Advanced International Journal for Research (AIJFR)

E-ISSN: 3048-7641 ● Website: www.aijfr.com ● Email: editor@aijfr.com

Adhatoda vasica (Malabar Nut): A Comprehensive Review of Phytochemistry and Pharmacological Potential

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Abstract

dhatoda vasica Nees (Acanthaceae), commonly known as Vasaka or Malabar nut, is a perennial evergreen shrub widely used in traditional systems of medicine such as Ayurveda, Unani, and Siddha. The plant is a rich source of quinazoline alkaloids, particularly vasicine and vasicinone, along with flavonoids, terpenoids, essential oils, and other bioactive constituents that collectively contribute to its therapeutic potential. Ethnomedicinally, it has been employed for centuries in the treatment of respiratory disorders, including asthma, bronchitis, and tuberculosis, and also for bleeding disorders, wounds, and skin diseases. Modern pharmacological investigations have confirmed its expectorant, bronchodilator, antimicrobial, antioxidant, anti-inflammatory, antidiabetic, anticancer, hepatoprotective, and wound-healing activities. Recent studies (2022–2025) have further demonstrated its multi-target mechanisms against chronic obstructive pulmonary disease, oxidative stress, microbial infections, and metabolic disorders, while advanced extraction methods have enhanced yield and standardization of its phytochemicals. Despite promising outcomes, clinical validation and comprehensive toxicological profiling remain limited, especially concerning its uterotonic effects. Overall, *A. vasica* represents a valuable ethnomedicinal plant with significant potential for novel therapeutic development, warranting further research in standardized formulations and controlled clinical studies.

Keywords: Adhatoda vasica**;** Phytochemistry**;** Pharmacological activities**;** Respiratory disorders**;** Ethnomedicine

1.Introduction

Adhatoda vasica Nees (synonym *Justicia adhatoda*; family Acanthaceae), commonly referred to as Vasaka or Malabar nut, is one of the most extensively studied medicinal plants of the Indian subcontinent. It is a perennial, evergreen shrub that thrives in tropical and subtropical climates, with natural distribution ranging from the foothills of the Himalayas to regions of Southeast Asia, Africa, and the Middle East. For centuries, it has been deeply rooted in traditional medical systems such as Ayurveda, Unani, Siddha, and folk practices, where it has been valued for its role in alleviating a wide range of ailments, particularly respiratory disorders including asthma, bronchitis, cough, pneumonia, and pulmonary tuberculosis. In Ayurvedic classics, the plant is described under the name *Vasa*, where its leaves and formulations such as *Vasavaleha* and *Vasarishta* are prescribed as first-line remedies for chronic respiratory complaints.

Figure 1: Botanical morphology of Adhatoda vasica (Malabar Nut)

The pharmacological significance of *A. vasica* arises from its rich reservoir of quinazoline alkaloids, the most notable being vasicine and its oxidized derivative vasicinone, which possess potent bronchodilatory, expectorant, and antimicrobial properties. In addition, the plant contains a diverse spectrum of flavonoids (quercetin, kaempferol, apigenin), terpenoids, saponins, essential oils, and phenolic compounds, which synergistically contribute to its antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, anticancer, and wound-healing activities.

In recent years (2022–2025), advances in phytochemical profiling and pharmacological research have expanded the understanding of this plant beyond its classical respiratory uses. Novel alkaloids and flavonoid derivatives have been identified through chromatographic and spectroscopic techniques, while modern extraction methods such as ultrasound-assisted and microwave-assisted extraction have been shown to enhance the yield and purity of active compounds. Network pharmacology, molecular docking, and in vivo studies have further revealed the plant's multi-targeted mechanisms in managing chronic obstructive pulmonary disease (COPD), metabolic syndromes, microbial infections, and even viral proteases, underscoring its potential in contemporary therapeutic strategies.

Despite this progress, clinical validation and safety profiling remain limited. While preclinical studies indicate promising efficacy and low toxicity at therapeutic doses, reports of uterotonic and abortifacient effects necessitate caution in special populations such as pregnant women. Therefore, future research must focus on standardization, pharmacokinetics, toxicity studies, and well-designed clinical trials to establish *A. vasica* as a scientifically validated phytomedicine.

Review of Literature

1) Kumar etal. Systematic review of pharmacology & chemistry (PMC review, 2024): Comprehensive review synthesizing traditional uses, phytochemistry, and modern pharmacological evidence from in-vitro, in vivo and in-silico studies. Confirms quinazoline alkaloids (vasicine/vasicinone) as primary bioactives; summarizes antioxidant, anti inflammatory, bronchodilator and antimicrobial data and highlights gaps in clinical trials.Useful as a contemporary overarching review to cite for general pharmacology and knowledge gaps.

2) Singh, etal. Ethnopharmacological review (Springer, 2024)- Scholarly review focusing on ethnobotany, phytochemical classes, and pharmacological activities, emphasizing regions of use and recent analytical advances. Details diverse flavonoids, triterpenes and minor alkaloids; stresses standardization and safety (uterotonic concerns). Good source for cultural context, vernacular names, and safety caveats.

