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AN OVERVIEW OF *ADHATODA VASICA* NEES ON PHARMACOGNOSTICAL, PHYTOCHEMISTRY AND PHARMACOLOGICAL ASPECTS

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ABSTRACT

Adhatoda vasica means untouched by goats is derived from the fact of animals such as goats avoid eating this plant owing to its intense bitterness. This plant is highly recognised in traditional medical systems. The study focused on pharmacological activities of vasicine from *Adhatoda vasica* namely anti-bacterial activity, antitubercular activity, insecticidal activity, muscle stimulant activity, allelopathic activity, anti pyorrhoeal activity, anti-ulcer activity, allopathic activity, sucrose inhibitory activity, anti- inflammatory activity, abortifacient activity, antioxidant activity, anti-alzheimer's activity, HIV-protease inhibitor activity, antifungal activity,WBC increasing activity, H1N1 flu prevention activity, anti-allergy activity, hepatoprotective activity, anti-diabetes activity, in-vitro antiurolithiatic activity, cholagogue activity, anti-asthmatic activity, anthelmintic activity, anticestodal activity, wound healing, digestion, radio modulation, anti-mutagenic activity, antiviral activity, anti-malarial activity, antimicrobial activity, antispasmodic activity, anticancer activity, thrombolytic activity and renal protective activities respectively. This plant is a sedative, expectorant, antispasmodic, and anthelmintic that helps to cure colds, coughs, whooping cough, chronic bronchitis, and asthma. Vasicine's anti-inflammatory, antibacterial, and antioxidant activities have also been studied, pointing to a larger therapeutic potential beyond respiratory health. The plant includes alkaloids such as vasicine, vasicinone, deoxyvasicine, vasicol, adhatodinine, and vasicinol.

Keywords: Vasicine, Chronic bronchitis, Pharmacological, Expectorant

INTRODUCTION

There are about 6000 higher plant species in India and 258,650 worldwide that are essential to human life. Traditional medical systems like as Ayurveda, Homoeopathy, Naturopathy, Siddha, and Unani use these plants because of their therapeutic qualities. Communities and cultures employ about 10% of these plants as remedies for a range of illnesses **[1]**. The shrub *Adhatoda vasica* (L.) (AV) Nees (Acanthaceae), often called the Malabar nut tree, is found abundantly throughout the Indian peninsula. In India, the plant is utilised in the traditional medical system **[2]**. The *A. vasica* plant holds significant importance in treating respiratory disorders, as indicated by the ancient Indian adage that declares, "As long as the vasaka plant (AV) exists, no man suffering from phthisis need despair" **[3]**. For more than 2000 years, the herb has been utilised in India's traditional medical system **[4]**. This plant is highly recognized in traditional medical systems, such as Ayurveda, for its healing effects. In Tamil, Adathoda means 'untouched by goats'. The term is derived from the fact that animals such as goats avoid eating this plant owing to its intense bitterness. A wide range of the plant's pharmacological characteristics were influenced by the quantity of alkaloids found in the adhatoda. The primary alkaloid present in adhatoda leaves is vasicine, a quinazoline alkaloid that has been extensively researched pharmacologically **[5]**. A wide range of pharmacological activities are demonstrated by this substance, such as cholagogue, anti-allergic, antitubercular, abortifacient, uterotonic, insecticidal, anti-bacterial, anticestodal, anti-inflammatory, antioxidant, hepatoprotective, antiviral, thrombolytic, antifungal, antidiabetic, and wound healing **[6]**. *Adhatoda vasica* is a sedative expectorant, antispasmodic, and anthelmintic that helps cure colds, coughs, whooping cough, chronic bronchitis, and asthma. The India Pharmacopoeia (1966) mentions it as an official medicament **[7]**.

Plant description:

Adhatoda vasica is a perennial shrub that grows to a height of 1 to 3 feet. It is a member of the Acanthaceae medicinal family and is distinguished by many long, opposing branches. The big, lance-shaped leaves of this plant have herbaceous characteristics above, which transition to woody below. The leaves have no stipulates and are arranged in an opposing manner. The tiny, asymmetric, zygomorphic, bisexual flowers are arranged underneath the ovary in spikes or panicles **[8]**. Fruits bearing four seeds per cap are produced by it. The flowers have two colours purple and white. Its commercial name comes from the Sanskrit name Vasaka **[9]**.



1: va

Vernacular names:

The vernacular names of *Adhatoda vasica* are depicted in **Table 1 [10]**.

