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REVIEW Article

Scientific Evidence on *Atlantia monophylla*: A Systematic Review of Its Phytochemistry, Bioactivity, and Safety Profile

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Abstract

Atlantia monophylla (L.) Correa, a member of the Rutaceae family, is a medicinal plant widely distributed in South and Southeast Asia and traditionally utilized for the treatment of various ailments including infections, inflammation, and metabolic disorders. In recent years, increasing scientific attention has been directed toward understanding the phytochemical composition and pharmacological properties of this plant. The present systematic review aims to comprehensively summarize the available literature on the phytochemistry, pharmacological activities, toxicity profile, and emerging therapeutic potential of *Atlantia monophylla*. Extensive studies have identified a wide range of bioactive constituents such as flavonoids, alkaloids, phenolic compounds, coumarins, terpenoids, and essential oils in different parts of the plant. These phytochemicals contribute to diverse biological activities including antioxidant, antimicrobial, anti-inflammatory, ant diabetic, and anticancer effects. Experimental investigations have demonstrated that extracts and isolated compounds from *A. monophylla* exhibit significant free radical scavenging activity, inhibition of pathogenic microorganisms, and modulation of inflammatory pathways. In addition, certain alkaloids and flavonoids isolated from the plant have shown promising cytotoxic activity against cancer cell lines, suggesting potential applications in oncology research. Toxicological evaluations indicate that plant extracts are relatively safe at moderate doses; however, further detailed safety assessments and clinical investigations are required. Recent advances in nanotechnology have also opened new opportunities for enhancing the therapeutic efficacy of *A. monophylla* phytochemicals through nanoparticle-based drug delivery systems, which may improve bioavailability, stability, and targeted delivery. Overall, the available evidence highlights the significant pharmacological potential of *Atlantia monophylla* and underscores the need for further mechanistic studies, isolation of novel compounds, and well-designed clinical trials to fully explore its therapeutic applications in modern medicine.

1. Introduction

Natural products have historically served as a cornerstone for the discovery of therapeutic agents, with a substantial proportion of modern drugs being derived from plant sources. Among medicinal plants belonging to the Rutaceae family, *Atlantia monophylla* (L.) Correa has attracted growing scientific interest due to its diverse phytochemical constituents and broad spectrum of biological activities[1-3]. This plant is widely distributed across South and Southeast Asia and has been traditionally used in indigenous medicine to treat inflammation, infections, and metabolic disorders[4]. Traditional medicinal knowledge has often guided the scientific exploration of plant-derived compounds, and *A. monophylla* is no exception. Over the past two decades, several phytochemical and pharmacological studies have attempted to elucidate the bioactive constituents responsible for the therapeutic properties of this plant. Investigations have revealed the presence of various secondary metabolites including flavonoids, alkaloids, coumarins, and essential oils that contribute to its pharmacological activities. In addition, emerging research suggests that these bioactive compounds may have potential applications in the management of chronic diseases such as cancer, diabetes, and neurodegenerative disorders. Therefore, a systematic synthesis of existing literature is necessary to consolidate the available knowledge and identify future research directions for *A. monophyla*.[5-7]

2. Botanical Description and Taxonomy[8-10]

Atlantia monophylla is a small evergreen shrub or tree belonging to the Rutaceae family, which includes many economically and medicinally important plants such as citrus species. The plant is commonly found in tropical and subtropical regions of India, Sri Lanka, Thailand, and Malaysia (8). It typically grows in dry deciduous forests and coastal areas, demonstrating remarkable adaptability to varying environmental conditions. The plant is characterized by simple, leathery leaves, fragrant white flowers, and small berry-like fruits. Taxonomically, *A. monophylla* is closely related to other citrus species and shares several morphological and phytochemical characteristics with them. The fruit peel and leaves are often rich in aromatic compounds, which contribute to the plant's characteristic fragrance. Traditional healers have used different parts of the plant, including leaves, fruits, and bark, for various medicinal purposes. Ethno botanical surveys indicate that the leaves have been used as insect repellents, while the roots and bark have been applied in traditional remedies for swelling and inflammatory conditions. Such ethno medicinal uses have encouraged scientific studies investigating the chemical composition and pharmacological activities of the plant.

