A Review on the Role of "*Adhatoda vasica*" in COPD Management

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Abstract: Chronic Obstructive Pulmonary Disease (COPD) is a progressive, non-communicable respiratory condition marked by persistent airflow limitation, chronic inflammation, oxidative stress, mucus hypersecretion, and mitochondrial dysfunction induced by hypoxia. Although advancements have been made in conventional pharmacotherapy, current treatments mainly offer symptomatic relief and do not sufficiently alter disease progression. This has led to increasing interest in complementary and plant-based therapies. *Adhatoda vasica* (Justicia adhatoda), commonly referred to as Vasaka, is a well-regarded medicinal plant in Ayurvedic and Unani medicine, traditionally utilized for treating asthma, bronchitis, cough, and other respiratory issues. This review critically examines the therapeutic potential of *A. vasica* in managing COPD by synthesizing findings from recent phytochemical, pharmacological, preclinical, and emerging clinical studies. The plant is abundant in bioactive compounds, especially quinazoline alkaloids (such as vasicine and vasicinone), flavonoids, phenolic acids, phytosterols, saponins, and tannins. Collectively, these constituents demonstrate bronchodilatory, mucolytic, anti-inflammatory, antioxidant, antimicrobial, and anti-hypoxic properties. Experimental research indicates that *A. vasica* modulates essential inflammatory pathways, mitigates oxidative damage, enhances mucus clearance, protects mitochondrial function via Nrf2 and HIF-1α signaling, and reduces airway remodeling—key pathological features of COPD. Recent advancements in formulation strategies, including standardized extracts and innovative pulmonary delivery systems, have further improved its therapeutic potential. Overall, *Adhatoda vasica* stands out as a promising multi-targeted herbal option for adjunctive COPD therapy. However, comprehensive clinical trials that are large-scale and well-structured, along with standardized phytochemical profiling and thorough safety and pharmacokinetic studies, are crucial to confirm its clinical efficacy and long-term therapeutic role in managing COPD.

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I. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent, preventable, and treatable condition characterized by ongoing respiratory symptoms and airflow limitations. These issues arise from abnormalities in the airways and/or alveoli, typically caused by significant exposure to harmful particles or gases. Common respiratory symptoms include dyspnea, cough, and/or sputum production, which patients may often underreport. [23]

COPD stands for Chronic Obstructive Pulmonary Disease, encompassing two types of long-term diseases that cause swelling and partial blockage of the airways (the breathing tubes) in the lungs. This condition worsens over time; while it cannot be cured, it can be effectively treated and managed. COPD primarily consists of two major breathing disorders: emphysema and chronic bronchitis. [1]

Emphysema affects the tiny alveoli (air sacs) located at the ends of your lungs. Under normal circumstances, these air sacs expand like balloons during inhalation and deflate during exhalation. However, emphysema stiffens these air sacs, trapping air inside them. This leads to difficulty in breathing and feelings of fatigue. Chronic bronchitis causes inflammation, swelling, and irritation in your airways. The glands within your airways produce excess mucus (phlegm), which obstructs airflow. This results in a persistent cough, the expulsion of mucus, and breathlessness. [1]

COPD has been considered a disease of the elderly. However, recent studies indicate that COPD can also occur in younger individuals, with an increasing burden observed among this population . The concept of "young COPD" is gaining attention, and the 2022 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report first introduced the concept of "young COPD," defining it as adult patients under the age of 50. [2]

Adhatoda vasica (synonym Justicia Adhatoda), commonly known as Vasaka, has been widely used in traditional Ayurvedic and Unani medicine to treat cough, asthma, bronchitis, and other pulmonary diseases. Phytochemical analyses reveal that the leaves and roots are rich in alkaloids such as vasicine, vasicinone, and various flavonoids that contribute to its pharmacological activity.

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Recent studies have validated its traditional use and highlighted its relevance in modern respiratory medicine, particularly for chronic airway disorders . [8]

Preclinical research indicates that extracts from A. vasica exhibit powerful bronchodilatory, mucolytic, anti-inflammatory, and antioxidant effects. Experimental models reveal notable reductions in airway resistance, improved mucus clearance, and inhibition of critical inflammatory mediators such as TNF α, IL-6, and IL-1β following the administration of Vasaka extracts. Additionally, vasicine, a primary alkaloid, demonstrates calcium-channel blocking activity, which aids in smooth muscle relaxation and enhances airflow—an essential mechanism in the treatment of COPD. [9]

One of the most intriguing discoveries is the capacity of *A. vasica* to modulate the Nrf2 pathway, a crucial regulator of antioxidant defense. Sundaram et al. (2019) demonstrated that Vasaka extract can reverse hypoxia-induced mitochondrial dysfunction—an important contributor to the progression of COPD—by activating Nrf2 and restoring cellular respiration. Likewise, research involving animal models of COPD induced by cigarette smoke revealed that standardized Vasaka extract decreased oxidative damage, enhanced lung tissue structure, and reduced airway remodeling. [10]

