Phytochemical and Pharmacological Investigations on *Adhatoda zeylanica* (Medic.): A Review

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**INTRODUCTION**

Nature is still mankind’s greatest chemist and many compounds that remain undiscovered in plants are beyond the imagination of even our best scientists. From time immemorial man has been interested in trying to control diseases. As the world’s population is nearing 5 billion, with this rate of growth, ¾th of the world’s population can’t afford the products of western pharmaceutical industries. Therefore, they have to rely upon the traditional medicine, which are derived from plants. One third of all pharmaceuticals are of plant origin. Though considerable advances are made in the pharmaceutical sciences, especially in synthetic chemistry, but plants and their derivatives continue to maintain their significance in medicines. In fact, modern people are now showing increased interest in natural drugs than synthetic once, primarily because of a high degree of adverse side effects caused by the latter. It is evident from the present scenario, that herbal cure is gaining world wide acceptance and has emphasized on modern scientific exploration, extraction and evaluation of folk medicines.

**ABSTRACT:** Plants have been one of the important sources of medicines since the beginning of human civilization. There is a growing demand for plant based medicines, health products, pharmaceuticals, food supplements, cosmetics etc. Medicinal plants have curative properties due to the presence of various complex chemical substances of different composition, which are found as secondary plant metabolites in one or more parts of these plants. The plant *Adhatoda zeylanica* Medic. syn. *A. vasica* Nees commonly known as vasaka, family Acanthaceae, is extensively used traditionally for treating cold, cough, whooping cough, chronic bronchitis, asthma and also used as a sedative, expectorant, antispasmodic. In recent years the interest in this plant has increased considerably with substantial progress on its chemical and pharmacological properties. *Adhatoda zeylanica* is an important source of phytoconstituents like quinazoline alkaloid vasicine, vasicinone, vasicinol, vasicinine and vasicoline. The alkaloids vasicine and vasicinone shows bronchodilatory action. Hence in view of immense medicinal importance of the plant this review is therefore an effort to compile all the information reported on its phytochemical and pharmacological activities, these information will be helpful to create interest towards the plant and may be useful in developing new formulations, which are more effective and have more therapeutic values.

**Keywords:** *Adhatoda zeylanica*, Acanthaceae, Vasicine, Vasicinone, Bronchodilator.

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from plants. These are either used directly as a plant extract or modified through further synthesis.\(^1\) Now a days natural medicines are gaining prominence, because they are economical, easily available and relatively free from side effects. The increased global demand for polyherbal formulations is a reflection of positive impact of consolidated efforts aimed at reviving science of phytopharmacy.\(^2\) *Adhatoda zeylanica* Medic. family Acanthaceae is an evergreen, gregarious, stiff, perennial shrub, 1–6 m in height, distributed throughout India, up to an altitude of 1300 m. Leaves elliptic-lanceolate or ovate-lanceolate, entire, 5–30 cm long, hairy, light green in colour. Shrub grows on waste lands and in variety of habitats and soil. There is considerable demand for this plant within the country for its beneficial effects, particularly in bronchitis. The leaves, flowers, fruits and roots are extensively used for treating cold, cough, whooping-cough and chronic bronchitis and asthma, as sedative-expectorant, antispasmodic and as anthelmintic.\(^3\) Hence in view of immense medicinal importance of the plant this review is therefore an effort to compile all the information reported on its phytochemical and pharmacological activities, these information will be helpful to create interest towards the plant and may be useful in developing new formulations, which are more effective and have more therapeutic values.

**PLANT PROFILE**

*Common vernacular names*\(^3\)

- **Arusa** (Hindi)
- **Adusoge** (Kannad)
- **Basak** (Bengali)
- **Aradusi** (Gujrati)
- **Adhatodai** (Tamil)
- **Bansa** (Panjabi)
- **Arusa** (Urdu)
- **Basongo** (Uriva)
- **Bangra** (Garhwal)
- **Addasaramu** (Telugu)
- **Bahekar** (Kashmir)

*Taxonomic Classification*\(^4\)

