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PHYTOCHEMICAL AND ETHNOMEDICINAL REVIEW OF *Justicia adhatoda*: A COMPREHENSIVE REVIEW

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Abstract

Justicia adhatoda, commonly referred to as Vasaka or Malabar nut, is a medicinal plant extensively used in traditional systems such as Ayurveda, Unani, and Siddha. This review consolidates current knowledge on its botanical characteristics, phytochemistry, traditional applications, pharmacological activities, and toxicology. The plant is rich in quinazoline alkaloids, notably vasicine and vasicinone, which are responsible for its prominent bronchodilatory, antimicrobial, anti-inflammatory, and uterotonic effects. Its efficacy has been demonstrated in preclinical studies against respiratory conditions, microbial infections, oxidative stress, and even in silico antiviral activity against SARS-CoV-2. While traditional use supports its safety, modern toxicological assessments highlight the need for dose standardization. This paper underscores the relevance of J. adhatoda as a therapeutic resource and calls for further pharmacological validation and clinical trials.

Keywords: *Justicia adhatoda, Vasaka, vasicine, bronchodilator, phytochemistry, Ayurveda, respiratory pharmacology, traditional medicine, natural products*

1. Introduction

Medicinal plants have been the cornerstone of traditional healthcare systems worldwide, offering diverse bioactive compounds that have served as templates for modern drug development. Among these, *Justicia adhatoda*, a member of the family Acanthaceae, holds a unique position due to its extensive therapeutic utility, especially in the management of respiratory disorders. Commonly known as Vasaka, Malabar Nut, or *adhatoda*, this plant has been recognized in traditional medical systems such as Ayurveda, Unani, Siddha, and folk medicine across South Asia and Southeast Asia for millennia. The earliest documented references to *J. adhatoda* appear in classical Ayurvedic texts including the Charaka Samhita and Sushruta Samhita, where it is described as a potent remedy for ailments characterized by excess *Kapha* and *Vata*, primarily involving respiratory tract diseases.

The global burden of respiratory illnesses such as chronic bronchitis, asthma, and tuberculosis remains high, necessitating efficacious, affordable, and accessible therapeutic options. Synthetic bronchodilators and corticosteroids, though effective, are often accompanied by adverse effects and resistance issues. This has reignited interest in phytotherapy and plant-derived compounds, with *Justicia adhatoda* emerging as a promising candidate due to its potent bronchodilatory, expectorant, and anti-inflammatory properties. The plant's pharmacological repertoire extends beyond respiratory benefits, encompassing antimicrobial, antioxidant, uterotonic, and potential anticancer activities.

Phytochemical investigations have identified a complex matrix of biologically active constituents within *J. adhatoda*, most notably quinazoline alkaloids such as vasicine and vasicinone, which are responsible for its characteristic pharmacodynamics. These compounds have been extensively studied in vitro and in animal models, elucidating mechanisms such as smooth muscle relaxation, mucolytic activity, and modulation of inflammatory pathways. Additionally, emerging studies employing in silico molecular docking have revealed promising antiviral activities against viruses including SARS-CoV-2, further broadening the scope of *J. adhatoda*'s medicinal potential.

Despite its widespread traditional use and promising preclinical data, comprehensive clinical validation and standardization remain limited, hindering its full integration into evidence-based medicine. Moreover, issues such as variability in phytochemical content, lack of standardized formulations, and safety concerns—particularly relating to its uterotonic effects—necessitate rigorous scientific scrutiny.

This review aims to present an exhaustive analysis of *Justicia adhatoda*, encompassing its botanical characteristics, ethnomedicinal significance, phytochemistry, pharmacological activities, toxicological profile, and future research directions. By synthesizing traditional knowledge with contemporary scientific insights, this paper endeavors to highlight *J. adhatoda*'s potential as a versatile medicinal resource and stimulate further research towards its clinical application and pharmaceutical development.

2. Botanical and Taxonomical Description

2.1 Taxonomy and Nomenclature

Justicia adhatoda, previously classified under the genus *Adhatoda* as *Adhatoda vasica* Nees, belongs to the family Acanthaceae, order Lamiales. The reclassification to the genus Justicia reflects advances in phylogenetic and molecular studies that grouped similar species based on genetic and morphological traits. The binomial nomenclature is as follows:

Kingdom: Plantae
Phylum: Tracheophyta (vascular plants)
Class: Magnoliopsida (dicotyledons)
Order: Lamiales
Family: Acanthaceae
Genus: Justicia
Species: *J. adhatoda* L.

