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Wonderful bronchodilatory indigenous plant (adhatoda vasica): A phyto-pharmacological profile

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Abstract
Adhatoda vasica Linn belongs to the family of Acanthaceae, commonly known as Basok is a well-known herb in indigenous systems of medicine for its bronchodilatory effects. The aim of the present study was to evaluate the update data on phytochemical compositions and pharmacological properties of different parts of *Adhatoda vasica* are reviewed. Adhatoda has been used for a variety of disorders including cold, cough, bronchitis, asthma, thirst, fever, vomiting, loss of memory, tumors, and mouth troubles. *Adhatoda vasica* L. also has anti-tubercular, anti-allergic, anti-asthmatic, anti-inflammatory, hepatoprotective, anthelmintic, antimicrobial, wound healing, anti-ulcer, antibacterial, antihistaminic, antimutagenic, uterotonic and abortifacient activities. This plant contains alkaloids, tannins, flavonoids, terpenes, and glucosides. The principle constituents of Adhatoda are its several alkaloids, the chief one being vasicine. The leaves contain two major alkaloids called vasicine and vasicinone. The leaves of Adhatoda are rich in vitamin C, carotene and essential oil. The roots are known to contain vasicinolone, vasicol, peganine, sitosterol, β-glucoside-galactose and deoxyvasicine and 2'hydroxy-4- glucosyl-oxychalcone. The flowers contain b-sitosterol-D-glucoside, kaempferol, its glycosides and quercetin, adhatonine, vasinol.

Keywords: adhatoda vasica, vasicine, vasicinone, pharmacological activity

1. Introduction
The use of the medicinal plants is increasing in many countries where 35% of drugs contain natural products [1]. Unani & Ayurvedic medicines mainly based on plants enjoy a respective position today, especially in the developing countries, where modern health services are limited. Safe effective and inexpensive indigenous remedies are gaining popularity among the people of both urban and rural areas especially in Bangladesh, India and China. Information from ethnic groups or indigenous traditional medicines has played vital role in the discovery of novel products from plants as chemotherapeutic agents. Herbal medicines have been main source of primary healthcare in all over the world. From ancient times, plants have been catering as rich source of effective and safe medicines. About 80 % of world populations are still dependent on traditional medicines [2]. *Adhatoda vasica* (Acanthaceae) is an important Unani & Ayurvedic medicinal plant distributed all over in Bangladesh and India. Beside India, it is found in Myanmar, Sri Lanka, Burma and Malaysia [3]. The plant has been used in the indigenous system of medicine in Indian sub-continent for more than 2000 years [4]. It is an evergreen, gregarious, stiff, perennial shrub, 1.2-6.0 m in height, distributed throughout India, up to an altitude of 1,300m2. Leaves of A. vasica are ellipticlanceolate or ovate-lanceolate, entire, 5-30 cm long, hairy, light green above, dark below, leathery; flowers are large, white with red- or yellow-barred throats, in spikes with large bracts; capsules are clavate, longitudinally channeled, 1.9-2.2 cm× 0.8 cm and seeds are globular [5]. Its leaves are extensively used for treating cold, cough, whooping cough and chronic bronchitis and asthma as sedative expectorant, antispasmodic and anti-inflammatory drug. There is considerable demand for this plant within the country. The demand is being met from natural sources [6, 7]. In indigenous system of medicine, *Adhatoda vasica* has been used for a variety of disorders including; cold, cough, asthma, whooping cough, chronic bronchitis, leprosy, blood disorders, heart troubles, thirst, fever, vomiting, loss of memory [8, 9]. The leaves, roots, flowers and bark of Adhatoda are all used for medicinal purposes. Glycodin®, a famous product used for the cure of bronchitis is extracted from the leaves of this plant [10]. A. vasica is recommended for the preparation of sputum more fluid and use to treat cough, asthma and bleeding piles and it can be used for both adults and children for a long period. Also, the plant is recommended for first-aid medicine in primary health care and can be used in both adults and children and for a long period without any restriction of use.