Fig.1A: Pictography of *Atlantia monophylla*

Kingdom:	Plantae
Clade:	Tracheophytes
Clade:	Angiosperms
Clade:	Eudicots
Clade:	Rosids
Order:	Sapindales
Family:	Rutaceae
Genus:	*Atalantia*
Species:	*A. monophylla*

3. Ethnomedicinal Uses[11-13]

Ethno medicinal knowledge provides valuable insights into the therapeutic potential of medicinal plants and often serves as a foundation for pharmacological research. In traditional medicine systems across India and Southeast Asia, *Atlantia monophylla* has been used for a variety of therapeutic purposes. The leaves are commonly applied externally to treat inflammatory conditions and skin infections. In some regions, crushed leaves are used as a natural insect repellent due to their strong aromatic properties. The fruits are occasionally used in traditional remedies for digestive disorders, while decoctions of the root bark have been employed to treat swelling and pain. In rural communities, plant-based preparations derived from *A. monophylla* are also used to manage fever and microbial infections. The widespread ethno medicinal use of this plant indicates that it contains biologically active compounds capable of exerting multiple therapeutic effects. Modern pharmacological investigations have provided scientific evidence supporting several of these traditional claims, thereby validating the importance of this plant in traditional healthcare systems.

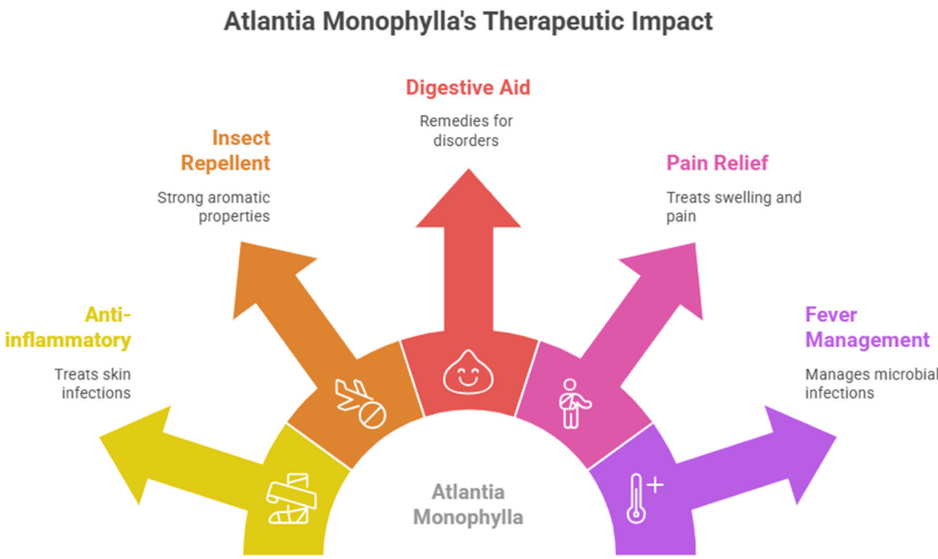

Fig.1B: Therapeutic potential of *Atlantia monophyla*

Leaf morphology

The leaves of *Atalantia monophylla* are simple and unifoliolate, meaning they appear as a single leaflet rather than a compound structure. They are arranged alternately along the stem and typically exhibit an elliptic to oblong or ovate shape. The leaf apex is usually acute or slightly obtuse, while the base may be rounded or tapering. The margins are entire and smooth, lacking serrations. The leaves possess a leathery (coriaceous) texture and are dark green and glossy on the upper surface, with a comparatively lighter underside. The petiole is short and may be wingless or narrowly winged. A characteristic feature is the presence of oil glands within the leaf tissue, which release a mild citrus-like aroma when crushed, reflecting its belonging to the Rutaceae family.

Root morphology

The root system of *Atalantia monophylla* is typically a well-developed taproot system, consisting of a prominent primary root that penetrates deeply into the soil. This main root is supported by numerous lateral roots that extend horizontally, enhancing stability and absorption capacity. The roots are woody and firm in mature plants, with a brown outer surface and a lighter internal tissue. This structure allows the plant to anchor effectively and efficiently absorb water and nutrients, particularly in dry or semi-arid environments. The deep taproot system also contributes to the plant's drought tolerance, making it well adapted to challenging ecological conditions.

4. Pharmacognostical Studies[14]

Pharmacognostic evaluation plays an essential role in the identification, authentication, and quality control of medicinal plants. Detailed macroscopic and microscopic examinations of different plant parts such as leaves, stems, and roots provide diagnostic characteristics useful for pharmacological and pharmaceutical investigations.