Table 1: Vernacular names of *Adhatoda vasica*

Language	Name
Urdu	Basa, Adusa
Persian	Bansa
Assamese	Titabahak, Bahak, Vachaka
Bengali	Baksa, Vasaka
English	Vasaka
Gujarati	Aduso, Ardusi, Adulso
Hindi	Aduss, Arusa
Kannada	Adsale, Adusoge, Atarusha, Adsole, Adasale
Kashmiri	Vasa
Malayalam	Attalatakam, Atalotakam
Marathi	Vasa, Adulsa
Punjabi	Bhekar, Vansa, Arusa
Sanskrit	Vasaka
Tamil	Adathodai
Telugu	Addasaram

Taxonomical classification:

Figure 1 mentions the taxonomical classification of *Adathoda vasica* **[11]**.

Figure 2: Taxonomical hierarchy of *Adhatoda vasica*

Geographical indication:

The evergreen shrub *Adhatoda vasica* is indigenous to the Indo-Malayan region and can be found in many places, such as Southern China, Myanmar, Laos, Malay Peninsula, Indonesia, Burma, Malaysia, India, and Sri Lanka **[12]**. India's primary crop is grown in tropical and subtropical regions, particularly in the lower Himalayas at 1350 m altitude. The states of Punjab, Bengal, Manipur, and Kerala are the primary locations for it **[13]**. Manas national park spans an area of 500 square kilometres and is situated between 26°45'- 26°50'N latitude and 90°30'-91°15'E longitudes **[14]**.

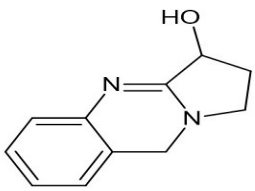
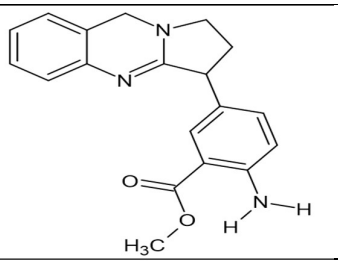
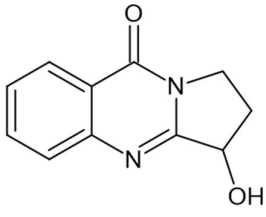
Medicinal uses:

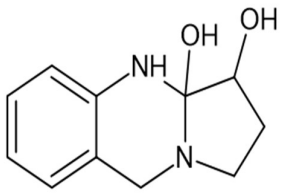
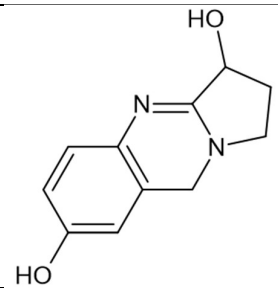
The leaves, petals, fruit, and roots are widely used to treat cold cough, whooping cough, as a sedative, expectorant, antispasmodic, chronic bronchitis and asthma. Antiseptic, anthelmintic, bronchodilator and uterotonic **[15]**. Vasicine and its derivative, vasicinone, are well-known for their bronchodilator and expectorant qualities, which make them useful therapies for respiratory disorders such asthma, bronchitis, and coughing. Vasicine's anti-inflammatory, antibacterial, and antioxidant activities have also been studied, pointing to a larger therapeutic potential beyond respiratory health **[16]**.

Chemical constituents:

The plant includes alkaloids as vasicine, vasicinone, deoxyvasicine, vasicol, adhatodinine, and vasicinol. Other ingredients include vitamin C, saponins, flavonoids, steroids, and fatty acids **[2]**.

Table 2: List of Chemical constituents present in *A. vasica*

Compound	IUPAC name	Molecular formula	Structure
Vasicine	1,2,3,9-tetrahydropyrrolo [2,1-b]quinazolin-3-ol	$C_{11}H_{12}N_2O$	
Adhatodinine	Methyl-2-(methyl amino)-5-(1,2,3,9-tetrahydropyrrolo[2,1-b]quinazoline-3-yl)benzoate	$C_{20}H_{21}N_3O_2$	
Vasicinone	(1*S*)-1-Hydroxy-2,3-dihydropyrrolo[2,1-b]quinazoline-5(1*H*)-one	$C_{11}H_{10}N_2O_2$	

Vasicol	(3R)-1-[(2-aminophenyl)methyl]-3-hydroxypyrrolidin-2-one	$C_{11}H_{14}N_2O_2$	
Vasicinol	3(s)-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazoline-3,7-diol	$C_{11}H_{12}N_2O_2$	

