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# REVIEW ON RESEARCH STUDIES OF *VASAPATRA* (LEAF OF *ADHATODA VASICA* NEES.)

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**ABSTRACT:** Plants have been used for health and medical purposes for several thousands of years. The clinical experience built over many centuries provides a substantial basis for the safe and effective use of herbal medicines, not just as a main form of therapy, but as a complement to the mainstream of western medical treatment in certain diseases. Till today, few plant species that provide medicinal herbs have been scientifically evaluated for their possible medical application and safety. Assurance of the safety, quality, and efficacy of medicinal plants and herbal products has now become a key issue in industrialized and in developing countries. Leaf of *Adhatoda vasica* Nees, classically known as a Vasapatra, is one of the important medicinal herbs as it was mentioned for the treatment of many diseases like Kasa (a cough), Swasa (dyspnoea), Ksaya (phthisis), Raktapitta (hemorrhagic diseases), Kamala (jaundice) and Kustha (skin disease). Many research studies have been conducted to evaluate its clinical efficacy. Keeping this view, a critical review of *Adhatoda vasica* Nees, an Ayurvedic medicinal plant, has been carried out based on authentic and scientific information documented in classics and various research studies.

**INTRODUCTION:** During the past decade, traditional systems of medicine have become a topic of global importance. Current estimates suggest that, in many developing countries, a large proportion of the population relies heavily on traditional practitioners and medicinal plants to meet primary health care needs. Concurrently, many people in developed countries have begun to turn to alternative or complementary therapies, including medicinal herbs [1].

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*Vasa*, botanically identified as an *Adhatoda vasica* Nees., belonging to Acanthaceae family is important Ayurvedic medicinal herb. It is an evergreen, gregarious, stiff, perennial shrub, 1.2-6.0 m in height, distributed throughout India, up to an altitude of 1,300 $m^2$. Leaves of *A. vasica* are elliptic-lanceolate 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 [3]. Its leaves are extensively used for treating cold, cough, whooping cough, and chronic bronchitis and asthma as a sedative expectorant, an antispasmodic and anti-inflammatory drug. There is considerable demand for this plant within the country. The demand is being met from natural sources [4-5].

The analysis was carried out basing on the collected information from various sources including review articles; Ayurvedic classical texts & lexicons; Ayurvedic pharmacopeia of India; as well as many other reference books.

**Properties and Actions According to Ayurveda: [5]**

***Rasa* (taste):** Tikta (Bitter), Kashaya (Astringent)
***Guana* (quality):** Laghu (light)
***Virya* (Potency):** Sheeta (cold)
***Vipaka* (post-digestive effect):** Katu / Laghu
***Karma*:** Hridya, Kaphapittahara, Raktasangrahika, Kasaghna

**Indication Described in Ayurvedic Medicine:** Raktapitta (Purpura/Hemorrhagic disorder), Kasa (Cough), Jwara (Fever), Kshaya (Phthisis), Kasa (Cough), Shvasa (Asthma), Raktapitta (Purpura/ Hemorrhagic disorder), Rajayakshma (Tuberculosis), Parshvashula (pain in flanks), Hritshula (Angina pectoris), Shotha (oedema) [7-10].

**Uses Described in Folk Medicine:** The leaves are used fever, rheumatism, bronchitis, asthma, cough, cold, menorrhagia, leprosy, jaundice, stomachic, wound healing, malaria, mumps, heart trouble, and delivery complaint [11].

**Formulation:** *Vasa Swarasa* (juice of *A. vasica* leaves), *Vasa Avaleha* (sugar formulation of *A. vasica* leaves), *Vasa Ghrita* (clarified butter of *A. vasica* leaves) and *Vasa Asava/Arista* (Alcoholic preparation of *A. vasica* leaves) [7-10]

**Major Chemical Constituents:** The Leaves have been found to be a rich source of alkaloids of which vasicine and vasicinone are bioactive. A non-nitrogenous neutral principle, vasakin, vasicinone, two new quinazoline alkaloids, one of which was named as adhvasinone and two new pyrroloquinoline alkaloids, desmethoxyaniflorine and 7-methoxyvasicinone were identified from the ethanolic extract of the leaves [6].

**Experimental Pharmacology:**
**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 estrogens [12].

Vasicine-induced abortion was studied in rats, guinea pigs, hamsters, and rabbits. The study showed that vasicine acted through the release of PGs [13].

