

Phytochemical Composition and Pharmacological Potential of *Adhatoda zeylanica* Medic. Syn. *A. vasica* L. Nees

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Abstract

Innumerable natural products with inherent potential biological activity procured from plants have played a significant role in improving the human health since the dawn of civilisation. As more than 50% of modern clinical drugs originate from natural products. Therefore, based on latter, the approach to new drug discovery and its development in the pharmaceutical industry has emerged significantly. *A. vasica* is a good source of pyrroloquinoline alkaloids such as vasicine, vasicol, adhatodine, vasicinone, vasicinol, vasicinolone etc. which are the chief constituents of different extracts of the plant. These compounds have shown many biological and pharmacological activities viz. anti-malarial, anti-inflammatory, antioxidant, antidiabetic, anti-bacterial, anti-cancer etc. Further, *Adhatoda* leaves have been used extensively in Ayurvedic medicine for the treatment of diarrhea, dysentery, tuberculosis, skin diseases, vomiting and leprosy etc. Herbal medicine is still the mainstay of about 75-80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. However, the last few years have seen a major increase in their use in the developed world. As far as contemporary drugs are concerned they must be further characterized after their pharmacological screening by studying the pharmacokinetic and pharmacodynamic properties, including toxicity. Therefore, the present communication enumerate the phytochemical composition and pharmacological potential of *A. vasica*.

Keywords: *Adhatoda vasica*; Secondary Metabolites; Pyrroloquinoline Alkaloids; Biological Activities

Introduction

Adhatoda vasica is popularly known as Basak in Bangla, Malabar Nut in English, Adosa in Hindi and Vasaka in Sanskrit. It has been used in preparation of herbal medicines for the past 2000 years. It is a medicinal plant native to Asia, widely used in Siddha Medicine, Ayurvedic and Unani system of medicine [1]. The plant's range includes Sri Lanka, Nepal, India, Pakistan, Indonesia, Malaysia and China as well as Panama where it is thought to have been introduced. This evergreen perennial shrub has leathery leaves. The flowers are dense and large having large bracts and whitish pink/purple colored. The herb is often grown as a hedge and its leaves and twigs are utilized as green-manure. The whole plant or its roots, leaves, bark and flowers are used in various herbal preparations. They are oppositely arranged, smooth-edged, and borne on short petioles [2-5].

It has been revealed from the literature that the quinazoline based alkaloids have been the major constituents present in the different parts of *A. vasica*, which have been mainly responsible for their wide range of pharmacological potential. Research performed has revealed that the alkaloids, vasicine and vasicinone (quinazoline ring derivatives) present in the leaves, possess respiratory stimulant activity whereas its roots contain vasicinolone, vasicol and pegamine [6]. Vasicine (1,2,3,9-tetrahydropyrrolo [2,1-b]quinazolin-3-ol, C₁₁H₁₂N₂O) also called Peganine [19]. Other chemical constituents of this plant include vasicinone (3-hydroxy-2,3-dihydropyrrolo[2,1-b]quinazolin-9(1H)-one, C₁₁H₁₀N₂O₂) (isolated from leaves, stem and roots) and deoxyvasicinone (derived from leaves) etc. Recent investigations on vasicine showed bronchodilatory activity comparable to theophylline, both *in vitro* and *in vivo*. Both the alkaloids in combination showed pronounced bronchodilatory activity.

Figure 1

Figure 2

Deoxyvasicinone possesses antimicrobial, anti-inflammatory and antidepressant activities. It is a primary medicinal plant for the respiratory tract ailments in the treatment of cough, bronchitis, asthma and symptoms of common cold. The medicinal uses of *Adhatoda* leaves are attributed to its antitussive, antimicrobial and anti-inflammatory properties. Its leaf juice is the most common home remedy for cough, respiratory diseases and bleeding disorders. It is also a highly effective natural medicine for respiratory infections. In ayurveda, *Adhatoda* juice is also called *Adhatoda Swarasa*, *Adhatoda Swarasa* and *Vasa Swarasa* [7-11].

Constituents of the plant have been exposed to have antistress effects, which might be occasioned partly by an endocrine and partly by an immunomodulatory mechanism of action. This plant has medicinal uses, mainly antispasmodic, fever reducer, anti-inflammatory, anti-bleeding, bronchodilator, anti-diabetic, disinfectant, anti-jaundice and oxytocic. It is antiperiodic, astringent,

diuretic, purgative and is also used as an expectorant in addition to liquefy sputum. The leaves, flowers and roots of this plant used in herbal drugs against tubercular activities cancer and possessed anti-helminthic properties [12-17].

