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Review article

# Exploring the pharmacological and chemical aspects of pyrrolo-quinazoline derivatives in *Adhatoda vasica*

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ABSTRACT

*Adhatoda or Justicia* is one of the biggest and complex genera of the Acanthaceae family. *Adhatoda vasica* is commonly known as 'Adosa'. It is an ayurvedic medicine with a medicinal history of more than a thousand years in India. Traditionally, it is used to treat cough, asthma, phlegm, bleeding hemorrhoids, for both adults and youth. This plant possesses antiarthritis, antiseptic, antimicrobial, anti-tuberculosis, anti-inflammatory and abortifacient properties. Alkaloids are the major phytoconstituents present in the plant in the form of pyrrolo-quinazoline derivatives *viz* vasicine, vasicinone, vasicinol, adhatodine, adhatodinine, adhavasinone and anisotine etc. The asserted objectives are to conduct a systematic review on the phytochemistry, pharmacology and traditional uses of *A. vasica*, as well as highlighting the challenges found in the research. This will promote the utilization of *A. vasica* at extract level and further development of new drug leads based on the compounds isolated and used for treatment of various ailments. The present review covers the literature survey from 1888 to 2023. The relevant data has been collected from various peer-reviwed journals, and books *via* Sci-Finder, PubMed, Science Direct, Google Scholar, EBSCO, online electronic journals, SpringerLink and Wiley. This paper aims to present a systematic review of known traditional applications, pharmacological and chemical aspects in *Adhatoda vasica*.

## 1. Introduction

Acanthaceae are the ninth largest pantropical family of dicotyledonous plants, including over 200 genera and 2000 species [1]. *Adhatoda* or *Justicia* is the one of the biggest genera of Acanthaceae family. This genera is an important source of therapeutic drugs and its species are distributed in all continents, mainly in tropical and subtropical regions. In America, only three species *viz Justicia spicigera, Justicia secunda* and *Justicia pectoralis* are most widely used for medicinal purposes, but very few studies related to their chemical composition and pharmacological properties have been done yet. Asian species *Justicia adhatoda, Justicia beddomei* and *Justicia adhatoda* are most promising species of this genus [2]. *Justicia adhatoda is also known as Adhatoda vasica. Adhatoda vasica* (L.) Nees (Fig. 1) is commonly known as *'Vasaka'* in Ayurveda *and* 'Malabar nut'in English. It is a very small, evergreen shrub that is geographically distributed throughout India up to altitude of 1300 m and mainly found in sub-Himalayan areas. It is also distributed in Nepal, Pakistan, Myanmar and Germany. The plant not only been used in the indigenous system of medicine in India since thousands of

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(a) (b)

**Fig. 1.** *Adhatoda vasica* plant: (a) Whole aerial part (b) Flowering twig.

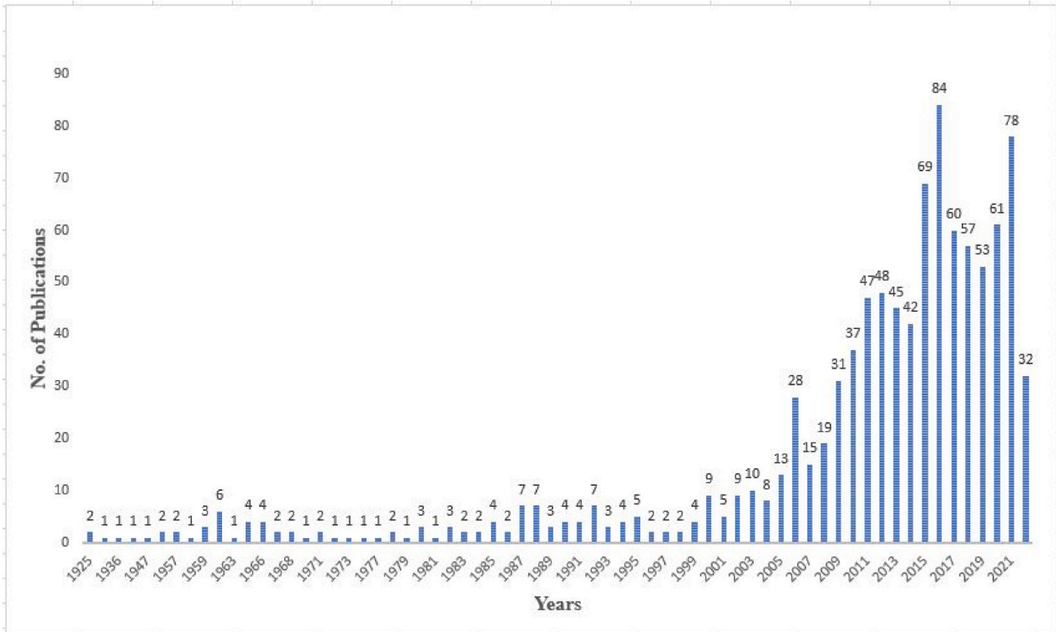



**Fig. 2.** The number of publications published on *Adhatoda vasica* and its medicinal applications since 1925.

years [3], but also a well-known drug in Ayurvedic and Unani medicine [4]. It is used as traditional Indian medicine for treating bronchitis, tuberculosis, other lung and bronchiole disorders. This plant is included in the "Manual of Traditional Medicine in Primary Health Care", published by the World Health Organization, as it has been traditionally used for treating young and old people suffering from cough, asthma, breathing trouble, phlegm, allergic conditions, bleeding hemorrhoids [5]. Several herbal remedies containing *A. vasica* are commercially available *viz* Kada [6]; Femiforte [7]; Salus Tuss [8]; Kan Jang, Spirote [1,9]. Adusa is well known for anthelmintic and weedicide properties [10]. Alkaloids like pyrrolo-quinazoline derivatives are the main classes of secondary metabolites that have been isolated from Adhatoda [11]. All findings about the pyrrolo-quinazoline derivatives and other phyto-constituents indicate that *Adhatoda* is an important genus of the Acanthaceae family having a commercial reputation and can be encouraged for diversified applications like medicinal and other potential uses [12].

(These photographs were taken from Gasiyaar near Iswal, Udaipur).

Research data on *Adhatoda vasica* was collected from Sci-Finder, PubMed, ScienceDirect, Google Scholar, EBSCO, online electronic journals, SpringerLink and Wiley and is shown in the form of the bar graph. This graph clearly indicates that it is an ancient plant being studied since 1925 and is being studied largely which is clear from the number of increasing publications in the recent years (Fig. 2).

Earlier reviews of *Adhatoda vasica* have incorporated its pharmacological activities [13–21], phytochemistry [22–29] and ethnomedicinal uses [30–33]. In this paper, we have discussed the bioactivities confirming the ethnopharmacological uses of *Adhatoda*

**Table 1**
Ethnomedicinal uses of plant parts of *A. vasica*.

| Plant part/s | Disease | Mode of administration | References |
|---|---|---|---|
| Leaves | Malaria | Leaves paste applied to body and left for 24 h, to cure chronic malaria | [47] |
| | Whooping cough and asthma | Leaves juice administered orally | [48] |
| | | Leaves decoction with honey taken thrice a day | [49] |
| | | Inhalation of smoke obtained from burning dry leaves by patients suffering from asthma, chronic bronchitis | [50] |
| | Diabetes | Leaves juice of *A. vasica* and *Andrographis paniculata* given together for 21 days | [51] |
| | | Chewing of young leaves empty stomach to cure diabetes | [52] |
| | Poisonous bites | Leaves paste applied externally and leaves juice taken internally as an antidote | [53] |
| | Fits | Juice of leaves of *A. vasica* along with *Piper nigrum*, *Zingiber officinalis* and beetle leaf given to cure epilepsy | [54] |
| | Ear pain | Leaves decoction is used | [55] |
| | Inflammation | Leaves applied externally as poultice | [56] |
| | Arthritis | Two tea spoons of leaves extract taken twice a day | [55] |
| | As antiseptic lotion | Leaves decoction is used | [55] |
| | Scabies | Use of leaves decoction | [55] |
| | Rheumatism | Leaves paste applied externally | [57] |
| | Jaundice | Two spoons of leaves extract with sugar taken twice a day for a month. | [58] |
| | Eczema, cuts and wounds. | Leaves paste applied externally. | [48] |
| | Diarrhoea and dysentery | Leaves extract used | [57] |
| | Sprains | Leaves paste applied externally | [59] |
| **Roots** | Snake bite | Roots and Leaves decoction of *A. vasica* mixed with the extracts of *Alangium salvifolium* and *Coccinia grandis* given orally as an antidote | [60] |
| | Gonorrhoea | Roots extract used as anti gonorrhoeal agent | [61] |
| | Leucorrhoea and gynaecological problems | Roots bark juice given along with honey | [62] |
| | Labour pains | Application of roots paste on the abdomen and vagina at the time of child birth. | [59] |
| | Rheumatism | Roots extract applied externally | [57] |
| | Dysentery | Fresh roots extract taken | [63] |
| | Asthma | Root bark decoction taken along with honey | [64] |
| **Flowers** | Asthma | Floral extract mixed with *Solanum surattense* and given | [65] |
| | Ophthalmia | Fresh flowers extract used | [66] |
| | Jaundice | Flowers extract given | [65] |
| | Diabetes | Flowers along with powdered neem leaves and gum of *Acacia nilotica* given to patients having diabetes. | [65] |
| | Muscular spasms | Flowers and fruits extract taken to cure spasms. | [61] |
| | Pimples | Application of floral extract along with mustard oil | [65] |
| | Tuberculosis | Flowers and raw roots chewed empty stomach once a day | [51] |
| **Whole plant** | Asthma, bronchitis, Cough and cold | Whole plant extract used | [66] |
| | Liver fever | Whole plant extract used to cure liver fever | [67] |
| | Jaundice | Decoction of whole plant taken | [68] |
| | Scabies | Extract of whole plant used | [69] |
| **Stem/Bark** | Stomach pain | Extract given | [70] |
| | Nausea | Bark and young leaves juice taken as anti- emetic tonic | [71] |
| | Intestinal worms | Bark and young leaves juice given to kill intestinal worms | [71] |

*vasica* and its potential for further investigation, exploitation, and utilization.

