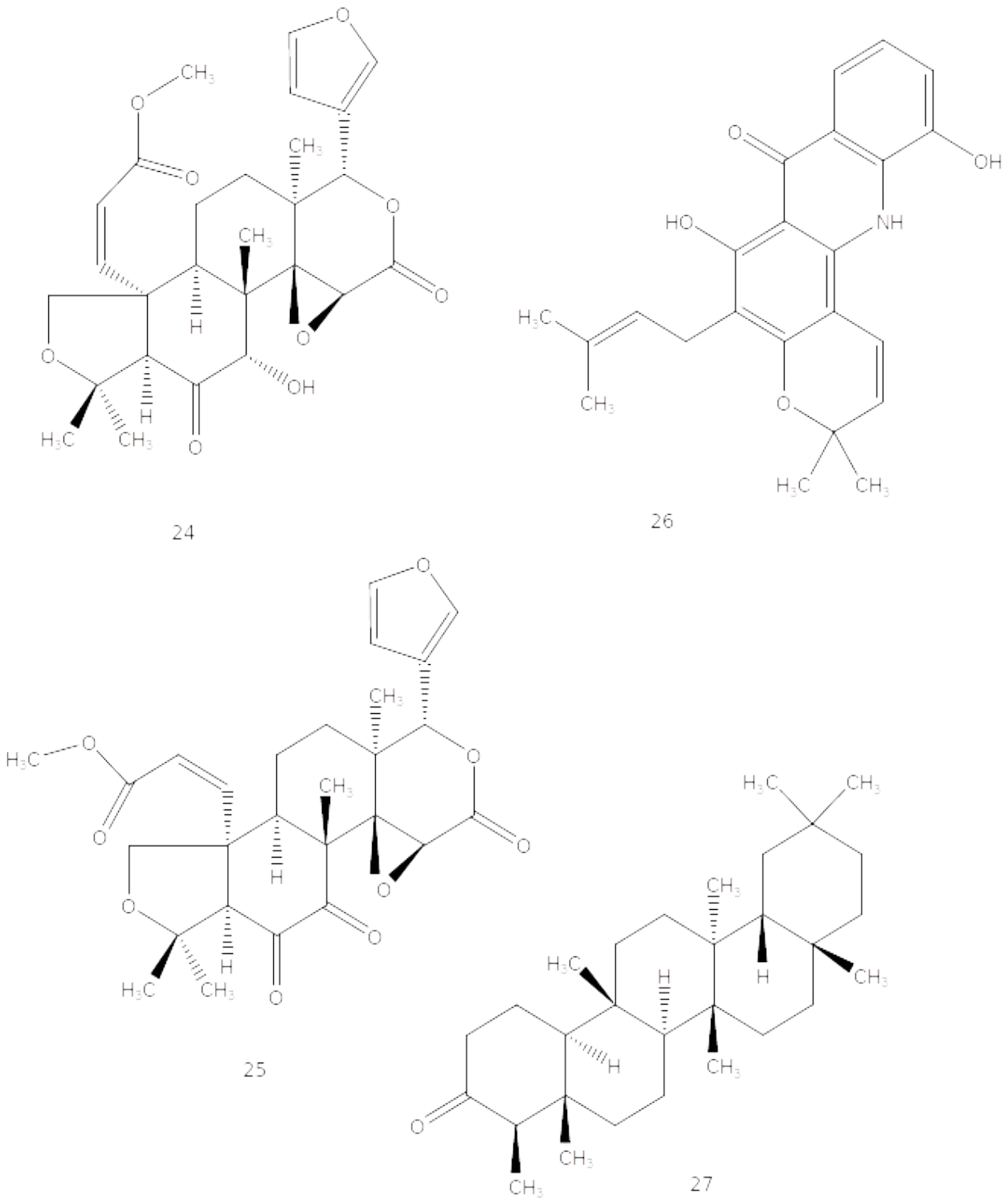

Figure 3: Structure of chemical moieties from *Atalantia wightii* Tanaka

3.3.3. Pharmacologıcal actıvities of *Atalantia wightii* Tanaka

Table 6: Pharmacological activities are summarized in the following table.

Activity	Part Used	Treatment	Method of preparation	References
Investigation and comparison of the chemical nature of oils from three Atalantia species	Fresh leaves	GC-MS analysis	The percentage of oil was found to be 0.2% in *A. monophylla*, 0.17% in *A. racemosa*, and 0.31% in *A. wightii*	47
Phytochemical investigation.	Leaves extracted using water, chloroform, and ethanol	Phytochemical screening	Alkaloids, glycosides, amino acids, phenolic compounds, proteins, and tannins were present	59
Antioxidant potential of 3 different species of the Atalantia genus	Fruits methanolic extract	Phospho-molybdenum method	Free radical scavenging was shown by all extracts	2

4 CONCLUSION

Based on ethnopharmacological claims of the genus *Atalantia*, the current review discusses conventional uses, phytochemical moieties, and pharmacological activities. A detailed literature survey indicated that most of the varieties are utilized traditionally in various countries including India. Only a couple of varieties have undergone scientific evaluation to determine which phytochemical components may be responsible for a certain pharmacological activity. This review is an in-depth explanation of the traditional use, chemical composition, and therapeutic aspects of the genus *Atalantia* using *Atalantia monoplylla, Atalantia racemosa, and Atalantia wightii*. The species *Atalantia monophylla* has received the most research attention and is crucial to the manufacture of biodiesel. Although these two species have ethnomedical claims to be useful for the human ailment, there hasn't been much of an evaluation. Therefore, additional meticulously planned and in-depth clinical research that concentrates on mechanism-based *in vitro* and *in vivo* studies is needed to comprehend the underlying mechanisms connected to ethnopharmacological applications.

5 CONFLICT OF INTEREST

The authors declare no conflict of interest in this article.

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