A phyto-pharmacological overview on
Adhatoda zeylanica Medic. syn. A. vasica (Linn.) Nees

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Abstract
Adhatoda zeylanica Medic. syn A. vasica (Linn.) Nees (Vasaka), a popular Indian medicinal plant, has long been used commonly in Ayurvedic system of medicine. The plant has been found to possess diverse number of pharmacological activities. The present paper gives an account of updated information on its phytochemical and pharmacological activities. The review reveals that wide range of phytochemical constituents have been isolated from the plant and it possesses important activities like antitussive, antibacterial, abortifacient, anti-inflammatory and antituber. Various other activities like radiomodulation, hypoglycaemic, cardiovascular protection, antitubercular, antiviral, hepatoprotective, antimutagenic and antioxidant have also been reported. These reports are very encouraging and indicate that herb should be studied more extensively for its therapeutic benefits. Clinical trials using vasaka for a variety of combinations in different formulations should also be conducted.

Keywords: Adhatoda vasica, Adhatoda zeylanica, Arusa, Malabar Nut, Vasaka, Vasicine, Phytoconstituents, Pharmacological activities.

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Introduction
Adhatoda zeylanica Medic. (Family — Acanthaceae) syn. A. vasica (Linn.) Nees and Justicia adhatoda Linn. It is commonly known as Basak (Bengali); Aradusi, adusa (Gujrati); Arusa, baansa, adulsa (Hindi); Bansa, basuti, bhekkar (Punjabi), and shwetavasa, vasa, vasaka (Sanskrit) and Malabar nut (English) in different languages and regions of India1-3. It has been used in Ayurvedic system of medicine for the treatment of various ailments of respiratory tract in both children and adults. All the parts of the plant have been used for their therapeutic beneficiary effect from ancient times4. It is also used for the treatment of bleeding piles5. The plant is used as an ingredient of numerous popular formulations including cough syrups used in combination with ginger and tulsi where it exerts its action as an expectorant and antispasmodic6. Bisolvon, a branded drug containing Vasaka as an ingredient is used to clear the airways by decreasing the mucus secretions and opening the air passages5. There are various herbal formulations, viz. Kada, Fermiforte, Spirote available for the treatment of various kinds of respiratory disorders6-9. It is an evergreen, gregarious, perennial shrub, 1-2.5 m in height, having opposite ascending branches1. The plant is distributed throughout India up to an altitude of 1300 m and mainly found in sub-Himalayan regions; also found in Nepal, Pakistan, Myanmar and Germany10. Leaves are simple, petiolate, ex-stipulate, 10-20 cm long and 3-10 cm broad, lanceolate to ovate lanceolate having crenate margin, tapering base and an acuminate apex with characteristic odor and bitter taste. Transverse section of the leaves showed two layers of palisade cells with diacytic stomata. Glandular and non-glandular trichomes are present on both the surfaces of the leaf. Elongated cystoliths, acicular and prismatic form of calcium oxalate crystals are present in the mesophyll. The midrib region composed of 4-6 layers of collenchyma just below the epidermis and 3-5 vascular bundles, central one being largest12. Adulteration of leaves with A. beddomei Clarke, Ailanthus altissima (Mill.) Swingle (syn. A. glandulosa Desf.) and A. excelsa Roxb. leaves is very common and can be distinguished from the genuine drug by their characteristic macroscopic and microscopic features12.

Phytochemical studies
A. zeylanica mainly consists of pyrroquinazoline alkaloids (Fig. 1 a-k), viz. vasicine, vasicol, vasicinone, peganine along with other minor constituents. Vasicine is a major bioactive pyrroquinazoline alkaloid of vasaka present in the concentration of 1.3%. Minor alkaloids include adhatonine, vasicinol and vasicinolone. Flowers mainly
consist of kaempferol and quercetin. A new moiety 2'-4-dihydroxy chalcone-4-glucoside has been identified in the flowers. Four quinazoline alkaloids: vasicoline, adhatodine, vasicolinone and anisotine have been obtained from the leaves and vasicinone, vasicol have been isolated from the inflorescence. Sitosterol, β-glucoside-galactose and deoxy vasicine have been isolated from the roots of the plant. Phytochemical investigations of leaves also yielded a quinazoline alkaloid identified as 1,2,3,9-tetrahydro-5-methoxypyrrolo[2,1-b] quinazoline-3-ol. HPTLC method has been developed for the determination of pharmacologically important quinazoline alkaloids vasicine and vasicinone in Vasaka. The assay combines the separation and quantification of analytes on silica gel 60 GF254 HPTLC plates with visualization under UV light and scanning at 270-281nm.

**Pharmacological activities**

Water and alcoholic extracts of Vasaka exerts significant pharmacological actions due to the presence of active constituents like vasicine and vasicinone. The pharmacological activities of vasicine and vasicinone are much more as compared to their racemic forms. Various activities reported are:

**Antibacterial**

Alcoholic extract of leaves and roots showed antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, whereas water extract showed activity against *S. aureus* only.

