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AN UPDATED REVIEW ON PHYTOCHEMICAL CONSTITUENTS AND PHARMACOLOGICAL ACTIVITIES OF *ADHATODA VASICA* (L). NEES

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ABSTRACT: *Adhatoda vasica* (L.) Nees is a well-known medicinal plant in both Ayurvedic and Unani traditions, widely used for treating various health issues, especially respiratory tract disorders. Over the past two decades, numerous scientific studies have highlighted the oxytocic and abortifacient properties of vasicine, an alkaloid derived from the plant. This paper provides an overview of the most recent research on its phytochemical and pharmacological properties. The review emphasizes the diverse range of phytochemical compounds extracted from the *Adhatoda vasica* plant and it possesses various activities like anti allergic, anti-tubercular, immunomodulatory, anti-asthmatic, bronchodilator, hepatoprotective, antiviral, anti-inflammatory, anti-fungal, anthelmintic, thrombolytic activities. Various phytochemicals like alkaloids, flavonoids, tannins, etc. were obtained from *Adhatoda vasica* (*A. vasica*). The active constituent of the plant is vasicine, l-vasicinone, deoxyvasicine, maiontone, vasicinolone and vasicinol etc. This review consists of updated information on the phyto-constituents isolated from *A. vasica* and their potential role in the treatment of various ailments traditionally and medically.

INTRODUCTION: *Justicia adhatoda* belongs to the family Acanthaceae, commonly known in English as Malabar nut, adulsa, adhatoda, vasa, vasaka [1, 2]. It is native to Asia [3] Adhatoda means 'untouched by goats' in Tamil. The name comes from the fact that animals, such as goats, avoid eating this plant because of its intensely bitter taste. This plant is native to tropical and subtropical regions, including Afghanistan, the Indian subcontinent (Bangladesh, India, Pakistan, Nepal, and Sri Lanka), as well as Laos, Myanmar, and Vietnam.

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It can be found in waste areas, roadside ditches, and dry, stony soils and it has also been introduced to other areas [4]. An evergreen plant with an average height of 1.0 to 2.5 m with a unpleasant smell and bitter taste [5]. Numerous studies have reported the use of the leaves and flowers for treating conditions such as asthma, cough, cold, as an expectorant, and for their antispasmodic effects. An *in-vivo* study on rats demonstrated that it can help prevent oxidative damage caused by carbon tetrachloride [6].

The phenolic compounds found in *A. vasica* are known to scavenge free radicals and exhibit strong antioxidant activity [7]. These medicinal properties make *Adhatoda vasica* a subject of great interest for studying its phytochemicals and active compounds in the field of drug discovery [8]. It is a well-known herbal remedy in both Ayurvedic and Unani medicine systems, and has been used in various traditional treatments for managing a range

of human diseases [9]. The primary chemical compounds in *A. vasica* belong to the quinazoline alkaloid group, which includes vasicine and vasicinone, a bronchodilator alkaloid [10].

FIG. 1: ***ADHATODA VASICA***

Taxonomy [14]:

Root	Root
Genus	Eriocaulon
Phylum	Tracheophyta
Kingdom	Plantae
Family	Eriocaulaceae
Order	Poales
Class	Liliopsida
Species	*Eriocaulon ansarii*

Vernacular Names [31]:

- Hindi -Adosa, adalsa, vasaka
- Sanskrit -Shwetavasa, vasa, vasaka, Vaidyamatasinghee
- Bengali -Basak
- Tamil- Adatodai
- Marathi- Vasuka
- Telugu -Adasaram
- Malayalam- Ata- lotakam
- Gujarati -Aradusi, adusa
- Punjabi- Bansa, basuti, bhekkar
- English- Malabur nut
- China -Ya-Zui-Hua
- Manipuri- Nongmangkha-agouba
- Kannada- Adusoge
- Arabic -Adusha

MORPHOLOGY:

Macroscopic Characters: This is a dense shrub that typically grows between 1.2 to 2.4 meters in height, although it can sometimes become arborescent, reaching up to 6 meters. It has many long, opposite, and ascending branches, with a stem that has yellowish, smooth, and round bark. The leaves are elliptical to lanceolate in shape, measuring 10-20 cm by 9-8 cm, and are acuminate at the tips.