The plant is known by various vernacular names across regions:

Sanskrit: Vasaka
Hindi: Adulsa, Vasaka
Tamil: Vasambu
Marathi: Adusa
Telugu: Vasakamu
English: Malabar Nut, *adhatoda*, Arusa

The genus Justicia comprises over 600 species, many of which are tropical shrubs and herbs known for their medicinal properties. *J. adhatoda* is among the most studied due to its pharmacological importance.

2.2 Morphological Characteristics

Understanding the detailed morphology of *J. adhatoda* is crucial for correct identification, cultivation, and quality control in herbal pharmacognosy.

2.2.1 Habit and Habitat

J. adhatoda is a fast-growing, evergreen, perennial shrub, typically attaining a height of 1.5 to 3 meters, sometimes reaching up to 4 meters under optimal conditions. It exhibits a bushy and erect growth habit with multiple woody stems branching from the base. The plant is hardy, drought-resistant, and thrives in tropical to subtropical climates, commonly found at altitudes up to 1500 meters above sea level.

It naturally colonizes disturbed sites such as roadsides, forest edges, wastelands, and homestead gardens. It prefers well-drained soils rich in organic matter but can tolerate a range of soil types including loamy and sandy soils with pH 6.5–7.5.

2.2.2 Stem
The stems are quadrangular (square in cross-section), woody at the base, and green or light brown in color. Younger stems are covered with fine pubescence (soft hairs), which decreases as the stem matures. The bark is thin and smooth, becoming slightly rough with age.

2.2.3 Leaves
Leaves are one of the primary identification features of *J. adhatoda*:
Arrangement: Opposite, decussate (each pair at right angles to the one below)
Shape: Lanceolate to ovate-lanceolate
Size: Typically 8–15 cm in length, 3–6 cm in width
Margin: Entire (smooth edges)
Apex: Acute to acuminate (tapering to a point)
Base: Attenuate (narrowing at the base)
Texture: Glabrous (smooth and hairless) on the upper surface; paler and slightly pubescent on the underside
Venation: Pinnate with a prominent midrib and lateral veins visible on the underside
Petiole: Short, about 1 cm long
The leaves emit a characteristic bitter and slightly pungent aroma when crushed, attributable to volatile oils and alkaloids present in the mesophyll cells.

2.2.4 Inflorescence and Flowers
J. adhatoda produces flowers in axillary or terminal spikes or racemes, generally 6–10 cm long. The floral structure is zygomorphic (bilaterally symmetrical) and tubular, characteristic of the family Acanthaceae.
Calyx: Five sepals fused into a tubular calyx, green in color, 1–1.5 cm long, with narrow teeth at the apex
Corolla: Tubular, approximately 2.5–3 cm long, bilabiate (two-lipped) with the upper lip being hooded and the lower lip spreading
Color: Usually white, occasionally tinged with purple or pink
Stamens: Four didynamous stamens (two long and two short) inserted near the corolla tube's base
Pistil: Single style, ending in a bifid stigma
Flowering Period: Mainly from August to November, varying with climatic conditions
The flowers are hermaphroditic and entomophilous (insect-pollinated), attracting bees and butterflies.

2.2.5 Fruit and Seeds
The fruit is a small, oblong, club-shaped capsule, measuring about 1.5 cm in length. It is dehiscent, splitting open on maturity to release 2 to 4 seeds.
Seeds: Small, angular, brownish-black, with a rough surface and a hard seed coat, aiding in protection during dispersal.
Seed dispersal is primarily through gravity (barochory), with occasional involvement of ants (myrmecochory).

2.2.6 Root System
The root system is predominantly taproot type with lateral branches. The roots are cylindrical, brownish on the outside with a white interior. They contain significant alkaloids but are less commonly used in herbal preparations compared to leaves and stems.

2.3 Cytology and Genetic Studies
Chromosome studies report the diploid chromosome number of *J. adhatoda* as 2n = 22, which aids in taxonomic classification and breeding studies.
Molecular marker techniques such as RAPD (Random Amplified Polymorphic DNA) and SSR (Simple Sequence Repeat) analyses have been employed to study genetic diversity among wild and cultivated populations. This genetic information supports conservation strategies and quality assurance in medicinal plant cultivation.

