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PHARMACEUTICAL ATTRIBUTES OF VASA (ADHATODA VASICA LINN.)-A REVIEW

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ABSTRACT

The present review on *Adhatoda vasica* Nees belonging to family Acanthaceae, commonly known as Adosa highlights that this have a lot of uses in traditional Ayurveda and most popular for its effectiveness in treating respiratory problems. In this paper general medicinal uses and pharmacological activities of various parts of the plants have been revived. The plant as a whole along with its root, leaves, bark and flowers are extensively used to relieve cough, cold, whooping-cough, asthma and bronchitis. Principle constituents of Malabar nuts are the several alkaloids present and chief principle being quinazoline alkaloid, vasicine. A considerable difference in chemical composition is found, which may be due to their occurrence in different eco-climatic zones and changes in edaphic factors. Attention is also focused on the pharmacological properties of which are related to their various interesting applications as antioxidant activity, anti-ulcer activity, hepatoprotective activity, bronchodilator alkaloid, useful in *tamaka shwasa* (asthma), abortifacient and uterotonic activity, anti-tubercular activity, anti-allergy activity, anti-diabetic activity, muscle stimulant activity, anti-ulcer activity, abortifacient and uterotonic activity, insecticidal activity, anticestodal activity and anti-helminthic agents.

KEYWORDS: bronchodilator alkaloid, *tamaka shwasa* (asthma), abortifacient and uterotonic activity, anti-diabetic activity.

1. INTRODUCTION

Srivastava *et al.*[1] mentions that plants have provided a source of inspiration for novel drug compounds and we are using crude plants as medicine since Vedic period. The multiple drug

resistance has developed due to the indiscriminate use of the commercial antimicrobial drugs commonly used in the treatment of infectious disease but with adverse effects on the host, including hypersensitivity, immune suppression, and allergic reactions. This situation forced scientists to search new and effective therapeutic agents. Pinner *et al*[2] stated that infectious disease is the number one cause of death accounting for approximately one-half of all deaths in tropical countries. Herbal have become increasingly popular because of their wide spread use. Clear-cut proof of their efficacy in microorganisms inducing pathogens is yet to be explored. *Adhatoda vasica* nees (Acanthaceae) commonly known as vasaka distributed throughout India up to an attitude of 1300m. is a medicinal plant native to Asia, widely used in Siddha Medicine, Ayurvedic and Unani systems of medicine. 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.

Justicia adhatoda(commonly known in English as Malabar nut, adulsa, adhatoda, vasa, or vasaka) are highly medicinal their leaves, flowers, fruit and roots are extensively used for treating cold cough, whooping cough, chronic bronchitis and asthma as sedative, expectorant and antispasmodic.[3,4] Asthma is a problem worldwide, with an estimated 300 million affected individuals, along with 250 000 deaths estimated worldwide annually.[3] The powder of herb when boiled with sesame oil is useful in healing ear infections and arrest bleeding and boiled leaves are used to treat rheumatic pain and urinary tract infections. It is also believed to have abortifacient properties and used in some parts of India to stimulate uterine contractions, thus speeding childbirth.[5] Acharya Charaka says that an ideal drug should be available throughout the year, that is, *Bahuta*, and it should be capable of converting into different dosages forms, that is, *Anekavidha Kalpana*[6] without altering its pharmacological actions.

However, it is not feasible as it is often seen that the plants, in the peak of their active principles are not available at all times and so it is essential to convert these plants into some formulation without losing their potency. The ancient scholars were specialists enough to utilize each and every bio-substance [plant–animals], metal and mineral, and every process in the nature was observed for the benefit of the human beings.