Phytochemistry and pharmacology

Water, ethanolic and petroleum ether extracts of *Adhatoda* leaves enriched with alkaloids, phenols, tannins and reducing sugars, main constituent vasicine etc. have been found to possess antibacterial activity (singularly or in combination) against *S. epidermidis*, *S. aureus*, *B. subtilis*, *E. faecalis*, *E. coli*, *P. aeruginosa*, *P. vulgaris*, *K. pneumoniae* and *C. albicans*. *Adhatoda vasica* possesses abortifacient and uterotonic properties [18-20]. The leaves of *Adhatoda vasica* are mostly used in the treatment of respiratory ailments in Ayurveda. The two main alkaloids, vasicine and vasicinone present in the leaves, possess respiratory stimulant activity. Vasicine, at low concentrations induces bronchodilation and relaxation of

the tracheal muscle. *Adhatoda vasica* also has immense potential as an anti-ulcer agent which is used to treat or ameliorate peptic ulcer or irritation of the gastrointestinal track of great therapeutic relevance [21].

A wide range of phytochemical constituents have been isolated from this plant having activities like antitussive, abortifacient, antimicrobial, insecticidal, hepatic protection, cardiovascular protection, anticholinesterase, antioxidant, anti-inflammatory and other important activities. Some important bioactive compounds have been reported in various part of *Adhatoda vasica* are essential oils and quinazoline alkaloids [22,23]. So this plant can form one of the best options for developing novel compounds having medicinal value. Two new aliphatic hydroxyketones, isolated from the aerial parts of *Adhatoda vasica* have been characterized as 37-hydroxyhexatetracont-1-en-15-one and 37-hydroxyhentetracont an-19-one, respectively, on the basis of spectral data and chemical studies. 2',4-Dihydroxychalcone 4-glucoside has been identified in the flowers of *Adhatoda vasica* (Bhartiya and Gupta, 1982). A novel alkaloid and a galactoside isolated from the roots of *Adhatoda vasica* have been characterized as 9-acetamido-3,4-dihydropyrido-(3,4-b)-indole and O-ethyl- α -D-galactoside respectively by chemical and spectroscopic methods. In addition, sitosterol β -D-glucoside, D-galactose and deoxyvasicine one have also been isolated from the roots of this plant (Jain., *et al.* 1980). Two new pyrroloquinoline alkaloids, viz. 1,2,3,9-tetrahydropyrrolo (2,1-b)-quinazolin-9-one-3Rhydroxy-3(2'-dimethylamino phenyl (desmethoxyaniflorine) and 7-methoxy-3R-hydroxy-1,2,3,9-tetrahydropyrrolo-[2,1-b]-quinazolin-9-one (7-methoxyvasicinone), together with several known compounds were isolated from the leaves of *Adhatoda vasica*. Their structures were established by spectroscopic and X-ray diffraction analyses [24-29].

Phytochemical composition

The chemical compounds found in *Adhatoda vasica* plant includes essential oils, fats, resins, sugar, gum, amino acids, proteins and vitamins 'C' etc [30]. The phytochemical analysis show that phenols, tannins, alkaloids, anthraquinone, saponins, flavonoids and reducing sugars were found in the leaves of plant. But the pharmacologically most studied chemical component in plant is vasicine, a bitter quinazoline alkaloid, the novel alkaloid isolated leaves and characterized as 1, 2, 3, 9-tetrahydro- 5-methoxypyrrol [2, 1-b] quinazolin-3-ol. It is present in the leaves, roots and flowers. Besides vasicine, the leaves contain several alkaloids (Vasicinone, Vasicinol, Adhatodine, Adhatodine, Adhvasinone, Anisotine and hydroxypeganine), betaine, steroids and alkanes. The leaves contain two major alkaloids called vasicine and vasicinone [30,31].

The pharmacological activities of vasicine and vasicinone are well known. Recent investigations on vasicine showed bronchodilatory activity comparable to theophylline, both *in vitro* and *in vivo*. Both the alkaloids in combination showed pronounced bronchodilatory activity. Vasicine also exhibits strong respiratory stimulant activity. There has also been a report of thrombopoietic4 (platelet increasing) activity with vasicine. Uterine stimulant activity and moderate hypotensive activity of the alkaloids have been observed. Vasicine is metabolized to vasicinone and analysis of plant leaf extract showed that it contained 0.85% vasicine and 0.027% vasicinone. Sitosterol, β -glucoside-galactose and deoxyvasicine have been isolated from the roots of the plant. 2'-4-dihydroxychalcone-4-glucoside has also been recognized in the flowers. Flowers of *Adhatoda vasica* mainly contain kaempferol and quercetin [32]. A new triterpenoid, 3-hydroxy-D-friedoolean-5-ene, along with the known compounds, epitaraxerol and peganidine have been isolated from the aerial parts of *Adhatoda vasica* Nees. The leaves also contain a very small amount of an essential oil and a crystalline acid. An analysis published in India in 1956 showed the seeds as containing 25.8% of deep yellow oil composed of glycerides of arachidic 3.1%, behenic 11.2%, lignoceric 10.7%, cerotic 5%, oleic 49.9% and linoleic acids 12.3% and β -sitosterol (2:6%). Elemental analysis using atomic absorption spectrophotometry revealed the presence of major (K, Na, Ca and Mg) and trace (Zn, Cu, Cr, Ni, Co, Cd, Pb, Mn and Fe) elements in *Adhatoda vasica*. *Adhatoda vasica* mainly consists of alkaloids containing pyrroquinazoline ring derivatives like vasicine, vasicol, vasicinone along with other mineral constituents. Vasicine is a major bioactive alkaloid of vasicine which contain pyrroquinazoline ring [33-35].

