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Importance of *Adhatoda Vasica* Nees In Traditional System of Medicines: A Review

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ABSTRACT

Adhatoda vasica Nees, (Family Acanthaceae), commonly known as vasa or vasaka, is a well-known herbal drug in Ayurvedic, Unani and Homeopathic system of medicines. Vasaka is widespread throughout India and tropical regions of Southeastern Asia. This plant is a source of vitamin C and has other phytoconstituents with their proven medicinal value. All parts of *A. vasica* are rich in alkaloids among which leaves and roots contain a bitter quinazoline alkaloid, adhatodine, vasicine, vasicinol, vasicinone, vasicinolone, vasicine and vasicinone, among which the latter two predominate. Other constituents include triterpenes, flavonoids, alkanes, steroid, daucosterol, β -sitosterol. Pharmacological properties of this plant are mainly due to vasicine, vasicinol and vasicinone. Vasicinone and vasicine are widely known for powerful bronchodilator action. The whole plant with its phytoconstituents has been studied for antiasthmatic, antitussive, antioxidant activity, hepatoprotective activity, antiulcer activity, uterotonic and abortifacient activity.

Keywords: *Adhatoda vasica*, vasaka, vasicine, quinazoline alkaloid, bronchodilator

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INTRODUCTION

Adhatoda vasica Nees is a well-known herbal drug in Ayurvedic and Unani system of medicines (Claeson *et al.*, 2000)¹. Drug known as vasa or vasaka consists of fresh dried leaves and roots of *Adhatoda vasica* Nees. (Family Acanthaceae) (Figure 1). The plant is widespread throughout the tropical regions of Southeast Asia including plains of India especially in the lower Himalayan regions up to range of 1000 meters above sea level (Kirtikar and Basu, 2005; Chakrabarty and Brantner, 2001)^{2,3,4}. The plant is known by multiple names in different languages, Vāsā (Sanskrit), atarusaka (Hindi), vasaka (Bengali), vasaka or malabar nut (Eng), vachaka (Assam), adulsa (Marathi), arusa (Punj). This plant is a source of vitamin C and has medicinal uses, mainly antispasmodic, antipyretic, antitussive, anti-inflammatory, anti-bleeding, bronchodilator, anti-diabetic, anti-jaundice and oxytocic (Karthikeyan *et al.*, 2009; Maurya and Singh, 2010)^{5,6}. It is astringent, diuretic, antiperiodic, purgative and expectorant. In homeopathy, the plant has been used in the treatment of cold, cough, pneumonia, fever, jaundice, whooping cough and asthma due to main action as expectorant and antispasmodic (Karthikeyan *et al.*, 2009)⁵. Moreover the importance of vasaka plant in the treatment of respiratory disorders can be understood from the ancient Indian saying, “No man suffering from phthisis need despair as long as the vasaka plant exists” (Dymock *et al.*, 1893)⁷. Bisolven and vasavleha, are the branded herbal formulations containing vasaka as main ingredient are used to clear the airways by decreasing the mucus secretions and opening the airway passages.



Figure 1. *Adhatoda vasica* Nees. Plant and roots

Scientific classification

Kingdom	:	Plantae
Division	:	Angiosperms
Class	:	Dicotyledonae
Order	:	Personales

Family	:	Acanthaceae
Genus	:	Adhatoda
Species	:	vasica
Binomial name	:	<i>Adhatoda vasica</i> Nees.
Synonym	:	<i>Justicia adhatoda</i> L., <i>Adhatoda zeylanica</i> Medik.

GENERAL DESCRIPTION

It is an evergreen shrub, about 2.2-3.5 meters high, with long leaves and white flowers in axillary spike. Shrub is highly branched, woody and has opposite ascending branches with white, pink or purple flowers. Root is normal with secondary and tertiary rootlets. Leaves are large, lance-shaped, opposite and exstipulate. Flower spikes or panicles. Inflorescences in axillary spicate cymes, densely flowered; peduncles short; bracts broadly ovate, foliaceous. Fruit is four seeded in the form of a capsule (Kirtikar and Basu, 2005)².