Additionally, Adhatoda vasica has shown significant anti-remodeling activity by decreasing collagen deposition, inhibiting neutrophil infiltration, and reducing goblet cell hyperplasia—changes that contribute to irreversible airway narrowing in COPD. Clinical observations from herbal formulations containing A. vasica indicate improvements in expectoration, reduction in dyspnea, and better overall respiratory performance with minimal side effects. These findings collectively support the use of A. vasica as a potential complementary therapeutic option in COPD management .[11] [12]

With its diverse mechanisms of action—such as bronchodilation, anti-inflammatory effects, antioxidation, hypoxia protection, and mucoregulation — *Adhatoda vasica* stands out as a promising candidate for effective plant-based therapies for COPD. Nonetheless, despite significant preclinical validation, comprehensive large-scale controlled clinical trials are essential to ascertain the optimal dosing, safety, and long-term effectiveness. Ongoing research into its bioactive components and pharmacokinetics could have the way for establishing *Vasaka* as a standardized herbal remedy for COPD in the realm of future respiratory medicine.. [7] [11]

Justicia adhatoda (L.), sometimes referred to as Malabar nut, Arusa, Adulsa, Vasa or Vasaka, is a plant of exceptional medicinal values whose leaves, blossoms, fruits and roots are widely used as sedative, expectorant and antispasmodic to treat asthma, chronic bronchitis, cold and whooping cough. It is significantly efficacious in chronic bronchitis and asthma. Justicia adhatoda is a small evergreen sub herbaceous plant which grows all over the plains of India and the lower Himalayan ranges. The plant has minutely pubescent entire leaves arising from swollen nodes, the flowers are white or purple in color. The leaves are opposite, short petioled, broad, lanceolate, long tapering or pointed, smooth on both surfaces, and of a yellowish green or dark green colour. The taste is bitter and aromatic. [13]

II. HISTORY OF COPD

Some of the earliest accounts of emphysema can be traced back to notable figures in medical history: Bonet (1679): Described “voluminous lungs.” Morgagni (1769): Documented 19 cases where the lungs were “turgid,” particularly due to air. Baille (1789): Provided illustrations of an emphysematous lung, believed to belong to Samuel Johnson. The clinical understanding of chronic bronchitis, a component of COPD, began with Badham (1814), who used the term catarrh to describe the chronic cough and mucus hypersecretion that are hallmark symptoms. He characterized bronchiolitis and chronic bronchitis as debilitating conditions. The emphysema aspect was notably described by Laënnec (1821) in his Treatise on Diseases of the Chest. A clinician, pathologist, and inventor of the stethoscope, Laënnec conducted meticulous dissections of patients he had observed during their lives. He recognized that emphysematous lungs were hyperinflated and poorly emptied. In his 1837 work, A Treatise on the Diseases of the Chest and on Mediate Auscultation (p. 81), Laënnec wrote: “The disease which I designate by this title is very little known and has not hitherto been correctly described by any author. I for a long time thought it very uncommon, because I had observed only a few cases of it: but since I have made use of the stethoscope, I have verified its existence as well on the living as the dead subject, and am led to consider it as by no means infrequent. I consider many cases of asthma, usually deemed nervous, as depending on this cause.” At this time, smoking was uncommon, yet emphysema could still occur in non-smokers, particularly those with a genetic predisposition or environmental triggers. Laënnec added: “In opening the chest, it is not unusual to find that the lungs do not collapse, but they fill up the cavity completely on each side of the heart. When experienced, this will appear full of air… The bronchus of the trachea are often at the same time a good deal filled with mucous fluid”. [3]

Thus, Laënnec articulated a combination of emphysema and chronic bronchitis. John Hutchinson invented the spirometer in 1846, a crucial tool for diagnosing and managing COPD, although its application remains limited in many areas today. Hutchinson’s device initially measured only vital capacity, and it would take another century for Tiffeneau to introduce timed vital capacity as a measure of airflow, completing spirometry as a diagnostic tool (Tiffeneau and Pinelli 1947).[3]

Osler’s Principles and Practices of Medicine (1916) provided minimal information on emphysema, with Osler attributing the condition to excessive pressure in the alveoli. Notably, references to the spirometer are absent in this classic text. In 1912, another author illustrated the sphygmomanometer, invented by Rico Rossi in 1896, but did