2.4 Identification and Quality Control
Macroscopic and microscopic examinations are essential for proper authentication:
- Macroscopic identification includes leaf size and shape, stem texture, flower morphology, and aroma.
- Microscopic features of powdered leaves show epidermal cells with anisocytic stomata, glandular trichomes, and calcium oxalate crystals.
- Physicochemical parameters such as moisture content, ash values, extractive values, and thin-layer chromatography (TLC) fingerprints are standardized for quality control.

3. Ethnomedicinal and Traditional Uses
J. adhatoda holds a revered position in traditional medicine due to its versatile therapeutic profile, including Ayurveda, Unani, Siddha, Traditional Chinese Medicine (TCM), and diverse folk medicinal practices across South Asia and

Southeast Asia. Its long-standing use across cultures underscores its pharmacological versatility, particularly in the management of respiratory disorders, bleeding conditions, skin diseases, and reproductive health.

3.1 Traditional Medical Systems

3.1.1 Ayurveda

In Ayurveda, *J. adhatoda* is classified under the "Kasahara" (anti-cough) and "Shwasahara" (anti-asthmatic) groups. Its fundamental properties are:
Rasa (Taste): Tikta (bitter), Kashaya (astringent)
Guna (Attributes): Laghu (light), Ruksha (dry)
Virya (Potency): Shita (cooling)
Vipaka (Post-digestive effect): Katu (pungent)
Effect on Doshas: Pacifies Kapha and Pitta
Ayurvedic physicians often prescribe Vasaka for:

- Chronic cough, asthma, and bronchitis
- Hemoptysis (coughing up blood)
- Excessive menstrual bleeding (menorrhagia)
- Bleeding piles and other hemorrhagic conditions
- Tuberculosis (Rajayakshma), as an adjunct therapy

The leaves, flowers, and roots are used individually or in polyherbal combinations, prepared as decoctions, powders, or ghrita (medicated ghee).

3.1.2 Unani Medicine

In Unani pharmacopoeia, *J. adhatoda* is known as "Arusa" and considered "Muqawwi-i-Riya" (tonic for the lungs) and "Munaffis-i-Balgam" (expectorant). The leaf juice is administered in:

- Diseases of the chest and lungs
- Pneumonia
- Pulmonary tuberculosis

Unani practitioners also use the root in hematuria and uterine bleeding.

3.1.3 Siddha System

In Siddha, the plant is called "Adathodai," and it is used extensively for:

- Bronchial asthma and productive cough
- Fever and body aches
- Skin eruptions and ulcers (topically)

The preparation "Adathodai Manapagu" (a herbal syrup) is commonly used in Tamil Nadu as a household remedy for children and adults alike.

3.1.4 Folk and Indigenous Use

Tribal communities in India (e.g., the Bhils of Rajasthan, the Santhals of Jharkhand, and various Northeast Indian tribes) utilize *J. adhatoda* in their ethnomedicinal practices:

- Leaf poultices are applied to wounds and boils to promote healing
- Leaf smoke inhalation is used for respiratory congestion
- Root extracts are used in treating intestinal worms
- Decoctions are used for fever and malaria
- Infusions of flowers and young leaves are given to women with excessive menstrual bleeding

Traditional healers often mix *J. adhatoda* with other medicinal plants such as Tulsi (Ocimum sanctum), Black Pepper (Piper nigrum), or Ginger (Zingiber officinale) to enhance its effects.

3.1.5 Traditional Applications

Ailment	Mode of Use	Preparation Form
Cough, bronchitis	Leaf decoction or juice	Syrup, tea, extract
Asthma	Mixed with honey and black pepper	Herbal paste
Tuberculosis	Regular decoction intake	Decoction
Bleeding disorders	Leaf extract orally	Juice
Skin infections	Topical application of crushed leaves	Paste
Diarrhea, dysentery	Leaf powder orally	Capsule or infusion
Menorrhagia	Flower and leaf extracts	Powder or decoction

3.3 Home Remedies and Folk Recipes

1. Vasaka Cough Syrup

- Ingredients: Fresh *J. adhatoda* leaf juice, honey, black pepper powder
- Preparation: Mix 2 tablespoons of leaf juice with 1 teaspoon honey and a pinch of black pepper.

• Use: Taken twice daily for chronic cough and bronchitis.

2. Decoction for Asthma

• Ingredients: Dried *J. adhatoda* leaves (5g), water (200 mL)
• Preparation: Boil leaves in water until reduced to half.
• Use: Consume warm twice a day to ease bronchial spasms.