Morphological Description[14]

The stem is woody and bears sharp spines, while the bark is smooth and greyish. Leaves are simple, ovate to elliptic, and glabrous with entire margins. The flowers are small, white, and arranged in clusters with a mild fragrance. The fruit is a subglobose berry containing few seeds, resembling small citrus fruits.

Pharmacognosy of Atalantia monophylla[15]

ROOT

The root of *Atalantia monophylla* is cylindrical, woody, and brown in color with a slightly aromatic odor. Microscopically, it shows well-developed secondary xylem, cork cells, and distinct medullary rays. It contains bioactive compounds like alkaloids and flavonoids. Traditionally, it is used for treating cough, rheumatism, and inflammatory conditions.

STEM

The stem is hard, woody, and characterized by the presence of sharp spines. Young stems are green and become brown upon maturation. Anatomically, it shows a thick cortex and well-developed vascular bundles arranged in a ring. It is used in traditional medicine for managing arthritis and rheumatic pain.

BARK (Stem Bark & Root Bark)

The bark is thin, smooth, and brownish-grey in appearance. Microscopically, it contains cork cells, phloem fibers, and calcium oxalate crystals. It is rich in tannins, glycosides, and alkaloids contributing to its medicinal properties. The bark is used in the treatment of rheumatoid arthritis, heart disorders, and postnatal conditions.

FRUIT

The fruit is a small, round berry resembling citrus fruits, turning yellow or orange upon ripening. It has a fleshy mesocarp and contains oil glands typical of Rutaceae plants. Phytochemically, it is rich in essential oils, flavonoids, and antioxidants. It is traditionally used for cough, gastritis, skin diseases, and as an anthelmintic agent.

PHYTOCHEMICAL CONSTITUENTS[16]

The plant contains a variety of bioactive compounds including alkaloids, flavonoids, phenolic compounds, and glycosides. Essential oils are also present, especially in the fruit and leaves. These compounds contribute to its antioxidant and antimicrobial activities. The phytochemical richness supports its wide ethnomedicinal applications.

PHARMACOLOGICAL ACTIVITIES[17-25]

Atalantia monophylla exhibits several pharmacological properties such as anti-inflammatory, antioxidant, and antimicrobial activities. It also shows immunomodulatory and anthelmintic effects in experimental studies. These activities are attributed to its diverse phytochemical composition. The plant has potential for further drug development and clinical research. Diagnostic characters such as lignified xylem vessels, thick periderm layers, and parenchymatous cortex are useful markers for the identification and standardization of the root material used in herbal preparations.

Table.1. Reported activities in *A. monophylla*

Sl. No	Plant Part	Biological Activity	Extract / NPs	In-vitro / In-vivo
1	Leaves	Antibacterial and antifungal activity	Aqueous leaf extract	In-vitro
2	Leaves	Antioxidant and antifungal activity (DPPH, NO, H_2O_2 scavenging)	Ethanol leaf extract	In-vitro
3	Bark	Antioxidant activity (DPPH, NO, H_2O_2 radical scavenging)	Methanolic bark extract	In-vitro
4	Fruit peel	Antidiabetic / hypoglycemic activity	Aqueous fruit peel extract	In-vivo (alloxan-induced diabetic mice)
5	Leaves	CNS activity (behavioral models for neurological disorders)	Hydro-alcoholic leaf extract	In-vivo (animal models)
6	Leaves	Mosquitocidal / larvicidal activity	Methanolic leaf extract	In-vitro (mosquito larvae assays)
7	Leaves	Antifeedant, larvicidal, pupicidal activity against insect pests	Hexane, chloroform, ethyl acetate extracts	In-vitro bioassay
8	Leaves	Ovicidal activity against agricultural pests	Hexane, ethyl acetate, chloroform leaf extracts	In-vitro

5. Phytochemical Composition[26]

Phytochemical investigations of *Atlantia monophylla* have revealed a complex mixture of secondary metabolites that contribute to its pharmacological activities. Preliminary phytochemical screening has demonstrated the presence of flavonoids, tannins, phenolic compounds, alkaloids, terpenoids, steroids, and glycosides in various plant extracts. These compounds are widely recognized for their biological activities, particularly their antioxidant, antimicrobial, and anti-inflammatory properties. Advanced analytical techniques such as gas chromatography–mass spectrometry (GC–MS), high-performance liquid chromatography (HPLC), and nuclear magnetic resonance spectroscopy have been employed to identify and characterize specific bioactive molecules present in the plant. The presence of these diverse phytochemicals suggests that *A. monophylla* may exert its therapeutic effects through multiple biochemical pathways. Such chemical diversity also enhances the potential of the plant as a source of novel drug leads for pharmaceutical development.

