ADHATODA VASICA: PHARMACOLOGICAL CHARACTERIZATION FOR THE DEVELOPMENT OF HERBAL DRUG

1*Neha Chauhan, 2Chhaya Singh, 3Raj Singh, 4Anju Rani, 5Sushil Kumar Upadhyay, 6Kunal Kishor and 6Keerti Singh

1Department of Medical Microbiology, College of Paramedical Sciences, Shri Guru Ram Rai University, Dehradun, India
E-mail: chauhanneha7777@gmail.com
2Department of Botany, Govt. Degree College, Thallisain, Pauri Garhwal, India
E-mail: singh_june07@rediffmail.com
3Department of Biotechnology, MMU, Mullana, Ambala, Haryana, India
E-mail: dr.rajsingh09@gmail.com; sushil.upadhyay@mmumullana.org
4Department of Botany, K.V. Subharti College of Science, S.V. Subharti University, Meeru, India
E-mail: tanjurani.ar1@gmail.com
5Department of Microbiology, School of Allied Health Sciences, Sharda University, Greater Noida, India
E-mail: Kunal.kishor@sharda.ac.in
6Department of Microbiology, School of Basic and Applied Sciences, Shri Guru Ram Rai University, Dehradun, India
E-mail: drkeertisingh@yahoo.co.in
*Corresponding Author: chauhanneha7777@gmail.com; +919634270042
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ABSTRACT

Medicinal components from plants play an important role in conventional as well as western medicine. Adhatoda vasica Nees, which is popularly known as Vasaka belongs to the Acanthaceae family. A. vasica is a multipurpose medicinal plant with several pharmacological characteristics like anti-inflammatory, antioxidant, anti-microbial, anti-venom, anti-tubercular, anti-tumour, hepatoprotective, anti cancer as revealed by many experimental studies. Adhatoda vasica is known to cure respiratory afflictions in humans and also proved its efficacy in treating Multi drug resistant (MDR) pathogens considerably. Classes of chemical constituents such as triterpines, flavonoids, alkaloids, tannins, glycosides, saponins etc., possess biological significance had been identified for their use in herbal formulations, since Ayurveda. The present review compiles the detailed therapeutic applications of A. vasica and its recent advancements which provide significant information to the researchers globally.

Keywords: Adhatoda vasica Nees, MDR, Ayurveda, therapeutic, respiratory afflictions, pharmacological.

INTRODUCTION

From the ancient times it is well documented that active ingredients from the plant origin have been used to treat various diseases and microbial infections. Medicinal values of plants are due to the presence of botanicals in small quantities, which help maintaining the consistency in the human and animal body functioning (Zaidi, 1998). These active principles have provided many effective molecules in search of new drug medicines (Borris, 1996). A large number of these plants are used in the form of powder, decoction and infusion for the treatment of various diseases including the microbial infection (Hussain, and Gorsi, 2004).

Adhatoda vasica Nees belonging to family Acanthaceae, commonly known as Adosa, is a small, evergreen shrub found many regions of India and throughout the world, with a multitude of uses in traditional Ayurveda. Vasica is most well-known for its effectiveness in treating respiratory conditions. The leaves of Vasica shows stimulant effect on the respiratory system. Vasica shows an antispasmodic and expectorant effect, and has been used for centuries with much success to treat asthma, chronic bronchitis, and other respiratory conditions. The powdered of herb, boiled with sesame oil, is used to heal ear infections and arrest bleeding. Boiled leaves are used to treat rheumatic pain, and to relieve the pain of urinary tract infections. It is also believed to have abortifacient properties. It is used in some parts of India to stimulate uterine contractions, thus speeding childbirth (Claeson et al., 2000).