2. Botanical description

2.1 Macroscopic: *Aadhatoda* is a shrub with lance-shaped leaves 10 to 15 centimeters in length by four wide. They are oppositely arranged, smooth-edged, and borne on short petioles

in dried form dull brownish-green colour and have bitter-tasting. When a leaf is stained with chloral hydrate and examined microscopically the oval stomata can be seen. They are surrounded by two crescent-shaped cells at right angles to the ostiole. The epidermis bears simple 1-3celled warty hairs and small glandular hairs. Cystoliths occur beneath the epidermis of the underside of the blade.[7] Trunk has many, long, opposite, ascending branches, where the bark is yellowish in color. Flowers are usually white and the inflorescence shows large, dense, axillary spikes. Fruits are pubescent, and are with club-shaped capsules(Fig 1,2).

Fig 1. Luxuriently growing arusa plants at Panchgaon, Gurgaon.

Fig 2. Arusa plants at flowering stage.

2.2.Scientific classification- Kingdom- Plantae; Subkingdom- Tracheobionta; Division- Magnoliophyta; Class- Magnoliopsida; Subclass- Asteridae; Order- Lamiales; Family- Acanthaceae; Genus- Adhatoda; Species-vasica.

2.3.Vernacular names: Hindi Name- Adosa, Arusha, Rus, Bansa, Adusa; English Name- Malabar Nut; Telugu Name- Addasaramu, Adamkabu, Adampaka; Bengali Name- Adulsa,

Bakash,Vasok; Punjabi Name-Vamsa, Bhekkar; Marathi Name- Adulsa; Gujarati Name-Araduso, Aradusī, Adulso, Aduraspee, Bansa; Tamil Name-Eidhadad, Adathodai; Nepali name – Asuro, Kalo vasak; Persian name – Bansa.

2.4. Sanskrit Synonyms: Vasa, Vasaka, Vasika – Vasayati Acchadayati – the herb which is thick and spreads its branches to create shade area; Simhi, Simhasya – the flower resembles the mouth of lion; Vajidanta – the flowers are as white as teeth of horse; Vrisha, Vrusha – Varshati Madhu – flowers attract bees Atarusha, Atarooshaka; Bhishagatma – mother medicine.

2.5. Classical Categorization: Charaka—Tikta Skandha – Bitter tasting group of herbs; Vagbhata- Durvadi Gana.

3. Chemical investigations

Time to time researchers have reported chemical investigations which is recorded in Table 1.

Table 1. Reported chemicals in vasaca plant.

SN	Name of chemical	Plant part	Name of investigator
	Vasicine/Peganine	leaves	First isolated by Sen and Ghose,1924[8]
	quinazoline alkaloid known as vasicine	leaves	Dhar *et al*[9]; Maikhuri and Gangwar,[10]; Shrivastava *et al*[11]
	alkaloids l-vasicinone, deoxyvasicine, maiontone, vasicinolone and vasicinol	Leaves and roots	Jain and Sharma[12]
	pyrroloquinazoline alkaloids, chiefly vasicine (1,2,3,9–Tetrahydropyrrolo[2,1–b]quinazolin–3–ol, C11H12N2O)	leaves	Haq *et al*[13]
	vasicinone (3–hydroxy–2,3-dihydropyrrolo[2,1–b]quinazolin–9(1H)–one, C11H10N2O2)	leaves	Amin and Mehta[14]
	adhatodine, anisotine, vasicoline and vasicolinone	leaves	Johne *et al*[15]
	β-sitosterol, tritricontane and vasicinine	leaves	Haq *et al*[13]
	1,2,3,9,-tetrahydro-5-methoxypyrrolo[2,1-b]quinazolin-3-ol	leaves	Chowdhury & Bhattacharyya, 1985[16]
	adhavasinone	leaves	Chowdhury & Bhattacharyya[17]
	phenols, tannins, alkaloids, anthraquinones, saponins, flavanoids, aminoacids and reducing sugars	leaves	Karthikeyan *et al*[18]
	alkaloids, flavonoids, saponins, sugars, tannins and glycosides	leaves	Prakash *et al*[19]
	0.096% (v/w) of essential oil. Eleven compounds viz.,1,2,3, trimethyl benzene (1.51 %), borneol (58.60 %),	leaves	Sarker *et al*[20]