Sl. No	Plant Parts	Phytochemicals	Presence in the Compounds	Molecular Formula
1	Heart wood	Alkaloid	5-Hydroxydictamine, β-sitosterol, Furoquinoline	$C_{29}H_{50}O$
2	Root bark	Alkaloid	Atalaphyllinine	$C_{23}H_{23}NO_4$
4	Root bark	Alkaloid	Acridone	$C_{13}H_9NO$
6	Root bark	Alkaloid	Acridone	$C_{13}H_9NO$
7	Root bark	Alkaloid	N-methylbicycloatalaphylline	—
8	Root bark	Alkaloid	Cloatalaphylline, Tetranortriterpenoids, Atalantolide, Atalantin, Limonoids	$C_{27}H_{32}O_9$
9	Root bark	Limonoids	Atalantin, Dehydroatalantin, Atalantolide	$C_{27}H_{30}O_9$
10	Leaf	Alkaloid	Caryophyllene oxide, α-Asarone	$C_{15}H_{24}O$, $C_{12}H_{16}O_3$

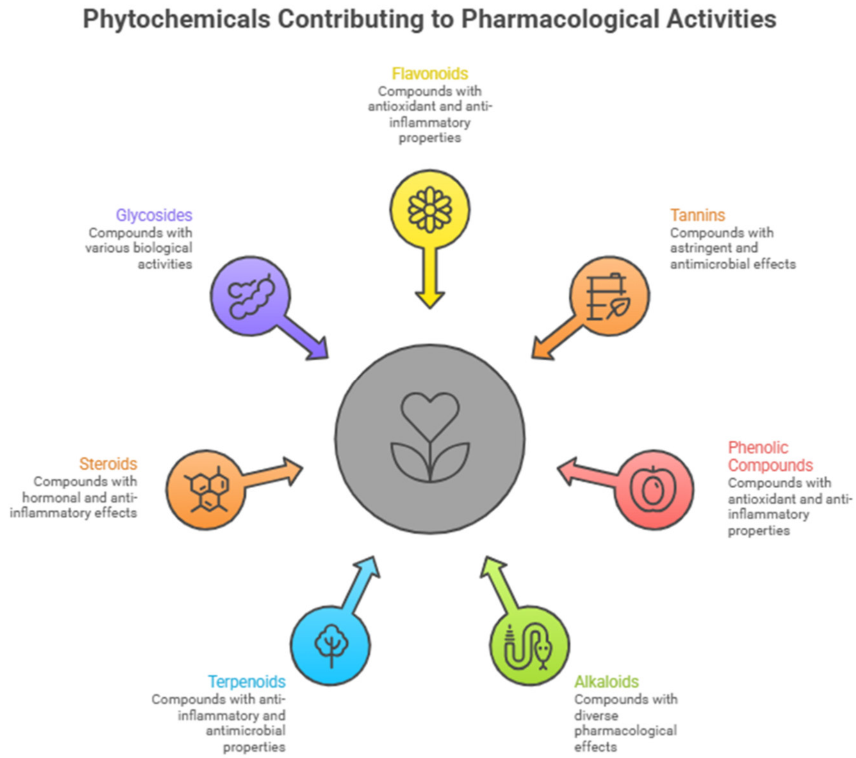

Fig.2: Phytoconstituents sources in *Atlantia monophylla*

6. Alkaloids and Flavonoids[27]

Among the various phytochemicals identified in *Atlantia monophylla*, alkaloids and flavonoids are considered the most pharmacologically significant. Researchers have isolated several benzoyltyramine alkaloids from the fruit peel of the plant, collectively known as atalantums. These compounds possess unique chemical structures and have demonstrated notable cytotoxic activity against certain cancer cell lines. For instance, studies have shown that some atalantum derivatives exhibit strong inhibitory effects on cholangiocarcinoma cells, suggesting their potential as anticancer agents. In addition to alkaloids, several flavonoid derivatives such as atalantraflavone and racemoflavone have been isolated from the leaves. Flavonoids are well known for their antioxidant and enzyme inhibitory activities, particularly their ability to inhibit acetylcholinesterase. This enzyme plays a key role in the pathogenesis of neurodegenerative diseases such as Alzheimer's disease. The presence of these compounds highlights the potential of *A. monophylla* as a valuable source of neuroprotective and anticancer agents.