Mechanism of action of Vasicine

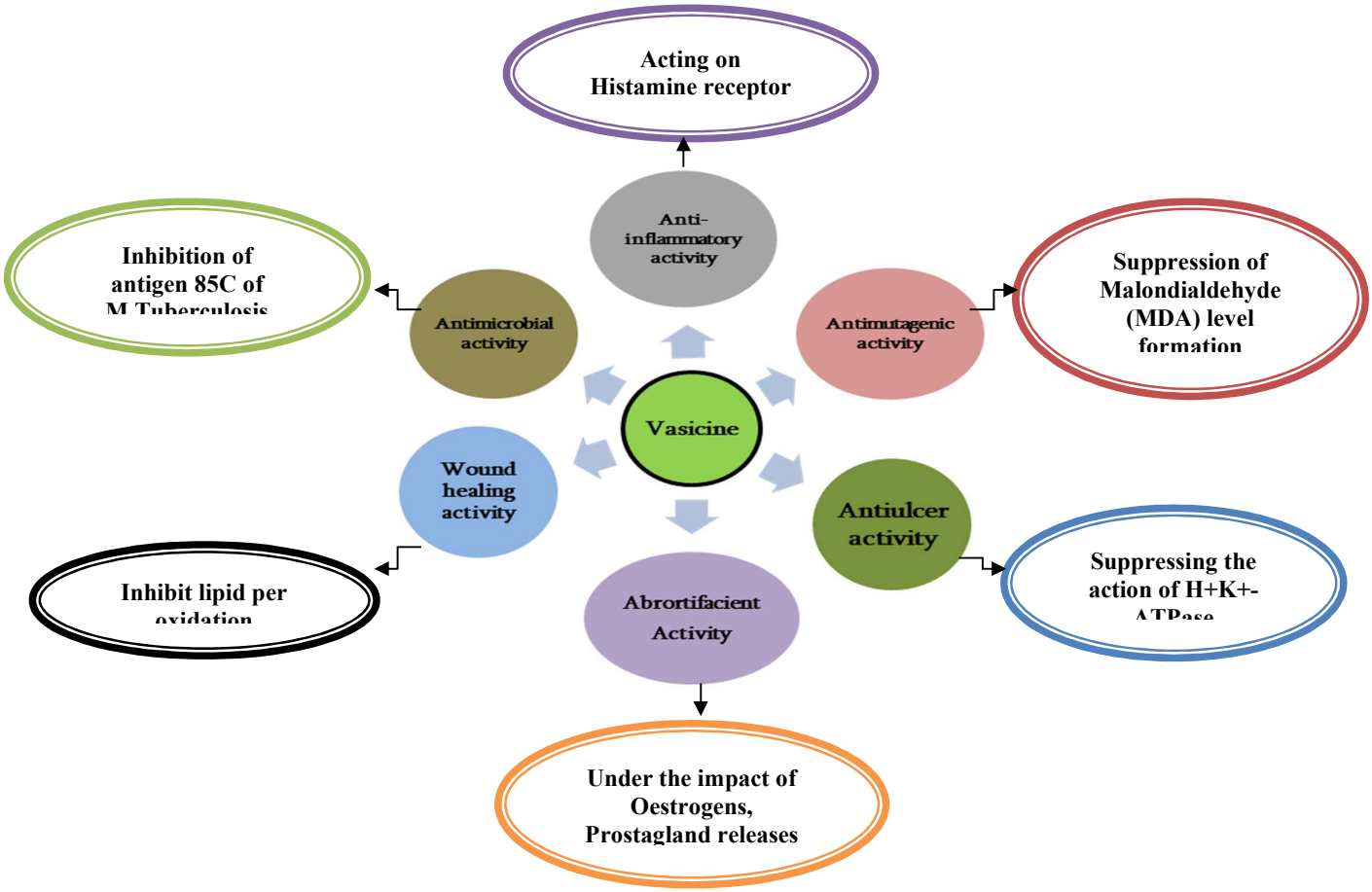


Figure 3: Mechanism of action of Vasicine

Pharmacological activities:

Anti bacterial activity:

An examination was conducted to test the antibacterial properties of a leaf extract using the paper disc and dilution methods. The in-vitro screening revealed that Adhatoda's alkaloids displayed strong activity against the bacterium Pseudomonas aeruginosa. Furthermore, the extract showed significant antibacterial effects against Gram-positive bacteria such as Streptococcus faecalis, Staphylococcus aureus, and Staph epidermidis, as well as the Gram-negative bacterium *E. coli* **[17]**.