Fig 1: Adhatoda vasica Linn

Synonyms

China - Ya-Zui-Hua
Sanskrit - Vasaka
Hindi - Arusha
Bengali - Basok
Manipuri - Nongmangkha-agouba
Gujarati - Alduso
Tamil - Adadodai

Phytoconstituents

Adhatoda vasica leaves have been found to be a rich source of two major alkaloids of which vasicine and vasicinone and also contains alkaloids such as deoxyvasicine, vasicol, adhatodinine, adhavasinone, adhavasine and vasicinol [11]. Other constituents include vitamin C, saponins, flavonoids as well as steroids, and fatty acids [12]. Vasicine is reported to have bronchodilatory, respiratory stimulant, and uterine stimulant effects [13]. The roots are known to contain vasicinolone, vasicol, peganine, sitosterol, β-glucoside-galactose and deoxyvasicine and 2'hydroxy-4- glucosyl-oxychalcone [14, 16]. The flowers contain b-sitosterol-D-glucoside, kaempferol, its glycosides and quercetin. Minor alkaloids include adhatonine, vasinol [17].

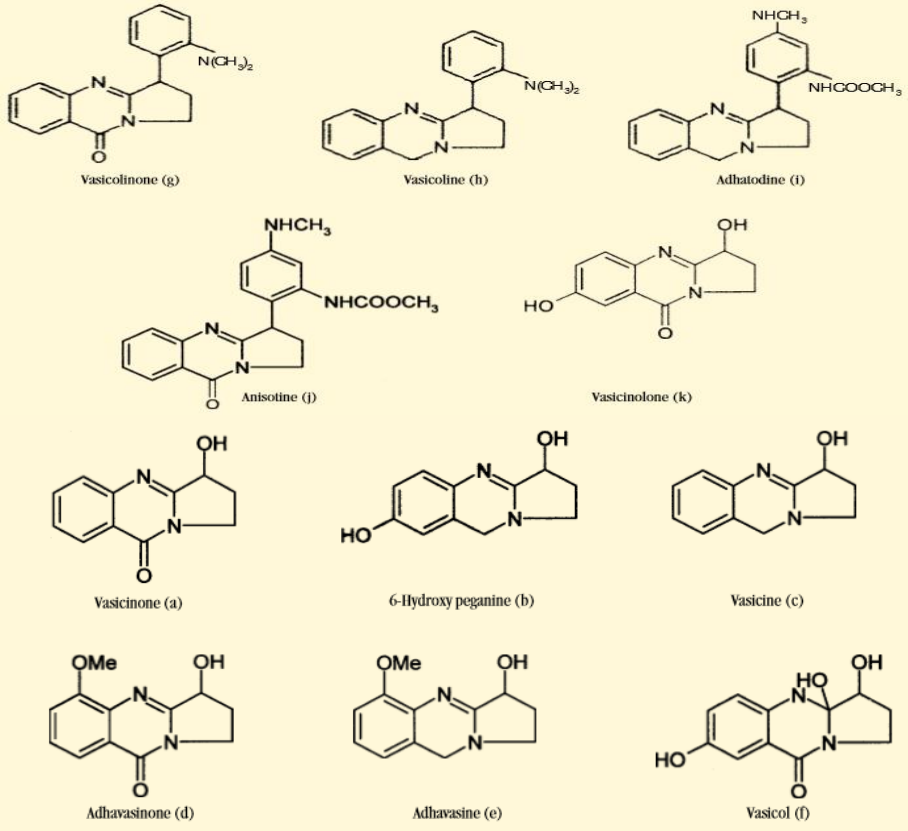

Fig 2: Phytochemical constituents

Pharmacological Activity

Bronchodilatory activity

Adhatoda has been used in traditional medicine to treat respiratory disorders. Both vasicine and vasicinone the primary alkaloid constituents of Adhatoda are well established as therapeutical respiratory agents [18]. Extract of Adhatoda's leaves and roots are useful in treating bronchitis, and other lung and bronchiole disorders, as well as common coughs and colds. A decoction of the leaves of Adhatoda has a soothing effect on irritation in the throat, and acts as an expectorant to loosen phlegm in the respiratory passages. To evaluate the antitussive activities of Adhatoda extract in anesthetized guinea pigs and rabbits and in unanesthetized guinea pigs showed the plant to have a good antitussive activity [19]. Recent investigations using vasicine showed bronchodilatory activity both in vitro and in vivo [20].

Both vasicine and vasicinone, the primary alkaloid constituents of Adhatoda are well-known for their therapeutical respiratory agents. Vasicine showed bronchodilatory activity both in vitro and in vivo [21]. Vasicinone, the main metabolite of vasicine, showed bronchodilatory activity in vitro but bronchoconstrictory activity in vivo, suggesting that it is probably biotransformed in vivo, causing bronchoconstriction. The two alkaloids in combination showed a bronchodilatory activity both in vitro and in vivo.