When young, the leaves are slightly pubescent, but they become glabrous as they mature. They are dark green on the upper surface and paler beneath, with a tapering base. The petioles are 1-2.5 cm long. The flowers grow in dense, axillary, pedunculate spikes that are 2-8 cm long, appearing toward the end of the branches. The peduncles are 3-10 cm long and stout, typically shorter than the leaves.

The calyx is less than 1.3 cm long, either glabrous or slightly pubescent, and is divided to within 2 mm of its base. The sepals are imbricate, oblong-lanceolate, acute, 3-nerved, and have a reticulate venation. The corolla is white with a few irregular pinkish bars in the throat and measures 2.5-3 cm in length, with pubescence on the outside. The tube of the corolla is 1-2 cm long, cylindrical for the lower half (4 mm in diameter), ovate-oblong, curved, obtuse, and notched. The filaments are hairy at the base, long, stout, and curved, with the lower anther-cells being minutely apiculate (not white-tipped) at the base. The ovary is pubescent, and the lower part of the style is also pubescent. The seeds are orbicular-oblong, 5-6 mm long, tubercular-verrucose, and glabrous [11].

Microscopic Characters: The transverse section through the midrib is highly convex on the lower side and centrally depressed on the upper side, with a central arc of meristeles and a few secondary meristeles on either side. The upper and lower epidermis consists of rectangular to square-shaped cells covered by a thin cuticle. The cell walls of the upper epidermis are more wavy than those of the lower epidermis. Beneath the upper epidermis, there are two layers of palisade cells containing oil globules and elongated, warty cystoliths that extend from the epidermis down into the lower palisade cells. On both sides of the midrib, there are 5–10 rows of collenchymatous tissue. The midrib itself contains 3–4 conjoint, collateral meristeles. Additionally, small glandular trichomes are present on the lower epidermis [12].

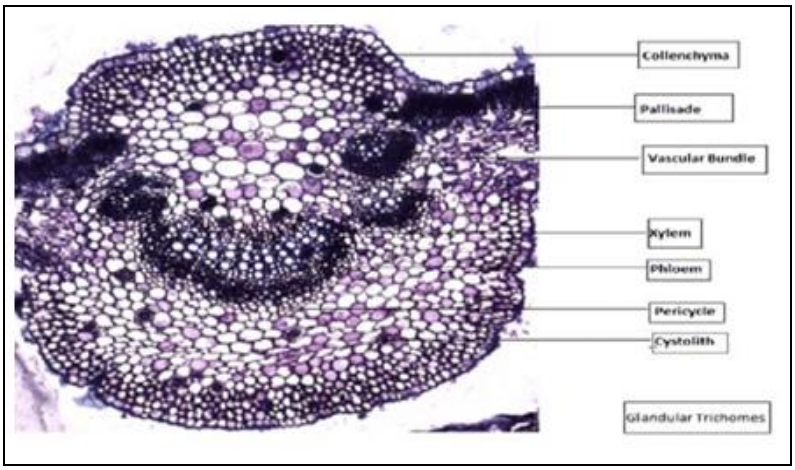
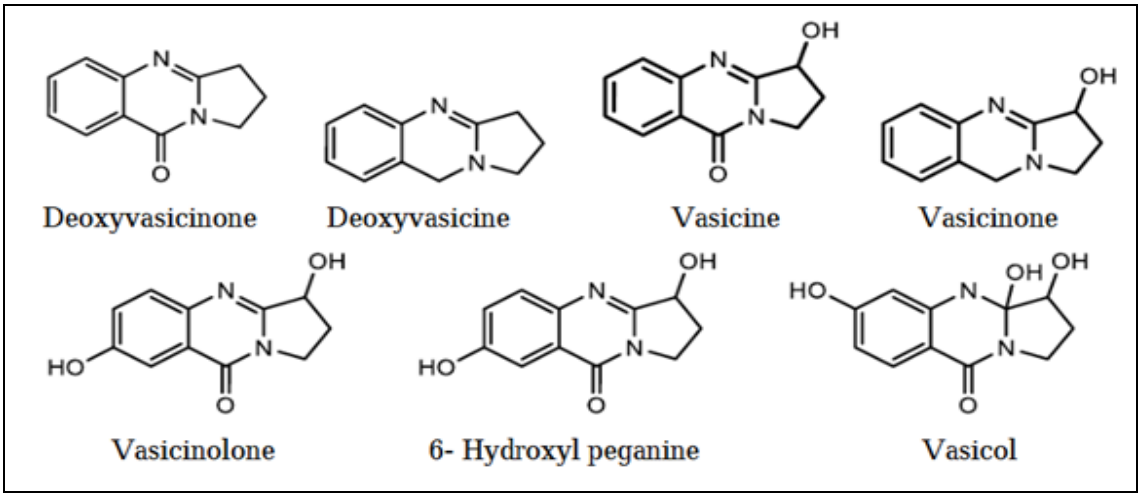