- **Kingdom** - **Plantae**
- **Subkingdom** - **Tracheobionta**
- **Superdivision** - **Spermatophyta**
- **Division** - **Magnoliophyta**
- **Class** - **Magnoliopsida**
- **Subclass** - **Asteridae**
- **Order** - **Spermatophytales**
- **Family** - **Acanthaceae**
- **Genus** - **Adhatoda**
- **Species** - **Adhatoda zeylanica**

**MORPHOLOGICAL CHARACTERS**

Plant is a dense shrub 1–6 m high with many long opposite ascending branches. Stem with yellowish bark. Leaves-12.5–20 by 3.8–6.3 cm, elliptic-lanceolate, acuminate, minutely puberulous when young, glabrous when mature, entire, dark green above paler beneath, base tapering, main nerves 10–12 pairs with reticulate venation between petioles 1.3–2.5 cm long. Flower short densely axillary pedunculate spikes 2.5–7.5 cm long, towards the ends of the branches, peduncles 3.8–10 cm, stout, shorter than the leaves, bracts reaching 2.2 by 1.3 cm. Calyx rather less than 1.3 cm. long glabrous or slightly pubescent, divided to within 2 mm. of the base, segments inbricate, oblong-lanceolate, acute, 3–nerved, reticulately veined. Corolla white, with a few irregular rose-coloured bars in the throat, 3.2 cm long, long pubescent outside, tube 1.3 cm long the lower half cylindrical, 4 mm. diameter upper half much laterally flatted. Filaments hairy at the very base, long, stout, curved lower anther-cells minutely apiculate, (not white spurred) at the base. Ovary pubescent, subacute shortly and bluntly pointed, pubescent, solid stalk flattened, 1 cm long, seeds 6 by 5 mm, orbicular-oblong.\(^5\)

**PHYTOCHEMICAL INVESTIGATION**

Plant contains chief active principal quinazoline alkaloids such as vasicine, adhatodine, vasicinone, deoxyvascinone.\(^5\) A novel alkaloid and galactoside isolated from the roots have been characterized as 9 – acetoamido–3, 4 – dihydro pyrido – (3, 4-b) – indole and O–ethyl – α – D galactoside respectively. In addition to sitosterol β-D – glucoside, D – galactose and deoxyvascinone have also been isolated from the roots of this plant.\(^6\) Vasicol a new alkaloid is also isolated from the plant.\(^7\) High-performance thin layer chromatographic method has been developed for the simultaneous determination of pharmacologically important quinazoline alkaloids vasicine and vasicinone in *Adhatoda zeylanica*.\(^8\) The alkaloid vasicine has been found to occur in higher plants. Minor alkaloids which include vasicinol, vasicinone, deoxyvascinone and deoxyvascine have been reported in lower plants.\(^9\) Two new aliphatic hydroxyketones, isolated from the aerial part have been characterized as 37- hydroxy hexatetracont - 1- en- 15 - one and 37- hydroxy pentatetracont - 19- one.\(^10,11\)