Anti-tubercular activity

A chemical constituent of Adhatoda alkaloids, vasicine, produces bromhexine and ambroxol – two widely used mucolytics. Both of these chemicals have a pH-dependent growth inhibitory effect on Mycobacterium tuberculosis. Indirect effects of Adhatoda on tuberculosis include increased lysozyme and rifampicin levels in bronchial secretions, lung tissue and sputum, suggesting that it may play an important adjunctive role in the treatment of tuberculosis [22, 23].

Anti-allergic and anti-asthmatic activities

The two main alkaloids vasicine and vasicinone are known to exhibit antiallergic activity. An extract containing the alkaloid

vascinol and 20% vasicine [24] inhibited ovalbumin-induced allergic reactions by about 37% at a concentration of 5 mg. Vasicinone has been shown to be a potent anti-allergen in tests on mice, rats and guinea pigs as studied by Wagner [25]. Also, the methanolic extract from the entire plant has been shown to possess anti-allergic and antiasthmatic activities in the guinea-pig after inhalation or intragastric administration at doses of 6 mg peranimal or 2.5 gm/kg, respectively [26].

Antimicrobial activity

The antimicrobial activity (MIC) of *Adhatoda vasica* was assessed against clinical pathogen solvents like methanol, ethanol, acetone, chloroform, diethyl ether and water were used for the preparation of plant extracts in various concentrations by disc diffusion method the antimicrobial activity (MIC) was measured. From this, solvents showed higher activity in the order of diethyl ether > methanol > ethanol > acetone > Chloroform> water. The plant extract of Adhatoda vasica showed higher activity for different clinical pathogens in the order of Klebsiella pneumoniae>Staphylococcus aureus > Proteus valgaris > Pseudomonas aeroginosa > Streptococcus Pyogens [27].

Anti-inflammatory activity

Vasicine, the main alkaloid of *Adhatoda vasica* showed anti-inflammatory activity [28]. The anti-inflammatory activity of the methanol extract, the non-alkaloid fraction, the saponins and the alkaloids were evaluated by the modified hen's egg chorioallantoic membrane test. The alkaloid fraction showed potent activity at a dose of 50 /pellet equivalent to that of hydrocortisone while the MeOH extract and the other fractions showed less activity [29].

Anti-tussive activity

The present study was carried out to evaluate antitussive activity of ethyl acetate and methanolic extract of leaves of *Adhatoda vasica* Nees. As cough is a natural reflex expulsive defense mechanism of the body, it is the most common symptom of respiratory disease. Ammonium hydroxide and Sulphur dioxide induced cough models in mice were used for evaluation of antitussive activity of ethyl acetate and methanolic extracts of leaves *Adhatoda vasica*. The ethyl acetate and methanolic extract of leaves Adhatoda vasica was orally administered at the dose levels of 500 mg/kg b.w. showed maximum inhibition of cough by 82% and 81% respectively .The standard antitussive drug Codiene phosphate (10mg/kg b.w.) showed maximum inhibition of cough by 84%. It was found that both extracts of *Adhatoda vasica* showed anti-tussive activity and obtained percentage inhibition of cough reflex is approximately comparable as standard drug [30].

Antimutagenic activity

Jahangir *et al*. [31] studied the antioxidant and anticlastogenic efficacy of A. vasica against cadmium chloride (CdCl2)–induced renal oxidative stress and genotoxicity in Swiss albino mice. A single intraperitoneal dose of CdCl2 (5 mg\kg b.wt.) resulted in significant (p<0.001) increase in chromosomal aberration and micronuclei formation. Oral administration of A. vasica at two doses (50 and 100 mg/kg BW) for seven consecutive days showed significant (p<0.001) suppression of mutagenic effects of CdCl2 in plant-pretreated groups. Cadmium intoxication altered the antioxidant levels and enhanced MDA formation significantly (p<0.001). A. vasica showed significant (p<0.001) recovery in antioxidant status, viz., GSH content, its dependent enzymes, and catalase activity. Prophylactic pretreatment of A. vasica extract in cadmium-intoxicated mice showed marked (p<0.001) inhibition of lipid peroxidation (LPO) and xanthine oxidase (XO) activity.