3. Topical Paste for Wounds and Skin Infections

• Ingredients: Fresh leaves
• Preparation: Grind into a paste and apply directly to the affected area.
• Use: Helps reduce inflammation, promotes healing, and prevents infection.

4. Anti-bleeding Flower Powder

Flowers are dried, powdered, and mixed with honey to treat bleeding gums and hemorrhoids.

3.4 Cultural and Ritual Use

In some rural traditions in India and Sri Lanka, *J. adhatoda* leaves are:
• Used in religious rituals to ward off "evil air" believed to cause respiratory illnesses
• Burned in households as an air purifier, especially during flu season
• Planted near homes due to belief in its protective and cleansing properties

3.5 Polyherbal Formulations in Traditional Medicine

In Ayurveda and Siddha, *J. adhatoda* is frequently used in combination with other botanicals to treat complex conditions:
• Sitopaladi Churna – for bronchitis (contains *J. adhatoda*, cardamom, and cinnamon)
• Vasavaleha – a herbal jam formulation with honey, ghee, and Vasaka for productive cough and hemoptysis
• Dashamoola Kwatha – used as an anti-inflammatory and expectorant, sometimes with *J. adhatoda* added

4. Phytochemical Profile

The pharmacological activities of *Justicia adhatoda* are fundamentally rooted in its diverse and rich phytochemical composition. The plant produces a wide spectrum of secondary metabolites, including alkaloids, flavonoids, phenolic compounds, essential oils, terpenoids, and saponins, which together contribute to its broad therapeutic potential.

4.1 Overview of Phytoconstituents by Plant Part

Plant Part	Major Phytoconstituents
Leaves	Quinazoline alkaloids (vasicine, vasicinone), flavonoids, tannins, essential oils
Flowers	Alkaloids, glycosides, flavonoids
Roots	Alkaloids (in lesser quantity), carbohydrates, trace volatile oils
Whole plant	Phenolics, saponins, terpenoids, steroids, reducing sugars

4.2 Major Classes of Phytochemicals and Their Roles

4.2.1 Alkaloids (Quinazoline-type)

The defining phytochemicals of *Justicia adhatoda* are quinazoline alkaloids, a class of heterocyclic nitrogen-containing compounds that exhibit a range of pharmacological effects.

Compound	Structure Type	Concentration Range	Biological Activity
Vasicine (peganine)	Quinazoline alkaloid	0.4%–1.2% in leaves (dry weight)	Bronchodilator, uterotonic, antimicrobial
Vasicinone	Oxidized derivative of vasicine	Formed by oxidation	Anti-inflammatory, ronchodilator
Deoxyvasicine	Reduced form	Trace	Antispasmodic
Adhatonine, Anisotine, Adhatodine	Minor alkaloids	Variable	Potential antiviral and CNS effects

Vasicine is the most studied, with proven efficacy as a bronchodilator and expectorant. It exerts a dual effect—bronchial smooth muscle relaxation and stimulation of the respiratory center.

Vasicinone, formed via enzymatic oxidation of vasicine, shows synergistic bronchodilatory effects when used in combination with vasicine. It also has anti-allergic and anti-inflammatory properties.

4.2.2 Flavonoids

Flavonoids are phenolic compounds with potent antioxidant, anti-inflammatory, and cytoprotective activities. Identified flavonoids in *J. adhatoda* include:

• Apigenin
• Luteolin
• Kaempferol
• Quercetin (in trace amounts)

These compounds act by:

• Scavenging reactive oxygen species (ROS)
• Inhibiting lipid peroxidation
• Modulating inflammatory cytokines (e.g., TNF-α, IL-6)
• Inhibiting enzymes such as cyclooxygenase (COX) and lipoxygenase (LOX)

4.2.3 Phenolic Compounds and Tannins

Phenolics contribute significantly to the astringent, antimicrobial, and antioxidant properties of the plant.

• Gallic acid
• Tannic acid
• Ferulic acid
• Ellagic acid (minor component)

These compounds aid in:

• Reducing mucosal irritation
• Preventing oxidative DNA damage
• Providing antibacterial activity via membrane disruption

4.2.4 Saponins

Saponins are glycosidic compounds with surfactant properties. They are responsible for:

• Enhancing expectorant action by stimulating mucus secretion
• Facilitating immune modulation
• Exhibiting antidiabetic effects via inhibition of glucose absorption

Quantitative studies indicate that the saponin content in dried leaves is approximately 1.2%–1.8%.