\(^{1}\) H NMR spectroscopy of l- vasicine by the use of Moher’s method using MTPA (α–methoxy–α – (trifluoromethyl) phenyl acetic acid) esters for establishing the absolute configuration was reported.\(^12\) Further a non nitrogenous neutral principle, vasakin,\(^13\) (+) -
vasicinone[14] and two new quinazoline alkaloids, one of which named as adhavasinone have been isolated[15] and two new pyrroloquinazoline alkaloids, desmethoxyamflorine and 7- methoxyvasicinone were identified from the ethanolic extract of the leaves.[16] A reverse phase HPLC method of estimating vasicine in the leaves was developed. Using this technique, vasicine was estimated in two polyherbal drug formulations as well as from the leaves and stem of the plant.[17] In another study, a rapid and accurate method using HPLC was developed for detection, monitoring and quantification of vasicine in the plant as well as herbal preparations containing plant.[18] Synthesis of analogues of vasicine, vasicinone and deoxyvasicinone were reported.[19] Leaves of vasaka were subjected to authentication and the marketed formulations containing the leaf extract were obtained from local pharmacies to estimate vasicine and vasicinone contents using HPLC method. The vasicine content of various formulations varied from 22.8 µg to 86.4 µg/10 ml of the marketed formulations. At the operative chromatographic conditions vasicinone was not detected in any of the formulation analyzed. The HPLC technique now allows routine analysis of vasicine containing complex traditional formulation.[20] The flavonoids in the leaves were identified as kaempferol, quercetin, vitexin and isovitexin while the phenolic acids were p-hydroxybenzoic acid, syringic acid and p-coumaric acid.[21] The leaves were found to contain free vitamin C and carotene.[22] Both leaves and flowers contained the flavones luteolin.[23] The mineral elements of the leaves were identified as calcium, magnesium, potassium, sodium and iron.[24] The petroleum ether extract yielded an aliphatic alcohol characterized as 29-methyltriacontan-1-ol.[25] The stalk, which is non woody, was found to contain the lignins composed of guaiacyl-, syringyl- and p- hydroxymethylphenyl propane building units similar to hardwood lignins.[26] The petroleum ether extract of the flowers contained a number of non-nitrogenous compounds viz., triatricontane, β-sitosterol, α-amyrin and β-sitosterol-D-glucoside; the ether extract yielded kaempferol and quercetin, the ethyl acetate and n-butanol extracts afforded kaempferol-3-β-D-glucoside and kaempferol-3-sophoroside.[27] The young inflorescence yielded (±) - vasicinone.[26,29] Flowers in addition yielded a fat containing traces of tridecenoic acid, pentadecanoic acid and a new glucoside identified as 2', 4-dihydroxychalcone-4-glucoside.[30] The fixed oil obtained from the seeds contained arachidic (3.1 percent), behenic (11.2 percent), lignoceric (10.7 percent), cerotic (5.0 percent), oleic (49.9 percent) and linoleic (12.3 percent) acids. The unsaponifiable matter yielded β-sitosterol.[31] The structure of vasicinol isolated from the roots was established as 6-hydroxypeganein.[32] The mass fragmentation of the alkaloids vasicine, vasicinol as well as its methyl ether was also studied.[33] The other alkaloids isolated were 9-acetamido-3,4-dihydropyrido-(3,4-b)-indole, O-ethyl-α-D-galactoside, 1,2,3,9-tetrahydropyrrolo(2,1-b) quinazolin-9 (1H) –one, sitosterol-β-D-glucoside, D-galactose and deoxyvasicinone;[34] vasicol (1,2,3,4,9, 11-hexahydropyrrolo(2,1-b) quinazolin-3,11-diol, vasicinone, adhatonine and vasicinolone.[35]Vasicinolone was reported as the oxidative product of vasicinol.[36] The total and reducing sugars present in the root and the bark were estimated.[37]

**PHARMACOLOGICAL INVESTIGATION**

Although many pharmacological studies have been performed on the basis of chemical constituents present, a lot more are still to be exploited, explored and utilized. Important pharmacological findings are summarized below:

**Bronchodilator activity**

Vasicinone isolated from the leaves has a bronchodilator action on the normal lungs and powerful bronchodilator action against the histamine-induced bronchoconstriction in guinea pig’s lungs and tracheal chain. 1 –Vasicinone was, however, stronger in action than dl-form.[38]Vasicine showed bronchodilator activity in both in vivo and in vitro experimental studies, its activity being comparable to theophylline.[39]

**Antitussive activity**

The antitussive activity of *Adhatoda zeylanica* extract was evaluated in anaesthetized guinea pigs and rabbits and in unanaesthetized guinea pigs. On oral administration to the guinea pigs, the antitussive activity of the extract was similar to codeine against coughing induced by irritant aerosols.[40]

**Hypoglycemic activity**

The non-nitrogenous principle obtained from the leaves as suspension administrated orally (25 mg/kg) to fasting male rabbits lowered the blood sugar of rabbits for a short period of two hours. The average fall over a period of four hours was 7.5 percent which was far less than the fall due to similar dosage of tolbutamide.[41] The ethanolic extract of the leaves exhibited hypoglycemic activity in rats.[42] The effect of the two unani drugs, Arusa (leaves of *Adhatoda zeylanica*) and Kalongi (seeds of *Nigella sativa*) was studied in induced diabetic rabbits. Both the extracts were compared for hypoglycemic effect with a standard drug glibenclamide. Diabetes was observed in...
rabbits (fasting blood glucose level ranged from 200–250 mg/100 ml) within 24 hrs after injection of alloxan and divided into four groups i.e. diabetic control (distilled water), diabetic standard (glibenclamide), diabetic test (Arusa) and diabetic test (Kalongi). The test drugs were administered to the treated group, while the vehicle was administered to the animals of control group, orally. Blood glucose was estimated by the end point o-toluidine. The study revealed that the aqueous extract of Arusa and Kalongi in the dose of 100 mg/kg and 200 mg/kg, respectively given orally reduced the blood glucose level in induced diabetic rabbits. The significant reduction (P less than 0.05) in blood glucose level started after 3 hrs which continued for 6 hrs in both the groups.\[43\]