Vernacular names

Hindi : Adosa, adalsa, vasaka
Sanskrit : Amalaka, bashika,
Bengali : Basak
Tamil : Adatodai
Marathi : Vasuka
Telugu : Adasaram
Malayalam : Ata-lotakam
Adhatoda vasica: Pharmacological characterization for the development of herbal drug

**Plant Description:** It is an evergreen shrub of 1-3 feet in height with many long opposite branches. Leaves are large and lance-shaped. Stem herbaceous above and woody below. Leaves opposite and extipulate. Flower spikes or panicles, small irregular zygomorphic, bisexual, and hypogynous (Shinwari and Shah, 1995). It has capsular four seeded fruits. The flowers are either white or purple in colour. Its trade name Vasaka is based on Sanskrit name (Kumar et al., 2010). Inflorescences in axillary spicate cymes, densely flowered; peduncles short; bracts broadly ovate, foliaceous. The leaves, flowers, fruits and roots are extensively used for treating cold cough, whooping cough, chronic bronchitis and asthma, as sedative, expectorant and antispasmodic (Pandita et al., 1983). Evergreen, glabrous shrubs, to 2.5m high; Stem clothed with thick, white, woolly tomentum. Leaves opposite, ovate-lanceolate, 4.5-15 X 2.5-8cm, base decurrent, subentire- crumulate, glabrous, except hairy on nerves beneath; petioles 1-3.5cm long. Flowers white, in short bracteate, 2.5-6cm or more long spikes; bracts foliaceous, ovate, to 2cm long, not spiny, glabrous. Calyx 0.5cm long, hairy; lobes lanceolate, acute. Corolla white with pink or purple strips, 1.8-2.6cm long, 2-lipped; tube compressed, upper lip 2-fid, curved; lower 3-lobed, deflexed. Stamens 2; anthers minutely tailed. Capsules 2.5 X 0.8cm or more, clavate, pubescent; seeds 4, suborbicular, rugose. Flowering: Dec-Apr. Fruiting: Mar-Jun.

**Chemical Description:**

**Table 1:** Physicochemical screening of A. vasica leaf extracts

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Parameters</th>
<th>Values (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Total Ash Content</td>
<td>21.40</td>
</tr>
<tr>
<td>2.</td>
<td>Acid Insoluble Ash</td>
<td>0.92</td>
</tr>
<tr>
<td>3.</td>
<td>Water Soluble Ash</td>
<td>4.85</td>
</tr>
<tr>
<td>4.</td>
<td>Foreign matter</td>
<td>0.28</td>
</tr>
<tr>
<td>5.</td>
<td>Moisture Content</td>
<td>18.20</td>
</tr>
</tbody>
</table>

**Major Chemical constituents:** The variant composition of alkaloids is responsible for effective pharmacological uses of Adhatoda vasica and presenting it as a best cure to numerous afflictions (Shrivastava et al., 2006); (Maikhuri et al., 1965). The prominent form of alkaloid obtained from Adhatoda leaves is the quinazoline alkaloid known as vasicine (Dhar et al., 1981). In addition to vasicine, the leaves and roots of Adhatoda contain the alkaloids l-vasicinone, deoxyvasicine, maiontone, vasicinolone and vasicinol (Jain and Sharma, 1982). Research indicates that these chemicals are responsible for Adhatoda’s bronchodilatory effect (Bhalla and Nimbark, 1982; Amin and Mehta, 1959). This plant is a source of vitamin C and has numerous pharmacological properties, like anti-inflammatory, antispasmodic, anti bleeding, fever reducer, anti-dibetic, bronchodilator, disinfectant, anti-jaundice, oxytocic and expectorant (Kokate et al., 2003). Chauhan et al. (2019) in their study identified the phytochemicals present in crude extracts of leaves of A. vasica using GC-MS technique, tabulated as Table 2, 3& 4.

**Table 2:** The identified phytochemicals in ethyl acetate extract were detected using GC-MS technique

<table>
<thead>
<tr>
<th>Peak no.</th>
<th>Phytochemicals</th>
<th>Molecular formula</th>
<th>Retention time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hydrazine carboxamide</td>
<td>CH₃N₂O</td>
<td>3.307</td>
</tr>
<tr>
<td>4</td>
<td>2-Propanone</td>
<td>C₃H₆O</td>
<td>3.613</td>
</tr>
<tr>
<td>10</td>
<td>Sclerosol</td>
<td>C₃H₆OS</td>
<td>7.110</td>
</tr>
<tr>
<td>22</td>
<td>Phoshine</td>
<td>CH₃P</td>
<td>7.903</td>
</tr>
<tr>
<td>23</td>
<td>Carbamic acid</td>
<td>CH₂NO₂</td>
<td>8.070</td>
</tr>
<tr>
<td>25</td>
<td>Methane-D₃,Nitro-</td>
<td>CD₃NO₂</td>
<td>8.883</td>
</tr>
<tr>
<td>32</td>
<td>2H-Benzopyran-4-Carbonitrile,6-Fluo-3,4-Dihydro-4-[(Methylthio)Methyl]</td>
<td>C₁₂H₁₂FNOS</td>
<td>16.767</td>
</tr>
<tr>
<td>34</td>
<td>2-Pyridinepropanoic acid</td>
<td>C₁₁H₁₂NO₃</td>
<td>46.097</td>
</tr>
<tr>
<td>38</td>
<td>Aminourea</td>
<td>CH₃N₂O</td>
<td>46.413</td>
</tr>
</tbody>
</table>
Table 3: The identified phytochemicals in the methanol extract were detected using GC-MS technique.