	ethanonaphthalene (2.82 %), 1,1,4a trimethyl-5,6-dimethylenedecahydro naphthalene (5.28 %), 2,tert-butyl-1,4-dimethoxy benzene (6.50 %), bicyclo[jundec-4-ene,4,11-trimethyl-8-methylene (14.56 %), hexa- methyl dewar benzene (0.87 %), alphacaryophyllene (1.95 %), cycloproplejazulene (1.48 %), caryophyllene oxide (2.35 %) and 2-naphthalenemethanol (1.46 %).		
	alkaloids, flavonoids, saponins, sugars, tannins and glycosides	leaves	Kamlesh *et al*[21]
	saponins, oils and fats, phytosterol, phenolic compounds, tannins, carbohydrate, alkaloids, flavanoids and proteins	leaves	Rao *et al*[22]
	Alkaloids(vasicine, a quinazoline alkaloid), tannins, saponins, phenolics and flavonoids	leaves	Kumar *et al*[23]
	vasicine, vasicinone, vasicine acetate, 2-acetyl benzyl amine, vasicinolone	leaves	Singh and Sharma[24]

4. Therapeutic powers of *Adhatoda vasica*

Medicinal qualities

Rasa (taste) – Tikta (bitter), Kashaya (astringent); Guna (qualities) – Laghu (light), Rooksha (dryness); Vipaka – Katu – undergoes pungent taste conversion after digestion; Veerya – Sheeta – cold potency; Karma- Balances Kapha and Pitta In ayurvedic medicine the plant as a whole along with its root, leaves, bark and flowers are extensively used to relieve cough, cold, whooping-cough, asthma and bronchitis due to their pharmacological properties. The extract from leaves has been used to relieve asthma, bronchitis, breathlessness and cough for centuries and to relieve other conditions like local bleeding due to piles, peptic ulcers and menorrhagia; and relief from bleeding gums and pyorrhea. Crushed leaves are applied to relieve conditions like skin ailments, worms and amavata. Warm crushes are effective to relive dislocated joint and rheumatic pain. Powder of Adhatoda boiled in sesame oil is an effective management for stopping bleeding and relieving ear infection. A paste of the leaves is applied on the abdomen for relieving urinary infection. The flowers are used to relieve burning micturation and as an effective expectorant to relive congestion and dyspnoea. The leaves of *Adhatoda vasica* are rich sources of carotene and Vitamin-C. In some parts of India like Bihar, a decoction from the leaves is used to induce abortion and facilitate child-birth.

The Khasi tribe in India cooks the leaves and vegetables to prepare a delicious vegetable. Herbal practitioners in Europe use this herb as a febrifuge, antispasmodic and expectorant.

CARE AILMENTS

Investigations have proved therapeutic effectiveness of *Adhatoda vasica* through various activities like

4.1. Anti-Microbial activity

Karthikeyan *et al*[18] studied the effect of ethanol, petroleum ether and water extracts were tested on*Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, Enterococcus faecalis, Escherichia coli, Pseudomonas aeroginosa, Proteus vulgaris, Klesiella pneumoniae* and *Candida albicans* . The minimum inhibitory concentration of the crude extracts was determined for various organisms and found effective.

