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ADHATODA VASICA: PHARMACOLOGICAL CHARACTERIZATION FOR THE DEVELOPMENT OF HERBAL DRUG

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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 bymany 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
Malayalum	:	Ata-lotakam

Fig. 1: *Adhatoda Vasica* (Whole Plant)

Fig. 2: Dried Leaves

Fig. 3: Powdered Leaves

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 exstipulate. 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, fruit 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- cranulate, 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

S.No.	Parameters	Values (%)
1.	Total Ash Content	21.40
2.	Acid Insoluble Ash	0.92
3.	Water Soluble Ash	4.85
4.	Foreign matter	0.28
5.	Moisture Content	18.20

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 Nimbkar, 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, antidibetic, 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.

Peak no.	Phytochemicals	Molecular formula	Retention time (min)
1	Hydrazine carboxyamide	CH_5N_3O	3.307
4	2-Propanone	C_3H_6O	3.613
10	Sclerosol	C_2H_6OS	7.110
22	Phoshine	CH_5P	7.903
23	Carbamic acid	CH_3NO_2	8.070
25	Methane-D3,Nitro-	CD_3NO_2	8.883
32	2H-Benzopyran-4-Carbonitrile,6-Fluoro-3,4-Dihydro-4-[(Methylthio)Methyl]	$C_{12}H_{12}FNOS$	16.767
34	2-Pyridinepropanoic acid	$C_{11}H_{13}NO_3$	46.097
38	Aminourea	CH_5N_3O	46.413

Table 3: The identified phytochemicals in the methanol extract were detected using GC-MS technique.

Peak no.	Phytochemicals	Molecular formula	Retention time (min)
3	N-(3,4,4-Trimethyl-1,2-Dioxethane-3-yl-MethoxyCarbonyl) Glycine	$C_9H_{15}NO_6$	3.620
6	Silane	$C_8H_{18}C_{12}OSi$	3.933
17	Acetamide	$C_2H_3C_{12}NO$	7.723
25	1H-Pyrimido[4,5,6-IJ][2,7]Naphthyridine-6-Carbonitrile,2-Ethyl-5,8-Dimethoxy-	$C_{14}H_{13}N_5O_2$	50.753
26	Acetonitrile-D3	C_2D_3N	50.860
28	3-Methoxy-5-(Methoxymethoxy)-7-Methyl-6-(3-(Trimethylsilyl)Propargyl)-1,4-Naphthoquinone	$C_{20}H_{24}O_5Si$	51.007
30	L-Alanine, Ethylester-	$C_5H_{11}NO_2$	52.513
32	Formamide,N-[(dibutylamino)methyl]-N-methyl-	$C_{11}H_{24}N_{20}$	53.240
34	Trans-2-((phenylthio)methyl)-1-(2-propenyl)-1,2,3,4-tetrahydronaphthalene	$C_{20}H_{22}S$	53.747
37	2-Acetonyl-3-cyano-2,3-dimethylcyclobutane-1-carboxylic acid	$C_{11}H_{15}NO_3$	54.043
45	5,5'-dicarboxy-3'-(2-chloroethyl)-4-(2-acetoxyethyl)-3,4'-dimethylpyrromethane	$C_{19}H_{23}ClN_2O_6$	56.893

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

Peak no.	Phytochemicals	Molecular formula	Retention time (min)
10	3,3'-[1,2-hydrazindiyl-bis(Carbonyloxymethylene)[Bis(3,4,4-trimethyl-1,2-dioxethane	$C_{14}H_{24}N_2O_8$	3.620
23	D5-Ethylnitrate	$C_2D_5NO_3$	7.740
25	Methane- D3	CD_3NO_2	8.850
20	Bis(Fluoromethyl)(Dimethyl)Silane	$C_4H_{10}F_2Si$	7.343
27	Erythro-1,2-Dimethyl-1-Methylthio-2-Hydroxyethane	$C_5H_{12}OS$	10.080