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not mention spirometry, occurring 50 years post-Hutchinson's invention. A textbook titled Disease in the Chest published in 1918 briefly mentioned spirometry without illustrations (Norris and Landis 1918). Gaensler later introduced the air velocity index based on Tiffeneau's findings, as well as the forced vital capacity, which underpins the FEV1 and FEV1/FVC percent measures (Gaensler 1950, 1951). In 1944, prominent emphysema educator Ronald Christie asserted: "The diagnosis should be considered certain when dyspnea on exertion, of insidious onset, not due to bronchospasm, or left ventricular failure, appears in a patient who has some physical signs of emphysema together with chronic bronchitis and asthma" (Christie 1944, p. 145). This statement highlights Christie's recognition of the individual components of COPD, relying on patient history and physical examination for diagnosis. Oswald (1953) documented the clinical features of 1,000 chronic bronchitis cases. Barach and Bickerman (1956) edited the first comprehensive textbook on pulmonary emphysema, detailing the era's treatment methods. These physicians were early advocates for emphysema treatment. Contributors included: Dayman: Recognized spirometric and flow volume patterns indicating dynamic expiratory airway collapse in emphysema. Dickerson Richards: Nobel Laureate who focused on pulmonary circulation and cor pulmonale. Reuben Cherniack: Described respiratory acidosis and significantly advanced our understanding of emphysema diagnosis and treatment over several decades. Menelee and Callaway: Provided insights into pulmonary function tests for emphysema patients. In total, 17 leading clinicians and clinical scientists contributed to this seminal work of the 1950s. The first edition of Hinshaw and Garland's (1956) *Textbook of Respiratory Medicine* featured a detailed illustration of a Collins 13.5-liter recording spirometer alongside capacity spirograms that demonstrated airflow limitations in emphysema. [3]

Chronic Obstructive Pulmonary Disease (COPD) is a significant non-communicable respiratory condition and continues to be one of the top causes of morbidity and mortality around the globe. Recent global estimates suggest that COPD affects roughly 390–400 million individuals, leading to over 3.2 million deaths each year, making it the third leading cause of death worldwide. The increasing burden of this disease is linked to ongoing exposure to tobacco smoke, environmental pollution, and aging populations in both developed and developing areas. [4]

III. PREVELENCE OF COPD

Epidemiological studies reveal that the burden of COPD is disproportionately greater in low- and middle-income countries (LMICs), where over 80% of COPD-related deaths occur. Factors such as rapid urbanization, occupational exposure to dust and chemicals, and the widespread use of biomass fuels for cooking and heating significantly contribute to the prevalence of the disease in these regions. South-East Asia and Africa are experiencing the most rapid increases in COPD prevalence, resulting in considerable healthcare and economic challenges The prevalence of COPD rises significantly with age, particularly among individuals aged ≥40 years, due to the cumulative effect of risk factors and declining lung function. Historically, COPD has been more common in men; however, recent data indicate a growing prevalence among women, especially in developing nations. This trend is linked to increasing tobacco use among women and extended exposure to indoor air pollution from burning biomass fuels. [5] [24]

In India, COPD poses a considerable public health challenge, with recent population-based research estimating a prevalence of 6.5–8.5% among adults. India accounts for nearly 15% of global COPD-related mortality, primarily driven by tobacco smoking, household air pollution, and occupational hazards. COPD significantly contributes to disability-adjusted life years (DALYs) and results in a heavy socioeconomic burden due to frequent exacerbations and hospitalizations. Despite its high prevalence and mortality, COPD remains significantly underdiagnosed, with estimates indicating that 70–80% of cases go unidentified, particularly in rural and resource-limited areas. Delayed diagnosis leads to disease progression, increased frequency of exacerbations, and higher mortality rates, highlighting the urgent need for early screening, improved access to spirometry, and public health initiatives aimed at addressing modifiable risk factors. [25] [4]