Kamlesh *et al*[21] Antimicrobial screening of hot aqueous, methanolic and chloroform extracts at 125, 250 and 500 mg/ml concentrations by disc diffusion assay method (25 µL/disc) against selected Gram positive (Staphylococcus aureus -MTCC 7405, Bacillus sp. -MTCC 4666) and Gram negative (E. coli – MTCC 1680, Klebsiella sp.- MTCC 4032) bacteria revealed that methanolic extract was moderately effective against Staphylococcus aureus and the zones of inhibition at 250 and 500 mg/ml concentrations were found to be 12.33+0.88 and 14.00+0.57 mm, respectively compared to the zone of inhibition of 19.33+0.57 mm of 0.02µg levofloxacin against Staphylococcus aureus. But hot methanolic extract almost lacked any such activity against rest of the three microbes. Hot chloroform and hot aqueous extracts were also found to be almost devoid of any antibacterial activity against these microbes. Sarker *et al*[20] reported anti microbial activity of the oil against *Bacillus subtilis, Salmonella typhimurium, Staphylococcus aureus,* and *E. coli.* It was found that all mentioned microorganisms were more or less sensitive to this essential oil. Josephin Sheeba and Selva Mohan[25] assesed the antimicrobial activity (MIC) of *Adhatoda vasica* 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. Rashmi and Mathew[26] investigated the antimicrobial

activity of methanolic leaf extracts of Justicia adhatoda and vasicine against *Staphylococcus aureus, Streptococcus pyogenes, Serratia marcescens, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, Candida albicans, Cryptococcus neoformans* and *Aspergillus flavus.* Studies on the minimum inhibitory concentration of the extracts on the test organisms showed that the lowest minimum inhibitory concentration and minimum microbicidal concentrations were demonstrated against *Serratia marcescens, Escherichia coli and Pseudomonas aeruginosa* and the highest minimum inhibitory concentration was exhibited against *Staphylococcus aureus, Streptococcus pyogenes, Klebsiella pnuemoniae.* Among fungi *Aspergillus flavus* showed lowest minimum inhibitory concentration whereas *Candida albicans* and *Cryptococcus neoformans* showed highest minimum inhibitory concentration. So this plant has broad spectrum of antimicrobial activity and a potential source of antimicrobial agents that could be useful for chemotherapy and control of infectious diseases.

Inderjit *et al*[27] evaluated antimicrobial activity of aqueous and methanolic extracts of *Adhatoda vasica* against the bacteria isolated from the sputum samples of asthmatic patients. *Adhatoda vasica* showed a broad spectrum of antibacterial activities against Gram-positive (*Staphylococcus aureus and Streptococcus pneumoniae*) bacterial species in comparison to the Gram-negative (*E.coli and Klebsiella pneumoniae)* bacterial species. On the basis of the results obtained in the present study, concluded that the aqueous and methanolic extract of *Adhatoda vasica* has significant amounts of antimicrobial agents

Sawant *et al.*[28] evaluated the hot and cold Methanolic extracts of *Adhatoda vasica* against clinically important bacteria such as *Staphylococcus aureus* ATCC 25923, *Staphylococcus aureus* NTCC 3750, *Escherechia coli* ATCC 25922, *Proteus mirabilis*, a Clinical isolate, *Salmonella typhi* NTCC 786, *Pseudomonas aeruginosa* ATCC 27853, *Candida albicans* MTCC 183 and *Cryptococcus neoformans* NCIM 3542. In vitro antimicrobial activity was performed using agar cup diffusion method. Both the (hot and cold) methanolic extracts of *Adhatoda vasica* were found to be active only against *S. aureus* and *P. aeruginosa*, but alkaloids isolated from these extracts` exhibited excellent antimicrobial activity against organisms investigated.

Meignanalakshmi *et al.*[29] at Kattankulathur-. India evaluated the antimicrobial activity of aqueous and methanol extracts of *Adhatoda vasica* against mastitis pathogens. The methanol extract was found to be having significant antibacterial activity against *Staphylococcus aureus, Streptococcus agalactiae, Klebsiella pneumonia, Streptococcus dysgalactiae* and

Escherichia coli with zone of inhibition 21.7±0.58 mm, 18.3±0.58mm, 21.3±0.58, 18.3±0.58 and 28.3±0.58mm respectively at 200 mg/ml concentration.Rao *et al* (2013).[22] demonstrated moderat antimicrobial and cytotoxic activity (brine shrimp lethality).