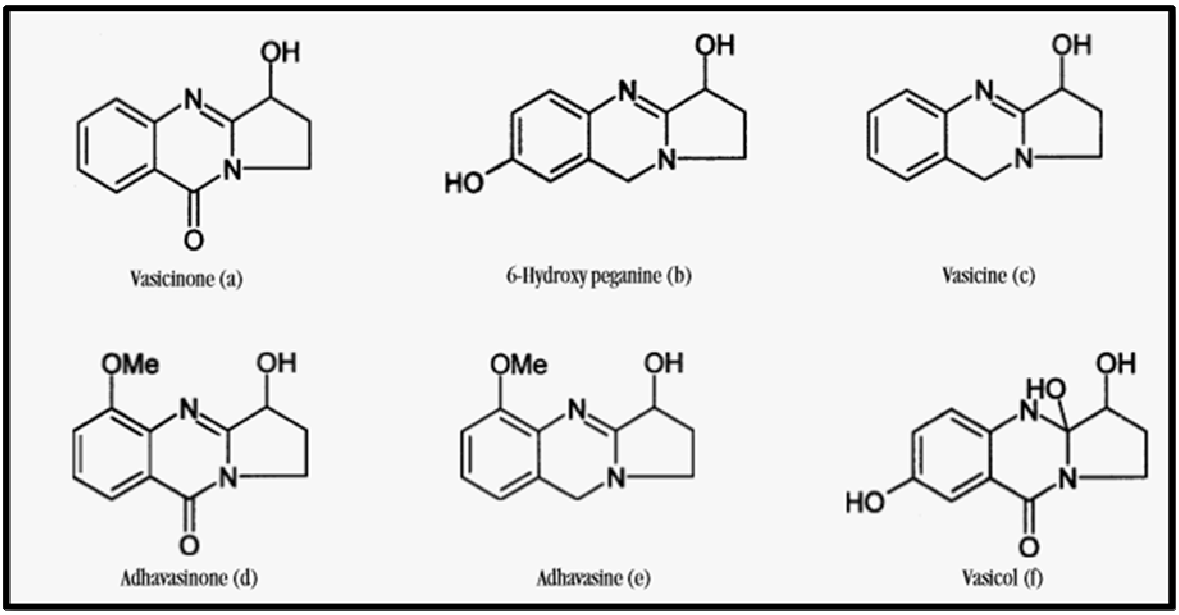

Fig. 4: Structural Representation of Phytochemicals (Nyeem *et al*., 2017)

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 therapeutical 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 vascinol 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 uterotonic activity: *Adhatoda vasica* has abortifacient and uterotonic 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 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 uterusi 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 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 (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 prostogladins (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 antifertility 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 Venkatakrishna, 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, Glyccyrhiza 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 ezymaytic and non enzymatic antioxidants were significantly more in *A. vasica* than *S. grandifllora*. 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.

Anti-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 carragennan-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 (Barry *et al*., 1955), cancer (Pandey, 2002) and possessed to have anti-helminthic 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 andrabbits. 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 oxytoxic 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 oxytoxics, 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 anticlastogenic efficacy of *A. vasica* against cadmium chloride ($CdCl_2$)– induced renal oxidative stress and genotoxicity in Swiss albino mice. A single intraperitoneal dose of $CdCl_2$ (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 $CdCl_2$ in plant-pretreated 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

Codienephosphate (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 vasnetine (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 Prahdan, 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 ardusi 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

Atal, C.K. (1980). The chemistry and pharmacology of vasicine, a new oxytocic and abortifacient. Regional Research Laboratory, CSIR, Jammu-Tawi.

Amin, A.H. and Mehta, D.R. (1959). A bronchodilator alkaloid (vasicinone) from *Adhatoda vasica Nees.* Nature, 184: 1317.

Balachandran, A.; Sangeetha, D.; Awale, E. and Ignacimuthu, P. (2017). *In vitro* and *in vivo* anticancer activity of 2-acetyl-benzylamine isolated from *Adhatoda vasica* L. leaves. *Biomed Pharmacother*, 796-806.

Bhalla, H.L. and Nimbkar, A.Y. (1982). Preformulation studies III. Vasicinone, a bronchodilatory alkaloid from *Adhatoda vasica Nees* (absorption, potency and toxicity studies). Drug Dev Indian Pharm, 8(6): 833.

Bhargava, M.K.; Singh, H. and Kumar, A. (1988). Evaluation of *Adhatoda vasica* as a wound healing agent in buffaloes. Clinical, mechanical and biochemical studies. *Indian Veterinary Journal*, 65(1):33.

Borris, R.P. (1996). Natural products research: perspectives from a major pharmaceutical company. *J Ethnopharmacol*. 51(1-3): 29-38.