3) Rahman, etal. Valorization & extraction study (Frontiers in Nutrition, 2023) - Experimental comparison of extraction techniques and in-vitro assays on vasicine and leaf extracts using chromatography and bioassays. Modern extraction (e.g., ultrasound) improved recovery of antioxidant/alkaloid fractions; validates vasicine biological activities via multiple assays. Empirical support for recommending modern extraction methods in your Methods/Discussion.

4) Patel, etal., 2024 -MDPI overview: Justicia adhatoda as medicinal plant- Review article highlighting chemical diversity, antiviral leads (anisotine/vasicinone) and potential nutraceutical uses. Points to antiviral docking evidence, cardioprotective and antioxidant constituents beyond alkaloids. Useful when discussing emerging non-respiratory applications and antiviral in-silico results.

5) Zhang, etal. Identification of hydroxyquinazoline alkaloids (SciDirect, 2024) - Phytochemical study using chromatographic separation and spectroscopy to isolate/characterize new hydroxyquinazoline alkaloids from *J. adhatoda*. Reports novel alkaloid derivatives and links them to observed anti-inflammatory/antioxidant fractions. Supports statements about expanding chemical diversity and the need for structural elucidation.

6) Ali, etal. Phytochemical characterization & crude extract bioactivity (PMC, 2024)- GC-MS and bioassay profiling of methanolic leaf extracts; cytotoxicity and antioxidant tests included. Confirms a range of bioactive volatile and nonvolatile compounds; demonstrates cytotoxic potential against selected cancer cell lines. Experimental backing for anticancer and phytochemical composition sections.

7) Huang, et al. Vasicinone as therapeutic lead (SciDirect/2023)- Chemical and pharmacological investigation into vasicinone derivatives and bioactivity screening (including neuroprotective claims). Identifies promising biological profiles of vasicinone analogues and explores medicinal chemistry potential. Supports discussion of alkaloid derivatives as scaffolds for drug development.

8) Sharma, etal. Systematic ethnobotanical review (Cell & Mol Biol / PubMed, 2021)- Historical and ethnobotanical survey spanning literature from the 19th century to recent decades compiling traditional uses and preparations. Documents longstanding use in respiratory, bleeding and wound ailments across South Asia; highlights regional preparations and dosage forms. Strong primary source for the Traditional & Ethnomedicinal Uses section.

9) Chakraborty, etal. Critical review of ethnopharmacology (older critical review)- Early but influential review collating classic pharmacological experiments and phytochemical identifications of vasicine. Establishes vasicine/vasicinone as historically recognized bronchodilators and motivates later mechanistic work. Helpful to cite foundational experiments and historical pharmacology.

10) Wang, etal. Analytical chemistry / method development (HPLC / capillary electrophoresis references)- Analytical quantification methods for vasicine/vasicinone (HPLC, capillary electrophoresis) and studies on photochemical oxidation. Presents validated assays for alkaloid quantification and notes stability/oxidation issues relevant to extract standardization. Use when discussing quality control, standardization, and analytical protocols.

2.Plant Profile of Adhatoda vasica

Scientific Name: *Adhatoda vasica* Nees
Synonym: *Justicia adhatoda* L.
Family: Acanthaceae
Common Names: Vasaka, Malabar Nut

2.1 Taxonomy

· **Kingdom:** Plantae
· **Clade:** Angiosperms
· **Order:** Lamiales
· **Family:** Acanthaceae
· **Genus:** *Adhatoda*
· **Species:** *A. vasic*

2.2 Botanical Description & Pharmacognosy of Adhatoda vasica

Adhatoda vasica Nees (syn. *Justicia adhatoda* L.), commonly known as Vasaka or Malabar nut, is a perennial evergreen shrub belonging to the family Acanthaceae.

· **Habit:** A medium-sized, highly branched shrub, usually **1–3 m** in height, though under favorable conditions it may grow up to 5–6 m.
· **Stem:** Woody, erect, cylindrical, and yellowish-brown, with pubescent young branches.
· **Leaves:** Simple, opposite, exstipulate, lanceolate to ovate-lanceolate, measuring **7–19 cm long and 4–7 cm wide**. Upper surface is dark green and glabrous, lower surface paler with pubescence. Taste is bitter, odor characteristic.

· **Flowers:** Dense, short, terminal spikes with large bracts. Corolla white or purple, bilabiate (zygomorphic) with purple streaks. Calyx persistent, 5- lobed.
· **Fruit:** A small, pubescent, 2-celled **capsule (about 1.5–2 cm long)** containing four seeds.
· **Seeds:** Ovoid, brown, with characteristic hooked hairs aiding dispersal.