## 2. Ethnomedicinal uses

*Adhatoda vasica* has been used in indigenous medicine to treat a number of ailments, including colds, coughs, asthma, whooping cough, leprosy, chronic bronchitis, heart problems, blood disorders, fever, vomiting, thirst and memory loss [33–36]. An ammonical vapour is formed when leaves are smoked in a pipe, which aids in breathing for asthma patients [14]. In Ayurveda, due to its properties like *Tikta-Kashaya rasa, katu vipaka and sheeta virya*, it is known for its use to cure diseases like *Gulma, Raktapitta, Swasa-kas*a etc. [37]. The herbal basak tea prepared from its leaves can be developed as a good expectorant for the treatment of asthma [38].

A decoction of leaves boiled in water is utilized to alleviate rheumatic pain and urinary tract infections [39]. In Ayurveda, leaves of Adhatoda vasica is an important drug, used as an expectorant [4]. Vasicine helps in condensing sputum and is therefore the vital component for throwing sputum out of the body [15]. Quinazoline alkaloids are active principles for this property. Traditionally, leaves' juice (swarasa) is obtained by subjecting a bolus of crushed fresh leaves to heat followed by squeezing out the juice [40,41]. Leaves extract is used to stimulate uterine contractions, thus speeding child birth in various parts of India [2]. A survey revealed that 70 % of the pregnant women had been previously using the leaves of *A. vasica* orally to induce abortion in Gora village, Lucknow [42]. This observation has been earlier mentioned by scientists from the same institute in a report on the abortifacient activity of *A. vasica* in rats [43]. There is one indication of use of the roots for facilitating the expulsion of foetus or helping parturition [44–46]. The route of administration is probably a local application as mentioned in one of references [45].

**Table 2**
Brief summary of the pharmacological properties.

| S. No | Pharmacological activities | Parts/extracts/ possible chemical constituents | Effective dose range | Test system for activity | Result | References |
|---|---|---|---|---|---|---|
| 1 | **Antibacterial/ Antimycobacterial activity** | Leaves: crude alkaloids, petroleum ether extract, alcohol extract and hot water extract | – | *Bacillus cereus, Bacillus subtilis, Bacillus-megaterium, Saimoneiia typhi, Staphylococcus aureus, Vibrio cholerae, E. coli* | Mild inhibition against subject microrganisms in different degrees was found. | [72] |
| | | Vasicine, vasicinone, vasicine acetate, 2-acetyl benzyl amine, vasicinolone<br>Vasicine acetate and 2-acetyl benzylamine isolated from hexane extract | 10–150 μg/mL<br>200 and 50 μg/ mL | *E. coli*<br>*Mycobacterium tuberculosis* | Vasicine at 20 μg/mL exhibited potent antibacterial activity against *E. coli.*<br>Significantly inhibited *M. tuberculosis* as well as one multidrug resistant (MDR) strain and one susceptible strain. | [73]<br>[74,75] |
| | | Vasicine acetate | 125 μg/mL | *E. aerogenes*, *S. epidermidis*, *P. aeruginosa*, *M. luteus* | Vasicine acetate exhibited good zone of inhibition against tested bacteria. | [72] |
| | | Phytol | 2, 5 and 8 mg/kg | *Bacillus licheniformis* PKBMS$_{16}$ injected experimentally challenged ornamental goldfish *Carassius auratus* | Phytol treated group significantly (P < 0.01 & P < 0.05) reduced the rate of fish mortality, thus supporting its potential as a new compound for inducing fish immunity. | [76] |
| | | Leaves extract | – | *Gram positive and gram-negative* bacteria | Gram-positive bacteria had the highest antibacterial activity. | [77] |
| | | Leaves extract | – | *P. aeruginosa, S. aureus, S. pyogenus, E. coli* | Largest zone of inhibition was found against *P. aeruginosa.* | [78] |
| 2. | **Antiallergic and anti-asthmatic activity** | *In vivo*: Ethanolic extract of plant | 250, 500, 750 mg/kg | Acetylcholine and histamine induced brancho-spasm in guinea pigs | Spasmolytic effect of ethanolic extract of *A. vasica* found similar to ketotifen (1 mg/kg). | [79] |
| | | *In vitro:* Ethanolic extract of plant | 250, 500, 750 μg/ mL | Isolated guinea pig ileum | Significant increase in the contractions to histamine and acetylcholine was observed. | [79] |
| | | Plant: Aqueous extract | 130 mg/kg | Ova-allergen mouse model | Extract attenuated the increased airway resistance and inflammation in acute allergic asthmatic mice. | [80] |
| 3. | **Radioprotective effects** | Leaves: ethanolic extract | 800 mg/kg | Swiss albino mice exposed to 8 Gy radiation | Significant prevention in chromosomal damage in bone marrow cells of radiation-induced mice. | [81] |
| 4. | **Antimutagenic activity** | Whole plant extract | 50 and 100 mg/ kg by weight | Swiss albino mice toxicated with $CdCl_2$ (5 mg/kg by weight) | Significant decrease in malanodialdehyde formation and xanthine oxidase levels was observed. | [82] |
| 5. | **Anti-tubercular activity** | Volatile extract from leaves | 340 mg/kg | Parkes albino mice infected intravenously with the *Ravenel Rv* strain of *M. tuberculosis* | Volatile principle showed no anti-tubercular properties in mice on oral administration. | [83] |
| | | Ambroxol and bromhexine (semi synthetic derivatives of vasicine) | 50 mg/L for ambroxol and 6 mg/L for bromhexine | Against *M. tuberculosis in vitro* | Ambroxol and bromhexine showed pH-dependent growth-inhibitory effect on *M. tuberculosis*. | [84] |
| 6. | **Anti-ulcer activity** | Leaves powder | 500 mg/kg in 0.2 % agar | Ethanol induced and Pylorus ligation plus aspirin-induced rats | The ethanol-induced ulceration model had the highest level of activity (80 %). | [85] |
| 7. | **Allelopathic activity** | Fresh and dried aqueous extract of leaves | 60 % concentration of extract | Seeds of *Capsicum annum* L. | Dry aqueous extract was found more phytotoxic than fresh aqueous extract. | [86] |
| 8. | **Antifeedant and toxic activity** | Leaves: Methanolic extract | 200–1000 ppm | *Spodoptera littoralis larvae* | Crude extract lowered growth, consumption, utilization of swallowed and digested food, | [87] |

(*continued on next page*)