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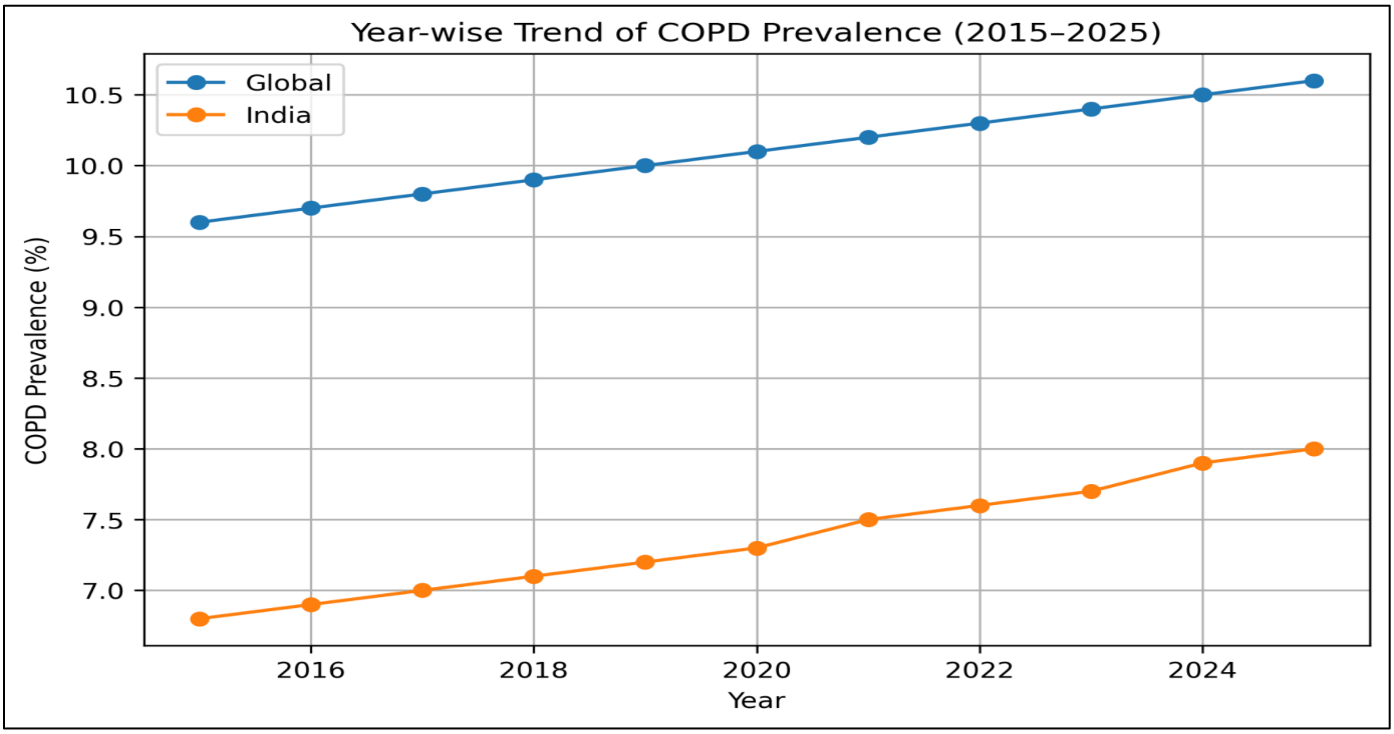

Fig 1 Year Wise Prevelence Rate of COPD

- *Adhatoda vasica*

Justicia adhatoda (L.), commonly referred to as Malabar nut, Arusa, Adulsa, Vasa, or Vasaka, is a plant renowned for its impressive medicinal qualities. This plant has been an integral part of traditional medicine systems for centuries, owing to its extensive range of therapeutic applications. The leaves, flowers, fruits, and roots of Justicia adhatoda are highly valued for their sedative, expectorant, and antispasmodic properties. These attributes make it particularly effective in the treatment of various respiratory ailments, such as asthma, chronic bronchitis, colds, and whooping cough. Among these, its effectiveness in managing chronic bronchitis and asthma stands out, providing significant relief to those suffering from these conditions. This small, evergreen, sub-herbaceous plant thrives in the diverse climatic conditions found across the plains of India and the lower Himalayan ranges. Its adaptability to different environments contributes to its widespread cultivation and use. The plant is characterized by finely pubescent, entire leaves that sprout from swollen nodes, adding to its distinct appearance. The flowers of Justicia adhatoda come in shades of white or purple, offering a subtle contrast to its lush foliage. The leaves themselves are opposite in arrangement, with short petioles that add to their structural elegance. They feature a broad, lanceolate shape that tapers to a pointed tip, with a smooth texture on both sides. The color of the leaves varies from a yellowish-green to a dark green, depending on the specific growing conditions. When tasted, the leaves have a unique combination of bitterness and a pleasant aromatic quality, which contributes to their medicinal efficacy. [13]


Fig 2 Adhatoda vasica Plant


Fig 3 Dry leaves of Adhatoda vasica

➢ *Vernacular Name*

Table 1 Vernacular Names of Adhatoda vasica [13]

Language	VERNACULAR NAME
Hindi	Adosa, Arusha, Bansa, Rus, Adusa, Adalsa,Adulaso, Adarsa, Adalsa
Sanskrit	Vasa, Vasaka, Acchadayati, Simhasya, Atarusha, Vrisha, Bhishagmata, Sinhaparni, Vansa, Amalaka, Bashika, Kanthiravi, Nasa, Pancha mukhi, Kasnotpatana, Rakrappittaghni
Marathi	Adulsa, Adusa, Adulsi, Baksa, Vasuka
Urdu	Bansa, Arusa
English	Malabar Nut, Vasaka
Tamil	Eadadad, Adathodai, Adadoda,Vachai, Abadodai
Konkani	Adolso, Kumaon, Bashangarus, Basinga
Punjabi	Vamsa, Bhekkar
Gujrati	Adusol, Araduso, Aduraspee, Bansa, Asoge, Alduso
Telugu	Addasaramu, Adam kabu, Adampaka
Kannada	Adusogae, Adu, Muttada, Soppu