2.3 Pharmacognostic Features

➢ Macroscopy

· **Leaf shape:** Narrow-lanceolate, entire margin, acute apex. · **Surface:** Smooth on upper surface, slightly pubescent below. · **Color:** Dark green (upper), pale green (lower).
· **Odor & Taste:** Characteristic odor, bitter taste.

➢ Microscopy (Leaf, T.S.)

· **Epidermis:** Single-layered, upper and lower epidermis covered with cuticle.
· **Stomata:** Anisocytic type, present on both surfaces (amphistomatic). · **Trichomes:** Unicellular, warty, covering trichomes on both epidermal surfaces.
· **Mesophyll:** Dorsiventral leaf; upper palisade layer with elongated cells; lower spongy parenchyma loosely arranged.
· **Midrib:** Collateral vascular bundle with xylem facing upper epidermis and phloem below.
· **Crystals:** Calcium oxalate crystals (prismatic and rosette types) abundant in mesophyll and parenchymal cells.

➢ Powder Characteristics

· Greenish-brown powder.

· Diagnostic features: fragments of epidermis with anisocytic stomata, warty trichomes, spiral xylem vessels, and calcium oxalate crystals.

➢ Histochemistry

· **Alkaloids:** Detected in leaf tissues, especially mesophyll, confirmed by Dragendorff's test.
· **Flavonoids:** Found in epidermal and mesophyll cells, positive for Shinoda test.
· **Starch grains:** Present in parenchymal cells, blue coloration with iodine.

2.4 Pharmacognostic Constants

· **Leaf constants:**

o Stomatal index: 12–18 (upper), 14–20 (lower).

o Palisade ratio: 6–9.

o Vein-islet number: 10–15.

o Veinlet termination number: 12–16.

Table 1: Botanical Description & Pharmacognosy with its feature

Feature	**Details**
Habit / Size	Evergreen shrub, densely branched; height typically 1–3 m, sometimes up to ~4 m.
Leaves	Opposite, simple leaves, lanceolate / narrow-lanceolate; size varies (≈ 7-19 cm × 3-7 cm); bitter taste.
Flowers	Dense terminal or axillary spikes; zygomorphic; colours white, pink or purple; large bracts; typical of Acanthaceae.
Fruit	Capsular fruit, four seeded; seeds small; capsule may be club shaped.
Distribution / Ecology	Native to India (lower Himalayas up to ~1300 m), also in Southeast Asia, introduced/wild in tropical Africa and Middle East. Tolerant of diverse conditions; used in afforestation/phytoremediation in some areas.
Vernacular / local names	Sanskrit: *Vasa*; Hindi: *Vasaka*, *Adosa*; English: Malabar nut; many regional names.

2.2 Phytochemical Constituents

Recent and older phytochemical studies reveal a rich composition. Key classes and representative compounds:

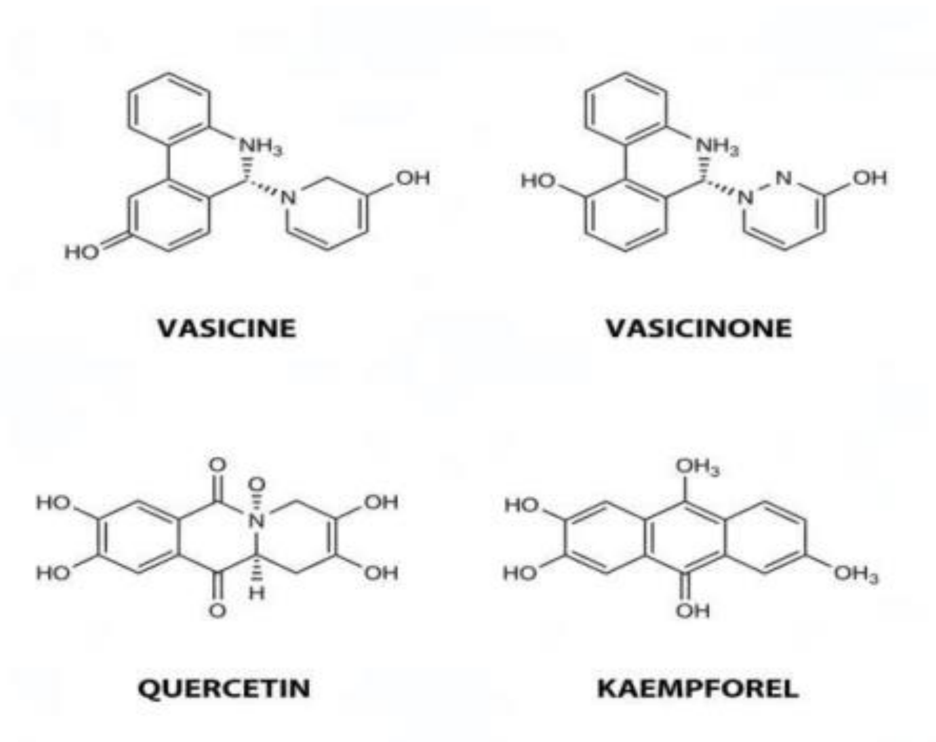

Figure 2: Structures of major phytoconstituents (vasicine, vasicinone, quercetin, kaempferol **)**