7. Antioxidant Activity[28-30]

Oxidative stress plays a crucial role in the development of numerous chronic diseases, including cancer, cardiovascular disorders, and neurodegenerative conditions. Several studies have evaluated the antioxidant activity of *Atlantia monophylla* extracts using in vitro assays such as DPPH radical scavenging, ABTS radical cation decolorization, and ferric reducing antioxidant power assays. These studies have demonstrated that the plant extracts exhibit significant free radical scavenging activity, which is primarily attributed to the presence of phenolic compounds and flavonoids. The antioxidant activity of the plant may help protect cells from oxidative damage by neutralizing reactive oxygen species and enhancing endogenous antioxidant defense systems. This property supports the potential use of *A. monophylla* in the prevention and management of diseases associated with oxidative stress.

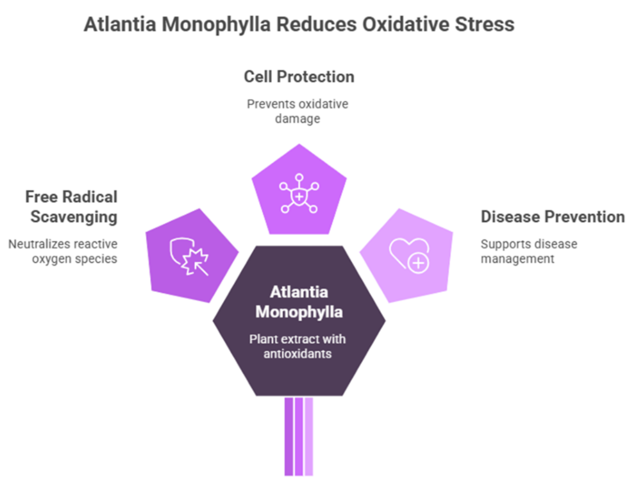

Fig.3. Antioxidant potentials of *Atlantia monophylla*

8. Antimicrobial and Anti-inflammatory Activities[31-33]

The antimicrobial properties of *Atlantia monophylla* have been extensively studied against a range of pathogenic microorganisms. Extracts of the plant have demonstrated inhibitory activity against both Gram-positive and Gram-negative bacteria as well as certain fungal species. These antimicrobial effects are believed to result from the presence of bioactive compounds that disrupt microbial cell membranes and interfere with essential metabolic processes. In addition to its antimicrobial properties, the plant also exhibits significant anti-inflammatory activity. Experimental studies using animal models such as carrageenan-induced paw edema have shown that plant extracts can effectively reduce inflammation. The anti-inflammatory effects are likely mediated through the inhibition of pro-inflammatory mediators such as prostaglandins and cytokines. These findings support the traditional use of the plant in the treatment of inflammatory conditions and infections.

9. Antidiabetic and Metabolic Effects[34]

Metabolic disorders such as diabetes mellitus have become major global health challenges, and there is increasing interest in plant-derived compounds for their management. Studies investigating the antidiabetic potential of *Atlantia monophylla* have demonstrated that plant extracts can significantly reduce blood glucose levels in experimental diabetic animal models. The hypoglycemic effects are believed to be mediated through several mechanisms, including enhancement of insulin secretion, inhibition of carbohydrate-digesting enzymes, and improvement of glucose uptake in peripheral tissues. In addition to lowering blood glucose levels, the plant extracts have been shown to improve lipid profiles by reducing cholesterol and triglyceride levels while increasing high-density lipoprotein levels. These findings suggest that *A. monophylla* may have potential applications in the management of metabolic syndrome and diabetes-related complications.