➢ *Morphology*

- *Macroscopic Characters:*

This is a dense shrub that generally reaches heights between 1.2 and 2.4 meters, though it can occasionally grow into a tree form, attaining up to 6 meters. It features numerous long, opposite, and ascending branches, supported by a stem with smooth, yellowish, rounded bark. The leaves are shaped elliptical to lanceolate, measuring 10-20 cm by 8-9 cm, and are acuminate at the tips. When young, the leaves have a slight pubescence but become glabrous as they mature. They display a dark green hue on the upper surface and a lighter shade underneath, tapering at the base. The petioles measure 1-2.5 cm in length. Flowers are borne in dense, axillary, pedunculate spikes measuring 2-8 cm long, appearing towards the branch tips. The peduncles are stout, typically 3-10 cm long and shorter than the leaves. The calyx is under 1.3 cm long, either glabrous or slightly pubescent, and divides up to 2 mm from the base. The sepals are imbricate, oblong-lanceolate, acute, with three nerves and a reticulate venation. The corolla is white, adorned with a few irregular pinkish bars in the throat, measuring 2.5-3 cm in length and pubescent on the outside. The corolla tube is 1-2 cm long, cylindrical in the lower half (4 mm in diameter), ovate-oblong, curved, obtuse, and notched. The filaments are long, stout, and curved, with hairy bases, while the lower anther-cells are minutely apiculate (not white-tipped). The ovary and the lower part of the style are both pubescent. The seeds are orbicular-oblong, measuring 5-6 mm long, tubercular-verrucose, and glabrous. [14]

- *Microscopic Characters:*

In a detailed transverse section through the midrib, the structure reveals a distinctive anatomy. The lower side is markedly convex, creating a prominent bulge, while the upper side exhibits a central depression, giving it a unique concave appearance. This configuration forms a central arc of meristeles, which are the vascular bundles, accompanied by a few secondary meristeles positioned symmetrically on either side. These meristeles are crucial for the transport of nutrients and water throughout the plant. The epidermis on both the upper and lower surfaces consists of cells that vary from rectangular to square shapes, enveloped by a thin, protective cuticle layer. This cuticle plays a crucial role in minimizing water loss and providing a barrier against pathogens. The cell walls of the upper epidermis are particularly notable for their pronounced waviness, a feature that is less evident in the lower epidermis. This waviness could contribute to the flexibility and strength of the leaf structure.Beneath the upper epidermis lies a well-organized layer of palisade cells, which are arranged in two distinct layers. These cells are rich in oil globules, which are likely involved in storing energy and contributing to the plant’s defense mechanisms. Additionally, these cells contain elongated, warty cystoliths—calcium carbonate deposits—that extend into the lower palisade cells, potentially playing a role in deterring herbivores and providing structural support. On either side of the midrib, the section reveals 5-10 rows of collenchymatous tissue. This tissue is known for its ability to provide mechanical support while maintaining flexibility, essential for the plant's growth and movement. The midrib itself houses 3-4 conjoint, collateral meristeles, indicating a complex vascular system that is vital for the plant's physiological functions.Moreover, the lower epidermis is dotted with small glandular trichomes. These structures may serve various functions, including secretion of substances that could deter herbivores or contribute to the plant's interaction with its environment. Overall, the section through the midrib highlights a sophisticated arrangement of tissues, each playing a critical role in the plant's survival and adaptation. [14]

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➢ *Taxonomic Classification*

Table 2 Taxonomical Classification of Adhatoda vasica

Taxonomical Rank	**Taxon**
Kingdom	Plantae
Division	Angiosperms
Class	Eudicots
Order	Lamiales
Family	Acanthaceae
Genus	Justicia
Species	J. adhatoda
Common name	Adulsa, Vasaka

IV. GEOGRAPHICAL DISTRIBUTION

This plant is extensively found throughout the Indian subcontinent, which includes India, Nepal, Sri Lanka, Pakistan, and Bangladesh. In India, it thrives in a range of environments, from sub-Himalayan areas (up to an altitude of 1,500 m) to tropical and subtropical plains. You can commonly find it along roadsides, forest edges, and in wastelands, showcasing its remarkable ecological adaptability. [15]

The plant can also be found in Southeast Asia (including Myanmar, Thailand, Malaysia, and Indonesia) and has been introduced to certain regions of the Middle East and East Africa due to its medicinal significance and ability to thrive in warm climates. [17]

V. PHYTOCHEMISTRY

Adhatoda vasica is primarily characterized by its rich content of quinazoline alkaloids, which are recognized as its key bioactive components. The main alkaloids include vasicine (peganine) and vasicinone, along with deoxyvasicine, adhatodine, vasicinol, and vasicinolone. These compounds are predominantly found in the leaves and are linked to bronchodilatory and anti-inflammatory effects.[15]