Traditional uses

Adhatoda vasica, an ayurvedic medicinal plant has been used in various chest and respiratory track infection viz.- whooping cough, chronic bronchitis, asthma and has been employed as sedative expectorant in the treatment of excessive phlegm (mucus with bacteria, debris, and sloughed-off inflammatory cells) and menorrhagia (abnormal blood clotting, disruption of normal hormonal regulation of periods or disorders of the endometrial lining of the uterus) in Sri Lanka. It is also used for the treatment of bleeding piles, impotence and sexual disorders. I, antispasmodic and an-

thelminthic drug. Glycodin, which is a famous product used for the cure of bronchitis has been a product extracted from the leaves of *Adhatoda vasica* [36]. Further, the extracts have been found to be quite effective against tuberculosis. Various parts of the plant have been used in Indian traditional medicine for the treatment of asthma, joint pain, lumber pain, sprains, cold, cough, eczema, malaria, rheumatism, swelling and venereal diseases. Roots: In India paste of the fresh root applied on abdomen and vagina minutes before childbirth facilitates easy delivery. The extract of roots of *Adhatoda vasica* has commonly been used by rural population against diabetes, cough and certain liver disorders. whereas its paste has been used for curing tuberculosis, diphtheria, malarial fever, leucorrhoea, eye diseases, acute nightfall [(paste mixed with sugar)] in Sitapur district, Uttar Pradesh, India. Further, the root's decoction has been used for gonorrhoea and as an expectorant, antispasmodial/anthelmintic agent [37].

The various preparations of leaves has been used for curing bleeding, hemorrhage, skin diseases, wounds, headache and leprosy (chronic infection) while their infusion or the solvent extract has been observed to be an excellent agent for the destruction of white ants, flies and mosquitoes. The fresh juice of leaves mixed with honey and ginger juice cures all types of acute cough, chronic bronchitis, breathlessness and liquefies sputum and asthma. The extract obtained by decoction of its leaves along with fruit of *Phyllanthus emblica*, mixed with honey has been effective against asthma. The crushed fresh leaves of the plant have been used to treat snake bites (India and Sri Lanka). Macerated extract from leaves/Yellow leaves/smoke from dry leaves acts against cough and phlegm blockage during cold (Bangladesh) and an infusion protects from headache (Myanmar and Pakistan). The leaf powder boiled in sesame oil stops bleeding, earaches as well as pus from ears and jaundice. Leaf juice has been used as the best medicine to enhance platelet count during dengue like viral fevers, postpartum hemorrhage, urinary trouble, acidity and belching and its mixture with jaggery reduces excessive menstrual flow get cured. Externally warmed leaves have been used for rheumatic pains and dislocation of joint, stomach catarrh with constipation, rheumatism, gout, fever and urinary stone. Juice made from the bark and leaves help against vomiting. Flowers: The flowers have been known to possess expectorant and antiasthmatic, antiseptic properties and have been used against of ophthalmia, cold, phthisis, asthma, bronchitis, cough, antispasmodic, high fever and gonorrhoea. Also, the flowers improve blood circulation and hectic heat of blood. Fruits: Fruits

of the *Adhatoda vasica* are four seeded capsules. In Pakistan, fruits of the plant are used for cold, antispasmodic and bronchitis. The fruit of the plant are also used for Diarrhea, Dysentery, Fever and as laxative [38-40].

Conclusion

A wide range of phytochemical constituents have been isolated from this plant having activities like antitussive, abortifacient, antimicrobial, insecticidal, hepatic protection, cardiovascular protection, anticholinesterase, antioxidant, anti-inflammatory and other important activities. A wide range of phytochemical constituents have been isolated from this plant having activities like antitussive, abortifacient, antimicrobial, insecticidal, hepatic protection, cardiovascular protection, anticholinesterase, antioxidant, anti-inflammatory and other important activities *A. vasica* has emerged as imperative medicinal herb well known for its applications in different traditional medicinal system such as Ayurveda, Siddha and Unani etc.

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