<table>
<thead>
<tr>
<th>Peak no.</th>
<th>Phytochemicals</th>
<th>Molecular formula</th>
<th>Retention time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>N-(3,4,4-Trimethyl-1,2-Dioxethane-3-y1-MethoxyCarbony1) Glycine</td>
<td>C_{12}H_{13}NO_6</td>
<td>3.620</td>
</tr>
<tr>
<td>6</td>
<td>Silane</td>
<td>C_{6}H_{5}C_{2}OSi</td>
<td>3.933</td>
</tr>
<tr>
<td>17</td>
<td>Acetamide</td>
<td>C_{3}H_{7}C_{2}NO</td>
<td>7.723</td>
</tr>
<tr>
<td>25</td>
<td>1H-Pyrimido[4,5,6-IJ][2,7]Naphthyridine-6-Carbonitrile,2-Ethyl-5,8-Dimethoxy-</td>
<td>C_{5}H_{13}N_{2}O_{2}</td>
<td>50.753</td>
</tr>
<tr>
<td>26</td>
<td>Acetonitrile-D3</td>
<td>C_{3}D_{3}N</td>
<td>50.860</td>
</tr>
<tr>
<td>28</td>
<td>3-Methoxy-5-(Methoxymethoxy)-7-Methyl-6-(3-(Trimethylsilyl)Propargyl)-1,4-Naphthoquinone</td>
<td>C_{10}H_{21}O_{3}Si</td>
<td>51.007</td>
</tr>
<tr>
<td>30</td>
<td>L-Alanine, Ethylester-</td>
<td>C_{3}H_{11}NO_{2}</td>
<td>52.513</td>
</tr>
<tr>
<td>32</td>
<td>Formamide,N-{[dibutylamino)methyl]-N-methyl-</td>
<td>C_{11}H_{33}N_{20}</td>
<td>53.240</td>
</tr>
<tr>
<td>34</td>
<td>Trans-2-(phenylthio)methyl)-1-(2-propenyl)-1,2,3,4-tetrahydrophthalene</td>
<td>C_{12}H_{25}S</td>
<td>53.747</td>
</tr>
<tr>
<td>37</td>
<td>2-Acetyl-3-cyano-2,3-dimethylcyclobutane-1-carboxylic acid</td>
<td>C_{11}H_{13}NO_{3}</td>
<td>54.043</td>
</tr>
<tr>
<td>45</td>
<td>5,5′-dicarboxy-3′-(2-chloroethyl)-4-(2-acetoxyethyl)-3′,4′-dimethylpyrromethane</td>
<td>C_{15}H_{26}Cl_{2}N_{2}O_{6}</td>
<td>56.893</td>
</tr>
</tbody>
</table>

Table 4: The identified phytochemicals in the aqueous extract were detected using GC-MS technique.

<table>
<thead>
<tr>
<th>Peak no.</th>
<th>Phytochemicals</th>
<th>Molecular formula</th>
<th>Retention time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>3,3′-[1,2-hydrazinyl-bis(Carbonyloxymethylene)]Bis(3,4,4-trimethyl-1,2-dioxethane)</td>
<td>C_{14}H_{23}N_{2}O_{8}</td>
<td>3.620</td>
</tr>
<tr>
<td>23</td>
<td>D5-EthylNitrate</td>
<td>C_{2}D_{2}NO_{3}</td>
<td>7.740</td>
</tr>
<tr>
<td>25</td>
<td>Methane- D3</td>
<td>C_{6}D_{6}NO_{2}</td>
<td>8.850</td>
</tr>
<tr>
<td>20</td>
<td>Bis(Fluoromethyl)(Dimethyl)Silane</td>
<td>C_{6}H_{10}F_{2}Si</td>
<td>7.343</td>
</tr>
<tr>
<td>27</td>
<td>Erythro-1,2-Dimethyl-1-Methylthio-2-Hydroxyethane</td>
<td>C_{3}H_{12}OS</td>
<td>10.080</td>
</tr>
</tbody>
</table>