Bhattacharyya, D.; Pandit, S. and Janab, U. (2005). Hepatoprotective activity of *Adhatoda vasica* aqueous leaf extract on D-galactosamine induced liver damage in rats. *Fitoterapia.*76: 223-225.

Bhatt, B.P. and Panwar (1990). M.S. Plants with fertility regulating potential of Garhwal Himalayas. *J Econ Bot Phyto Chem.*, 1: 33-34.

Bhaduri, N.; Shri, R. and Patil, B.D. (1985). Evaluation of some plant extracts on protectants against the pulse

beetle *Callosobruchus maculates* (Fabricans) infecting cowpea seed. *J Entomol Res.* 9:183-187.

Claeson, U.P.; Malmfors, T.; Wikman, G. and Bruhn, J.G. (2000). *Adhatoda vasica :* a critical review of ethnopharmacological and toxicological data. *Journal of Ethnopharmacology*, 72:1.

Chauhan, N.; Singh, C. and Gupta, S. (2019). Screening antibacterial efficacy and anticancer studies of *A. vasica* leaf crude extracts for formulation of potential herbal drug. *Journal of Pharmacognosy and Phytochemistry*, 8(1): 428-434.

Chandokhe, N. (1987). Vasicine-the alkaloid of *Adhatoda vasica* a novel abortifacient. *Indian Drugs,* 24:425-429.

Chaturvedi, G.N.; Rai, N.P.; Dhani, R. and Tiwari, S.K. (1983). Clinical trial of *Adhatoda vasica* syrup (vasa) in the patients of non-ulcer dyspepsia (Amlapitta). *Ancient Science of Life*, 3(1):19.

Chakraborty, A. and Brantner, A.H. (2001). Study of alkaloids from *Adhatoda vasica* Nees on their anti-inflammatory activity. *Phytother. Res*. 15: 532-534.

Doshi, J.J.; Patel, V.K. and Venkatakrishna, B.H. (1983). Effect of *Adhatoda vasica* massage in Pyorrhoea. *Int J Crude Drug Res*, 21:173-176.

Dhar, K.L.; Jain, M.P.; Koul, S.K. and Atal, C.K. (1981). Vasicol, a new alkaloid from Adhatoda vasica. *Phytochemistry*, 20(2):319.

Dhankhar, S.; Kaur, R.; Ruhil, S.; Balhara, M.; Dhankar, S. and Chhillar, A.K. (2011). *Afr. J. Plant Sci,* 5: 620–627.

Dorsch, W. and Wagner, H. (1991). New antiasthmatic drugs from traditional medicine. Int Arch Allergy Appl. Immunol, 94(1-4): 262-265.

Dhuley, J.N. (1999). Antitussive effect of *Adhatoda vasica* extract on mechanical or chemical stimulation-induced coughing in animals. *J Ethnopharmacol*, 67(3):361-5.

Gao, H.; Huang, Y.N.; Gao, B.; Li, P.; Inagaki, C.K. (2008). *J. Food Chem*, 108: 965–972.

Grange, J.M. and Snell, N.J.C. (1996). Activity of bromhexine and ambroxol, semi-synthetic derivatives of vasicine from the Indian shrub *Adhatoda vasica,* against Mycobacterium tuberculosis in vitro. *Journal of Ethnopharmacology*, 50(1):49.

Gupta, O.P.; Anand, K.K.; Ghatak, B.J. and Atal, C.K. (1978). Vasicine, alkaloid of *Adhatoda vasica,* a promising uterotonicabortifacient. *Indian Journal of Experimental Biology*, 16(10):1075.

Gupta, A.; Joshi, A.; Joshi, V.K. (2014). *Int. J. Herb. Med*, 1:1–4.

Pandey, G. (2002). Anticancer herbal drugs of India with special reference to Ayurveda. Sri Satguru Publications; Delhi, pp. 18-121.

Gupta, O.P.; Wakhloo, R.L.; Sharma, M.L. and Atal, C.K. (1979). Vasicine-a potent uterine stimulant. Studies on human myometrium. *J Obstet Gynaecol India.* 29: 935-938.

Hussain, M.A. and Gorsi, M.S. (2004). Antimicrobial activity of *Nerium oleander* Linn. *Asian Journal of Plant sciences*. 3(2): 177-180.