**Platelet activity**

On repeated oral and intramuscular administration of vasicine hydrochloride resulted in a dose related increased in platelet count in normal rats, mice, rabbits and dogs. This increase in platelets was also associated with significant hyperplasia of megakaryocytes in the bone marrow. The findings revealed that vasicine could hold promise for control of capillary haemorrhages and for correction of drug-induced bone marrow depression.\[44\]

**Antitumour activity**

The alcoholic extract of the leaves did not show antitumour activity against various transplantable tumours.\[45\]

**Wound healing activity**

The activity of alcoholic extract of leaves was studies for its wound healing effect in buffalo calves. A significant increase in rate of healing, breaking strength, tensile strength, energy absorption and extensibility was observed. The treated wounds revealed significantly higher values of these parameters in comparison to control.\[46,47\]

**Enzyme activity**

The decoction of the leaves of the plant activated the trypsin enzyme in *in vitro* studies, which in turn stimulated the digestive process.\[48\]

**Antimicrobial activity**

The alcoholic extracts of the leaves and root showed antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. The water extract of the leaves also showed activity against *Staphylococcus aureus*.\[49–52\]

Aqueous and ethanolic extracts from various parts of seven plants were screened against three gram – negative bacteria. Of the twenty - four extracts assayed by agar well diffusion method, ethanolic extract from the shoots of *Adhatoda zeylanica* was the most active, exhibiting greatest inhibitory activity against multi-drug resistant *E. coli*.\[53\]

**Antiviral activity**

The crude extract of the leaf and bark showed 20–39.9 percent inhibition of potato virus X and 85 percent inhibition against bean common mosaic virus.\[54,55\]

**Insecticidal activity**

The powder of the leaves was a non-poisonous indigenous insecticide and recommended for controlling the insect pests for stored seeds.\[56\]

**Antifeedant and toxic activity**

The effect of crude methanolic extracts of *Adhatoda zeylanica* leaves on the feeding and performance of *spodoptera littoralis* larvae was investigated in the laboratory. The extract exhibited strong antifeedant and toxic activity against the larvae when applied either on leaf discs or incorporated into artificial diet.\[57\]

**Radiomodulatory influence**

The radiomodulatory influence of ethanolic extract of *Adhatoda zeylanica* leaf extract against radiation induced hematological alterations in peripheral blood of Swiss albino mice was studied at various post-irradiation intervals between 6 h to 30 days.\[58\]

**Immunostimulant activity**

V asaka exhibited marginal increase in the WBC count to the extent of 16%. Vasaka showed statistically significant protective effect against cyclophosphamide induced myelosuppression to an extent of 80%.\[59\] Effect of alcoholic extract of plant leaf (500 mg/kg, p.o.) on haematological profile, splenic lymphocytes and peritoneal macrophages was studied 5, 10, 15 and 20 days after treatment in swiss albino mice. Its effect on macrophages phagocytic index, *E.coli* induced abdominal peritonitis and SRBC induced delayed type hypersensitivity was also evaluated. Plant showed significant increase in total WBC, blood lymphocytes, splenic lymphocytes and peritoneal macrophages. It also showed significant protection against *E. coli* induced abdominal peritonitis.\[60\]

**Uterine activity**

Vasicine showed uterotonic activity in human myometrium strip and abortifacient activity in guinea pigs.\[61\]
Effect on Chikungunya

The symptoms and signs of Chikungunya were studied among 500 patients and the methods to fight the disease with traditional Siddha medicines are described. The patients were administered doses of decoction prepared with the powder of various plants including decoction prepared with Adhatoda zeylanica leaves. In the first 12 hrs, pain was reduced but fever persisted. In the next three hrs, pain was reduced further and fever came down by 2°C. In next 6 hrs normality was attained. Out of 500 patients treated, 450 got cured of the diseases.[62]