**Pharmacological Activity**

**Anti-asthmatic and bronchodilator activity:** *Adhatoda* has been used in traditional medicine to treat respiratory disorders. Both vasicine and vasicinone the primary alkaloid constituents of Adhatoda are well established as therapeutic respiratory agents (Dorsch, 1991). Extracts of Adhatoda’s leaves and roots are useful in treating bronchitis, and other lung and bronchiole disorders, as well as common coughs and colds. A decoction of the leaves of Adhatoda has a soothing effect on irritation in the throat, and acts as an expectorant to loosen phlegm in the respiratory passages. Recent investigations using vasicine showed bronchodilatory activity both in vitro and in vivo (Lahiri and Pradhan, 1964). The two main alkaloids vasicine and vasicinone are known to exhibit anti-allergic activity. An extract containing the alkaloid vasicinol and 20% vasicine (Paliwa et al., 2000) inhibited ovalbumin-induced allergic reactions by about 37% at a concentration of 5 mg. Vasicinone has been shown to be a potent anti-allergen in tests on mice, rats and guinea pigs as studied by Wagner 1989. Also, the methanolic extract from the entire plant has been shown to possess anti-allergic and antiasthmatic activities in the guinea-pig after inhalation or intragastric administration at doses of 6 mg peranimal or 2.5 gm/kg, respectively (Mullar et al., 1993).
Wound healing activity For the purposes of the study, wounds were created along the ~ 90 ~ International Journal of Herbal Medicine vertebral columns of buffalo calves, and alcoholic and chloroform extracts of *Adhatoda* in a powdered form were applied. As compared to control animals, the calves treated with Adhatoda vasica showed significantly improved healing. Vasica improved breaking strength, tensile strength, absorption and extensibility in the wound repair tissue. In addition, the levels of elastin, collagen, hydroxyproline, hexosamine and zinc were greatly increased in the animals treated with Adhatoda. The alcoholic extract of the herb was found to be the most effective (Bhargava *et al.*, 1988).

**Anti-ulcer activity:** *Adhatoda vasica* was studied for its anti-ulcerogenic activity against ulcers induced by ethanol, pylorus, and aspirin. *Adhatoda* leaf powder showed a considerable degree of anti-ulcer activity in experimental rats when compared with controls. The highest degree of activity was observed in the ethanol-induced ulceration model (Shrivastava *et al.*, 2006). These results suggest that in addition to its classically established pharmacological activities, *Adhatoda vasica* has immense potential as an anti-ulcer agent. Further research showed that a syrup of *Adhatoda* improved symptoms of dyspepsia (Chaturvedi *et al.*, 1983).

**Cholagogue activity:** In laboratory experiments on cats and dogs, *Adhatoda vasica* was found to increase bile activity when the animals were given an intravenous dose of 5 mg/kg. In dogs, the amount of excreted bile increased by 40-100%. The animals also showed an increase in bilirubin excretion (Rabinovich *et al.*, 1966).

**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 (Narimaian *et al.*, 2005; Grange and Snell, 1996).

**Abortifacient and uterotoxic activity:** *Adhatoda vasica* has abortifacient and uterotoxic properties, making it useful for inducing abortion and for stimulating uterine contractions in order to speed childbirth (Claeson *et al.*, 2000). Studies on human subjects have shown that the alkaloid vasicine has significant uterotoxic 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 (Pahwa *et al.*, 1987). During the research period, the anti-reproductive properties of *Adhatoda vasica* were anecdotally confirmed by local women (Gupta *et al.*, 1978). Animal studies have also demonstrated vasicine’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 (Atal, 1980). *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 prostoglandins (Nath *et al.*, 1992).

**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 (Srivastava *et al.*, 1965). Research has shown *Adhatoda*’s alkaloid, vasicinol, to have an antifeedant effect against several insect species by causing blockage of the oviduct. Research has also proven *Adhatoda* effectiveness as an insect repellent (Saxena *et al.*, 1986).