Singh and Sharma[24] reported antimicrobial activity in vasa phytochemicals viz., vasicine, vasicinone, vasicine acetate, 2-acetyl benzyl amine, vasicinolone present in the chloroform fraction having anti-inflammatory and antimicrobial activities. The antimicrobial activity of isolated compounds was assessed by using the microdilution method. The strong antibacterial activity was exhibited by vasicine at 20µg/ml dose against *E. coli* and also demonstrated maximum antifungal activity against *C. albicans* at the dose of >55µg/ml. All the five alkaloids demonstrated significant anti-inflammatory and antimicrobial activities.

4.2. Anti-inflammatory

Vasicine, the main alkaloid of *Adhatoda vasica* showedanti-inflammatory activity.[30] The antiinflammatory activ-ity of the methanol extract, the non-alkaloid fraction, thesaponins and the alkaloids were evaluated by the modifiedhen's egg chorioallantoic membrane test. The alkaloid frac-tion showed potent activity at a dose of 50/pellet equiva-lent to that of hydrocortisone while the MeOH extract andthe other fractions showed less activity (Chakraborty and Bartner, 2001).[31] Singh and Sharma[24] tested the anti-inflammatory activity by using carrageenan and CFA-model induced paw oedema. The observed results revealed that vasicine showed most potent anti-inflammatory effects (59.51%) at the dose of 20.0mg/kg at 6h after carrageenan injection and maximum inhibition rate was observed of vasicinone (63.94%) at the dose of 10.0mg/kg at 4 days after CFA injection.

4.3. Antioxidant activity

Inderjit *et al*[27] found from antioxidant study the SOD activity was observed to maximum in methanolic extract as compared to aqueous extract of *Adhatoda vasica*. Among the two extracts of *Adhatoda vasica*, the highest activity of catalase was observed in aqueous extract and lowest in methanolic extract.

Antioxidant activity of methanol extract of *A. vasica* was estimated by total antioxidant activity, 2,2 diphenyl-1-picrylhydrazyl radical scavenging activity, reducing power potential and iron chelating activity. Extract showed high antioxidant activity in various antioxidant experiments. The extract of *A. vasica* showed presence of high levels of polyphenolic

compounds (phenolic compounds and flavonoids), which could be the possible reason behind the antioxidant activity of the plant.[22]

4.4. Anti-ulcer activity

Shrivastava *et al*[11] studied the anti-ulcer activity of *Adhatoda vasica* leaves using two ulcer models (1) Ethanol-induced, and (2) Pylorus ligation plus aspirin-induced models. *Adhatoda vasica* leaf powder showeda considerable degree of anti-ulcer activity in experimental rats when compared with a control. The highest degree of activity (80%) was observed in the ethanol-induced ulceration model. Results of the study suggest that in addition to its classically established pharmacological activities, the plant also has immense potential as an anti-ulcer agent of great therapeutic relevance.

4. 5. Hepatoprotective activity

Rayese *et al*[32] investigated the hepatoprotective activity of Ethyl acetate extract of *Adhatoda vasica* against CCl4 induced liver damage in Swiss albino rats. At the dose of 1ml/kg, CCl4 induced liver damage in rats as manifested by statistically significant increase in serum Alanine aminotransferase, (ALT), Aspartate aminotransfrase (AST), Alkaline Phosphatase (ALP) and also in serum Bilirubin. Pre-treatment of rats with the ethyl acetate Extract of *Adhatoda Vasica* (100mg/kg and 200mg/kg) prior to the CCl4 dose at 1ml/kg statistically lowered the three serum level enzymes and also Bilirubin. Current results suggest that Ethyl acetate extract of *Adhatoda vasica* has potent hepatoprotective effect against CCl4 - induced liver damage.