In addition to alkaloids, A. vasica also features flavonoids and phenolic compounds such as quercetin, kaempferol, luteolin, apigenin, rutin, caffeic acid, and ferulic acid. These substances play a crucial role in providing significant antioxidant and anti-inflammatory benefits, aiding in the reduction of oxidative stress and chronic inflammation related to respiratory conditions. [19] [16]

➢ *Quinazoline Alkaloids (Vasicine, Vasicinone)*

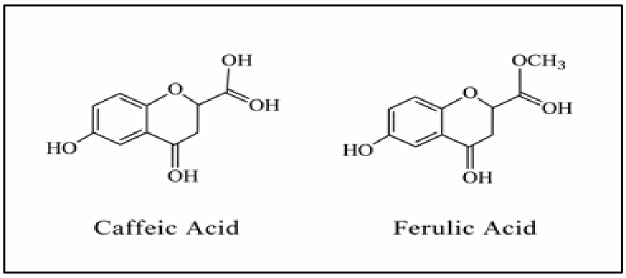

Fig 4 Quinazoline Alkaloids (Vasicine, Vasicinone)

The quinazoline alkaloids vasicine and vasicinone are key bioactive components of *Adhatoda vasica* and are crucial in managing COPD. These compounds demonstrate bronchodilatory and expectorant properties by relaxing bronchial smooth muscles and improving mucociliary clearance. They function by inhibiting phosphodiesterase activity, which leads to elevated intracellular cAMP levels, promoting relaxation of airway smooth muscles. Furthermore, these alkaloids decrease pro-inflammatory cytokines (TNF-α, IL-6) and diminish neutrophilic infiltration, effectively addressing chronic airway inflammation and airflow limitation—two defining characteristics of COPD. [15][22]

➢ *Flavonoids (Quercetin and Luteolin)*

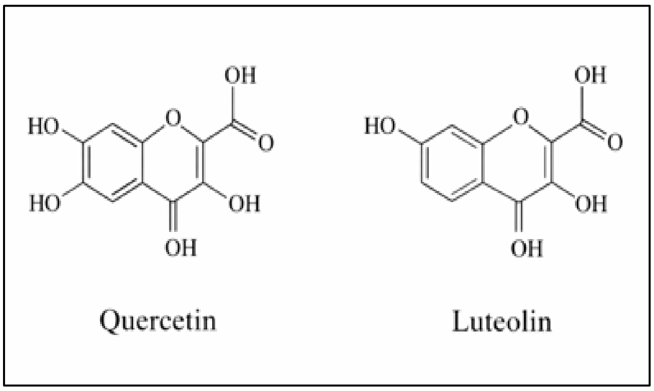

Fig 5 Flavonoids (Quercetin and Luteolin)

Flavonoids found in *A. vasica* serve as powerful antioxidants and anti-inflammatory agents, effectively combating oxidative stress-related lung injury in COPD. Quercetin and luteolin work to inhibit NF-κB and MAPK signaling pathways, resulting in reduced expression of inflammatory mediators such as IL-8, COX-2, and iNOS. These effects help alleviate inflammation caused by cigarette smoke, minimize epithelial damage, and address corticosteroid resistance, all of which pose significant challenges in the treatment of COPD. [18]

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➢ *Phenolic Compounds (Caffeic Acid, Ferulic Acid)*

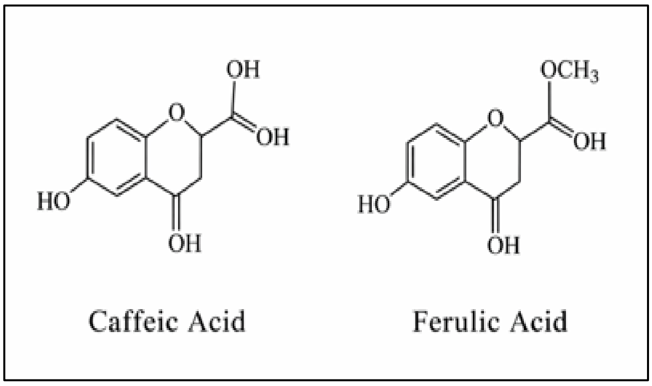

Fig 6 Phenolic Compounds (Caffeic Acid, Ferulic Acid)

Phenolic acids play a crucial role in the free-radical scavenging activity of *A. vasica*. In the context of COPD, the overproduction of reactive oxygen species (ROS) results in mitochondrial dysfunction, an imbalance between proteases and antiproteases, and hastened lung aging. Caffeic and ferulic acids effectively neutralize ROS and enhance the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD) and catalase, thus safeguarding alveolar structures and diminishing emphysematous transformations. [19][22]