**Table 2** (*continued*)

| S. No | Pharmacological activities | Parts/extracts/ possible chemical constituents | Effective dose range | Test system for activity | Result | References |
|---|---|---|---|---|---|---|
| | | | | | and approximate digestibility substantially. | |
| 9. | **Sucrase inhibitory activity** | Leaves: Methanolic extract, vasicine, vasicinol | – | Screening experiment for rat intestinal α -glucosidase | IC50 values were 125 μM and 250 μM for vasicine and vasicinol respectively. | [88] |
| 10. | **Anti-inflammatory activity** | Vasicine | 0.2 mg/kg body weight | Wistar strain of albino rats with induced lung damage | Decrease in lipid peroxidase and increase in antioxidants catalase, superoxide dismutase, glutathione peroxidase was observed. | [89] |
| | | Methanol extract, saponins and alkaloids, non-alkaloid fraction | 50 μg/pellet | Hen's egg (Chorioallantoic membrane test) | Potent anti-inflammatory activity was shown by the alkaloid fraction at a dose of 50 μg/pellet whereas less activity was shown by MeOH and the other fractions. | [90] |
| | | Vasicine, vasicinone, vasicine acetate, 2-acetyl benzyl amine, vasicinolone | 20 mg/kg for vasicine and 10 mg/kg for vasicinone | Carragenan and CFA-model induced paw oedema. | Most potent anti-inflammatory effects by vasicine and maximum inhibition rate was observed for vasicinone. | [73] |
| | | Methanolic extract of leaves | 200,400,600 mg/kg | Carrageenan-induced paw Oedema in wistar albino rats | 400 mg/kg dose showed significant inhibition of carrageenan-induced inflammation. | [91] |
| 11. | **Abortifacient activity** | Leaves: aqueous extract | 175 mg/kg | Female albino rats | 100 % abortifacient activity was observed. | [92] |
| | | Vasicine | 2.5–10 mg/kg | Hamsters, rabbits, rats and guinea pigs | Uterotonic and abortifacient effects shown by vasicine probably by enhancing the release and synthesis of prostaglandins. | [93] |
| 12. | **Antiviral activity** | Methanolic and aqueous extracts of whole plant | 10 mg/mL | Influenza virus | 100 % and 33 % Reduction in hemagglutination by methanolic and aqueous extract respectively. | [94] |
| 13. | **Hypoglycemic activity** | Ethanolic extract of the leaves | – | Rats | – | [95] |
| | | Non nitrogenous principle from leaves | – | Rabbits | Lowering of blood sugar level was observed. | [3,96] |
| 14. | **Anticholinesterase activity** | Root/Vasicinol | – | Cats, guinea pigs | Contraction of the isolated gut and depression of the isolated heart were noted in guinea pigs, as well as hypotension in cats. | [97] |
| 15. | **Cardioprotective activity** | Vasicine and vasicinone | – | – | Significant reduction in cardial depressant effects by vasicine, whereas no effect by vasicinone was observed. | [3] |
| 16. | **Thrombolytic activity** | Root extract | 5 mg/mL NaCl solution | *In vitro* thrombolytic model | *Adhatoda* showed 19.63 % clot lysis activity. | [98] |
| 17. | **Wound-healing activity** | Methanolic, chloroform and diethyl ether extracts | 10 % w/w | Excision wound model in albino rats | 98.50, 87.46, 80.65 and 68.70 % wound contraction observed for nitrofurazone, methanolic, chloroform and diethyl ether extract treated groups respectively. | [99] |
| | | Chloroform and alcoholic extracts of leaves | – | Male buffalo calves | Increase in tensile strength, breaking strength, collagen, elastin, hydroxyproline etc. were observed. | [100,101] |
| 18. | **Anti-tussive activity** | Vasicinone and vasicine | – | Unanaesthetized guinea pigs and anaesthetized guinea pigs and rabbits | Action found similar to codeine. | [102] |

(*continued on next page*)

**Table 2** (*continued*)

| S. No | Pharmacological activities | Parts/extracts/ possible chemical constituents | Effective dose range | Test system for activity | Result | References |
|---|---|---|---|---|---|---|
| 19. | **Hepatoprotective activity** | Leaves: aqueous extract | 50–100 mg/kg | D-galactosamine liver damage induced in rats | Results supported the use of the plant as hepatoprotective element in traditional medicine. | [103] |
| | | Vasicinone | 25 mg/kg/day for 7 days | $CCl_4$ induced acute hepatotoxicity model in mice | Normal hepatic cords and absence of necrotic changes suggested recovery from $CCl_4$ induced liver damage in rats. | [104] |
| 20. | **Anti pyorrhoeal activity** | Leaves extract massaged on the inflamed gums | Application twice a day for three weeks. | Patients with pyorrhoea complain | Reduction and relief in the inflammatory and bleeding conditions of gums was observed. | [105] |
| 21. | **Anticancer activity** | Whole plant | Prophylaxis dose (50 and 100 mg/ kg BW) | Ferric nitrilotriacetate (Fe-NTA)–induced renal oxidative stress and tumor promotion in rats | Results showed that *A. vasica* can reduce hyperproliferative response toxicity and carcinogenic activity of Fe-NTA. | [106] |
| | | Leaves extract | 10,50,100 μg/mL | Human lung epithelial adenocarcinoma cell line (HCC-827) using 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl-tetrazolium bromide (MTT) assay | Methanolic extract showed cytotoxic effect on the cancerous cells which increased with the increase in dose of the extract. | [107] |
| | | Ethanolic extract | – | *In-vitro* studies on Hela, HepG2, MCF-7, MDAMB-231 cell lines with normal cells as positive control | Ethanolic extract showed good cytotoxic activity (60 %, 60 %, 85 % and 65 %) on Hela, HepG2, MCF-7, MDAMB-231 cell lines respectively. | [108] |
| | | Vasicine acetate | 2000, 1000, 500, 250, 125, and 62.5 μg/mL | A549 human adenocarcinoma cancer cell line using 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl-tetrazolium bromide (MTT) assay | Vasicine acetate showed prominent *in vitro* cytotoxic activity against A549 lung adenocarcinoma cancer cell line. | [109] |
| | | 2-acetyl benzyl amine | 0.42 mM | NB-4, MOLM-14, CEM, Jurkat, K562, IM-9, and HL-60 | 2-Acetyl-benzylamine was shown to be cytotoxic to MOLM-14 and NB-4 cells, with IC50 values of 0.40 and 0.39 mM, respectively. | [110] |
| 22. | **Radioprotective effect** | Ethanolic extract of the leaves | 800 mg/kg body weight | Swiss albino mice exposed to 8.0 Gy radiation | Pretreatment with *A. vasica* leaf extract resulted in a considerable rise in GSH content and a decrease in LPO level in irradiated animals. | [81,111] |
| 23. | **Immuno-stimulant activity** | Ethanolic extract of the leaves | 500 mg/kg | Swiss albino mice | Protection against *E. coli* induced abdominal peritonitis, increase in blood lymphocytes, total WBC, splenic lymphocytes and peritoneal macrophages was observed. | [112] |
| | | Methanolic extract of plant | 200 mg/kg | Mice | Increase in the WBC count to 16 % and significant protective effect against cyclophosphamide induced myelosuppression upto 80 % were observed. | [113] |
| 24. | **HIV-Protease inhibitor activity** | Crude extract of whole plant | – | Pepsin assay | *A. Vasica* exhibited pot inhibitory activity of enzyme Pepsin. | [114] |
| 25. | **Anti-typhoid activity** | Leaves: methanolic extract | 2.50 mg/mL | *Salmonella typhi* | Methanolic extract proved effective against *Salmonella typhi* as an antityphoid agent. | [115] |
| 26. | **Renal protective activity** | Leaves: ethanolic extract | 1000–5000 mg/ kg | Albino rats with gentamicin-induced nephrotoxicity | Prevention in elevated serum creatinine and serum urea level and significant reduction in elevated level of urinary protein in albino rats. | [115] |
| 27. | **Muscle stimulant activity** | Vasicine | 1 &10 g/mL | Isolated uterus and mammary gland of rat/guinea pig. | Increase in amplitude of contractions in uterus, | [116] |

(*continued on next page*)

Table 2 (*continued*)

| S. No | Pharmacological activities | Parts/extracts/ possible chemical constituents | Effective dose range | Test system for activity | Result | References |
|---|---|---|---|---|---|---|
| | | | | | potentiated the action of oxytocin in mammary strip. | |
| 28. | **Anticestodal activity** | Whole plant: extract | 800 mg/kg | Hymenolepis diminuta-rat experimental model | The reduction in eggs per gram count of 79.57 % and the percentage worm recovery rate of 16.60 % indicated that Adhatoda has anticestodal action. | [117] |
| 29. | **Anti-Alzheimer activity** | Whole plant | 294 μg/mL | *in vitro*: acetylcholinesterase (AChE) and cycloxygenase-1 (COX-1) enzymes | *Adhatoda vasica* showed inhibitory effect on AChE at $IC_{50}$ 294 μg/mL. | [118] |
| 30. | **Analgesic activity** | Methanolic extract of leaves | 200,400,600 mg/kg | Hot plate and tail immersion method in albino rats | Significantly ($P < 0.05$) inhibit the inhibition and pain in rats. | [91] |
| 31. | **Anthelmintic activity** | Aqueous and ethanolic extracts of aerial parts | 25–50 mg/mL | Gastrointestinal nematodes of sheep | The gastrointestinal nematode egg hatching and larval growth was inhibited more effectively by ethanolic extract at 50.0 mg/mL ($P < 0.05$). | [119] |
| 32. | **Antioxidant activity** | Vasicine acetate | 125–1000 μg/mL | 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay | Vasicine acetate had the highest radical-scavenging efficiency (66.15 %) at a concentration of 1000 μg/mL. | [120] |
| | | Ethanolic extract of leaves | 25–150 μg/mL | 1,1-diphenyl-2-picrylhydrazyl (DPPH) Radical Scavenging Assay | 69.23 % inhibition of the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical was observed. | [121] |

Ethno-medicinal uses of *A. vasica* have been described in Table 1.