4.6. Bronchodilator Alkaloid

A alkaloid has been isolated by us in the crystalline form from the leaves of *Adhatoda vasica* Nees (Indian Patent No. 62349 of November 21, 1957. Patent application No. 64603 of July 9, 1958). The alkaloid, which has been named vasicinone, has been found to be a much weaker base than vasicine, an alkaloid which is already known to be present in this plant. Elementary analysis gave, C = 65.33, H = 4.93, N = 13.65 per cent. The molecular weight (Rast) was found to be about 210 and the molecular formula $C_{11}H_{10}N_2O_2$. The alkaloid was found to be identical with 2,3-(α-hydroxytrimethylene)-4 quinazolone which had been prepared earlier by the oxidation of vasicine with 30 per cent hydrogen peroxide.[14]

AV is well known for its use in respiratory ailments. Taking a lead from the nature, scientists are trying to synthesize molecules similar to, or derivatives of vasicine. Both pure vasicine

and its derivatives are worked upon to investigate their bronchodilatory and antitussive effects. One of those derivatives is Bisolvon/bromhexine (N-cyclo-N-methyl-(2-amino-3,5-dibromo-benzyl)amine hydrochloride). It has been reported to possess mucus liquefying/expectorant activity.[14,33]

A clinical trial was conducted with the derivative: bromhexine (bisolvon) with 30 patients (20 d, 8 mg, thrice a day) suffering from variety of respiratory complaints.[34] It was found that, there was a major change in the viscosity and acid mucopolysaccharide (AMPS) structure in the mucus of infected and uninfected patients. Similar study was conducted by Gent et al.[35] also in 1969.

A total of 100 human patients were given this drug for trial and were reported to respond well for the ease for expectoration of less viscous sputum. On the contrary, Langlands[36] did not observe any significant change after this treatment. In this study, Bromhexine was compared with a placebo in a double-blind clinical trial in patients with exacerbations of chronic bronchitis who had mucoid sputum. Treatment with either Bromhexine 8 mg, three times a day or with identical placebo tablets was continued for 14 days. There was no significant effect on the characteristics of the sputum, improvement in ventilatory capacity, or clinical advantage in patients on Bromhexine. Similarly, a report with usage of a higher dose of Bromhexine was published in "*British Journal of Disease Chest*" in 1973.[37] It states that 48 mg Bromhexine dosage daily for 2-3 weeks brought about an indistinguishable effect with the placebo tablets with respect to stickiness of sputum, difficultly of expectoration or time taken to clear the chest in the morning.Thomson[38] investigated the effect of Bromhexine on 9 patients for its (16 mg, thrice a day) mucociliary clearance rate of removal of previously inhaled particles tagged with a radioisotope (99 mTc). Serial whole lung gamma counts showed on average a small but, statistically significant faster clearance after the drug administration than in identical control runs ($P < 0.05$). The effect of Bromhexine after 72 h of treatment in 23 patients with chest infection was also tested.[39]

Racle *et al*[40] investigated the effect on 40 patients in a randomization, half of whom received Bisolvon intravenously. Observations were made for the following parameters: fewer bronchial aspirations, less fluid secretions, a decrease in alveolar cells, an increase in bronchial cells, a reduced increase in total mucus. These results evidenced an original action ascribable to Bisolvon on the bronchial cells.

Antitussive effect of AV extract was also investigated in mechanical or chemical induced coughing in guinea-pigs.[41] Oral administration of AV extract (ED50: 75.6-20 mg/kg) inhibited chemically induced coughing, in dose dependent manner (up to 75%) and was comparable to codeine. Cumulative dose response study with acetylcholine and histamine indicated its non specific direct effect on smooth muscle.[42] Ambroxol, a widely used secretolytic agent developed from vasicine, is found to inhibit IgE-dependent mediator secretion from human mast cells and basophils, which are the main effector cells of allergic inflammation. This compound was found to be more potent than vasicine in attenuating basophil IL-4 and IL-13 secretions respectively. It also reduced IgE-dependent p38 MAPK phosphorylation in basophils.[43] Richardson and Phipps[44] reviewed the drugs including Bromhexine and briefed the studies conducted around the world. Very few studies from India were included in the same. It is interesting to note that, the results obtained in those studies were not consistent and were contradictory.