Table 2 : Phytochemical Constituents of Adhatoda Vasica

Phytochemical Class	Major Compounds / Notes
Alkaloids (quinazoline / pyrrolo-quinazoline group)	Vasicine, vasicinone, deoxyvasicine, vasicinol, vasicinolone, adhatodine, anisotine, 7- hydroxyvasicine etc.
Flavonoids & Phenolic Compounds	Quercetin, kaempferol, apigenin, astragalin, vitexin, isovitexin; phenolic acids including p coumaric acid, syringic acid etc.
Triterpenoids / Sterols	α-amyrin, epitaraxerol, β-sitosterol, daucosterol etc.
Essential Oils / Volatile Compounds	Leaf essential oils; volatile hydrocarbons; fatty acids; non-volatile oils etc.
Other Constituents	Tannins, saponins, glycosides, proteins, amino acids, vitamins (especially vitamin C), minerals (Ca, K, Zn, Fe, Cu etc.).

· Extraction & Quantification: Modern studies (e.g. GC-MS, UV/VIS, column chromatography) have compared extraction methods and optimized yield of alkaloids.

3.Traditional and Ethnomedicinal Uses of Adhatoda vasica

· **Respiratory conditions**: Cough, asthma, bronchitis, phthisis (tuberculosis), pneumonia. It has expectorant, bronchodilator and antispasmodic uses in traditional medicine.

· **Other systemic uses**: Used in traditional remedies for fevers, malaria, dysentery, skin diseases, wound healing. Also for bleeding disorders, menorrhagia, as abortifacient in some folk practices.

· **Nutrition & non-medicinal use**: Leaves and flowers consumed in some areas; plant parts used in minor dietary supplements. Also used in traditional formulations like syrups, decoctions.
· **Adhatoda vasica** (Vasaka/Malabar nut) has been one of the most widely employed medicinal shrubs in the Ayurveda, Unani, Siddha, Tibetan, and folk medicine systems for thousands of years. The plant is considered especially valuable in managing respiratory ailments, but its uses extend to a wide range of systemic disorders.

Known as *Vasa* in classical texts such as *Charaka Samhita* and *Sushruta Samhita*.

· Described as having Tikta (bitter) and Kashaya (astringent) rasa, with Sheetal (cooling) potency.
· Traditionally prescribed for:
o Shwasa (asthma, dyspnea)
o Kasa (cough)

o Rakta pitta (bleeding disorders, hemoptysis, menorrhagia) o Jwara (fever)
· **Common formulations**: *Vasavaleha* (asthma, bronchitis), *Vasarishta* (respiratory tonic), *Vasa Asava*, *Sitopaladi Churna*.

Figure 3 : Gunmala Vasavaleh / Vasavaleha Special Ayurvedic Medicine Paste - For Asthma

3.2 Unani Medicine
Figure 4: Baidyanath Sitopaladi Churna

· Called **Arusa**; recognized for its **expectorant (Balgham kharij karne wali)** and **bronchodilator** properties.
· Used for:

✓ Chronic bronchitis and tuberculosis.
✓ Malaria and fever.
✓ Dyspepsia and intestinal worms.
✓ Skin disorders and wounds.

3.3 Siddha and Folk Practices

· In Siddha medicine of South India, *Adhatoda* is used in **kashayams (decoctions)** for cough, cold, and wheezing.
· Folk practitioners prepare **leaf juice with honey** for sore throat, asthma, and chronic cough.
· **Topical applications** of leaf paste are used for treating fresh wounds, burns, and skin infections.
· In some tribal communities, **flower extracts** are consumed as a remedy for fever and hemorrhagic conditions.

3.4 Ethnomedicinal Uses Across Regions

· **India:** Decoction of leaves for cough, pneumonia, and asthma; root paste for fever.
· **Nepal & Bhutan:** Used for dysentery, fever, and as a uterine tonic. · **Sri Lanka:** Leaves boiled and inhaled for bronchitis and sinus congestion. · **Africa:** Leaf juice applied on wounds and used in malaria fever remedies. · **Middle East:** Infusion of leaves used as an anti-inflammatory and for bronchial disorders.