➢ *Terpenoids and Phytosterols (β-Sitosterol)*

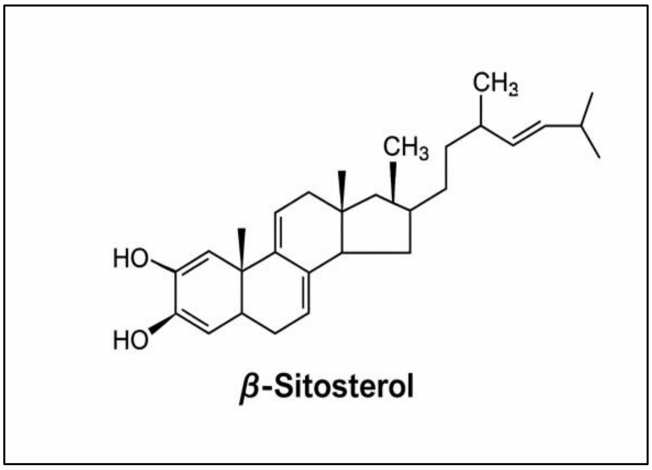

Fig 7 Terpenoids and Phytosterols (β-Sitosterol)

Terpenoids and phytosterols, such as β-sitosterol, play a vital role in regulating immune responses by inhibiting macrophage activation and the release of cytokines. In the context of COPD, persistent macrophage-driven inflammation contributes to tissue remodeling and narrowing of the airways. Research indicates that β-sitosterol effectively suppresses TNF-α and IL-1β while simultaneously promoting anti-inflammatory cytokines, thus helping to reduce airway remodeling and chronic inflammation. [20]

➢ *Saponins and Tannins*

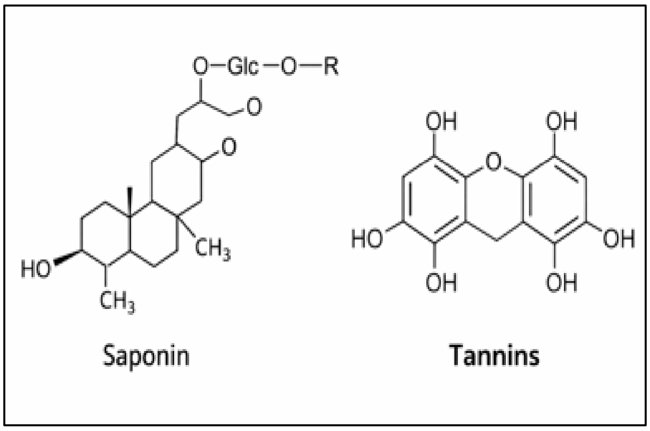

Fig 8 Saponins and Tannins

Saponins boost expectorant activity by decreasing mucus viscosity and aiding in sputum clearance, effectively addressing mucus hypersecretion linked to chronic bronchitis in COPD. Tannins provide antimicrobial and astringent properties, helping to lessen recurrent respiratory infections that worsen the progression of COPD. When combined, these components enhance airway hygiene and decrease the frequency of exacerbations. [21]

VI. PHARMACOLOGICAL ACTION OF "*Adhatoda vasica*" RELAVENT TO COPD

➢ *Anti-Inflammatory Mechanism*

Adhatoda vasica is a medicinal plant known for its therapeutic properties, particularly in alleviating airway inflammation through its active alkaloids, vasicine and vasicinone. Key mechanisms include: Inhibition of NF-κB signaling, reducing pro-inflammatory cytokines (TNF-α, IL-6, IL-1β). Downregulation of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), decreasing prostaglandins and nitric oxide production. Suppression of neutrophil recruitment, minimizing tissue damage and improving airway histology, especially in chronic obstructive pulmonary disease (COPD). [26]

➢ *Bronchodilatory Mechanism*

Extracts of Adhatoda vasica are known to induce relaxation of the airway smooth muscle through several mechanisms. One of the key actions involves the inhibition of phosphodiesterase (PDE) enzymes. This inhibition leads to an increase in the levels of intracellular cyclic adenosine monophosphate (cAMP). Elevated cAMP levels are crucial because they promote smooth muscle relaxation, which in turn eases the contraction of airway muscles and facilitates breathing. Active compound called vasicine. Vasicine exhibits activity that is similar to that of β2-agonists, which are commonly used in bronchodilator medications. This β2-agonistic-like activity of vasicine further enhances bronchodilation. [27] [28]

➢ *Antioxidant Mechanism*

A. vasica enhances the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and

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glutathione (GSH). These enzymes play crucial roles in the body's defense against oxidative stress. SOD converts superoxide radicals into less harmful molecules, CAT further breaks down these molecules into water and oxygen, and GSH helps detoxify harmful substances. By boosting the activity of these enzymes, A. vasica strengthens the lungs' natural defense mechanisms against oxidative damage. [29] [30]