4.7.Tamaka Shwasa *(asthma):* *Vasa (Adhatoda vasica* Linn.) is a well known and easily available drug in almost all the seasons. Easy availability of any drug gains popularity among physicians as well as pharmaceuticals and this is the reason why almost every *Kalpana* of *Vasa* is found described in the *Ayurvedika* text. The different dosage forms of *Vasa* like *Kvatha, Avaleha, Sneha*, and *Sandhana* have been used for the treatment of *Shwasa Roga*. A number of research studies have been performed on different formulations of *Vasa* and its effect on *Shwasa Roga.*[45] The chief quinazoline alkaloid vasicine is reported in all parts of the plant, the highest being in inflorescence. (The modern drug Bromhexin is the synthetic form of vasicine) It is a bitter bronchodilator, respiratory stimulant, hypotensive, cardiac depressant, uterotonic and abortifacient. An aqueous solution of vasicinone hydrochloride, when studied in mice and dogs, was found to potentiate the bronchodilatory activity of aminophylline also that of isoprenaline. Vasicinone exhibited smooth muscle-relaxant properties of airways. Alkaloids present in the plant showed significant protection against allergen-induced bronchial obstruction in guinea pigs.

4.8. Abortifacient and uterotonic activity

Animal studies have also demonstrated vasica's abortifacient properties. Aqueous or 90% ethanol plant extracts were given orally to test rats and guinea pigs for 10 days after insemination. Leaf extracts of Adhatoda vasica were 100% abortive at doses equivalent to 175 mg/kg.[46] Studies on human subjects have shown that the alkaloid vasicine has

significant uterotonic activity. This action appears to be influenced by the presence or absence of certain estrogens. In research on the activity of vasicine in stimulating uterine contractions, human myometrial strips taken from the uterus of both pregnant and non-pregnant women were treated with Adhatoda. The herb was found to induce uterine contractions, with effectiveness similar to the drug oxytocin.[47] During the research period, the anti-reproductive properties of *Adhatoda vasica* were anecdotally confirmed by local women.[48] Adhatoda vasica was also shown to have an abortifacient effect on guinea pigs, with effectiveness varying depending on the stage of pregnancy. The effects were more marked when estrogens were used as a priming influence, indicating that the actions of vasicine was probably mediated via the release of prostogladins.[49]

4.9. 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.[50,51]

4.10. Anti-allergy activity

The extract containing the alkaloid vascinol and 20% vasicine inhibited ovalbumin-induced allergic reactions by about 37% at a concentration of 5 mg.[52] Vasicinone has been shown to be a potent anti-allergen in tests on mice, rats and guinea pigs.[53]

4.11. Anti-diabetic activity

Bromhexine, as it found to have effect on mucus glycoproteins, was tried on diabetic patients and it was reported by Clamp *et al*[54] that, it can restore the balance in glucose level in the urine of diabetic patients but, has no effect on normal patient. They suggested that, this change may be due to reduction in the amount of glycoprotein and related material in the body, or from a change in the catabolism of these materials. Gao *et al*[55] highlights the role of vasicine in sucrose metabolism. Epidemiological studies and clinical trials conducted by them strongly support that, control of hyperglycemia is critical in treatment of not only, diabetic patients but also, individuals with impaired glucose tolerance.