Folks and tribes have been using *A. vasica* to cure ailments and diseases, thus, it would be interesting to explore inception time of usage the plant for medicinal purposes to have better understanding of significance of *A. vasica.*

## 3. Pharmacology

Over the past decades, numerous researchers have investigated the pharmacological activities of *A. vasica*. Summary of the pharmacological properties is given in Table 2.

The details enumerated above in the table is indicative of the fact that the different plant parts demonstrate large number of pharmacological activities. As major number of activities have been conducted at the extract level, the possibilities and scope for further research is widened, viz through the identification of the active phytoconstituents responsible for the activities, conduction of clinical trials to validate the use of specific phytoconstituents like vasicine, vasicine acetate etc for their manifold therapeutic activities, comparison with prevailing drugs to assess the efficacy, and preparation of synthetic modification of compounds to enhance efficacy and reduce toxicity.

### *3.1. Bronchodilatory and antiasthmatic activities*

Both *in vivo* and *in vitro*, vasicine and vasicinone exhibited bronchodilatory activity [97]. Bronchodilating effect of ethanolic extract of *Adhatoda vasica* was tested on histamine aerosol and acetylcholine induced broncho-constriction in guinea pigs. The broncho-dilating effect of *A. vasica* was found similar to ketotifen [79]. Hence, pyrrolo-quinazoline compounds like vasicine and vasicinone exerted potential antiasthamatic activity.

### *3.2. Wound-healing activity*

Wound healing effect of methanolic, chloroform and diethyl ether extract ointment (10%w/w) of *Adhatoda vasica* was evaluated using excision wound model in albino rats. The methanolic extract ointment (10%w/w) showed significant effect as compared to the standard drug [99]. The chloroform and alcoholic extracts of *Adhatoda vasica* were also studied for wound healing potential on male buffalo calves. Increase in tensile strength, breaking strength, collagen, elastin and hydroxyproline etc. were observed [100]. Hence, *Adhatoda vasica* exerted potential wound healing activity.

### 3.3. Antiallergic activity

Some studies showed that alkaloids vasicinol and vasicine can inhibit significantly ovalbumin-induced allergic reactions [81]. Vasicinone has also proved to be efficient anti-allergen when studied on mice, guinea pigs and rats [82]. Compound 73/602 (AA), which is a structural analogue of vasicinone, possesses potent antiallergic activity in mice, rats and guinea pigs [122].

### 3.4. Anti-inflammatory activity

Anti-inflammatory potential of non-alkaloid fraction, methanol extract, alkaloids and saponins was established using modified hen's egg chorioallantoic membrane test. Alkaloid fraction displayed influential activity, whereas the methanolic extract alongwith the other fractions exhibited less activity [90]. The anti-inflammatory activity of vasicine, vasicinone, vasicine acetate, 2-acetyl benzyl amine, vasicinolone was conducted on carrageenan and CFA model induced paw oedema. Vasicinone at the dosage of 10.0 mg/kg in 4 days followed by CFA injection exhibited maximum inhibition rate (63.94 %) and vasicine at a dose of 20.0 mg/kg at 6 h after carrageenan injection, presented most effective anti-inflammatory properties (59.51 %) [73].

Vasicine is a pyrrolo-quinazoline alkaloid found as large as 12 % in the alkaloid fraction of *Adhatoda vasica*, thus proving it to be a potential therapeutic agent against different inflammation mediated diseases [123]. The alkaloid fraction exercises effective anti-inflammatory activity by deciphering the regulation of protein expression of some pro-inflammatory cytokines, mRNA down regulation and NO production inhibition. Further, clinical therapeutics in this direction will bring it as a potential anti-inflammatory agent.

### 3.5. Antimicrobial activity

The antimicrobial activity of vasicine, vasicinone, vasicine acetate, 2-acetyl benzyl amine, vasicinolone was assessed by using the microdilution method. Vasicine exhibited strong antibacterial activity at 20 g/mL dose against *E. coli* and also showed maximum antifungal activity against *C. albicans* at the dose of 55 g/mL [73].

Both 2-acetyl benzylamine and vasicine acetate were bioassayed against *Mycobacterium tuberculosis* exhibiting significant inhibition of the *Mycobacterium species,* one sensitive and one MDR (multi-drug-resistant) strain at 50 and 200 μg/mL, respectively [74]. Pyrrolo-quinazoline like vasicine and vasicine acetate have the potential to be developed as potent antimicrobial agents of future.

### 3.6. Abortifacient activity

Vasicine also displayed uterotonic activity. A study showed that vasicine started rhythmic contractions of human myometrial strips from both pregnant and non-pregnant uteri, similar to that of oxytocin and mathergin [3]. Another more study revealed that vasicine exhibited uterotonic and abortifacient effects on hamsters, rabbits, rats, and guinea pigs, basically due to increased synthesis and release of prostaglandins [93]. Hence, further study should concern about the utility of *A. vasica* as herbal drug.

### 3.7. Immunostimulant activity

Effect of alcoholic extract of leaves of *Adhatoda vasica* on splenic lymphocytes, peritoneal macrophages and haematological profile were examined in swiss albino mice by Thakur. Increase in splenic lymphocytes, blood lymphocytes, total WBC and peritoneal macrophages was observed [112]. *Adhatoda* displayed protective effect against cyclophosphamide induced myelosuppression and marginal increase in WBC count to a significant extent [113]. These studies suggested that *Adhatoda vasica* showed immunostimulant activity.

### 3.8. Hepatoprotective activity

Aqueous extract of *A. vasica* leaves at doses of 50–100 mg/kg displayed effective hepatoprotective activity on D-galactosamine induced damged liver in rats [103]. Recent study showed that hepatotoxicity due to anti-TB drugs can be ameliorated by ethanolic leaf extract of Adhatoda vasica Nees [124]. Hence, *A. vasica* can effectively abolish drug mediated hepatic impairments.

### 3.9. Antitussive activity

Muscle relaxing activity of essential oil of aerial parts of *A. vasica* on tracheal vascular smooth muscle of guinea pigs had been carried out by Cruz [125]. Further antitussive activity of *A. vasica* extract was studied on unanaesthetized and anaesthetized guinea pigs and rabbits. Action was found similar to codeine. It was suggested that it may be attributed to specific site of action of vasicinone and vasicine, which act on neuronal system and thus suppress coughing [102]. Therefore, mechanistic studies should be focused in this direction.

### 3.10. Prevention of aflatoxin-induced toxicity

Chemopreventive effect of leaf extract *A. vasica* was studied on aflatoxin B1 induced biochemical changes in the serum and liver of

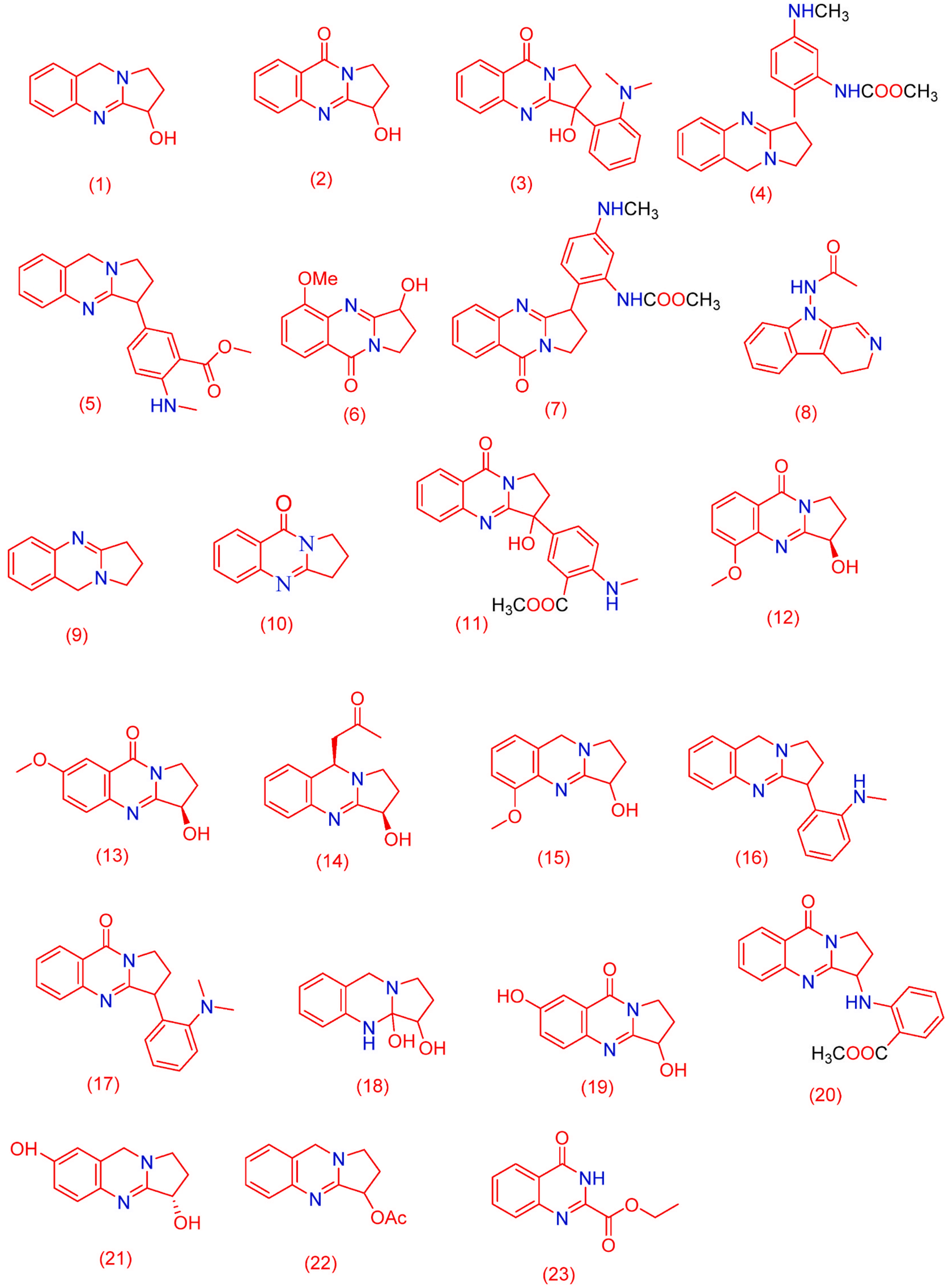
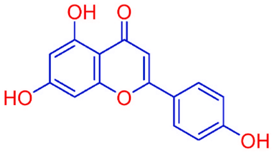