ETHNOMEDICINAL USES

All the parts of *A. vasica* have been used for their medicinal value since time immemorial. Vasaka is used in Indian traditional medicine for the treatment of asthma, joint pain, lumber pain, sprains, cold, cough, eczema, malaria, rheumatism, swelling and venereal diseases. Vasaka has also been used by the European medical practitioners. In England, the fluid extract and tincture was used as an antispasmodic, expectorant and febrifuge and was said to be useful in intermittent, typhus fever and diphtheria. In Germany and Sweden, the leaves are used for their expectorant and spasmolytic action (Farnlof, 1998). The plant is used for treatment of excessive phlegm and menorrhagia in Sri Lanka (Kirtikar and Basu, 2005)². It is also used for the treatment of bleeding piles (Ahmad *et al.*, 2009)⁹, impotence and sexual disorders. In Southeast Asia, the paste, powder and decoction of root is used for curing tuberculosis, diphtheria, malarial fever, leucorrhoea and eye diseases (Dymock *et al.*, 1890; Kirtikar and Basu, 2005)^{10,2}. The root decoction is also used for gonorrhoea (Siddiqui and Hussain, 1993)¹¹. Mainly yellow leaves of the plant are exploited for cough and smoke and ash of leaves is used for asthma (Jain and Puri, 1984)¹².

In India, leaves of the plant are used for checking postpartum haemorrhage and urinary trouble (Pushpangadan *et al.*, 1995) and pregnant women in the Gora village of Lucknow (Uttar Pradesh) use them to induce abortion. A decoction of the leaves is used by Neterh at people in Bihar (India) to stimulate and heal before and after delivery (Jain *et al.*, 1994)¹³. In Sitapur district of Uttar Pradesh, people use the paste of roots mixed with sugar for treatment of acute nightfall. Moreover, the macerated roots of *A. vasica* are applied on vagina to help parturition. The leaf powder boiled in sesame oil is used to stop bleeding, earaches as well as pus from ears and jaundice.

REPORTED PHYTOCHEMISTRY

The most studied important chemical component in *A. vasica* is a bitter quinazoline alkaloid, vasicine (1, 2, 3, 9-tetrahydropyrrole [2, 1-b] quinoxalin-3-ol, C₁₁H₁₂N₂O) which is present in the leaves, roots and flowers. Besides vasicine, other alkaloids present in the leaves are adhatodine, adhatonine, adhavasine, anisotine, vasakine, vasicine, deoxyand N-oxide vasicine, vasicinol, vasicinone, vasicinolone, vasicol, and 6-hydroxy preganine. Betaine, steroid β -sitosterol and alkanes are also present in leaves (Jain *et al.* 2001; Jain and Puri, 1984; Chowdhury and Bhattacharyya, 1987). Vasicine is metabolized to vasicinone. The absolute stereochemistry of (-)-vasicine and (-)-vasicinone have been shown as 3S configuration on the basis of X-ray analysis of the alkaloid hydrobromides. Similarly, vasicinol and vasicinolone which have been interrelated also have the 3S configuration (Joshi *et al.*, 1996)¹⁵. The novel alkaloid isolated from leaves and characterized as 1, 2, 3, 9-tetrahydro-5-methoxypyrrol [2, 1-b] quinoxalin-3-ol (Chowdhury and Bhattacharyya, 1987). The roots also contain alkaloids adhatodine, vasicine, vasicinol, vasicinone, vasicinolone, deoxyvasicinone (Jain *et al.*, 1984), a steroid, daucosterol, carbohydrates and alkanes. In the flowers alkaloids vasicine, vasicinone triterpenes (α -amyrin), flavonoids (apigenin, astragaline, kaempferol, quercetin, vitexin), alkanes, steroid, daucosterol, β -sitosterol have been found.

REPORTED BIOLOGICAL ACTIVITIES

Pharmacological properties of this plant are mainly due to vasicine, vasicinol and other active principle of this medicinal plant. Vasicine is an optically active molecule and gets racemized on extraction. Various derivatives such as bisolvon/bromhexine and ambroxol have been developed and are present in marketed cough formulations as an expectorant. Now a days ambroxol, a widely used secretolytic agent is developed from vasicine to inhibit IgE mediated histamine release from mast cells (Rachana *et al.*, 2011)¹⁶. Various activities biological reported for *A. vasica* are described briefly below:

Anti-inflammatory activity

Aqueous and alcoholic extract of *Adhatoda vasica* Nees showed anti-inflammatory in rats using carrageenan induced rat paw edema model. The efficacy was found to be comparable to diclofenac sodium (Rajput *et al.*, 2004; Chakraborty and Brantner, 2001)¹⁷.

Antioxidant activity

Oral administration of *A. vasica* leaves extract at 800 mg/kg controlled hematological parameters to normal like GSH and LPO level in post irradiated animals. Pretreatment with *A. vasica* Nees at

100 and 200 mg/kg also significantly improved SOD, catalase and GSH levels in CCl₄-induced hepatotoxicity (Pandit *et al.*, 2004).¹⁸

Hepatoprotective activity

Ethanol extract of *A. vasica* Nees exhibited significant reduction of liver enzymes such as SGOT, SGPT and ALP in CCl₄ induced hepatotoxicity model of rats and offered protection of hepatocytes against damage by toxin (Pandit *et al.*, 2004)¹⁸.