Ilango, K.; Chitra, V.; Kanimozhi, P. and Balaji, G. (2009). Antidiabetic, Antioxidant and Antibacterial Activities of Leaf extracts of *Adhatoda zeylanica*. Medic (Acanthaceae). *J. Pharm. Sci. &* Res. 1(2): 67-73.

Josephin, S.B. and Selva, M.T. (2012). Antimicrobial activity of Adhatoda vasica against clinical pathogens. *Asian Journal of Plant Science and Research*, 2(2):83-88.

Jahangir, T.; Khan, T.H.; Prasad, L. and Sultana, S. (2006). Reversal of Cadmium chloride–induced oxidative stress and genotoxicity by *Adhatoda vasica* extract in Swiss albino mice. *Biol. Trace Element Res*., 111: 217-228.

Jain, M.P. and Sharma, V.K. (1982). Phytochemical investigation of roots of *Adhatoda vasica.* Planta Medica, 46: 250.

Karthikeyan, A.; Shanthi, V. and Nagasathaya, A. (2009). Preliminary phytochemical and antibacterial screening of crude extract of the leaf of *Adhatoda vasica* . L. *International Journal of Green Pharmacy*. 3(1): 78-80.

Kumar, K.P.S.; Debjit, B.; Chiranjib, P.T. and Rakesh, K. (2010). Indian traditional herbs *Adhatoda vasica* and its Medicinal application. *J Chem Pharm Res*., 2(1): 240-245.

Lahiri, P.K. and Pradhan, S.N. (1964) Pharmacological investigation of vasicinol, an alkaloid from *Adhatoda vasica Nees. Indian Journal of Experimental Biology*, 2: 219.

Ayyanar, M. and Ignacimuthu, S. (2008) Medicinal uses and pharmacological Actions of five commonly used Indian Medicinal plants: A mini-review. *Iranian Journal of Pharmacology and Therapeutics*, 7: 107-114.

Mohammad, A.B.N.; Mustofa, N.B.M.; Rabiul Islam, Md. Moksed Ali, Sanjeeda Sultana, Rabeya Siddika (2017). Wonderful bronchodilatory indigenous plant (Adhatoda vasica): A phyto-pharmacological profile. *International Journal of Advanced Research and Development*. 2(1): 86-90.

Kumar, M.; Samarth, R.; Kumar, M.; Selvan, S.R.; Saharan, B. and Kumar, A. (2007). Evid Based Complement Alternat Med, 4(3): 343–350.

Mullar, A.; Antus, S.; Bittinger, M.; Dorsch, W.; Kreher, B.; Neszmelyi, A.; Stuppner, H. and Wagner, H. (1993). Chemistry and pharmacology of the antiasthmatic plants, *Galpinia glauca*, *Adhatoda vasica* , Picrorrizhakurroa. *Planta Med*, 59: 586-587.

Narimaian, M.; Badalyan, M.; Panosyan, V.; Gabrielyan, E.; Panossian, A. and Wikman, G. (2005). Randomized trial of a fixed combination (KanJang) of herbal extracts containing *Adhatoda vasica, Echinacea purpurea* and *Eleutherococcus senticosus* in patients with upper respiratory tract infections. *Phytomedicine*, 12(8): 539-47.

Nath, D.; Sethi, N.; Singh, R.K. and Jain, A.K. (1992). Commonly used Indian abortifacient plants with special reference to their teratologic effects in rats. *J Ethnopharmacol*, 36(2):147-54.

Pa Rashmi and Mathew, L. (2012). Antimicrobial activity of leaf extracts of *Justicia adhatoda* L. in comparison with vasicine, *Asian Pacific Journal of Tropical Biomedicine*, 1556-1560.

Paliwa, J.K.; Dwivedi, A.D.; Singh, S. and Gupta, R.C. (2000). Pharmacokinetics and in-situ absorption studies of a new anti-allergic compound 73/602 in rats. *Int J Pharm*, 197(1-2): 213-20.

Pahwa, G.S.; Zutshi, U. and Atal, C.K. (1987). Chronic toxicity studies with vasicine from *Adhatoda vasica Nees.* in rats and monkeys. *Indian J Exp. Biol*, 25(7): 467-70.

Patel, V.K. and Venkatakrishna, B.H. (1984). *In vitro* study of antimicrobial activity of *Adhatodavasika Linn.* (leaf

extract) on gingival inflammation a preliminary report. *Indian J Med Sci*, 38(4): 70-72.