**Fig. 3.** Chemical structures of pyrroloquinazoline alkaloids.

Wistar rats. Its potential to be used in the poultry industry to lower aflatoxicosis was demonstrated by the significant reduction in the activities of catalase and superoxide dismutase in liver tissues, the increase in the activities of alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase, and the levels of cholesterol, VLDL, and LDL in blood serum [126].



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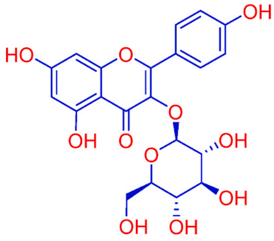

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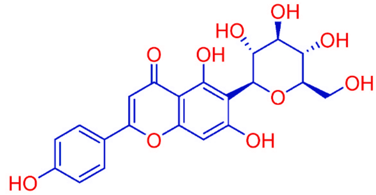

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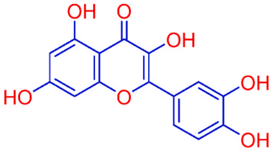

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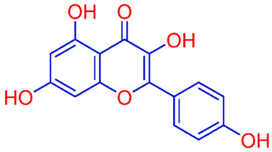

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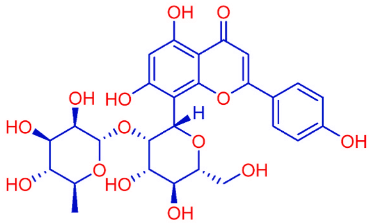

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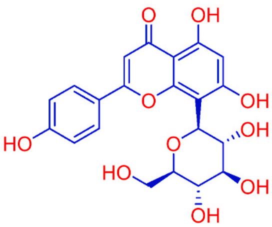

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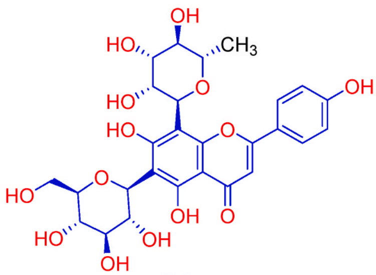

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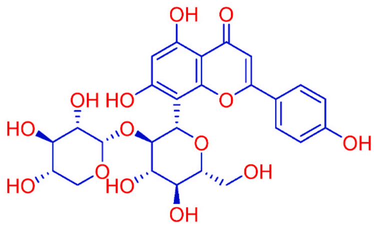

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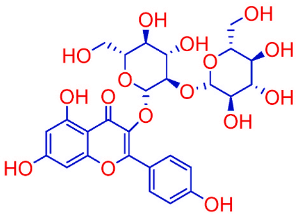

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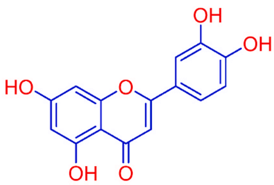


(34)

**Fig. 4.** Chemical structures of flavonoids.

### *3.11. Antibiotic property against fibroblasts*

Vizic acid, psacbumin C, 8′z-enzyme conjuger, 5- (8′z, 11′z-heptodecadinyl) −1,3-benzinol, 9 ’- (o-methyl) protocoteric acid and caliphenic acid isolated from *Adathoda vasica* were checked for their collagenase inhibition assay, elastase inhibition assay, hyaluronidase inhibition assay and tyrosinase inhibition assay by Ahmed et al. Their study revealed that the above isolated compounds can be used as novel antibiotics and can be further used in creams, lotions and tablets for future skin diseases control [127].

### *3.12. ACE inhibitory activity*

Recently molecular docking studies of isolated pyrroquinazoline alkaloids viz. vasicinol, vasicine and vasicinone were carried out by Tehreem et al. Vasicinol showed binding as effectively as captopril, a standard drug of ACE inhibition. Vasicine displayed the highest ACE inhibitory activity and its $IC_{50}$ was 2.60 mM. The $IC_{50}$ values of vasicinol and vasicinone were found to be 6.45 and 13.49 mM, respectively [128].

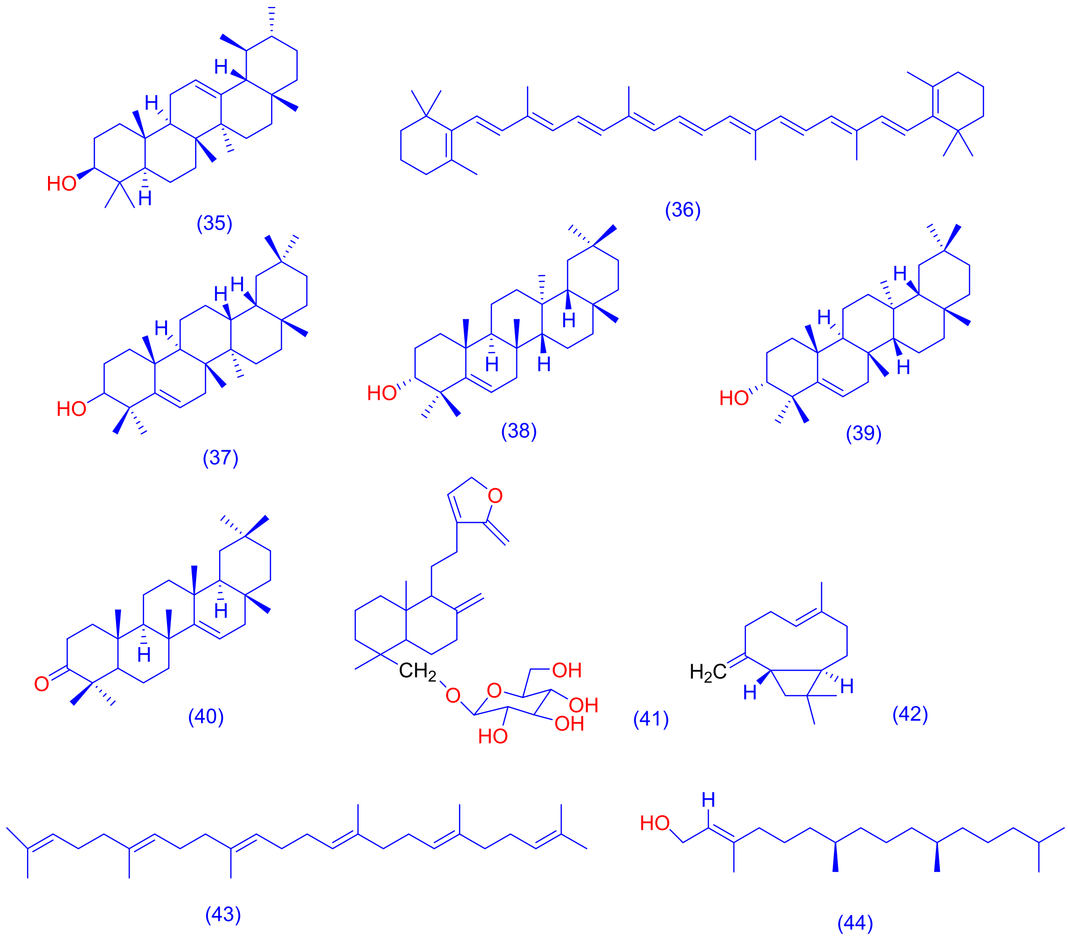


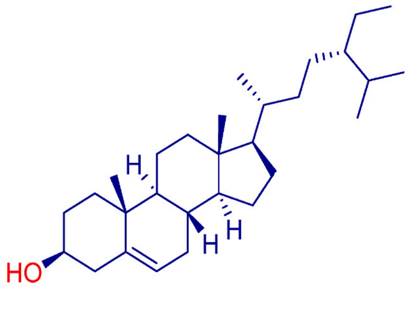

**Fig. 5.** Chemical structures of terpenoids.

### *3.13. Anti- Alzheimer activity*

Anti-AChE activity was performed to elicit the possible role of the active compounds in the treatment of Alzheimer disease. Docking was carried out using a flexible ligand–rigid protein. Vasicine showed binding similar to tacrine and galantamine in the catalytic site and inhibited AChE reversibly and competitively with a Ki (inhibition constant) value of 11.24 μM, but vasicinone, vasicole, and anisotine shown weak or no binding. As a result, it can be utilized directly or indirectly to create effective anti-Alzheimer drugs [118].