4.2.5 Essential Oils and Volatile Constituents

GC-MS analysis of the volatile oil from *J. adhatoda* reveals the presence of:

• Eucalyptol (1,8-cineole)
• Terpineol
• α-Pinene
• Thymol
• Limonene

These essential oils contribute to:

• Antiseptic and decongestant effects
• Mucolytic action
• Enhancement of airway clearance

Inhalation of steam containing leaf decoction is a common traditional method to deliver these volatiles directly to the respiratory tract.

4.2.6 Steroids and Terpenoids

• β-Sitosterol, stigmasterol, and campesterol have been identified in petroleum ether and chloroform extracts.
• These phytosterols exhibit anti-inflammatory, hypolipidemic, and immune-regulatory activities.
• Terpenoids contribute to the cytoprotective, anti-microbial, and hepatoprotective actions.

4.3 Quantitative Phytochemical Estimates

Phytochemical Group	Reported Quantity (per 100 g dry leaf)
Alkaloids	0.5–1.2 g
Flavonoids	1.0–1.8 g
Phenols	0.6–0.9 g
Saponins	1.2–1.8 g
Tannins	0.3–0.5 g
Essential Oils	0.1–0.2 mL

Values vary significantly based on geographical origin, harvest season, plant age, and extraction method.

4.4 Analytical Techniques for Identification

To authenticate and quantify the bioactive constituents of *J. adhatoda*, several analytical tools are employed:

• TLC (Thin-Layer Chromatography): Preliminary screening for alkaloids and flavonoids.
• HPLC (High-Performance Liquid Chromatography): Quantitative estimation of vasicine and vasicinone.

• GC-MS (Gas Chromatography-Mass Spectrometry): Identification of volatile components in essential oil.
• UV-Vis Spectroscopy: Used in colorimetric assays to determine total phenolic and flavonoid content.
• NMR (Nuclear Magnetic Resonance) and FTIR (Fourier Transform Infrared Spectroscopy): For structural elucidation of isolated compounds.

4.5 Synergistic Interactions
Recent pharmacological studies suggest that vasicine and vasicinone exhibit synergistic effects when administered together:
• Improved bronchodilation
• Enhanced anti-inflammatory response
• Reduced toxicity compared to isolated use
Moreover, the presence of flavonoids and phenolic acids further potentiates the therapeutic effects of quinazoline alkaloids by mitigating oxidative stress and inflammation.

4.6 Chemotaxonomic Significance
The unique presence of vasicine, a quinazoline alkaloid, in *Justicia adhatoda* serves as a chemotaxonomic marker for distinguishing it from other species in the Acanthaceae family. This property is critical for authentication in pharmacognosy and herbal medicine standardization.

5. Pharmacological Activities
The pharmacological properties of *Justicia adhatoda* L. are attributed primarily to its quinazoline alkaloids (notably vasicine and vasicinone), flavonoids, phenolics, and essential oils. The plant demonstrates a multifaceted pharmacological profile, with significant effects on the respiratory system, immune function, oxidative stress, inflammation, and microbial pathogens. Below is a detailed analysis of its major pharmacological activities as reported in various in vitro, in vivo, and in silico studies.

5.1 Antitussive and Expectorant Activity
Vasicine, the chief alkaloid, stimulates bronchial glands to increase secretion, thereby liquefying and expelling sputum. This expectorant activity is complemented by the antitussive effect of vasicinone, which inhibits cough reflex via peripheral and central mechanisms.
Mechanism:
• Enhances ciliary motility in the respiratory tract.
• Modulates cholinergic pathways to facilitate mucus clearance.
Evidence:
• Animal studies (e.g., guinea pigs exposed to irritant aerosols) showed significant reduction in cough frequency.
• Clinical formulations such as Vasaka syrup demonstrate therapeutic efficacy in productive and dry cough.

5.2 Bronchodilatory Activity
One of the most validated effects of *J. adhatoda* is bronchodilation, beneficial in asthma, COPD, and bronchitis.
Active Compounds: Vasicine and vasicinone
Mechanism:
• Vasicine acts as a β2-adrenergic receptor agonist-like compound.
• Relaxation of bronchial smooth muscle by phosphodiesterase inhibition.
• Increased cAMP levels in smooth muscle cells.
Evidence:
• Preclinical studies in guinea pigs and mice demonstrate reduced bronchoconstriction.
• Synergistic action observed when vasicine is combined with salbutamol.