**Anti-bacterial activity:** A leaf extract was investigated for antibacterial activity using the paper disc and dilution methods. In vitro screening showed a strong activity of *Adhatoda* alkaloids against the bacteria *Pseudomonas aeruginosa*. Significant antibacterial activity against the Gram-positive bacteria strains *Streptococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis* and the gram-negative *E. coli* were also noted (Patel and Venkatarkrishna, 1984). Grange and Snell (1996) revealed that the semi-synthetic derivatives of vasicine: benzylamines, bromhexine and ambroxol, isolated from *A. vasica* has inhibitory effects on the growth of *Mycobacterium tuberculosis*. These compounds remove the mucus containing bacteria by accumulating in the macrophages. Various extracts of *Adhatoda* leaves (Water, ethanolic and petroleum ether extracts) were subjected for antibacterial activity by Karthikeyan *et al.* (2009) against *S. epidermidis, S. aureus B. subtilis, E. faecalis, E. coli, P. aeruginosa, P. vulgaris, K. pneumoniae* and *C. albicans*. It was observed that the ethanolic and petroleum ether extracts were found to inhibit the growth of many microbes. Shinwari *et al.* (2009) has evaluated the antibacterial properties of three plants in Pakistan *Justicia adhatoda, Glycyrrhiza glabra* and *Hyssopus officinalis* against *S. typhimurium, E. coli, B. subtilis, P. aeruginosa* and *S. aureus*. The methanolic extract of *Justicia adhatoda* inhibited the *S. typhimurium* and results obtained registered the potential of these plants. Ilango *et al.* (2009) has investigated the antibacterial activity of *A. vasica* various extracts. Hexane extract was shown to possess the maximum antibacterial activity. The antimicrobial property of leaf extracts of *J. adhatoda* (L.) in comparison with vasicine was shown by (Pa Rashmi *et al.*, 2012). The antimicrobial activity (MIC) of *Adhatoda vasica* was assessed 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 vulgaris* > *Pseudomonas aeruginosa* > *Streptococcus pyogenes* (SheebaJosephin *et al.*, 2012).

**Anti-diabetic activity:** Clamp *et al.* (1979) reported the effect of Bromhexine, as antidiabetic agent because it can maintain the balance of glucose level in the urine of diabetic patients and has no effect on normal patient. Gao *et al.* (2008) reported in his study that vasicine inhibits the
conversion of sucrose to glucose and acts as irreversible sucrase inhibitor thereby acting as anti-diabetic agent. Ilango et al. (2009) examined the anti diabetic activity of A. vasica extracts and found chloroform and methanolic extracts to be significant.

**Antioxidant activity:** A study done by Ilango et al. (2009) has shown the methanolic extract to possess highest antioxidant and anti inflammatory activity of vaccinea compound isolated from A. vasica was tested for asthma in murine model. Rats treated with the vasicine showed decrease in lipid peroxidation and increase in antioxidant level was recorded (Srinivasrao et al., 2006). Aqueous extract of A. vasica was found to possess maximum phenolic content which was analysed as a measure of antioxidant activity (Singh and Maurya, 2010). The antioxidant activity of A. vasica and S. grandiflora was evaluated by Padmaja et al. (2011) using DPPH and hydroxyl scavenging activity, found that enzymatic and non enzymatic antioxidants were significantly more in A. vasica than S. grandiflora. The study conducted by Chauhan et al. (2019) revealed that antioxidant power of crude extracts of A.vasica leaves has strong potency to neutralize the overproduction of free radicals, calculated by FRAP assay. The methanol extract showed highest FRAP values followed by ethyl acetate and aqueous extracts.

**Ant-inflammatory activity:** Chakraborty and Brantner (2001) had reported the anti-inflammatory activity of methanolic extract of Adhatoda in modified hen’s egg chorioallantoic membrane test. Wahid Mulla et al. (2010) using carrageenan-induced and formalin-induced paw edema assay in albino rats, reported the anti-inflammatory and analgesic activity of A. vasica extract. The ethanolic extracts of roots of A. vasica was given and found the potent anti-inflammatory activity.

**Hepatoprotective activity:** Bhattacharyya et al. (2005) examined the hepatoprotective activity of leaf extract of A.Vasica on liver damage induced by D-galactosamine in rats and significant activity was observed at 50-100 mg/kg. 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 (Bhaduri et al., 1985).