### *3.14. Potential as repurposed drugs for COVID-19 like conditions*

Recent studies by Gheware and coworkers [129] revealed that the aqueous extract of *Adhatoda vasica* (AV) can ameliorate the hyperinflammation and hypoxic features like thrombosis, lung injury and fibrosis, thus highlighting this herbal medicine as a potent repurposed drug for COVID-19 like conditions. The AV extract has beneficial effects on systemic inflammation and phenotypic features of the lungs, sounding the extracts to be useful for the COVID-19 pandemic situations. **Anisotine** and **vasicoline** of AV are found to be very good inhibitors when tested on protease inhibitor and replicase inhibitor of COVID-19 virus using COVID-19 Docking Server [130]. Six well-known alkaloids from AV were docked against SARS CoV-2 Mpro to study their binding properties. Only anisotine interacted with both the catalytic residues (His41 and Cys145) of Mpro and exhibited good binding affinity (−7.9 kcal/mol), thus revealing anisotine's potency to inhibit the proteolytic activity of SARS CoV-2 Mpro [131]. In another study, Adhatodine and vasnetine showed a binding affinity of −9.60 kJ/mol and −8.78 kJ/mol, respectively when docked with SARS-CoV-2 main protease (PDBID:6Y84), viral protein targets [132]. Recently the first clinical evidence of HIF-1 reduction in COVID-19 patients receiving AV herbal extract treatment established the potential of AV to be safe and efficacious interventions for COVID-19 [133]. The *in-vitro* and in-silico analysis strongly suggest that it may have the ability to inhibit the SARS-CoV2 infection and its progression sequelae, thus AV being relevant treatment to the global pandemic of the microscopic demon COVID-19.



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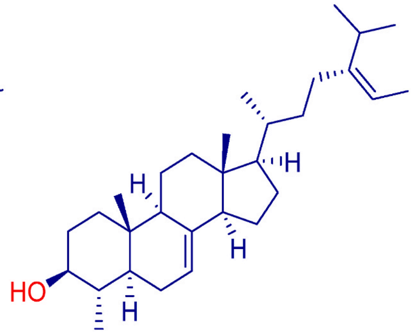

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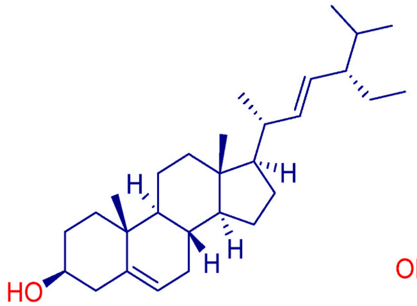

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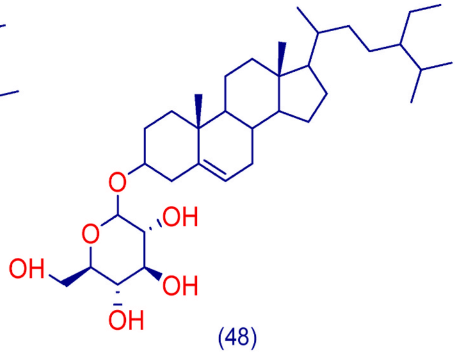

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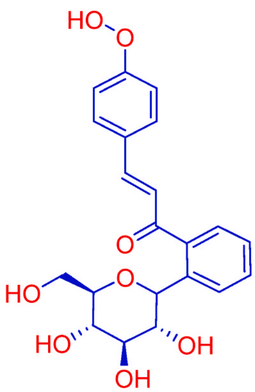
**Fig. 6.** Chemical structures of steroids.



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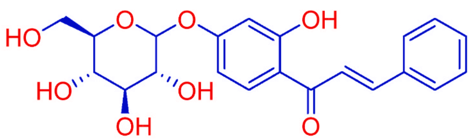

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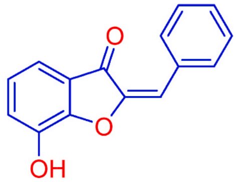

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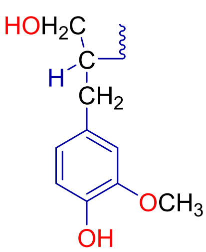
**Fig. 7.** Chemical structures of chalcones.

## 4. Major milestone of Adosa chemistry

A number of pyrroloquinazoline alkaloids have been discovered from this plant. D. Hooper in 1888 first isolated the alkaloid vasicine. According to him the alkaloid occurs in the leaves as a salt with “adhatodic acid” [134]. Leaves of this plant has two major quinazoline alkaloid, vasicine and vasicinone [135]. Vasicine is one of the major bioactive alkaloid, present in the concentration of 1.3 %. Pharmacological investigations of vasicine showed bronchodilatory activity *in vitro* and *in vivo* both; while vasicinone showed only *in vitro* bronchodilatory activity [97]. Later in 1965, Inamdar et al. isolated a neutral, non-nitrogenous crystalline material *viz*. vasakin, which melts at 273–274° C with decomposition. Its pharmacological studies revealed that it obstructs the functioning of exogenous adrenaline, moreover it had local anesthetic activity, so it resembled atropine. But it varied from atropine as it depresses heart and was found to be nontoxic at higher doses [136]. In 1967, Huq et al. isolated β-sitosterol, tritricontane, adhatonine, anisotine, vasicinine,



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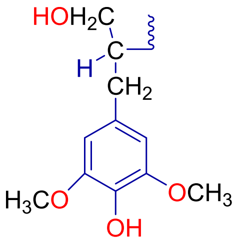

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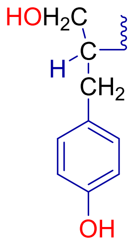

(54)

**Fig. 8.** Chemical structures of lignins.

vasicine and vasicinone from the leaves of this plant. Other alkaloids such as vasicinone, vasicinol, adhatodinine, adhavasinone, vasicoline and vasicolinone [137–142] have been isolated from its leaves and roots.

A new quinazoline alkaloid 1,2,3,9-tetrahydro-5-methoxypyrrolo [2,1-b]-quinazolin-3-ol was isolated from its leaves [141]. Flavonoids like isovitexin, astragaline, kaempferol, quercetin, as well as the triterpenoid $\alpha$-amyrin have been detected from its flowers [137]. Dihydroxychalcone 4-glucoside was also isolated from the flowers of *Adhatoda vasica* in 1982 [142]. In addition to these, *A. vasica* also contains several other phytochemicals and miscellaneous compounds, as these are present in complex mixture. These discrepancies suggest that re-investigation of the chemical constituents of *A. vasica* will provide interesting information regarding the phytochemistry.

## 5. Compounds present in *Adhatoda vasica*

It is essential to identify which secondary metabolites are present in plant as it may provide a basis for its traditional uses. In more than 80 years of intensive research, a number of compounds have been isolated from different parts of the plant. Alkaloids are one of the major secondary metabolites, which are present in the form of pyrrolo-quinazoline derivatives (Fig. 3). In addition to these, Adosa also contains several other phytochemicals such as flavonoids (Fig. 4), terpenoids (Fig. 5), steroids (Fig. 6), chalcones (Fig. 7), lignins (Fig. 8), glucoside and galactoside, amino acids, phenolic acids, fatty acids, and other miscellaneous compounds. Here we have tabulated molecular formula and the part from which these compounds were isolated in Table 3.