Padmaja, M.; Sravanthi, M. and Hemalatha, K.P.J. (2011). Evaluation of Antioxidant Activity of Two Indian Medicinal Plants. *Journal of Phytology*. 3(3): 86-91.

Pandita, K.; Bhatia, M.S.; Thappa, R.K.; Agarwal, S.G.; Dhar, K.L. and Atal, C.K. (1983). Seasonal variation of alkaloids of *Adhatoda vasica* and detection of glycosides and N-oxides of vasicine and vasicinone. Planta Medica, 48: 81-82.

Rabinovich, M.I.; Leskov, A.I. and Gladkikh, A.S. (1966). Cholegogic properties of peganine. Vrachei, 181.

Rana, A.; Arnab, M.; Sayantika, M. and Biswadev, B. (2014). *Journal of Pharmacy Research,* Vol.8 Issue 10. 8(10) 1520-1537.

Rao, M.N.A.; Krishnan, S.; Jain, M.P. and Anand, K.K. (1982). Synthesis of vasicine and vasicinone derivatives for oxytoxic and bronchodilatory activity. *Indian J Pharmaceutic Sci*, 44: 151-152.

Shrivastava, N.; Shrivastava, A.; Banerjee, A. and Nivsakar, M. (2006). Anti-ulcer activity of *Adhatoda vasica Nees. J Herb Pharmacother*, 6(2):43-9.

Shinwari, Z.K. and Shah, M. (1995). The Ethnobotany of Kharan district, Balochistan, Pakistan. ProcSym Med Pl, 12: 35-38.

Shrivastava, N.; Srivastava, A.; Banerjee, A. and Nivasarkar, M. (2006). Anti-ulcer activity of *Adhatoda vasica Nees. J Herb Pharmacother*, 6(2):43-49.

Sweta, S. and Choudhary, G.P. (2016). Anti-tussive activity of ethyl acetate and methanol extracts of *Adhatoda vasica*. *International Journal of Pharmaceutical Sciences and Research*, 7(10): 4180-4183.

Srivastava, A.S.; Saxena, H.P. and Singh, D.R. (1965). *Adhatoda vasica,* a promising insecticide against pests of storage. Lab Dev, 3(2):138.

Saxena, B.P.; Tikku, K. and Atal, C.K. (1986). Insect antifertility and antifeedant alleochemics in *Adhatoda vasica. Insect Sci Appl*, 7(4): 489.

Shinwari, Z.K.; Khan, I.; Naz, S. and Hussain, A. (2009). Assessment of antibacterial activity of three plants of Pakistan to cure respiratory disorders. *African Journal of Biotechnology*. 8(24): 7082-7086.

Singh, D. and Maurya, S. (2010) *Int. J. Pharm Tech Res*. 2(4): 2403-2406.

Srinivasarao, D.; Jayarraj, I.A.; Jayraaj, R. and Prabha, M. (2006). A study on antioxidant and anti-inflammatory activity of vasicine against lung damage in rats. *Indian J. Allergy Asthma Immunol*. 20: 1-7.

Sethi, N.; Nath, D.; Shukla, S.C.; Dayal, R. and Sinha, N. (1987). Abortifacient activity of a medicinal plant Adhatoda vasica in rats. *Arogya J Health Sci*, 13: 99-101.

Tafazul, M.; Badkhane, Y.; Raghuvwanshi, D.; Shabir, K.L.; Yadav, A.; Sharma, A.S. and Ajit, K. (2013). *Indo Am. J. Pharma. Res*, 3: 3341–3360.

Barry, V.C.; Conalty, M.L. and Rylance, H.J.R. (1955). Antitubercular effects of an extract of *Adhatoda vasica*, Nature, 176: 119-120.

Mulla, W.A.; Suyog, D.M.; Suraj, B.J.; Ajinkya, M.P.; Mukhtar, S.K. and Madhukar, R.V. (2010). Evaluation of anti-inflammatory and analgesic activities of ethanolic extract of roots of *Adhatoda vasica* Linn. *Int. J. Pharma Tech Res*. 2(2): 1364-1368.

Wagner, H. (1989). Search for new plant constituents with potential antiphlogistic and antiallergic activity. *Planta Med*, 55(3):235- 241

Zaidi, S.H. (1998). Existing indigenous medicinal plant resources of Pakistan and their prospects for utilization. *J. Pakistan Forest.* 48(2): 5-9.