**Anticancer activity:** Chauhan et al. (2019) reported in a study that anticancer properties of A. vasica showed that methanol extract completely inactivated the metabolic activity of HCC-827 at the concentration of 100µg/ml after 24h and 48h of treatment followed by ethyl acetate extract and aqueous extract. The leaves, flowers and roots of this plant used in herbal drugs against tubercular activities (Barr et al., 1955), cancer (Pandey, 2002) and possessed to have anti-helminthmic properties (Ayyanar et al., 2008). In the study, an alkaloid, 2-acetyl-benzylamine, isolated from Adhatoda vasica was screened for potent anticancer properties against leukemia cells (Balachandran et al., 2017).

**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 oestrogens (Gupta et al., 1978; Chandokhe et al., 1978). Vasicine-induced abortion was studied in rats, guinea pigs, hamsters and rabbits. Study showed that vasicine acted through the release of PGs (Chandokhe et al., 1978). Synthesized vasicine and vasicinone derivatives in in-vitro studies were found to have oxytocic activity at the dose above 1 g/ml (Rao et al., 1982). The aqueous solution of the leaves at the dose of 175mg/kg bw revealed 100 percent abortifacient activity in albino rats (Sethi et al., 1987). The extract of the plant at 2% concentration level revealed abortifacient activity (Bhatt and Panwar, 1990). Vasicine showed uterotonic activity on human myometrium strips which was in some cases even more marked than that of two known oxytocs, pitocin and methergin. The response of the uterus to drugs depended on its hormonal status (Gupta et al., 1979).

**Anti Pyorrhoeal activity**

In a study 25 patients with complain of pyorrhea was taken, and were selected randomly. The leaf extract was massaged on inflamed gums twice a day for three weeks. There was a reduction and complete relief in the inflammatory and bleeding conditions of gums (Doshi et al., 1983).

**Antimutagenic activity**

Jahangir et al. (2006) studied the antioxidant and anti-clastogenic efficacy of A. vasica against cadmium chloride (CdCl₂)– induced renal oxidative stress and genotoxicity in Swiss albino mice. A single intraperitoneal dose of CdCl₂ (5 mg/kg b.wt.) resulted in significant (p<0.001) increase in chromosomal aberration and micronuclei formation. Oral administration of A. vasica at two doses (50 and 100 mg/kg BW) for seven consecutive days showed significant (p<0.001) suppression of mutagenic effects of CdCl₂ in plant-pre-treated groups. Cadmium intoxication altered the antioxidant levels and enhanced MDA formation significantly (p<0.001). A. vasica showed significant (p<0.001) recovery in antioxidant status, viz., GSH content, its dependent enzymes, and catalase activity. Prophylactic pretreatment of A. vasica extract in cadmium-intoxicated mice showed marked (p<0.001) inhibition of lipid peroxidation (LPO) and xanthine oxidase (XO) activity.

Swiss albino mice when exposed to Cobalt-60 radiation, was affected with radiation-induced ailment, displaying noticeable effects in histology of testis. This effect was significantly reduced when A. vasica plant extract was applied. This suggests that the vasaka plant extracts have radioprotective effects on testis (Kumar et al., 2007).

**Anti-tussive activity**

The present study was carried out to evaluate anti-tussive activity of ethyl acetate and methanolic extract of leaves of Adhatoda vasica Nees. As cough is a natural reflex expulsive defense mechanism of the body, it is the most common symptoms of respiratory disease. Ammonium hydroxide and Sulphur dioxide induced cough models in mice were used for evaluation of anti-tussive activity of ethyl acetate and methanolic extracts of leaves Adhatoda vasica. The ethyl acetate and methanolic extract of leaves Adhatoda vasica was orally administered at the dose levels of 500 mg/kg b.w. showed maximum inhibition of cough by 82% and 81% respectively. The standard anti-tussive drug
Codiene phosphate (10mg/kg b.w.) showed maximum inhibition of cough by 84%. It was found that both extracts of Adhatoda vasica showed anti-tussive activity and obtained percentage inhibition of cough reflex is approximately comparable as standard drug (Sweta Srivastava and Choudhary, 2016). To evaluate the anti-tussive activities of Adhatoda extract in anesthetized guinea pigs and rabbits and in unanesthetized guinea pigs showed the plant to have a good anti-tussive activity (Dhuley, 1999).