- *Anti-Hypoxic & Mitochondrial Protection*

Recent studies show that Adhatoda vasica, a traditional medicinal plant, protects lung mitochondria and improves oxygen homeostasis by modulating Hypoxia-Inducible Factor 1-alpha (HIF-1α). This modulation reduces inflammation caused by hypoxia, which is beneficial for conditions like Chronic Obstructive Pulmonary Disease (COPD). Additionally, Adhatoda vasica enhances mitochondrial respiration, leading to increased ATP production, essential for lung health. It also reduces apoptosis of epithelial cells, maintaining lung structure and function, and offers potential therapeutic benefits for managing COPD symptoms. [31] [32]

- *Mucolytic & Expectorant Mechanism*

Adhatoda vasica has been shown to reduce the expression of mucin, specifically MUC5AC, a key component in mucus production that often becomes overexpressed in chronic respiratory diseases. By downregulating MUC5AC expression, the plant helps in managing excessive mucus production, thereby aiding in clearer airways and improved breathing. These combined effects make Adhatoda vasica a valuable natural remedy for managing symptoms associated with COPD and chronic bronchitis, providing relief from persistent coughing and aiding in overall respiratory health.[33] [34]

- *Anti-Microbial Mechanism*

Alkaloids and flavonoids inhibit respiratory pathogens linked to Chronic Obstructive Pulmonary Disease (COPD) exacerbations. These compounds effectively combat harmful bacteria such as Staphylococcus aureus, Pseudomonas aeruginosa, and Klebsiella pneumoniae by disrupting bacterial cell membranes and interfering with enzyme activity, leading to bacterial death. Their ability to reduce infection frequency and severity suggests potential for new COPD treatments. [35] [36]

VII. FORMULATION APPROCHES IN PHARMACOGNOSY

Recent research highlights various formulation strategies for Adhatoda vasica aimed at improving its therapeutic effectiveness in respiratory conditions. Standardized leaf extractshigh in vasicine are frequently utilized to create tablets, syrups, and herbal lozenges, nebulizers, all designed to enhance stability and bronchodilator effects. Innovative delivery systems, such as vasicine-loaded nanoparticles and inhalable herbal fractions, have been introduced to optimize pulmonary targeting and bioavailability. Collectively, these formulations underscore the promising role of A. vasica in managing COPD. [16] [41]

VIII. FUTURE PROSPECTS

The future potential of Adhatoda vasica in managing COPD rests on several key areas: the advancement of standardized alkaloid-rich formulations, enhancements in inhalation-based delivery systems, and the development of high-quality clinical evidence. Recent research highlights the necessity for standardized phytochemical profiling, validated safety/toxicity assessments, and biomarker-guided trials to validate its bronchodilatory, mucolytic, and anti-inflammatory properties. Future investigations should also focus on disease-modifying effects, the possibility of combination therapies with existing bronchodilators, and the regulatory pathways for botanical drug development. In summary, while A. vasica shows promise as a valuable adjunct, successfully translating it into clinical practice demands well-structured Phase I–III trials, consistent extract quality, and comprehensive pharmacokinetic data. [37] [38] [39]

IX. CONCLUSION

Chronic Obstructive Pulmonary Disease (COPD) continues to pose a significant global and national health challenge, marked by progressive airflow limitation, chronic inflammation, oxidative stress, and hypoxia-induced mitochondrial dysfunction. Although there have been advancements in conventional pharmacotherapy, current treatments primarily offer symptomatic relief and do not sufficiently alter disease progression or address the complex pathophysiology of COPD. This gap has sparked growing interest in complementary and alternative therapies with multi-targeted mechanisms. This project thoroughly emphasizes the therapeutic potential of Adhatoda vasica (Vasaka) as a promising plant-based intervention for managing COPD. Extensive phytochemical and pharmacological research indicates that its bioactive constituents—especially quinazoline alkaloids (vasicine, vasicinone), flavonoids, phenolic acids, phytosterols, saponins, and tannins—exhibit bronchodilatory, mucolytic, anti-inflammatory, antioxidant, antimicrobial, and anti-hypoxic effects. These actions directly address critical pathological processes of COPD, including airway obstruction, mucus hypersecretion, chronic inflammation, oxidative stress, airway remodeling, and mitochondrial dysfunction.

Preclinical and emerging clinical studies support Adhatoda vasica's role in improving airway function, reducing inflammation, protecting lung tissue, and enhancing respiratory performance with a good safety profile. Advances in formulation, like standardized extracts and nanoparticle delivery, have improved its bioavailability and potential applications. In summary, Adhatoda vasica is a promising herbal candidate for COPD management. However, to integrate its benefits into clinical practice, large-scale trials, standardized profiling, safety assessments, and pharmacokinetic studies are necessary. This could make it an effective and affordable therapy in respiratory medicine, especially in resource-limited areas affected by COPD.

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