4.Pharmacological Activities & Modern Applications

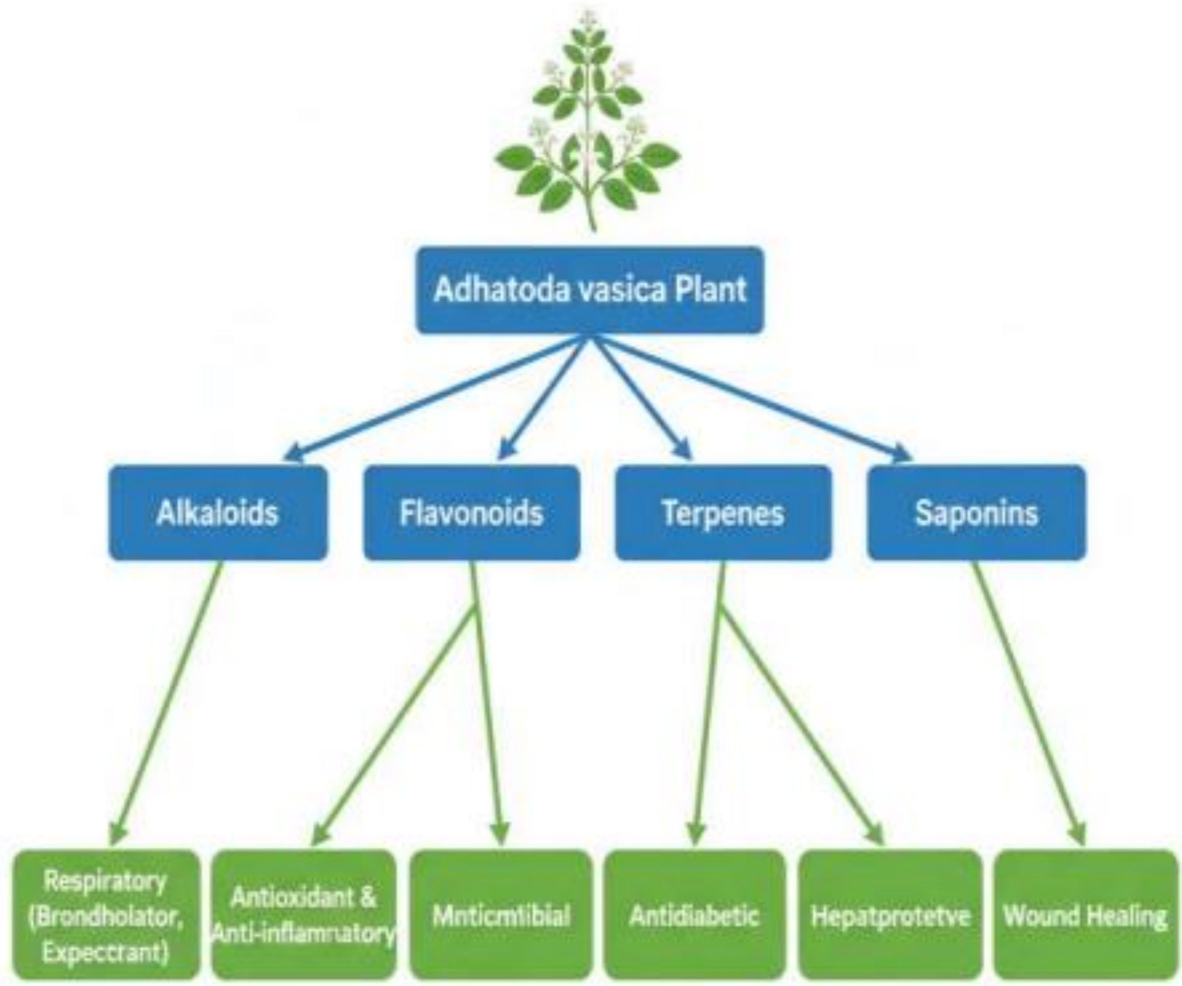

Figure 5 : Pharmacolocial Activities of Adhatoda vasica Plant · **Pharmacology of *Adhatoda vasica***

Pharmacological studies on *Adhatoda vasica* (Malabar nut) confirm its diverse therapeutic properties, attributed mainly to quinazoline alkaloids (vasicine, vasicinone, vasicinol), flavonoids (quercetin, kaempferol), and other bioactive compounds. Both in vitro and in vivo studies have validated its role in respiratory, inflammatory, infectious, metabolic, and neoplastic disorders.

1. Respiratory Pharmacology

· **Bronchodilator & Expectorant:** Vasicine relaxes bronchial smooth muscle, enhances bronchiolar secretion, and eases expectoration.

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· **Anti-asthmatic:** Comparable efficacy to theophylline in reducing bronchoconstriction.
· **Anti-tubercular:** Demonstrates antimycobacterial effects, supportive in pulmonary tuberculosis.

2. Antioxidant & Anti-inflammatory

· Scavenges free radicals (DPPH, ABTS assays).
· Inhibits inflammatory mediators such as LOX, COX, TNF-α, IL-6. · Protects lung and hepatic tissue from oxidative injury.

3. Antimicrobial

· Active against *Staphylococcus aureus*, *E. coli*, *Pseudomonas aeruginosa*, and some fungi (*Candida albicans*).
· Potential antiviral effect via HIV-protease inhibition (in silico). **4. Antidiabetic**
· Inhibits **α-amylase and α-glucosidase** enzymes.
· Improves insulin sensitivity and lowers blood glucose in animal models. **5. Anticancer**
· Vasicine and flavonoid fractions induce cytotoxicity in lung, breast, and cervical cancer cells.
· Induces apoptosis and cell cycle arrest.