Some recent studies also showed that ethyl acetate extract of *Adhatoda vasica* helps to maintain the redox homeostasis of hepatic cells hence it can be well-thought-out as an effective candidate against liver disorders due to oxidative stress [173]. Another study showed that pyrroquinazoline alkaloids like vasicine, vasicinone and deoxyvasicine have 5-LOX inhibitory potential [174]. All studies suggested that this plant is rich source of pyrroloquinazoline derivatives and their pharmaceutical applications prove that these candidates have the potential to develop as drugs. It is necessary to study the structure activity relation of the active chemical constituents for discovery and design of novel drugs with improved efficacy from traditionally vital natural products/plant *Adhatoda vasica.*

## 6. Conclusion and future directions

The present review summarizes the traditional importance, folklore uses, research progress in pharmacology and phytochemistry, importance in Ayurvedic and Unani medicinal systems, and scope for future research related to *Adhatoda vasica.* This plant has been used for a variety of disorders including; cold, cough, asthma, whooping cough, chronic bronchitis, heart troubles etc. Merit of many of therapeutic applications relates to important alkaloids of AV *viz.* vasicine, vasicinol, anisotine etc. After reviewing we came across the following areas where further research can be supervised. (1) Investigation regarding inception time of traditional uses. (2) Further in-depth clinical trials of important pharmacological activities *viz* anti-asthamatic and bronchodilatory. (3) Analysis of the structure activity relationships of pyrrolo-quinazoline alkaloids. In view of its multiple uses, more activity screening and structure-activity relationship studies are to be explored. (4) Many scientific reports suggested that vasicine has abortifacient and oxytocic effects. Therefore, further research may be focused on toxicity and safety of *A. vasica* as an herbal medicine. (5) Recent studies reveal that AV has potential to be developed as repurposed drugs for COVID-19 like conditions, further clinical trials can be carried out in this direction as WHO has declared JN.1 covid variant as variant of interest. (6) Synthetic modification of the compounds having important therapeutic activities like vasicine, vasicinol and anisotine can be conducted to increase their efficacy. (7) As this plant represents a class of herbal drugs with very strong conceptual or traditional as well as a strong experimental base for its use without any harm in human beings, hence it would be a matter of interest for chemists to isolate potent bioactive compounds from Adosa as a potential phyto-pharmaceutical agent for preventing ailments. *Adhatoda vasica* being biologically rich in pyrroloquinazoline alkaloids develops possibilities for further research through *in vivo* and *in silico* studies to confirm the therapeutic usefulness or medication potency of these bioactive compounds. The review validates the ethnomedicinal, phytochemical and pharmacological significance of *Adhatoda vasica* in management of different ailments in humans.

**Table 3**
Compounds isolated from *A. vasica*.

| S.No. | Compound name (Molecular formula) | Plant part & References |
|---|---|---|
| Pyrroloquinazoline alkaloids rowhead | | |
| 1 | Vasicine or Peganine ($C_{11}H_{12}N_2O$) | Roots [143], Young plants [139], Leaves, Part not specified [144,145] |
| 2 | Vasicinone ($C_{11}H_{10}N_2O_2$) | Aerial parts [146], Leaves [ [135,147–149]], Part not specified, Roots [150] |
| 3 | 1,2,3,9-tetrahydropyrrolo (2,1-b) quinazolin-9-one-3R hydroxy- 3 (2 dimethyl-amino) phenyl or Desmethoxyaniflorine ($C_{19}H_{19}N_3O_2$) | Leaves [151] |
| 4 | Adhatodine ($C_{21}H_{26}N_4O_2$) | Roots [143], Young plants [139], Leaves [ [152,153]] |
| 5 | Adhatonine ($C_{20}H_{21}N_3O_2$) | Leaves [147] |
| 6 | Adhavasinone ($C_{12}H_{12}N_2O_3$) | Leaves [141] |
| 7 | Anisotine ($C_{20}H_{20}N_4O_3$) | Roots [143], Young plants [139], Leaves [ [147,153]] |
| 8 | 9-Acetamido-3,4-dihydropyrido-(3,4-*b*)-indole ($C_{13}H_{13}N_3O$) | Roots [154] |
| 9 | Deoxyvasicine ($C_{11}H_{12}N_2$) | Leaves [142] |
| 10 | Deoxyvasicinone ($C_{11}H_{10}N_2O$) | Roots [154] |
| 11 | 3-Hydroxyanisotine ($C_{20}H_{19}N_3O_4$) | Leaves [153] |
| 12 | 5-Methoxy-vasicinone ($C_{12}H_{12}N_2O_3$) | Leaves [151] |
| 13 | 7-Methoxy-3*R*-hydroxy-1,2,3,9-tetrahydropyrrolo-[2,1-*b*]-quinazolin-9-one (7-methoxy-vasicinone) ($C_{12}H_{12}N_2O_3$) | Leaves [151] |
| 14 | Peganidine ($C_{14}H_{16}N_2O_2$) | Aerial parts [151] |
| 15 | 1,2,3,9-Tetrahydro-5-methoxy-pyrrolo [2,1-b] quinazoline-3-ol ($C_{12}H_{14}N_2O_2$) | Leaves [140] |
| 16 | Vasicoline ($C_{19}H_{21}N_3$) | Leaves [152]; Young plants [139] |
| 17 | Vasicolinone ($C_{19}H_{19}N_3O$) | Leaves [152]; Young plants [139] |
| 18 | Vasicol (1,2,3,4,9, 11-hexahydropyrrolo (2,1-b) quinazolin-3,11-diol, ($C_{11}H_{14}N_2O_2$) | Leaves [145]; Roots [150]; Leaves [153] |
| 19 | Vasicinolone ($C_{11}H_{10}N_2O_3$) | Roots [154]; Leaves [142]; Aerial parts [155] |
| 20 | Vasnetine ($C_{19}H_{17}N_3O_3$) | Leaves [153] |
| 21 | Vasicinol or 7-Hydroxypeganine ($C_{11}H_{12}N_2O_2$) | Roots [143]; Leaf [88] |
| 22 | Vasicine acetate ($C_{13}H_{14}N_2O_2$) | Roots [75] |
| 23 | Ethyl 4-quinazoline-2-carboxylate ($C_{11}H_{10}N_2O_3$) | Leaves [156] |
| **Flavonoids** rowhead | | |
| 24 | Apigenin ($C_{15}H_{10}O_5$) | Aerial parts [157] |
| 25 | Astragalin or Kaempferol 3-β-D-glucopyranoside ($C_{21}H_{20}O_{11}$) | Flowers [147] |
| 26 | Isovitexin ($C_{21}H_{20}O_{10}$) | Leaves and Flowers [157] |
| 27 | Quercetin ($C_{15}H_{10}O_7$) | Flowers [ [143,147,158]] |
| 28 | Kaempferol ($C_{15}H_{10}O_6$) | Flowers [ [143,147,158]] |
| 29 | Rhamnosylvitexin ($C_{27}H_{30}O_{14}$) | Flowers [143] Leaves and Flowers [157] |
| 30 | Vitexin ($C_{21}H_{20}O_{10}$) | Leaves and Flowers [157] |
| 31 | Violanthin ($C_{27}H_{30}O_{14}$) | Leaves and Flowers [157] |
| 32 | 2″ O-Xylosylvitexin ($C_{26}H_{28}O_{14}$) | Leaves and Flowers [157] |
| 33 | Kaempferol 3-*O*-sophoroside ($C_{27}H_{30}O_{16}$) | Flowers [159] |
| 34 | Luteolin ($C_{15}H_{10}O_6$) | Leaves and flowers [160] |
| **Terpenoids** rowhead | | |
| 35 | α-Amyrin ($C_{30}H_{50}O$) | Flowers [143,147,158] |
| 36 | β-Carotene ($C_{40}H_{56}$) | Part not specified [161] |
| 37 | 3α-Hydroxy-Oleanane-5-ene ($C_{30}H_{50}O$) | Aerial parts [162] |
| 38 | 3α -hydroxy-D-friedoolean-5-ene ($C_{30}H_{50}O$) | Aerial parts [146] |
| 39 | Epitaraxerol ($C_{30}H_{50}O$) | Leaves and Flowers [157], Aerial parts [146] |
| 40 | Taraxerone-14-ene ($C_{30}H_{48}O$) | Aerial parts [162] |
| 41 | Neoandrographolide ($C_{27}H_{42}O_7$) | Leaves [163] |
| 42 | Caryophyllene ($C_{15}H_{24}$) | Leaves [156] |
| 43 | Squalene ($C_{30}H_{50}$) | Leaves [156] |
| 44 | Phytol ($C_{20}H_{40}O$) | Leaves [156] |
| **Steroids** rowhead | | |
| 45 | β-Sitosterol ($C_{29}H_{50}O$) | Roots, Aerial parts [162] |
| 46 α-Sitosterol ($C_{29}H_{50}O$) Leaves [155] | | |
| 47 Stigmasterol ($C_{29}H_{48}O$) Leaves [155] | | |
| 48 Daucosterol ($C_{35}H_{60}O_6$) Roots [143] | | |
| **Chalcones** rowhead | | |
| 49 | 2′-Glucosyl-4-hydroxyl – oxychalcone ($C_{21}H_{22}O_8$) | Roots [143] |
| 50 | 2′,4-Dihydroxychalcone-4-*O*-β-D-glucopyranoside or 2′,4-Dihydroxychalcone 4-glucoside ($C_{21}H_{22}O_8$) | Flowers [142] |
| 51 | Hydroxyl oxychalcone ($C_{15}H_{10}O_3$) | Part not specified [164] |
| **Lignins** rowhead | | |
| 52 | Guaiacyl (polymer) | Wood [165] |
| 53 | Syringyl (polymer) p- Hydroxyl phenyl propane (polymer) | Wood [165] |
| 54 | | Wood [165] |

(*continued on next page*)