FIG. 2: MICROSCOPIC CHARACTERISTICS OF *JUSTICIA ADHATODA* LINN., T.S. OF LEAF THROUGH MIDRIB SHOWING GROUND TISSUE OF COLLENCHYMA CELL WITH ABUNDANT CYSTOLITH AND GLANDULAR TRICHOMES [12]

Phytochemical Constituents: The leaves, roots, seeds, fruit, and flower stem of *J. adhatoda* contain a variety of chemical constituents, including essential oils, fats, sugars, gum, resins, amino acids, proteins, and Vitamin C. Analysis has revealed that the leaves of *J. adhatoda* contain phenols, flavonoids, alkaloids, anthraquinones, saponins, and reducing sugars. Among the pharmacologically significant phytochemicals, the most extensively studied is the bitter quinazoline alkaloid Vasicine (1, 2, 3, 9-tetrahydropyrrole [2, 1-b] quinazoline-3-ol, C11H12N2O), which is found in the flowers, roots, and leaves. In addition, the triterpenoid 3-hydroxy-D-friedoolean-5-ene, along with two other compounds, epitaraxerol and peganidine, have been identified in the aerial parts of *Adhatoda vasica* Nees [13]. Main alkaloids- Vasicine Vasicol Vasicinone, Minor alkaloids- Adhatonine Vascinol Vasicinolone. Flower- Kaempferol Quercetin, new moiety in flower 2,4dihydroxychalcone and glucoside, leaves- Vasicoline adhatodine Vasicolinine Anisotine [25].



Pharmacological Activity:

Anti-allergic Activity: Studies have shown that vasicinone, a constituent of the *J. adhatoda* plant, exhibits anti-allergic properties when tested in mice, rats, and guinea pigs [15]. The methanolic extract of the plant, when administered to guinea pigs, demonstrates both anti-allergic and anti-asthmatic activity, either when inhaled at a dose of 6 mg per animal or given at 2.5 g/kg body weight [16].

Anti-tubercular Activity: A reported study found that *Adhatoda vasica* exhibits anti-tubercular activity. In an *in-vitro* study conducted against *Mycobacterium tuberculosis*, it was observed that two derivatives of vasicine, Bromohexine and Ambroxol, demonstrated a growth-inhibitory effect on *M. tuberculosis* [17, 18].

Immunomodulatory Activity: The methanolic, chloroform, and diethyl ether extracts of *Adhatoda vasica* Linn. leaves were pharmacologically assessed for their immunomodulatory properties in experimental animals. Oral administration of these extracts at a dose of 400 mg/kg to adult male Wistar rats significantly increased neutrophil adhesion to nylon fibers ($P<0.001$). Additionally, the extracts were shown to induce a Delayed Type Hypersensitivity reaction using sheep erythrocytes ($P<0.001$). The results observed at various doses were statistically significant compared to the control groups. These findings suggest that *A. vasica* Linn. extracts positively influence the modulation of the host's immune response [19].

Anti-asthmatic and Bronchodilator Activity: The alkaloids, primarily Vasicine and vasicinone, have demonstrated medicinal properties in treating respiratory disorders. Extracts from the leaves and roots have shown soothing effects for conditions such as throat issues, bronchitis, bronchiolar, and lung disorders, and they function as expectorants [20]. In experiments conducted on both anesthetized and unanaesthetized guinea pigs and rabbits, the substances exhibited antitussive properties [21]. Studies also revealed that Vasicine possesses bronchodilator activity, observed in both in vitro and *in-vivo* experiments [22].

Hepatoprotective Activity: The ethyl acetate extract of *Adhatoda vasica* demonstrates hepatoprotective effects when administered at doses of 50-100 mg/kg, as evaluated in CCL4-induced liver damage in Swiss albino rats [23].