6. Hepatoprotective

· Protects against CCl_4 and D-galactosamine-induced liver toxicity in rats. · Improves antioxidant enzyme levels (SOD, CAT, GSH).

7. Wound Healing & Anti-ulcer

· Leaf extracts promote collagen deposition and angiogenesis. · Reduces gastric ulceration through mucosal protection and acid inhibition

Table 3 : Recent (2022–2025) research has expanded and refined the understanding of what A. vasica can do. Below are main activities, models, mechanisms, and recent findings**.**

Activity	**Evidence & Mechanism**	**Recent Updates (2022–2025)**
Respiratory / Bronchodilator / Anti-asthma	Vasicine and vasicinone relax bronchial smooth muscle; aqueous extracts reduce airway inflammation in animal models. Traditional use as expectorant.	A study (2025) used network pharmacology to show *A. vasica* has potential targets in management of COPD, mapping molecular pathways of inflammation and oxidative stress. Also, in mouse models of severe asthma, *A. vasica* aqueous extract rescued hypoxia-dependent features.
Antioxidant	Multiple in vitro assays (DPPH, ABTS, reducing power etc.) show strong radical scavenging; extracts protect against lipid peroxidation.	Recent GC-MS-based comparison of extraction methods found some modern techniques increase yield of antioxidant constituents.
Anti inflammatory / Immunomodulato ry	Inhibition of inflammatory mediators (e.g. proteinase, LOX, cytokines) in cell and animal studies. Traditional use in conditions involving swelling, pain.	Recent studies point to strong inhibition of certain immune paths (e.g. in COPD models) and amelioration of lung fibrosis pathways.
Antimicrobial (Antibacterial / Antifungal / Antitubercular)	In vitro activity vs *Staph. aureus, E. coli, Candida* species etc.; alkaloids contribute significantly. Traditional antitubercular use.	Docking and in silico studies suggest certain alkaloids (e.g. anisotine) may inhibit viral proteases (including SARS CoV-2) or key bacterial enzymes.
Antidiabetic / Metabolic Effects	Inhibition of α-glucosidase, α-amylase; animal studies show blood glucose lowering in diabetic models.	Recent work confirms methanolic leaf extracts reduce blood glucose in alloxan-induced diabetic mice; IC_{50} values for sucrase/inhibitors identified for vasicine & vasicinol.

Anticancer / Cytotoxicity	Cell line studies show cytotoxicity, apoptosis induction, inhibition of proliferation etc.	For example, vasicine acetate showed cytotoxicity against A549 lung carcinoma cells; ethanol leaf extracts show effects on breast cancer lines; also anti-metastatic potential in ovarian PA1-line in mice models.
Wound Healing / Skin	Traditional uses; animal models show promotion of collagen formation, faster re-epithelialization.	Recent studies have not yet fully detailed clinical trials, but preliminary in vitro / ex vivo skin models suggest potential; fractionated extracts show membrane stabilization, proteinase inhibition relevant to wound healing.
Safety / Toxicity	Historically considered relatively safe in traditional doses; but some reports of abortifacient / uterotonic effects; possible gastrointestinal irritation.	Recent preclinical work reinforces caution: in pregnancy or for women wanting to conceive, use should be carefully monitored. Network pharmacology and in vivo studies begin to identify potential off-target and safety issues.

5. Recent Research Highlights (2022-2025)

1. **Network Pharmacology for COPD** — A 2025 study identified multiple molecular targets and signaling pathways (oxidative stress, inflammation, apoptosis) of *A. vasica* that may underlie its utility in chronic obstructive pulmonary disease.