Fig.4. Pictogram of multifaceted benefits of Atlantia monophylla

10. Nanoparticle-Based Approaches for *Atlantia monophylla* in Drug Delivery and Therapeutic Applications[35-40]

Nanotechnology has emerged as a transformative platform in biomedical research, enabling improved delivery, bioavailability, and therapeutic efficacy of plant-derived bioactive compounds. Many phytochemicals present in medicinal plants exhibit poor water solubility, low bioavailability, and rapid metabolic degradation, which limit their clinical applications. The integration of nanoparticles with plant-derived compounds has significantly improved the pharmacokinetic and pharmacodynamics profiles of phytochemicals. In the case of *Atlantia monophylla*, the presence of flavonoids, alkaloids, phenolic compounds, and essential oils suggests a strong potential for nanoparticle-based formulations aimed at enhancing therapeutic performance. Nanoparticle-mediated delivery systems can improve stability, enable targeted drug delivery, reduce systemic toxicity, and allow controlled drug release. Recent advancements in green nanotechnology have also enabled the use of plant extracts as reducing and stabilizing agents during nanoparticle synthesis. Although direct nanoparticle formulations specifically using *A. monophylla* remain limited, the phytochemical composition of the plant strongly supports its suitability for nanoparticle-based therapeutic strategies similar to those developed for other Rutaceae medicinal plants.

Plant-mediated synthesis of nanoparticles is gaining attention due to its eco-friendly nature, cost-effectiveness, and avoidance of toxic chemical reagents. Phytochemicals such as flavonoids, phenolic acids, terpenoids, and alkaloids act as both reducing and capping agents during nanoparticle formation. These molecules stabilize nanoparticles and often enhance their biological activity. Therefore, extracts derived from *A. monophylla* could potentially be used to synthesize various metal nanoparticles including silver, gold, zinc oxide, and iron oxide nanoparticles. Such nanoparticles may exhibit enhanced antimicrobial, antioxidant, and anticancer activities due to synergistic interactions between phytochemicals and metallic nanostructures. Furthermore, nan formulations may facilitate targeted delivery to specific tissues such as tumors or inflamed tissues, thereby improving therapeutic outcomes.

Nanoparticle systems also enable encapsulation of plant extracts within polymeric or lipid carriers. These carriers protect bioactive compounds from degradation and allow sustained release. Polymeric nanoparticles such as PLGA nanoparticles have been widely used to encapsulate phytochemicals for anticancer therapy. Liposomal nanoparticles and solid lipid nanoparticles are also effective carriers for hydrophobic phytochemicals, improving their solubility and bioavailability. Such approaches may be particularly beneficial for flavonoids and alkaloids isolated from *A. monophylla*, which often suffer from limited stability in physiological environments. Additionally, nanoformulations may reduce toxicity by enabling controlled drug release and minimizing off-target effects.

Another promising approach involves the use of metal oxide nanoparticles synthesized using plant extracts. Zinc oxide nanoparticles, for example, have demonstrated strong antimicrobial and anticancer activities. When synthesized using plant extracts, these nanoparticles often exhibit enhanced biological properties due to the presence of phytochemical coatings on their surfaces. Similarly, iron oxide nanoparticles can be used for targeted drug delivery and magnetic hyperthermia therapy in cancer treatment. Gold nanoparticles synthesized using plant extracts have shown excellent biocompatibility and are widely used in biosensing, imaging, and targeted drug delivery applications.

The potential integration of *Atlantia monophylla* phytochemicals with nanotechnology therefore represents an exciting avenue for developing advanced therapeutic systems. Future studies should focus on the synthesis, characterization, and biological evaluation of nanoparticles derived from *A. monophylla* extracts. Such investigations could significantly enhance the therapeutic potential of this medicinal plant and contribute to the development of novel nanomedicines.

Table 2: Potential Nanoparticle Systems for *Atlantia monophylla*-Derived Phytochemicals

Nanoparticle Type	Synthesis Method	Key Components	Average Particle Size	Major Characterization Techniques	Potential Biomedical Applications
Silver Nanoparticles (AgNPs)	Green synthesis using plant extract	*A. monophylla* leaf extract + $AgNO_3$	10–80 nm	UV–Vis spectroscopy, TEM, SEM, XRD, FTIR	Antibacterial, antifungal, wound healing
Gold Nanoparticles (AuNPs)	Plant-mediated reduction	Plant phenolics + $HAuCl_4$	15–100 nm	TEM, DLS, UV–Vis spectroscopy	Cancer therapy, biosensing, targeted drug delivery