Synthesized vasicine and vasicinone derivatives in *in-vitro* studies were found to have oxytocic activity at the dose above 1 µg/ml.[14]

The aqueous solution of the leaves at the dose of 175 mg/kg bw revealed 100 percent abortifacient activity in albino rats [15].

The extract of the plant at 2 percent concentration level revealed abortifacient activity [16].

Vasicine showed uterotonic activity on human myometrium strips which were in some cases even more marked than that of two known oxytocics, pitocin and methergine. The response of the uterus to drugs depended on its hormonal status [36].

**Expectorant:** The petroleum ether extract of the leaves 50 mg/kg b/w i.p. and i.v.[17]

**Bronchodilator:** Vasicinone isolated from the leaves had a bronchodilator action [18]. Vasicine showed bronchodilator activity in both *in-vivo* and *in-vitro* experimental studies [19].

**Antitussive:** The plant extract was evaluated in experimental models for antitussive activity [20].

**Anti-tubercular Activity:** It was found that bromhexine and ambroxol, the semi-synthetic derivatives of vasicine have activity against Mycobacterium tuberculosis *in-vitro* [21].

**Hypoglycaemic:** Ethanolic extract of the leaves [22].

**Platelet Activity:** Vasicine hydrochloride –alkaloid from leaves [23].

**Wound Healing:** Alcoholic and chloroform extracts in the form of ointment [24].

**Enzyme Activity:** The decoction of the leaves of the plant activated the trypsin enzyme [25].

**Anti-inflammatory Activity:** 50% ethanolic extract of the plant (excluding root) [26].

**Antimicrobial:** 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 [27].

**Antiviral:** The crude extract of the leaf, the bark and the plant [28].

**Anthelmintic:** The leaves (oil), as well as the alkaloids, vasicine and vasicinone, were screened against Ascaris lumbaricoides neuromuscular preparations [29].

**Insecticidal:** The powder of the leaves [30], alcoholic, and petroleum ether and benzene leaf extracts [31].

**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 [32].

**Preclinical Safety Data:**

**Safety & Toxicological Studies of Vasicine:** Acute toxicity in mice and absorption pattern in dogs of vasicinone administered by different routes confirmed activity and safety of vasicinone. Acute and chronic toxicity studies proved the use of vasicine and vasicinone comparatively safe.

Clinical trials of a drug containing vasicine and vasicinone have not revealed any side effects while treating bronchial asthma.

Wakhloo *et al.* (1980) investigated the safety of use of vasicine in 24 human volunteers using 0.5-16 mg dose of vasicine injected i.v. in 500 ml saline in 3 h with the objective of determining any acute human toxicity, tolerance, pharmacological action, any untoward effect and safe dosage range [33].

Vasicine tried up to 16 mg dose on the hospital in-patients on 2$^{nd}$ to 8$^{th}$ day of normal puerperium was well tolerated and showed no undesirable effect in clinical observations, hematological and bio-chemical investigations and kidney and liver function tests carried out before, during and after vasicine treatment. However, uterus became firm and contracted after vasicine treatment which indicated its effectiveness as an oxytocic and having abortifacient activity.

Pahwa *et al.,* (1987) have conducted the chronic toxicity study of *Adhatoda vasica* in rats (2.5 mg/kg, 5 mg/kg and 10 mg/kg, low dose, 2x ED50, med dose, 4x $ED_{50}$ and 8x $ED_{50}$ respectively) and monkeys (5, 10 and 20 mg/kg as above criteria) for 6 months. They reported that there is no change in mortality rate and body weight. Autopsy and histological examination of major organs did not reveal any abnormality [34].

**Pharmacokinetic Properties:**

**Vasicine:** The absorption and distribution of $^{14}$C-vasicine (30 mg/kg) were studied in mice by administering it in three different modes, *i.e.* i.v., i.m. and s.c. Within 10 min the maximum concentration of drug was monitored in the uterus and was maintained up to 30 min. Within 40 min most of the activity was distributed in various tissues and very little was found in the blood. Accumulation of the drug in other smooth and skeletal muscles was noticed 90 min after administration. There was no appreciable accumulation of the drug in the liver [44].

The *in-vivo* metabolism of vasicine on oral administration in rats revealed that the process of metabolism was very fast and first pass effect was appreciably pronounced and this might be the cause of loss of efficacy of vasicine as an abortifacient when administered orally [45.]