4.12. Muscle Stimulant activity

Madappa *et al*[56] studied the effect of vasicine (1 and 10 µg/ml) on uterus, mammary gland, guinea pig ileum and guinea pig tracheal muscle. They found that, vasicine has stimulatory effects on rat/guinea pig uterus and tracheal muscle as well as, on other tissues. They compared its effect with (+) INPEA (nifenolol). The effect of (+) INPEA showed selectivity for uterine tissue. Vasicine potentiated the action of oxytocin in isolated rat mammary strip preparation. It also showed smooth muscle stimulant activity and is thus used for bronchodilation, abortion.

4.13. Anti-ulcer activity

Adhatoda vasica has immense potential as an anti-ulcer agent. The research showed that a syrup of Adhatoda improved symptoms of dyspepsia.[57]

It is also reported to be an antiulcer agent[58] against ulcer caused by ethanol and pylorus with aspirin. 80% recovery was observed in case of ethanol-induced ulcer in rats in comparison to the control rats and 41% in case of pylorus+aspirin induced peptic ulcer.

4.14. 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 ‘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.[59]

4.15. Anticestodal activity

The plant AV has been used indigenously by Naga tribes for curing intestinal worm infections. The study has been conducted byYadav and Tangpu[60] with the methanolic plant extract using *Hymenolepis diminuta* model for rat. 800 mg/kg double dose was found to be profoundly efficacious and the egg number/gm of the feces was reduced to 79.6%. The percentage recovery from the eggs was found to be 16.6% with comparison to the control. Although, it does not specifically indicate that only vasicine is responsible for its activity, the fact that the methanolic extract of the leaves contains mainly vasicine and vasicinone and glycosides and might indicate the reason for its possible anticestodal activity.

4.16. Anti-helminthic activity: Al-Shaibani *et al*[61] studied the ovicidal and larvicidal properties of AV extracts against gastrointestinal nematodes of sheep *in vitro*. The aqueous

and ethanolic extracts of the plant at 25-50 mg/ml concentration were studied and shown to be ovicidal and larvicidal. The effect was dose dependent and ethanolic extract was more effective. The highest ED50 values of AV extracts were recorded against the eggs of *Chaberita ovina* (18.2 mg/ml for both the extracts). The lowest values were recorded against the eggs of *O. circumcinta* as 12.59 and 11.48 mg/ml for ethanolic and aqueous extracts, respectively. Similarly, the ED50 values of AV extracts against larvae, the highest ED50 values for *O. Columbianum* was 19.5 and 18.62 mg/ml and lowest against the *H. contotus* larvae : 15,14 and 12.88 mg/ml for aqueous and ethanolic extracts respectively.

5. CONCLUSIONS

There are many herbal plants in the world among which Adhatoda vasica is considered to be the ruler of herbs due to its great medicinal ethics. Various medicinal properties are well documented in the Hindu mythology. The literature revealed that this species from different geographical origins existed variety of chemical constituents, and the researchers found vide and varied application in traditional healthcare system. The review of past studies which has been discussed in this chapter showed that plants have gained much appreciation among scientists and researchers because of their multifold biological activities. The reviewed results aimed at attracting the attention of scientists and researchers looking for new drugs from natural products as well as those investigating the pharmaceutical diversity. Probably, such natural components might prove to be potentially beneficial but comparatively less toxic. From the study it is concluded that different formulations of *Vasa* have been used for the treatment of *Shwasa.* Vasaka is a well-known herb in indigenous systems of medicine for its beneficial effects, particularly in bronchitis.

But the modern medicine searched its active ingradients and found out that vasicine, oxyvascicine and vasicinone are the alkaloids present in vasaka and in which vasicine is the active ingradient for expelling sputum from the body .The present study revealed that this plant has broad spectrum of antibacterial activity and a potential source of antibacterial agents that could be useful for chemotherapy and control of infectious diseases. This plant has great potential to be developed as drug pharmaceutical industries, but before recommending it for clinical use in these conditions, there is a need to conduct clinical use in these conditions, there is a need to conduct clinical trials and prove its clinical utility.

CONFLICT OF INTEREST STATEMENT

I declare that I have no conflict of interest.

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