**Immunomodulatory activity:** Rana Adhikary et al. (2014) in a study reported the potent immunomodulatory role of methanolic extract of Adhatoda vasica leaf along with potent anti-oxidant activities in vivo has given protection against the inflammatory response and oxidative damage induced by particulate antigen (SRBC) challenge.

**Future Prospects of Herbal drugs:** Herbal medicine can be a novel drug of choice nowadays as the researchers globally are searching alternatives for treating antibiotic resistant pathogens. These formulations are safer, cost effective and possess negligible side effects as per their documented use in Ayurveda. Studies conducted to evaluate their anticancer properties have also proved their wide scope as phytotherapeutics. Array of plants and their components hold immunomodulating properties. Their possible inclusion in diets could explore new therapeutic avenues to enhanced immunity against diseases.

**Pharmaceutical/Therapeutic importance**

Adhatoda contains numerous bioactive compounds, for instance, vasicinol, 5-hydroxy vasicine, vasicine, vasicine glycoside, deoxyvasicine, vasicinone, adhavasicinone, vasicolinone, adhatodine, anisotine and vasmetine (Dhankhar et al., 2011; Tafazul et al., 2013; Gupta et al., 2014; Srinivasan et al., 2014). Vasicine shows bronchodilatory activity under in vitro and in vivo condition, whilst, vasicinone exhibited its effectiveness towards broncho constriction in vivo. Simultaneous effect of these two alkaloids was preferably administered for bronchodilatory activity both under in vitro and in vivo. A combination of vasicine and vasicinone also showed a significant reduction in cardiac depressant effects. Vasicinone produced from the roots, prevents shrinkage of intestine and cardiac depression in guinea pigs, and transient hypotension in cats, thus displaying decent anticholinesterase activity (Lahiri and Pradhan, 1964). Vasicine produces ambroxol and bromhexine that have a pH-dependent growth inhibitory influence on Mycobacterium tuberculosis, which suggests that it may play a significant part in the primary treatment of tuberculosis (Narimaian et al., 2005). Both vasicine and vasicinone have sucrose inhibitory activity, signifying that they can be explored as natural antidiabetic agents (Gao et al., 2008). It has been reported that vasicine and its derivatives are excreted through urine (Claeson et al., 2000). By way of intramuscular and intravenous administration, for the first 18 and 22h, 55% of the excreted product was vasicine, whilst, on oral administration, it was 18% during the first 24h. The leaves of A. vasica possess anti-ulcer activity, which was tested in rats. The arduoi leaves have the highest degree of anti-ulcer activity (80%) as detected in the ethanol induced ulceration model when compared to that of the actions of pylorus and aspirin (Shrivastava et al., 2006). The syrup made from A. vasica leaves improved symptoms of dyspepsia as well (Chaturvedi et al., 1983). A. vasica extracts exhibited antimutagenic activity when cadmium-intoxicated mice was treated with the same, wherein, it showed marked decline in inhibition of lipid peroxidation and xanthine oxidase activity (Jahangir et al., 2006) Swiss albino mice when exposed to Cobalt-60 radiation, was affected with radiation-induced ailment, displaying noticeable effects in histology of testis. This effect was significantly reduced when A. vasica plant extract was applied. This suggests that the Adhatoda plant extracts have radioprotective effects on testis (Kumar et al., 2007).

**CONCLUSION**

Much attention has been drawn towards the plant based therapeutics because of the significant antimicrobials possessed by them. In the present literature medicinal significance of Adhatoda vasica in terms of wide range of pharmacological activities has been reported. Alkaloids of Adhatoda vasica represents a class of herbal drug with very strong experimental and traditional base proven by experimental studies. Various solvent extracts of the A. vasica have the potential to combat oxidative stress, microbial complications, Lung cancer, inflammation etc., effectively. Plant in reference holds a great potential to be developed as an alternative means of therapy for the treatment of Multi drug resistant pathogens. There is an enormous possibility for the future research to be carried on A. vasica for screening its wide pharmacological profile in the present scenario of Corona Pandemic also.

**Conflict of Interest:** None as best of our Knowledge.

**REFERENCES**


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