Ram *et al.,* (2007) determined the site of absorption of vasicine in the intestine. They used the everted sac method to assess the absorption. Duodenum was reported to have the maximum capacity to absorb isolated vasicine from the methanolic and ethanolic extracts of Vasaka (82.3 ± 5.3%) [46].

Pharmacokinetics studies of vasicine were conducted on 6 healthy human volunteers after a bolus i.v. dose of 1.5 mg/kg was given. The peak plasma concentration was detected in the plasma [47].

**Clinical Studies:**

1. **Oxytocic Effect:** The safety study of vasicine hydrochloride was carried out on 24 human volunteers, up to 16 mg i.v. dose was given on

2nd to 8th day of normal puerperium. No undesirable effect was found during and after vasicine treatment. However, uterus became firm and contracted after vasicine treatment which exhibited its effectiveness as an oxytoxic [35].

2. **Gastric Acidity Or Dyspepsia:** In an uncontrolled clinical trial 60 ml of a *A. vasica* syrup (30g of crude drug) was given daily in four divided doses for six weeks in 20 patients of '*amlapitta'* (Dyspepsia). Clinical improvement along with a reduction in gastric acidity was observed in 85 percent of the patients [37].

   The efficacy of '*vasaka'* (*A.vasica*) syrup given at 30g per day in 4 divided doses for a period of 6 wk was tried in 20 cases of non-ulcer dyspepsia. The drug reduced the total and free HCl in the patients of hyperacidity and hyperchlorhydria; 7 patients were cured, 10 improved, while 3 remain unchanged [38].

3. **Pyorrhoea:** In a study, 25 patients with complain of pyorrhea were taken and were selected randomly. The leaf extract was massaged on inflamed gums twice a day for three weeks. There were a reduction and complete relief in the inflammatory and bleeding conditions of gums [39].

4. **Asthma and Bronchitis (Shwasa):** In a study, comparative efficacy of Vasa-arishta and Vasaka-asava were assessed on 24 patients for the management of Shwasa. Effect of therapy showed that marked improvement was found more in Vasa arishta group while the improved patients were in Vasakaasava treated group [40].

   32 patients were taken in a study and randomly divided into three groups consisting of Vasa avleha, Vasa arishta and Vasa ghrita. Overall effectiveness of test samples on shwasa was observed more in Vasa avleha than Vasa arishta and Vasa ghrita [41]. In a comparative study of Vasa avleha prepared from swarasa and kwathakalpana in the management of shwasa, 35 patients were taken and randomly divided in two groups. Both the preparation of Vasa avleha showed statistically highly significant results on shwasa. From both preparations, Vasa avleha (prepared from swarasa) was better clinically effective in compare to Vasa avleha (prepared from kwath) [42].

5. **Labour (Prasava):** Clinical study on 23 patients shows that the combined application of Vasa swarasa and Nabhilepa to minimize the total labour duration is comparatively more effective that only application of swarasa [43].

**Pregnancy:**

**Abortifacient- Vasicine Hydrochloride:** A preliminary clinical trial was carried out on 25 cases of mid-trimester pregnancy. Intraamniotic injection of 10-80 mg of vasicine hydrochloride in aqueous solution was given in a single dose. Doses above 60 mg were given in 12 cases and all of them aborted. The installation of abortion time was observed to be directly related to the dose of the drug employed. There were no untoward side effects, and the drug was safe [48].

**Lactation:** Excretion of the drug into breast milk and its effects on the newborn has not been established.

**CONCLUSION:** In Ayurvedic materia medica, Vasa is included under the list of prime drugs for the management of Raktapitta (hemorrhagic diseases), Kasa (Bronchitis) and Rajayakshma (phthisis). The folk medicine enumerates the therapeutic application of Vasa in the diseases namely fever, asthma, cough, cold, menorrhagia, leprosy, jaundice, wound, malaria, mumps, and delivery complaints. The analysis of various pharmacological and clinical studies indicates that Vasa leaf is reported to possess expectorant, bronchodilator, antitussive, anti-tubercular, hypoglycaemic, enhancer of platelet count, anti-inflammatory, antimicrobial, antiviral, anthelmintic and hepatoprotective activities. Given these reported activities, Vasa may also be prescribed in viral diseases like idiopathic thrombocytopenic purpura (ITP), Dengue and severe acute respiratory syndrome (SARS).

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## CONFLICT OF INTEREST: Nil

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