Antitubercular activity:

Vasicine, a chemical component of *Adhatoda alkaloids*, is the source of the widely used mucolytics ambroxol and bromhexine. Both of these substances limit the growth of Mycobacterium TB in a pH-dependent manner. Raising lysozyme and rifampicin levels in lung tissue, sputum, and bronchial secretions are some of Adhatoda's indirect effects on tuberculosis, which suggests that it may be a valuable adjuvant in the disease's treatment **[17]**.

Insecticidal activity:

India has been using *Adhatoda vasica* as a pesticide for generations. In lab and storage settings, its leaves have been demonstrated to reduce insect pests in oil seeds. Investigate

has demonstrated that the alkaloid vasicinol from Adhatoda exerts antifertility effects on a variety of insect species by obstructing the oviduct. The efficacy of Adhatoda as an insect repellent has also been demonstrated by research **[17]**.

Muscle stimulant activity:

Vasicine at concentrations of 1 and 10 g/mL was tested on the isolated uterus and mammary gland of rat/guinea pig. Resulted in an increase in the amplitude of contractions in the uterus **[18]**.

Allelopathic activity:

The aqueous extract of fresh and dried leaves contains 60% concentration of extract from *Capsicum annum* L. The dry aqueous extract from seeds was discovered to be more phytotoxic compared to the fresh aqueous extract **[18]**.

Anti pyorrhoeal activity:

Patients with pyorrhea demonstrated relief when a rubbed extract of leaves was applied twice a day for three weeks to the swollen gums. They noted that the bleeding and inflammatory symptoms in their gums had decreased and subsided **[18]**.

Anti-ulcer activity:

Adhatoda vasica leaves had anti-ulcer properties. Compared to pylorus and aspirin, adhatoda leaf powder demonstrated a significant level of anti-ulcer action in rats, with the maximum level of efficacy (80%) seen in the ethanol-induced ulceration paradigm **[19]**.

Allopathic activity:

*Adhatodavasica's*alleopatic activity has been recently investigated. Aqueous extracts of leaves and flowers were found to have inhibitory effects on turnip seed germination and seedling survival. At all dosages, the flower extract's inhibitory action was dramatically reduced. On the other hand, both extracts had a stimulating effect on turnip seed weight, especially at the lower and moderate doses **[19]**.

Sucrase inhibitory activity:

Utilising sucrose as a substrate, the methanolic extract of (AV) *Nees* (Acanthaceae) leaves exhibited remarkable sucrose inhibitory action. Vasicine and vasicinol, two alkaloids, both had an IC50 value of 250 ~M and 125 ~M, respectively, which meant that they inhibited sucrose action. However, intestinal maltase, isomaltase, and amylase did not exhibit inhibitory effects (IC50 > 1 mM) from the alkaloids **[19]**.

Anti- inflammatory activity:

In the modified hen's egg chorioallantoic membrane test, it was found that a dose of 50 µg/pellet alkaloid fraction (methanol extract) exhibited strong anti-inflammatory properties **[20]**.

Abortifacient activity:

The presence of vasicine in its extracts gives *Adhatoda vasica* abortifacient and uterotonic properties, which have been tested in different species, including human beings. The substance caused regular contractions in human myometrial strips from both non-pregnant and pregnant uteri, with an effect similar to that of oxytocin and mathergin. When estrogens were administered as a priming factor, the abortifacient impact on guinea pigs was more noticeable, suggesting that the effects of vasicine were likely strengthened by the production and discharge of prostaglandins **[20]**.

Antioxidant activity:

An important feature of antioxidants is their ability to capture harmful free radicals produced within the body, which can lead to the oxidation of proteins, lipids, or nucleic acids and trigger various degenerative diseases. All extracts of the *A. vasica* plant exhibited antioxidant potential at a concentration of 337µg/ml. additionally; the antioxidant, antidiabetic, and antibacterial properties of different *Adhatoda vasica* extracts have been studied. Among the plant's hexane, chloroform, and methanolic extracts, the methanolic extract demonstrated the highest antioxidant activity as well as the ability to lower blood cholesterol levels. *Adhatoda vasica* also demonstrates antioxidant and anti-clastogenic effects against cadmium chloride (CdCl2)-induced renal oxidative stress and genotoxicity in Swiss albino mice, supporting its anti-mutagenic efficacy **[20]**.