5.3 Anti-inflammatory Activity
The anti-inflammatory effect of *J. adhatoda* is relevant for both respiratory and non-respiratory inflammatory conditions.

Mechanism:
• Downregulation of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β).
• Inhibition of cyclooxygenase (COX) and lipoxygenase (LOX) pathways.
• Suppression of NF-κB signaling.
Evidence:
• Ethanolic extracts reduced paw edema in carrageenan-induced inflammation models in rats.
• Flavonoids (e.g., luteolin, apigenin) demonstrated COX-2 selective inhibition.

5.4 Antimicrobial and Antibacterial Activity
Both alcoholic and aqueous extracts of *J. adhatoda* possess significant antibacterial and antifungal activities.
Active Compounds: Alkaloids, flavonoids, terpenoids
Mechanism:

• Disruption of microbial cell membranes.
• Inhibition of bacterial DNA gyrase and topoisomerase IV (suggested via docking studies).
Effective Against:
• Gram-positive bacteria: *Staphylococcus aureus, Bacillus subtilis*
• Gram-negative bacteria: *E. coli, Pseudomonas aeruginosa*
• Fungi: *Candida albicans, Aspergillus niger*
• Applications: Topical use for skin infections, wound healing; oral use in respiratory infections.

5.5 Antioxidant Activity
Oxidative stress contributes to inflammation, cancer, and chronic diseases. Flavonoids and phenolic acids in *J. adhatoda* provide free radical scavenging activity.
Mechanism:
• Donation of electrons to neutralize ROS (reactive oxygen species)
• Inhibition of lipid peroxidation and enhancement of endogenous antioxidant enzymes (e.g., SOD, catalase)
Assays Used:
• DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging
• ABTS and FRAP assays
Outcomes:
Ethanolic and methanolic leaf extracts showed up to 80% inhibition in DPPH assays.

5.6 Antiviral Activity
Recent studies have explored the antiviral potential of *J. adhatoda*, especially in light of the COVID-19 pandemic.
Mechanism (In silico and In vitro):
• Vasicine and anisotine showed strong binding affinity to SARS-CoV-2 main protease (Mpro) and ACE2 receptor in docking studies.
• Possible inhibition of viral replication enzymes.
Other Viruses Studied:
• Influenza virus (H1N1)
• Herpes Simplex Virus (HSV-1)
Note: Antiviral effects need clinical validation, but preliminary results are promising for drug development.

5.7 Uterotonic and Abortifacient Activity
Traditionally used for treating excessive menstrual bleeding, *J. adhatoda* shows strong uterotonic effects, but this can be dangerous during pregnancy.
Mechanism:
• Vasicine stimulates uterine smooth muscle contractions.
• Potential activation of prostaglandin pathways.
Implication:
• Used in traditional medicine for postpartum hemorrhage and menstrual regulation.
• Contraindicated during pregnancy due to risk of miscarriage.

5.8 Antidiabetic and Hypoglycemic Activity
Experimental studies suggest that *J. adhatoda* may modulate glucose metabolism.
Mechanism:
• Inhibition of α-glucosidase and α-amylase enzymes.
• Enhancement of insulin secretion and glucose uptake.
Evidence:
• Streptozotocin-induced diabetic rat models showed significant reduction in blood glucose and HbA1c levels after treatment with leaf extract.
• Flavonoids and saponins are believed to be responsible for this effect.

5.9 Hepatoprotective Activity
Ethanolic leaf extracts have shown protective effects against chemically-induced liver damage.
Mechanism:
• Antioxidant defense enhancement
• Stabilization of liver enzymes (ALT, AST, ALP)
Model Systems:
Carbon tetrachloride (CCl_4)-induced hepatotoxicity in rats
Histological Evidence:
Reduction in hepatic necrosis and improved liver architecture after treatment

5.10 Wound Healing and Skin-Protective Activity

The topical application of *J. adhatoda* is supported by its antimicrobial, anti-inflammatory, and astringent properties.
Mechanism:
• Promotes fibroblast proliferation
• Increases collagen synthesis and re-epithelialization
Studies:
Excision and incision wound models in rats showed accelerated healing with Vasaka leaf ointment.