**Anticholinesterase**

Vasicinone obtained from the roots produced transient hypotension in cats, contraction of isolated intestine and depression of isolated heart in guinea pigs, thus showing good anticholinesterase activity.

**Wound healing**

The rate of healing was found to be higher in the plant extract treated wounds in buffaloes as compared to pancreatic tissue extracts.

**Hypoglycaemic**

Ethanolic extract of the leaves exhibited hypoglycaemic activity in the rats. Modak and Rao found that when non-nitrogenous principle of the leaves in suspension form administrated orally at the dose of 25 mg/kg, lowered the blood sugar level of rabbits for a short period of time.

**Abortifacient/Oxytocic**

Vasicine possesses uterine stimulating and oxytocic activity and causes abortifacient effect by the release of prostaglandins under the influence of oestrogens. The activity was found almost similar to oxytocin.

In a study conducted on rats, rabbits, hamsters and guinea pigs it was found that vasicine has uterotonic and abortifacient effects possibly by enhancing the synthesis and release of prostaglandins. In this study dose dependent effect was observed with effective doses ranging between 2.5-10 mg/kg. However, administration of estradiol dipropionate potentiated the abortifacient effect in...
Fig. 1(a-k): Quinazoline ring containing constituents of *Adhatoda zeylanica*
guinea pigs whereas treatment with aspirin inhibited the abortifacent activity due to inhibition of release of prostaglandins.30

**Antitussive**

Vasicine and vasicinone showed bronchodilatory activity *in vitro* and bronchoconstrictory activity *in vivo*, however, combination of both the alkaloids (1:1) showed bronchodilatory activity *in vivo* as well as *in vitro*.4 Evaluation of antitussive effect of *vasaka* on anesthetized guinea pigs and rabbits was confirmed electrically and mechanically and found to be 1/20th and 1/40th as active as codeine intravenously and almost similar in activity as by oral administration.31 *Kanjang*, a fixed combination of *A. zeylanica*, *Echinacea purpurea* (Linn.) Moench. and *Eleuthrococcus senticosus Maxim.* showed a significant efficacy in acute upper respiratory infections.32

**Digestive**

Decoction of the leaves activated the trypsin enzyme in *in vitro* studies and thus stimulated the digestion process.33

**Cardioprotective**

In combination of vasicine and vasicinone, a significant reduction in cardiac depressant effect was observed. No effect was shown by vasicinone (dl-form), however l-form was found to be weakly effective in stimulating cardiac muscles.4

**Anti-inflammatory**

Anti-inflammatory activity of methanolic extracts (a non alkaloid fraction, saponins and the alkaloids) were evaluated by using modified hens egg chorioallantoic membrane showing potent activity at a dose of 50 µg/pellet equivalent to that of hydrocortisone whereas methanolic extract showed lesser activity.34

**Hepatoprotective**

The leaves showed significant hepatoprotective effect at a dose of 50-100 mg/kg on the liver damage induced by d-galactosamine in rats.35

**Antiulcer**

Leaf powder of this plant showed considerable antiulcer activity in experimental rats in ethanol induced ulceration model.36

**Antimutagenic**

Antimutagenic and antioxidant status have also been attributed for *A. zeylanica*. It exerts antioxidant effect against lipid peroxide and xanthine oxidase induced oxidation.37

**Radiomodulation**

Leaf extract showed a radiomodulatory influence against radiation induced hematological alterations in the peripheral blood of swiss albino mice. A significant increase in serum alkaline phosphatase activity and decrease in acid phosphatase activity was observed in leaf extract pretreated irradiated animals during the entire period of study.38

**Antituberculer**

Growth of *Mycobacterium tuberculosis* was found to be inhibited by benzyl amine, ambroxol, bromhexine (semisynthetic derivatives of vasicine) due to their mucolytic action. These have ability to concentrate in the macrophages and enhance the level of lysozyme in bronchial secretions along with level of Rifampicin in the lung tissue and sputum, acting as adjunctive for the therapy of tuberculosis.39

**Toxicity studies**

Vasicine hydrochloride was subjected to chronic toxicity studies in rats and monkeys for six months, where the mortality and body weight of treated animals were found comparable to control. Hematological and biochemical parameters were with in the normal physiological range. No abnormality was found in the major organs while carrying out their autopsy and histopathological examination indicating the relatively non toxic nature of vasicine hydrochloride.40

**Conclusion**

The literature survey revealed that *A. zeylanica* is an important source of many pharmacologically and medicinally important chemicals such as vasicine, vasicinone, vasicolone and other various useful minor alkaloids. The pyrroquinazoline group of alkaloids is the most searched chemical constituents of it. The plant has been widely studied for its pharmacological activities and regarded as universal panacea in Ayurvedic medicines and finds its position as a versatile plant having a wide spectrum of medicinal activities. As the global scenario is now changing towards the use of non toxic plant products, development of modern drugs from *Vasaka* should be emphasized. Clinical trials should be conducted to support its therapeutic use. It is also important to recognize that its extracts may be effective not only in the...
isolation, but may actually have a modulating effect when given in combination with other drugs.

References