Anti-Alzheimer's activity:

(AV) was found in about 23 of the plants that were examined for the Alzheimer's medication. They were seen to operate against cycloxygenase-1 (COX-1) and acetylcholinesterase. At an inhibitory dosage of 294µg/ml, it interacted with AChE and had a reversible action on the enzyme **[21]**.

HIV-protease inhibitor activity:

In the evaluation of HIV-1-protease inhibitors, researchers examined aqueous, ethanol, methanol, and chloroform extracts. Instead of HIV-1-protease, they utilized the Pepsin Assay as an alternative method. The researchers observed that the aqueous extract effectively inhibited HIV, whereas the other extracts did not exhibit any effectiveness. Nonetheless, the chloroform extract displayed slight activity in inhibiting the enzymatic action of pepsin (>99%) **[21]**.

Antifungal activity:

The antifungal effect of the crude methanol extracts of 11 plant species, such as *A. vasica ,* was investigated. It showed effectiveness against human pathogenic fungus. The maximum antifungal activity was observed against *Candida albicans* at a dose of less than 55 µg/ml (>55 µg/ml).A second study that looked at the 18 extracts from medicinal plants found that they had only weak antifungal effects against Trichophytonterrestre, Microsporumgypseum, and *Chrysosporiumtropicum* **[21]**.

WBC increasing activity:

Another study discovered that the *Adhatoda vasica* plant was able to boost overall WBC count, blood lymphocytes, splenic lymphocytes, and peritoneal macrophages. Additionally, it was significantly effective in protecting against Escherichia coli, which caused abdominal peristomitis **[22]**.

H1N1 flu prevention activity:

Considering the current state of diseases, one study claims that *Adhatoda vasica* may be able to stop the swine flu. Patients with the H1N1 flu reported it. Experiencing body aches, sneezing, sore throat, malaise, and running nose. The investigation of *Adhatoda vasica* 30 c's activity involved the administration of 4 globules 4 times a day for 7 days as a treatment. It was discovered that 95% of cases not only had their symptoms resolved but also served as a "prevention" measure. According to the study's findings, *Adhatoda vasica* 30 C can effectively prevent H1N1, albeit more clinical validation is needed **[22]**.

Anti-allergy activity:

The research carried out on vasicinone activity demonstrated its effectiveness in reducing allergic reactions in mice and guinea pigs. Both the alkaloid vasicinone and 20% vasicine showed inhibitory properties at a 5 mg dose, with an inhibition rate of up to 37% **[22]**.

Hepatoprotective activity:

The hepatoprotective activity of the ethyl acetate extract of *A. vasica* was investigated by inducing liver damage in albino rats using carbon tetrachloride. It was observed that the 100mg/kg dose of the ethyl acetate extract of *A. vasica* reduced the levels of ALT, AST, and ALP, while the 200 mg/kg dose showed greater effectiveness against carbon tetrachloride-induced hepatotoxicity at a dosage of 1 ml/kg **[23]**.

Anti-diabetes activity:

The ethanolic extract of *A. vasica* was utilized for its antidiabetic effects using streptozocin (STZ) to induce diabetes in Wistar rats. It was observed that rats treated with *A. vasica* showed a notable rise in AchE, TNF-alpha, and nitrate levels, indicating the protective activity of *A. vasica* against diabetic encephalopathy **[23]**.

In-vitro antiurolithiatic activity:

They were employed to test the ethanolic extract of *A. vasica 's* antiurolithiatic efficacy. An equimolar solution of sodium oxalate and calcium chloride was used in an experimental setting to create kidney stones. It was discovered that the 200 mg/kg dose of *A. vasica* 's ethanolic extract had more activity **[23]**.

Cholagogue activity:

In laboratory experiments with cats and dogs, *Adhatoda vasica* was observed to enhance bile activity when the animals received an intravenous dose of 5 mg/kg. Dogs showed a 40-100% increase in the amount of ejected bile. Furthermore, the animals exhibited a rise in bilirubin excretion **[24]**.

Anti-asthmatic activity:

A. vasica treatment was observed to reduce asthma symptoms and improve lung function parameters in clinical studies **[25]**.

Anthelmintic activity:

The leaves of *A. vasica* produced a 10% aqueous extract that resulted in a 73% mortality rate for Meloidogyne incognita, according to chit wood **[25]**.