Antiviral Activity: The influenza virus is a significant cause of respiratory infections in humans, leading to considerable health and economic impacts. This study investigates the in vitro antiviral effects of *Justicia adhatoda* crude extracts against the influenza virus, using Hemagglutination (HA) reduction in two assay methods: simultaneous and post-treatment. Both aqueous and methanolic extracts were tested for antiviral activity within non-cytotoxic concentrations. The methanolic extract demonstrated a 100% reduction in HA in both the simultaneous and post-treatment assays at a concentration of 10 mg/ml. In the simultaneous assay, the aqueous extract reduced HA by 33% at 10 mg/ml and 16.67% at 5 mg/ml. These findings suggest that *Justicia adhatoda* extracts exhibit strong anti-influenza virus properties, potentially inhibiting viral attachment and/or replication, and could serve as a viral prophylactic [24].

Anti-Inflammatory Activity: Rat paws were used to assess the anti-inflammatory effects of carrageenan and formalin with an ethanolic extract of *Adhatoda vasica* (200–400 mg/kg, orally). The study revealed significant anti-inflammatory activity [26]. Another research team evaluated the potential anti-inflammatory effects by comparing the aqueous and butanol fractions with metabolites of arachidonic acid. The results indicated that the aqueous fraction of the plant inhibits the arachidonic acid pathway, acting on mechanisms such as platelet-activating factor, thromboxane, or cyclooxygenase. These findings highlight the underlying processes through which the plant exerts its anti-inflammatory effects [27].

Antifungal Activity: Plants have emerged as valuable sources of novel, biologically active natural products with potent medicinal properties. The use of these natural products and plant extracts has increased in recent years, with new drugs being discovered thanks to advancements in technology. This study focuses on the phytochemical components of *Adhatoda vasica* and their efficacy against human pathogenic fungi.

The minimum inhibitory concentration of the plant extract was determined, and further analysis was performed using TLC for partial characterization. Antifungal activity was assessed through the agar disc diffusion method and germ tube formation inhibition. The study specifically investigates the antifungal effects of *A. vasica* against *Aspergillus ruber* and *Trichophyton rubrum*, two pathogenic fungi [28].

Anthelmintic Activity: This study aimed to assess the anthelmintic activity of *Adhatoda vasica* (Acanthaceae) in vitro against gastrointestinal nematodes in sheep. The aqueous and ethanolic extracts from the aerial parts of *Adhatoda vasica* were tested using egg hatching and larval development assays. At concentrations of 25-50 mg/ml, both extracts exhibited significant ovicidal and larvicidal effects ($P<0.05$) on gastrointestinal nematodes, with dose-dependent inhibition ($P<0.05$). The ethanolic extract at 50.0 mg/ml was particularly effective in inhibiting egg hatching and larval development. The effective dose (ED50) for both extracts was determined using linear regression and probit scale, with $y = 5$. These findings suggest that *Adhatoda vasica* extracts could be effective for controlling gastrointestinal nematodes in sheep [29].

Thrombolytic Activity: In the study aimed at discovering cardio-protective drugs from natural sources, the extractives of *Adhatoda vasica* were evaluated for their thrombolytic activity, with the results summarized in **Table 1.** When 100 µL of SK (30,000 I.U.), used as a positive control, was added to the clots and incubated for 90 minutes at 37°C, it resulted in an 80.65% clot lysis. In comparison, distilled water, used as a negative control, caused only a minimal lysis of the clot (4.08%). Among the tested fractions, the methanolic fraction (MF) demonstrated the highest thrombolytic activity, showing a 53.23% lysis [30].

CONCLUSION: This overview provides a comprehensive review of the traditional uses of *Adhatoda vasica* in treating various diseases, along with the extensive biological activities that have been well-documented. Its broad pharmacological effects, such as anti-allergic, anti-tubercular, immunomodulatory, anti-asthmatic, bronchodilator hepato-protective, anti viral and anti-inflammatory properties, are largely attributed to its bioactive compounds, especially the alkaloids vasicine and vasicinone. Scientific studies have shown that formulations derived from this plant are particularly beneficial for treating respiratory diseases in humans.

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CONFLICT OF INTEREST: No conflict of interest.

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