**Table 3** (*continued*)

| S.No. | Compound name (Molecular formula) | Plant part & References |
|---|---|---|
| **Glucoside and Galactoside** rowhead | | |
| 55 | Sitosterol-β-D-glucoside ($C_{35}H_{60}O_6$) | Roots [154] |
| 56 | Ethyl-α-D-galactoside ($C_8H_{16}O_6$) | Roots [154] |
| 57 | D-Glucoside ($C_6H_{12}O_6$) | Roots [143] |
| 58 | D-Galactose ($C_6H_{12}O_6$) | Roots [154] |
| 59 | β-glucoside-galactose ($C_{12}H_{22}O_{11}$) | Roots [6] |
| 60 | β-Sitosterol-D-glucoside ($C_{35}H_{60}O_6$) | Part not specified [6] |
| 61 | N oxide and glycoside of Vasicine ($C_{11}H_{12}N_2O_2$) | Aerial parts [166] |
| 62 | N oxide and glycoside of vasicinone ($C_{11}H_{10}N_2O_3$) | Aerial parts [166] |
| **Amino acid** rowhead | | |
| 63 | Betaine or vasicinine ($C_5H_{11}NO_2$) | Flowers [147] |
| 64 | Amino-*n*-butyric acid ($C_4H_9NO_2$) | Pollen [167] |
| 65 | Glycine ($C_2H_5NO_2$) | Pollen [167] |
| 66 | Proline ($C_5H_9NO_2$) | Pollen [167] |
| 67 | Serine ($C_3H_7NO_3$) | Pollen [167] |
| 68 | Valine ($C_5H_{11}NO_2$) | Pollen [167] |
| **Phenolic acids** rowhead | | |
| 69 | *p*-Hydroxybenzoic acid ($C_7H_6O_3$) | Leaves [168] |
| 70 | Syringic acid ($C_9H_{10}O_5$) | Leaves [168] |
| 71 | *p*-Coumaric acid ($C_9H_8O_3$) | Leaves [168] |
| **Fatty acids** rowhead | | |
| 72 | Pentadecanoic acid ($C_{15}H_{30}O_2$) | Leaves [156] |
| 73 | Arachidic acid ($C_{20}H_{40}O_2$) | Seeds [169] |
| 74 | Behenic acid ($C_{22}H_{44}O_2$) | Seeds [169] |
| 75 | Lignoceric acid ($C_{24}H_{48}O_2$) | Seeds [169] |
| 76 | Cerotic acid ($C_{26}H_{52}O_2$) | Seeds [169] |
| 77 | Oleic acid ($C_{18}H_{34}O_2$) | Seeds [169] |
| 78 | Linoleic acid ($C_{18}H_{32}O_2$) | Seeds [169] |
| 79 | 9,12,15-Octadecatrienoic acid ($C_{18}H_{30}O_2$) *n*- Hexadecanoic acid ($C_{16}H_{32}O_2$) | Leaves [156] |
| 80 | | Leaves [156] |
| **Alkanones** rowhead | | |
| 81 | 3-Methylheptanone ($C_8H_{16}O$) | Flowers [164] |
| 82 | 4-Heptanone ($C_7H_{14}O$) | Flowers [164] |
| **Hydrocarbon** rowhead | | |
| 83 | Tritriacontane ($C_{33}H_{68}$) | Roots [139] |
| 84 | 2-Cyclohexyl-eicosane ($C_{26}H_{52}$) | Leaves [156] |
| **Alkyl Hydroxyketones** rowhead | | |
| 85 | 37-Hydroxy-hexatetracont-1-en-15-one ($C_{46}H_{90}O_2$) | Aerial parts [155] |
| 86 | 37-Hydroxy-hentetracontan-19-one ($C_{41}H_{82}O_2$) | Aerial parts [155] |
| **Vitamin** rowhead | | |
| 87 | Vitamin C ($C_6H_8O_6$) | Part not specified [161] |
| **Alkanol** rowhead | | |
| 88 | 29-Methyl -triacontan-1-ol ($C_{31}H_{64}O$) | Aerial parts [162] |
| 89 | 2,4- Dihydroxynonane ($C_9H_{20}O_2$) | Aerial parts [170] |
| **Others** rowhead | | |
| 90 | 2-Acetyl benzyl amine ($C_9H_{11}NO$) | Roots [75] |
| 91 | 1,3,5-Triazine-2,4,6-triamine ($C_3H_6N_6$) | Leaves [171] |
| 92 | 2,3-Dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one ($C_6H_8N_4$) | Leaves [171] |
| 93 | 5-Hydroxymethylfurfural ($C_6H_6O_3$) | Leaves [171] |
| 94 | 2-Butylphenol ($C_{10}H_{14}O$) | Leaves [171] |
| 95 | 3,4-Dihydroxy-5-methyl-dihydro-furan-2-one ($C_5H_8O_4$) | Leaves [171] |
| 96 | 2–(1,1-Dimethylethyl)-4-methoxyphenol ($C_{11}H_{16}O_2$) | Leaves [171] |
| 97 | Megastigmatrienone ($C_{13}H_{18}O$) | Leaves [171] |
| 98 | Tetradecanoic acid ($C_{14}H_{28}O_2$) | Leaves [171] |
| 99 | Vomifoliol ($C_{13}H_{20}O_3$) | Leaves [171] |
| 100 | Oxalic acid, cyclobutylhexyl ester ($C_{12}H_{20}O_4$) | Leaves [171] |
| 101 | Hexadecanoic acid ($C_{16}H_{32}O_2$) | Leaves [171] |
| 102 | 4-Ethyl-2-oxo-2,5,6,7-tetrahydro-1H-cyclopenta [B]pyridine-3-carbonitrile ($C_{11}H_{12}N_2O$) | Leaves [171] |
| 103 | Vitamin E ($C_{29}H_{50}O_2$) | Leaves [171] |
| 104 | 1,2,3-Trimethyl benzene ($C_9H_{12}$) | Leaves [72] |
| 105 | Borneol ($C_{10}H_{18}O$) | Leaves [72] |
| 106 | Ethanonaphthalene ($C_{12}H_{10}$) | Leaves [72] |
| 107 | 1,1,4a-Trimethyl-5,6-dimethylenedecahydronaphthalene ($C_{15}H_{24}$) | Leaves [72] |
| 108 | 2-Tert-butyl-1,4-dimethoxybenzene ($C_{12}H_{18}O_2$) | Leaves [72] |
| 109 | α-Caryophyllene ($C_{15}H_{24}$) | Leaves [72] |
| 110 | Caryophyllene oxide ($C_{15}H_{24}O$) | Leaves [72] |
| 111 | 2-Naphthalenemethanol ($C_{11}H_{10}O$) | Leaves [72] |
| 112 | Stictic acid ($C_{19}H_{14}O_9$) | Plant parts [172] |

(*continued on next page*)

**Table 3** (*continued*)

| S.No. | Compound name (Molecular formula) | Plant part & References |
|---|---|---|
| 113 | Usnic acid ($C_{18}H_{16}O_7$) | Plant parts [172] |
| 114 | Epigallocatechin gallate ($C_{22}H_{18}O_{11}$) | Plant parts [172] |
| 115 | Epigallocatechin ($C_{15}H_{14}O_7$) | Plant parts [172] |
| 116 | Catechin ($C_{15}H_{14}O_6$) | Plant parts [172] |
| 117 | Epicatechin ($C_{15}H_{14}O_6$) | Plant parts [172] |
| 118 | Morin ($C_{15}H_{10}O_7$) | Plant parts [172] |
| 119 | Naringenin ($C_{15}H_{12}O_5$) | Plant parts [172] |
| 120 | Viscic acid ($C_5H_{10}O_2$) | Leaves and seeds [172] |
| 121 | Pasakbumin ($C_{20}H_{24}O_9$) | Leaves and seeds [172] |
| 122 | 8′Z-Enyl congener ($C_{18}H_{16}O_7$) | Leaves and seeds [172] |
| 123 | 5-(8′Z,11′Z-heptadecadienyl)-1,3- benzene diol ($C_{23}H_{34}O_2$) | Leaves and seeds [172] |
| 124 | 9’-(*O*-Methyl) protocetraric acid | Leaves and seeds [172] |
| 125 | Calophynic acid ($C_{15}H_{10}O_7$) | Leaves and seeds [172] |

## Consent for publication

Not applicable.

## CRediT authorship contribution statement

**Poonam Khandelwal:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Barkha Darra Wadhwani:** Writing – review & editing. **Ravindra Singh Rao:** Writing – review & editing. **Deepak Mali:** Writing – review & editing, Investigation. **Pooja Vyas:** Writing – review & editing, Writing – original draft. **Tarun Kumar:** Writing – review & editing. **Rashmy Nair:** Writing – review & editing, Supervision.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Barkha Darra Wadhwani reports financial support was provided by India Ministry of Science & Technology Department of Science and Technology. Poonam Khandelwal reports administrative support was provided by Ministry of Education and SPD-RUSA Rajasthan. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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