Wound healing activity

For the purposes of the study, wounds were created along the vertebral columns of buffalo calves, and alcoholic and chloroform extracts of Adhatoda in a powdered form were applied. As compared to control animals, the calves treated with Adhatoda vasica showed significantly improved healing. Vasica improved breaking strength, tensile strength, absorption and extensibility in the wound repair tissue. In addition, the levels of elastin, collagen, hydroxyproline, hexosamine and zinc were greatly increased in the animals treated with Adhatoda. The alcoholic extract of the herb was found to be the most effective [32].

Anti-ulcer activity

Adhatoda vasica was studied for its anti-ulcerogenic activity against ulcers induced by ethanol, pylorus, and aspirin. Adhatoda leaf powder showed a considerable degree of anti-ulcer activity in experimental rats when compared with controls. The highest degree of activity was observed in the ethanol-induced ulceration model [33]. These results suggest that in addition to its classically established pharmacological activities, *Adhatoda vasica* has immense potential as an anti-ulcer agent. Further research showed that a syrup of Adhatoda improved symptoms of dyspepsia [34].

Insecticidal activity

Adhatoda vasica has been used for centuries in India as an insecticide. Its leaves have been shown to control insect pests in oil seeds, in both laboratory and warehouse conditions [35]. Research has shown Adhatoda's alkaloid, vasicinol, to have an antifertility effect against several insect species by causing blockage of the oviduct. Research has also proven Adhatoda's effectiveness as an insect repellent [36].

Anthelmintic activity

Anthelmintic activity of *Adhatoda vasica* in vitro against the gastrointestinal nematodes of sheep was evaluated. The aqueous and ethanolic extracts of *Adhatoda vasica* aerial parts were evaluated by egg hatching and larval development assays. The aqueous and ethanolic extracts at 25-50 mg/ml concentrations exhibited ovicidal and larvicidal (p<0.05) activity against gastrointestinal nematodes. The plant extracts showed dose-dependent inhibition (P<0.05). The ethanolic extract at the concentration of 50.0 mg/ml was more effective in inhibiting egg hatching and larval development of gastrointestinal nematodes. The effective dose (ED50) of aqueous and ethanolic extracts were determined graphically from linear regression equation with probit scale, y = 5. The results of this study suggested that *Adhatoda vasica* extracts may be useful in the control of gastrointestinal nematodes of sheep [37].

Uterine activity

The uterotonic activity of vasicine was studied in detail both by in vitro and in vivo methods employing the uteri under different hormonal influences and of different species of animals. The uterotonic activity seemed to be similar to that of oxytocin and methylergometrine. The abortifacient effect of vasicine like its uterotonic effect was more marked under the priming influence of oestrogens [38]. Vasicine-induced abortion was studied in rats, guinea pigs, hamsters and rabbits. Study showed that vasicine acted through the release of PGs [39]. Synthesized vasicine and vasicinone derivatives in in-vitro studies were found to have oxytoxic activity at the dose above 1 g/ml [40]. The aqueous solution of the leaves at the dose of 175mg/kg bw revealed 100 percent abortifacient activity in albino rats [41]. The extract of the plant at 2 per cent concentration level revealed abortifacient activity [42].Vasicine showed uterotonic activity on human myometrium strips which was in some cases even more marked than that of two known oxytoxics, pitocin and methergin. The response of the uterus to drugs depended on its hormonal status [43].

Hepatoprotective activity

Biologically active phytoconstituents such as Alkaloids-Quinazoline, Flavonoids, Tannins, Vasicinone, Essential oil which are present in the various extracts of Adhatoda vasica are accountable for the significant hepatoprotective activity [44].

Anti Pyorrhoeal activity

In a study 25 patients with complain of pyorrhea was taken, and were selected randomly. The leaf extract was massaged on inflamed gums twice a day for three weeks. There was a reduction and complete relief in the inflammatory and bleeding conditions of gums [45].

Conclusions

Adhatoda vasica is a small, evergreen, perennial shrub, which reaches an average height of three meters. Its branches are opposite and ascending. Traditionally Adhatoda vasica treating various ailments have been well documented in this brief review and a wide range of pharmacological activities are well reported. The present study would be helpful in promoting research to go deep in this area as plant indicate vast range of phytochemical related to origin so it can be suggested the further work can be done on *Adhatoda vasica*

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