Anticestodal activity:

The Naga tribes have traditionally used the plant AV to treat intestinal worm infections. Yadav and Tangpu conducted a study using the methanolic plant extract on a rat model infected with Hymenolepis diminuta. They found that a double dose of 800 mg/kg was highly effective, reducing the number of worm eggs in the feces by 79.6%. The recovery rate from the eggs was 16.6% compared to the control group. While the study doesn't conclusively attribute the activity to vasicine alone, the presence of vasicine, vasicinone, and glycosides in the methanolic extract of the leaves might explain its potential effectiveness against intestinal worms **[26]**.

Wound healing:

The wounds treated with plant extract showed a higher healing rate in buffaloes compared to wounds treated with pancreatic tissue extracts **[27]**.

Digestion:

In vitro experiments using a decoction of the leaves, the trypsin enzyme was activated, which prompted the process of digestion **[27]**.

Radio modulation:

In the peripheral blood of Swiss albino mice, leaf extract demonstrated a radiomodulatory effect against radiation-induced haematological changes. During the whole study period, leaf extract pre-treated irradiated animals showed a significant decrease in acid phosphate activity and an increase in serum alkaline phosphate activity **[27]**.

Anti-mutagenic activity:

A group showed that the plant Vasaka exhibited anti-mutagenic effect against cadmium chloride-induced kidney oxidative stress and genotoxicity in a rat model. Plant extracts pre-treatment results in prophylaxis and a notable decrease in the level of oxidative biomarkers. According to a different study, the Vasaka fractions' flavonoids and phenolic acids may have anti-mutagenic properties. Hexane, chloroform, and water have the greatest control potential of all the fractions. The investigation's findings are consistent with its potential use as a chemo preventive agent in the future. Unexpectedly, vasicine shows a dose-dependent action against the 2 amino fluorine-produced mutations. Additionally, the data show that the chemical causes the PC 3 cancer cell to undergo apoptosis **[28]**.

Antiviral activity:

The plant's aqueous and methanolic extracts exhibit strong antiviral action against the influenza virus by preventing the virus from attaching to the host surface or from replicating. As a result, we can state that it can be applied as a preventative measure to cure viral infections **[28]**.

Anti-malarial activity:

The schizont maturation inhibition assay and lactate dehydrogenase inhibition assay, which are based on morphological criteria and biochemical reaction, respectively, demonstrated antiplamodial activity in vasicine, pyrrolquniazoline alkaloid, and embelin, as well as a benzoquione derived from *A.vasica* and Embeliaribes, respectively **[29]**.

Antimicrobial activity:

Effectiveness against the microbial flora that causes gingivitis was shown by the water extract. The ethanolic leaf extracts showed antimicrobial efficacy against Bacillus subtilis, Streptococcus faecalis, Pseudomonas aeruginosa, and Staphylococcus epidermidis [30].

Antispasmodic activity:

Vasicine is an alkaloid with a bitter taste that is used as an antispasmodic and expectorant. In the isolated guinea-pig tracheal chain, the

essential oil extracted from the leaves demonstrated smooth muscle relaxant action **[30]**.

Anticancer activity:

The dosage for whole plant prophylaxis is 50 and 100 mg/kg BW. Rats' increased tumour growth and renal oxidative stress due to ferric nitrilotriacetate (FeNTA). The findings indicated that *A. vasica* can lessen Fe-NTA's carcinogenic potential and hyper proliferative response toxicity **[31]**.

Thrombolytic activity:

When combined with a 5 mg/mL Nacl solution, the root extract showed 19.63% clot lysis activity in an in vitro thrombolytic model of Adhatoda **[32]**.

Renal protective activity:

The leaves' ethanolic extract, which ranges in concentration from 1000-5000 mg/kg, has demonstrated the ability to protect albino rats from gentamicin-induced nephrotoxicity by preventing elevated serum creatinine and urea levels **[33]**.

CONCLUSION

Vasicine is a naturally occurring alkaloid predominantly found in the plant *Adhatoda vasica*, also known as Vasaka or Malabar nut. Vasicine possesses a complex chemical structure and is classified as an indole alkaloid. Its basic properties are typical of alkaloids, and its molecular formula is $C_{12}H_{16}N_2O$.From the various reported studies it is clear that vasicine is an important phytoconstiuent of *Adhatoda vasica* it plays significant role in the treatment of cough, cold, asthma, bronchitis etc. it showed many pharmacological activities. These activities have been plays a major role in the herbal medicine system.

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