Traditional Uses

The plant is pungent, bitter, acrid, cooling, useful in bronchitis, leprosy, blood impurities, heart troubles, thirst, asthma, fever, vomiting, loss of memory, leucoderma, constipation, jaundice, tumors, and diseases of the mouth.[5] The root is diurectic, useful in bronchitis, asthma, bilious vomiting, sore eyes, fevers, gonorrhoea. The leaves are emmenagogues, useful in gonorrhoea. The flowers improve the circulation of the blood. The fruit is useful in bronchitis.[63] The leaves and the roots of this plant are considered a very efficacious remedy for all sorts of coughs, being administered along with ginger.[64] The leaves are also used for rheumatism. The flower, leaves, and root but especially the first, are supposed to possess antispasmodic qualities. The flowers and the fruit are bitter, aromatic and antispasmodic.[65] The fresh flowers are used in ophthalmia.[66] The powdered root is used in Mysore by native doctors in cases of malarial fever. It has expectorant and antispasmodic properties and its use has been recommended in the treatment of cold, cough, asthma and even diphtheria.[67] Fresh juice of leaves with honey relieves the irritable cough by its soothing action on the nerves and by liquefying the sputum which makes expectoration easier.[68] Both the decoction and powder form constitutes of many Ayurvedic preparations for infection of the respiratory tract.[69] Plant is one of the ingredients of the preparations known as Vasavaleha (Dabur), Kasamrit Herbal (Baidyanath) and Vasaka capsule (Himalaya Drug Company). The plant is recommended for snake bite. Daily application of massage of leaf extracts effectively reduces the inflammatory and bleeding condition of gums.[70]

TOXICOLOGICAL STUDIES

The allergenic pollen grains of the plant were common during the months of October and November in Pondicherry.[71] A pilot survey of air borne pollen grains as well as clinical survey of pollen allergy conducted at Kolhapur during monsoon season revealed that only two patients with asthma/rhinitis gave a significant positive reaction on skin testing.[72] In another survey at Nagpur, 7 of the 50 patients treated at the allergy and chest clinic, Jasleen Hospital, Nagpur showed allergy due to the pollens of Adhatoda zeylanica.[73]

ETHNOBOTANICAL STUDIES

An ethnomedical exploration was carried out during 2001–2002 in village Barali Kass and its allied areas, revealed that 47 species were used as folk medicine for curing of several diseases. The data was collected from the local peoples including reliable hakims, physicians and old villagers. Plant species with their botanical names, local names, status and folk medicinal uses have been collected and enlisted. Some of the medicinal plants used from the study area includes Adhatoda vasica, Phoenix sylvestris, Plumbago zeylanica, Clematis grata, Adiantum caudatum.[74]

CONCLUSION

Adhatoda zeylanica is highly regarded as an universal panacea in the Ayurvedic medicine because it is extensively used for treating cold, cough, whooping-cough and chronic bronchitis and asthma, as sedative-expectorant, antispasmodic and as anthelmintic. However, well controlled double-blind clinical trials are lacking. It is one of the most versatile plants having a wide spectrum of medicinal activities. This medicinal plant is the unique source of various type of compounds chief principle is a quinazoline alkaloid, vasicine accompanied by vasicinone, vasicinol, vasicinine, vasicoline and adhatodine. Very little work has been done on the medicinal applications of these compounds and hence extensive investigation is needed to exploit their therapeutic utility to combat diseases. A drug development programme should be undertaken to develop modern drugs with the compounds isolated from Adhatoda zeylanica. Although crude extracts from leaves of Adhatoda zeylanica have medicinal applications from time immemorial, modern drugs can be developed after extensive investigation of its bioactivity, mechanism of action, pharmacotherapeutics, toxicity, proper standardization and well controlled double-blind clinical trials. As the global scenario is changing towards the use of nontoxic plant products having traditional medicinal use, development of modern drugs from Adhatoda zeylanica should be emphasized for the control of various diseases. Therefore it is necessary to exploit its maximum potential in the field of medicinal and pharmaceutical science for novel and fruitful application.
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