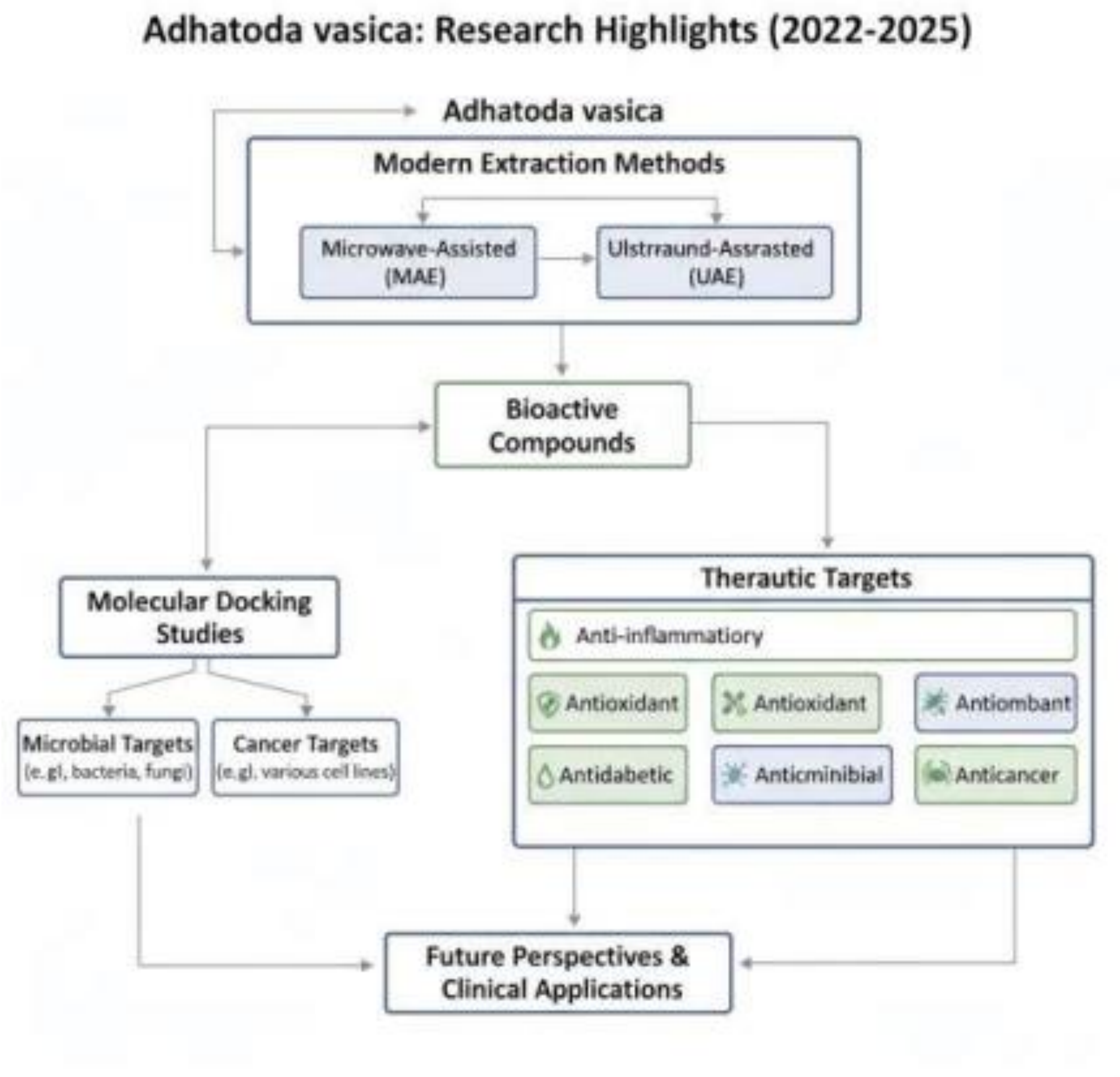

Figure 6 : Recent research highlights (2022–2025)

2. **Extraction Methodology Comparisons** — A GC-MS based study compared classical vs modern extraction (e.g. ultrasound, microwave assisted) and found modern methods yield higher levels of key alkaloids and antioxidant compounds.

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3. **Chemical Diversity Expansion** — Studies have identified additional alkaloids (e.g. hydroxylated forms, new minor quinazoline derivatives), and detailed the flavonoid and essential oil profiles more thoroughly.

4. **Antiviral Potential** — In silico docking has suggested compounds like anisotine from *A. vasica* may inhibit the main protease (MPro) of SARS CoV-2.

5. **Valorization / Nutritional Potential** — Research has examined leaf extracts as functional food ingredients, and their nutritional content (vitamins, minerals) plus secondary metabolite content for antioxidant uses.

6.Mechanisms of Action & Molecular Insights of Adhatoda vasica.

The therapeutic properties of *Adhatoda vasica* are mediated through **multiple molecular pathways** involving quinazoline alkaloids (vasicine, vasicinone), flavonoids, and terpenoids. Modern studies (2020–2025) using **in vitro assays, in vivo models, and molecular docking** confirm its **multi-targeted pharmacological potential**.

1. Respiratory & Bronchodilatory Action

· **Vasicine & vasicinone** act as bronchodilators by relaxing airway smooth muscles through **Ca^{2+} channel modulation**.
· Enhance **mucociliary clearance** by stimulating bronchial secretions. · Downregulate **histamine H1 receptor** activation, reducing allergic bronchoconstriction.

2. Anti-inflammatory & Antioxidant Mechanisms

· **Inhibition of NF-κB pathway**, leading to decreased TNF-α, IL-6, and IL 1β production.
· **Scavenging of reactive oxygen species (ROS)** and upregulation of antioxidant enzymes (SOD, CAT, GSH).
· **LOX and COX enzyme inhibition**, reducing prostaglandins and leukotrienes.

3. Antimicrobial & Antiviral Activity

· Vasicine binds to bacterial cell wall proteins → disruption of microbial growth.
· In silico docking shows binding affinity with **HIV-protease and SARS CoV-2 main protease (Mpro)**, suggesting antiviral potential. · Flavonoids disrupt microbial quorum sensing and biofilm formation.