Zinc Oxide Nanoparticles (ZnO NPs)	Green synthesis using aqueous extract	Zinc acetate + plant phytochemicals	20–90 nm	XRD, SEM, FTIR, UV–Vis	Anticancer, antimicrobial, anti-inflammatory
Iron Oxide Nanoparticles (Fe_3O_4 NPs)	Co-precipitation with plant extract	$FeCl_2/FeCl_3$ + phytochemical stabilizers	10–50 nm	TEM, VSM, XRD, FTIR	Magnetic drug targeting, cancer therapy
Copper Oxide Nanoparticles (CuO NPs)	Plant-assisted synthesis	Copper sulfate + plant extract	20–100 nm	SEM, TEM, UV–Vis, XRD	Antibacterial, anticancer activity

Table 3: Nano-Drug Delivery Systems for *Atlantia monophylla* Bioactive Compounds

Nanocarrier System	**Encapsulated Compounds**	**Preparation Method**	**Advantages**	**Therapeutic Target**
Polymeric Nanoparticles (PLGA)	Flavonoids and alkaloids	Emulsion solvent evaporation	Controlled release, improved stability	Cancer therapy
Liposomes	Phenolic compounds	Thin film hydration	Enhanced bioavailability	Anti-inflammatory therapy
Solid Lipid Nanoparticles (SLNs)	Essential oils	High-pressure homogenization	Improved solubility of hydrophobic compounds	Antimicrobial treatment
Nanostructured Lipid Carriers (NLCs)	Mixed phytochemicals	Melt emulsification	High drug loading capacity	Metabolic disorders
Nanoemulsions	Volatile oils from fruit peel	Ultrasonication	Improved absorption and stability	Antioxidant and antimicrobial therapy

11. Toxicological Evaluation[41]

Although *Atlantia monophylla* exhibits numerous pharmacological benefits, its safety profile must be carefully evaluated before therapeutic application. Acute toxicity studies conducted in experimental animal models have indicated that the plant extracts are relatively safe at moderate doses. However, excessive consumption or prolonged exposure to high concentrations of bioactive compounds may produce adverse effects. Toxicological evaluations have also been conducted on the essential oils of the plant, particularly in relation to their insecticidal properties. These studies revealed that certain compounds present in the essential oil can interfere with enzymatic pathways in insects, leading to toxicity. While this property is advantageous for pest control, it underscores the importance of detailed toxicity assessments when considering the plant for medicinal use. Further studies including chronic toxicity and clinical safety evaluations are necessary to establish the safe therapeutic dosage of *A. monophylla*.

12. Therapeutic Potential and Future Perspectives[42]

The increasing body of scientific evidence suggests that *Atlantia monophylla* possesses significant therapeutic potential due to its diverse phytochemical composition and pharmacological activities. The discovery of bioactive alkaloids and flavonoids with anticancer and neuroprotective properties highlights the importance of this plant as a promising source for drug discovery. Furthermore, its demonstrated antioxidant, antimicrobial, anti-inflammatory, and antidiabetic activities support its potential use in the development of herbal formulations and pharmaceutical agents. Future research should focus on isolating and characterizing additional bioactive compounds from the plant, as well as elucidating their mechanisms of action at the molecular level. Advances in modern drug discovery techniques such as molecular docking, network pharmacology, and nanotechnology-based drug delivery systems may further enhance the therapeutic applications of compounds derived from *A. monophylla*. Comprehensive clinical trials will also be necessary to validate the efficacy and safety of these compounds in human populations. Such investigations could ultimately lead to the development of novel therapeutic agents derived from this medicinal plant.

13. Conclusion

Atalantia monophylla is a valuable medicinal plant with rich phytochemical constituents such as flavonoids, alkaloids, phenolics, and essential oils. Various plant parts (leaf, root, bark, fruit) exhibit important pharmacological activities including antioxidant, antimicrobial, anti-inflammatory, and antidiabetic effects. Emerging approaches like nanotechnology further enhance its therapeutic potential for advanced drug delivery. Although preliminary studies indicate safety, more detailed toxicological and clinical research is required to confirm its efficacy and establish its role in modern medicine.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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CRediT authorship contribution statement

Ashwaq Basheer Ahmed and Parthasarathi: conceptualization, methodology, Writing, editing, and reviewing for All authors have read and agreed to the published version of the manuscript.

Declaration of competing interest

The studies described in this publication could not have been influenced by any known conflicting financial interests or close relationships of the authors.

Data availability

Data will be made available on request.

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