Antiulcer activity

In ethanol and aspirin induced ulcer model of rats treatment with *A. vasica* leaves extract exhibited significant antiulcer activity in experimental animals compared to control. Results were better in ethanol induced ulceration mode (Srivastava *et al.*, 2006)¹⁹.

Wound healing activity

Topical application of alcoholic and CHCl₃ extract of *A. vasica* leaves in buffalo calves showed significant increase in rate of wound healing, tensile strength, energy absorption and extensibility with increase of collagen, elastin, hydroxyproline and zinc compared to control from 3rd day of treatment (Bhargava *et al.*, 1988)²⁰.

Uterotonic and abortifacient activity

Vasicine induced abortifacient effects were dose related and stage of pregnancy in rats, guinea pigs, rabbits. Aqueous solution of *A. vasica* leaves at 175 mg/kg in guinea pigs revealed abortifacient activity (Sethi *et al.*, 1987)²¹. Petroleum ether, alcoholic and aqueous extract of leaves did not show any antifertility activity in rats and mice, however, 50% ethanolic extract of leaves showed 66.6% anti-implantation activity in rats.

Antitussive activity

Intravenous administration of the extract exhibited 1/20–1/40 as active as codeine on mechanically and electrically induced cough in rabbits and guinea pigs. Oral administration of plant extract to guinea pigs showed antitussive activity against irritant induced aerosols comparable to codeine (Dhuley, 1999)²². Petroleum ether extract of *A. vasica* caused stimulation of respiratory tract fluid more than ammonium chloride and eucalyptol in atropinised rats. Respiratory secretions were reduced by 78.5%, 47% and 36%, respectively.

Bronchodilator activity

Vasicinone, important alkaloid, exhibited powerful bronchodilator action both in normal and histamine induced bronchoconstriction in guinea pigs' lungs but vasicine exhibited bronchoconstriction with negative inotropic effects on heart. In *in vitro* studies, vasicinone produced tracheal relaxation comparable to theophylline, carbachol and histamine induced

constriction. It showed inhibitory effects on histamine release and showed anti-anaphylactic activity in both *in vitro* and *in vivo* studies in rats. However, vasicine exhibited bronchoconstrictor, cardiac depressant and devoid of anti-anaphylactic activity. Contrarily, in another study, vasicine exhibited marked bronchodilatory effects comparable to theophylline *in vivo* and *in vitro* studies which could be explained on the basis of fast degradation of vasicine in the body (Sharma *et al.*, 1983b).²³ Vasicine exhibited significant respiratory stimulant activity that was found to be increased in the presence of vasicinone (Gupta *et al.*, 1977a)²⁴. Aerosol inhalation of alkaloids of *A. vasica* at 10 mg/ml exhibited significant protection against allergen induced bronchoconstriction (Dorch and Wagner, 1991)²⁵.

Anti-asthmatic activity

In clinical trials, treatment of asthmatic patients with *A. vasica* was found to decrease asthmatic symptoms and increase lung function parameters (Chaudry *et al.*, 2005).²⁶

Antimicrobial activity

Ethanollic and petroleum ether extarct of *A. vasica*were found to be antibacterial against *S. epidermidis*, *S. aureus* *B. subtilis*, *E. faecalis*, *E. coli*, *P aeruginosa*, *P. vulgaris*, *K. pneumoniae* and *C. albicans* (Karthikeyan *et al.*, 2009). In *in vitro* study, aqueous and ethanolic extracts at 25-50 mg/ml concentration showed ovicidal and larvicidal effects against gastrointestinal nematodes of sheep (Al-Shaibani *et al.*, 2008)²⁷.The aqueous extract of leaves was found to decrease fungal growth through inhibition of their spore germination.

Anthelmintic activity

10% aqueous extract of leaves of *A. vasica* exhibited mortality rate of 73% on *Meloidogyne incognitachit* wood (Masood *et al.*, 1985).²⁸

Insecticidal activity

Oral administration of methanolic, chloroform and diethyl ether extracts of leaves of Indian medicinal plant *Adhatoda vasica* at a dose of 400 mg/kg in adult male wistar rats significantly increased the percentage neutrophil adhesion to nylon fibers ($p < 0.001$) and positively modulated the immunity (Vinothapooshan and Sundar, 2011)²⁹. Vasicine and vasicinol, the main alkaloids from AV inhibited sucrose hydrolyzing activity of rat intestinal α -glucosidase competitively with K_i values of 82 μ M and 183 μ M, respectively (Ilango *et al.*, 2009)³⁰.

Toxicity studies

Chronic oral toxicity studies with vasicine HCl in arts and monkeys for six months administered orally at 2.5-20 mg/kg did not produced any toxic effects (Pahwa *et al.*, 1987)³¹.

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