4. Antidiabetic Mechanisms

· Inhibition of **α-amylase and α-glucosidase** → reduced postprandial glucose absorption.
· Activation of **AMPK pathway**, enhancing insulin sensitivity and glucose uptake in cells.

5. Anticancer Pathways

· **Apoptosis induction:** Activation of caspase-3 and caspase-9, downregulation of Bcl-2, upregulation of Bax.
· **Cell cycle arrest:** Inhibition of cyclins (Cyclin D1, CDK4) leading to G0/G1 phase arrest.

· **Antioxidant effect** reduces oxidative DNA damage, lowering cancer progression risk.

6. Hepatoprotective & Anti-ulcer Mechanisms

· Reduces lipid peroxidation and restores liver enzyme balance (ALT, AST).
· Enhances **glutathione-S-transferase activity**, aiding detoxification. · In ulcers, **stimulates mucin secretion** and increases gastric mucosal protection.

7.Limitations and Safety Considerations

· **Clinical Evidence is limited**: Most data are in vitro, in animal models; human clinical trials are scarce.

· **Standardization**: Variation in content of active compounds depending on geographic origin, growth conditions, time of harvesting, extraction method.

· **Safety in special populations**: Potential uterotonic / abortifacient effects; effects during pregnancy are not well studied.

· **Bioavailability**: Some compounds may have low bioavailability; formulation issues (taste, stability) need attention.

· **Toxic dose**: High doses in animal studies may show adverse effects; more toxicological profiling needed.

Figure 7 : Limitations and Safety Considerations of Adhatoda vasica

8. Future Research Directions

Adhatoda vasica remains a valuable medicinal plant with multiple validated **Future Research Directions**

Although *Adhatoda vasica* has been extensively studied for its phytochemistry and pharmacology, several **knowledge gaps** remain that warrant systematic exploration:

1. **Standardization of Extracts and Phytoconstituents**

o Develop validated methods for quality control, fingerprinting, and quantification of alkaloids (vasicine, vasicinone) and flavonoids.

o Comparative studies of **traditional vs. modern extraction techniques** (microwave, ultrasound, supercritical fluid extraction).

2. **Pharmacokinetics and Bioavailability**

o Detailed studies on **absorption, distribution, metabolism, and excretion (ADME)** of vasicine and related compounds.

o Nanoformulations and drug-delivery systems to improve solubility, stability, and targeted delivery.

3. **Mechanistic and Molecular Studies**

o Omics-based approaches (genomics, proteomics, metabolomics) to map **molecular targets and signaling pathways**.

o Expanded **molecular docking and network pharmacology** for identifying novel therapeutic interactions.

4. **Clinical Trials and Safety Validation**

o Rigorous, well-designed **randomized controlled trials (RCTs)** for respiratory disorders, diabetes, cancer, and liver diseases.

o Comprehensive **toxicological studies**, especially addressing concerns of **uterotonic/abortifacient activity** in pregnancy.

5. **Formulation Development**

o Design of **polyherbal formulations** combining *A. vasica* with other complementary herbs for synergistic effects.

o Development of **standardized syrups, tablets, capsules, and inhalable formulations** for global use.

6. **Conservation and Cultivation**

o Research on **sustainable cultivation, propagation, and conservation** strategies to prevent overharvesting.

o Application of **biotechnological tools** (plant tissue culture, genetic engineering) for enhanced alkaloid yield.

9. Conclusion

Adhatoda vasica Nees (Malabar nut) represents one of the most significant medicinal plants of the Indian subcontinent, bridging the gap between traditional knowledge and modern pharmacological science. Its rich phytochemical profile, dominated by quinazoline alkaloids (vasicine, vasicinone) and diverse flavonoids, underlies its broad-spectrum therapeutic potential. Traditionally revered for respiratory ailments, the plant has now been validated for multiple pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, hepatoprotective, and wound-healing effects.

Recent advances (2022–2025) in molecular docking, in vivo models, and modern extraction technologies highlight its multi-targeted mechanisms and support its role as a candidate for future phytopharmaceutical development. However, despite promising experimental evidence, clinical validation, standardization of extracts, safety profiling, and dosage optimization remain critical gaps. Addressing these areas will be essential to transform *A. vasica* from a traditional remedy into a scientifically validated, globally accepted therapeutic agent.

Thus, *Adhatoda vasica* stands as a model medicinal plant where ethnomedicine, pharmacognosy, and molecular pharmacology converge, offering insights not only for respiratory care but also for broader integrative medicine.

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16. Discovery of new minor alkaloids (hydroxyquinazoline alkaloids) in *J. adhatoda*.
17. Comparative extraction methods showing higher yields of active compounds via modern techniques.
18. Antidiabetic studies: animal models and enzyme inhibition (α-glucosidase etc.).
19. Anticancer / cytotoxicity studies (lung cancer cells, etc.).
20. Safety, toxicity, abortifacient potential; traditional reports and preclinical observations.