5.11 Anticancer and Cytotoxic Potential
Although still in early stages of investigation, some in vitro studies suggest cytotoxic activity against cancer cell lines.
Possible Targets:
• Breast cancer (MCF-7)
• Lung cancer (A549)
Mechanism:
• Apoptosis induction
• Cell cycle arrest (G0/G1 phase)

5.12 . Formulation and Standardization
Several herbal products incorporate *J. adhatoda*:
• Cough syrups: Vasaka syrup, Sitopaladi churna
• Tablets: Bronkoherb, Vasa gutika
• Inhalers: Polyherbal inhalants for bronchitis
Standardization is essential to ensure vasicine content (usually 0.5–1.0%) and to maintain batch-to-batch consistency.

6. Toxicology and Safety Assessment
6.1 Reproductive Toxicity
High doses of vasicine (>25 mg/kg) may induce miscarriage due to uterine contractions. Use during pregnancy should be strictly avoided.

6.2 Side Effects
• Nausea
• Vomiting
• Diarrhea (at high doses)
• Long-term toxicity studies are limited and represent an area for future research

9. Conclusion and Future Perspectives
Justicia adhatoda L. (commonly known as Vasaka or Malabar nut) has established itself as a plant of significant therapeutic importance in both traditional and modern medicine. It is one of the most widely used herbs in the treatment of respiratory tract ailments, especially asthma, bronchitis, tuberculosis, and chronic cough. The presence of unique quinazoline alkaloids, particularly vasicine and vasicinone, forms the biochemical cornerstone of its pharmacological actions, including bronchodilation, expectorant, and anti-inflammatory properties.
In addition to its pulmonary benefits, *J. adhatoda* has demonstrated a broad pharmacodynamic profile encompassing antioxidant, antimicrobial, hepatoprotective, antidiabetic, wound-healing, uterotonic, and emerging antiviral and anticancer activities. The ethnopharmacological relevance of the plant, deeply embedded in Ayurvedic, Unani, Siddha, and various tribal systems, has been strongly supported by preclinical and pharmacological studies.
Advancements in phytochemical research, using techniques such as HPLC, GC-MS, and NMR, have enabled the identification of key bioactive compounds across different parts of the plant. Despite the growing body of scientific literature, comprehensive validation and clinical translation of its therapeutic potential remain incomplete.
Despite the vast ethnomedicinal use and promising pharmacological potential of *Justicia adhatoda*, several critical research gaps remain. One of the most pressing issues is the lack of robust human clinical trials to validate its therapeutic efficacy, particularly for respiratory disorders, inflammatory conditions, and emerging viral infections. Although numerous in vitro and animal studies support its medicinal claims, these findings have yet to be systematically translated into clinical practice.
Additionally, there is an urgent need for the standardization of plant extracts. Variability in the concentration of bioactive compounds—especially vasicine and vasicinone—due to differences in geography, harvest time, and processing methods poses a challenge to reproducibility and therapeutic consistency. Without standardized formulations and pharmacopoeial benchmarks, dosage optimization and regulatory approval remain difficult.
Long-term toxicity and safety profiles are inadequately studied. While traditional use suggests a relatively wide margin of safety, comprehensive toxicological evaluations—particularly chronic toxicity, reproductive toxicity, and teratogenicity—are lacking. This is especially crucial given the plant's known uterotonic activity.
Mechanistic studies at the molecular and cellular levels also remain insufficient. Although certain pathways such as NF-κB, COX, and cytokine signaling have been implicated, the precise biochemical mechanisms of *J. adhatoda*'s pharmacological effects are not fully understood. Furthermore, in the context of antiviral research, especially against pathogens like SARS-CoV-2, promising in silico findings require validation through in vivo and clinical studies.

Potential herb-drug interactions have not been well-documented, raising concerns about its use in combination with conventional pharmaceuticals, particularly in patients with polypharmacy. In the realm of drug development, there has been minimal exploration of advanced delivery systems such as nanoformulations or controlled-release preparations to enhance the bioavailability of key compounds.

Moreover, research utilizing modern omics technologies—such as genomics, transcriptomics, and metabolomics—to investigate the biosynthetic pathways of its active constituents is still in its infancy. This limits the potential for metabolic engineering or synthetic production of vasicine and related compounds.

Finally, sustainability concerns must be addressed, as much of the current supply relies on wild harvesting. There is a need to develop scalable, eco-friendly cultivation practices and conservation strategies to ensure the long-term availability of this valuable medicinal resource.

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