# Overview of Phytochemistry and Pharmacology of *Adhatoda vasica*

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**Abstract**

Secondary metabolites obtained from traditional medicinal plants are known to play immortal roles in ancient and modern medicinal system. These compounds are ecofriendly and act as versatile source of agrochemicals and other drugs. Further, these compounds have shown numerous biological activities such as antiseptic, anti-asthmatic, diuretic, antispasmodic, antipyretic, diaphoretic, analgesic, sedative, fungicidal, herbicidal, insecticidal, insect repellent etc. So, in the present times new and efficient methodologies are needed to be developed for the production of drugs and agrochemicals of botanical origin. *Adhatoda vasica* commonly known as Vasaka in *Ayurveda* belongs to family Acanthaceae. This plant has been used in the indigenous system of medicine in India for over 2000 years. *A. vasica* is a good source of pyrroloquinazoline alkaloids such as vasicine, vasicol, adhatonine, vasicinone, vasicinol, vasicinolone etc., which are the chief constituents of different extracts of the plant. These compounds have shown many biological and pharmacological activities viz. anti-malarial, anti-inflammatory, antioxidant, antidiabetic, anti-bacterial, anti-cancer etc. Further, *Adhatoda* leaves have been used extensively in *Ayurvedic* medicine for the treatment of diarrhea, dysentery, tuberculosis, skin diseases, vomiting and leprosy etc. This paper reviews the phytochemical composition and pharmacological potential of *A. vasica.*

**Key words:** *Adhatoda vasica*, secondary metabolites, pyrroloquinazoline alkaloids, biological activities.

## 1. Introduction

Innumerable natural products with inherent potential biological activity procured from plants have played a significant role in improving the human health since the dawn of civilisation. As more than 50% of modern clinical drugs originate from natural products [1], therefore based on latter, the approach to new drug discovery and its development in the pharmaceutical industry has emerged significantly [2,3].

Medicinal plants, (rich bio-resources of drugs of traditional systems of medicines, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceuticals intermediates and chemical entities for synthetic drugs) naturally synthesize and accumulate biologically active secondary metabolites**,** like alkaloids, sterols, terpenes, flavonoids, saponins, anthraquinones, glycosides, tannins, resins, lactones, quinines, volatile oils etc. that have been extracted and used in different forms such as infusions, syrups, concoctions, decoctions, infused oils, essential oils, ointments and creams for the well being of human life [4,5,6]. Traditional medicine (Ayurveda, Unani, Homeopathy, Naturopathy, Sidha medicinal system), as old as the origin of man has been reported to be popular amongst more than two-third of the world population (mainly in the developing countries: WHO 80%) for primary health care [7,8,9].

A numerous families of medicinal plants exist, out of which Euphorbiaceae, Asteraceae, Labiatae, Fabaceae, Meliaceae and Solanaceae, Acanthaceae happen to be noteworthy. The metabolites extracted from the plants of these families show significant biological activities with a special mention of *Acanthaceae* family. Widely spread *Adhatoda*

*vasica (now Justicia Adhatoda) of* family *Acanthaceae* –a well-known drug plant in Ayurvedic and Unani medicine [10] has been known to possess enormous biological potential. The plant has been used in the indigenous system of medicine in India for more than 2000 years [11]. Different names for the plant in different regions/languages of India have been reported as: English (Arusa, adusa, rusa, baansa, adulsa), Hindi (Baansa, adulsa), Bengali (Basak, bakas), Gujrati (Aradusi, adulso), Kannada (Adusoge, kurchigida, pavate, bansa), Malayalam (Adalodakam), Manipuri (Nongmangkha-agouba), Marathi (Adulsa), Punjabi (Bhekkar, bansa, basuti), Tamil (Adhatadai, Pavettai), Telugu (Adasaramu), Kashmiri (Bahekar, baikar, bansuth, babading), Konkani (Adusogae), Sanskrit (Vasaka), Oriya (Arusa, basung), Sinhala (Pawatta) and Peasian (Bansa)

*Adhatoda vasica* - a small (1.0 m to 2.5 m height), dense, evergreen shrub with 10-15 cm long and 3-10 cm broad leaves, herbaceous woody stem, large and dense flowers, small and clavate fruit is widely distributed throughout the tropical regions of Southeast (Malaya and Singapore, Sri Lanka, Upper and Lower Myanmar, southern China, Laos, and the Malay-Peninsular and Indonesian Archipelago) [13,14,15,16]. In India the plant is distributed all over the plains, in lower Himalayan ranges, Punjab, Bengal and Assam [16].

Research performed over the last three decades has revealed that the alkaloids, vasicine and vasicinone (quinazoline ring derivatives) present in the leaves, possess respiratory stimulant activity whereas its roots contain vasicinolone, vasicol and peganine [17, 18]. Vasicine (1,2,3,9–tetrahydropyrrolo [2,1-b]quinazolin-3-ol, $C_{11}H_{12}N_2O$) also called Peganine [19]. Other chemical constituents of this plant include vasicinone (3–hydroxy–2,3-dihydropyrrolo[2,1–b]quinazolin–9(1H)–one, $C_{11}H_{10}N_2O_2$) (isolated from leaves, stem and roots) [20] and deoxyvasicinone (derived from leaves) etc. Recent investigations on vasicine showed bronchodilatory activity comparable to theophylline, both in vitro and in vivo. Both the alkaloids in combination showed pronounced bronchodilatory activity. Deoxyvasicinone

possesses antimicrobial, anti-inflammatory and antidepressant activities [21]. The botanical description of the plant is as follows: [22]

| | | |
|---|---|---|
| Kingdom | : | Plantae |
| Division | : | Angiosperms |
| Class | : | Eudicots |
| Order | : | Lamiales |
| Family | : | *Acanthaceae* |
| Genus | : | *Justicia* |
| Species | : | *Adhatoda (Adhatoda vasica)* |

**2. Traditional uses**

*Adhatoda vasica*, an ayurvedic medicinal plant has been used in various chest and respiratory track infection [23] viz.- whooping cough, chronic bronchitis, asthma and has been employed as sedative expectorant in the treatment of excessive phlegm (mucus with bacteria, debris, and sloughed-off inflammatory cells) and menorrhagia (abnormal blood clotting, disruption of normal hormonal regulation of periods, or disorders of the endometrial lining of the uterus) in Sri Lanka. It is also used for the treatment of bleeding piles, impotence and sexual disorders [24]. I, antispasmodic and anthelmintic drug [25]. Glycodin, which is a famous product used for the cure of bronchitis has been a product extracted from the leaves of *Adhatoda vasica*. It has also been reported that 70% of the pregnant women in the Gora village of Lucknow (Uttar Pradesh, India) use the leaves of plant to induce abortion [26]. Further, the extracts have been found to be quite effective against tuberculosis. Various parts of the plant have been used in Indian traditional medicine for the treatment of asthma, joint pain, lumber pain, sprains, cold, cough, eczema, malaria, rheumatism, swelling and venereal diseases [27].

**Roots:** In India paste of the fresh root applied on abdomen and vagina minutes before childbirth facilitates easy delivery [28,29]. The extract of roots of *Adhatoda vasica* has commonly been used by rural population against diabetes, cough and certain liver disorders

[30] whereas its paste has been used for curing tuberculosis, diphtheria, malarial fever, leucorrhoea, eye diseases, acute nightfall [(paste mixed with sugar) in Sitapur district, Uttar Pradesh, India] [31]. Further, the root's decoction has been used for gonorrhoea [31] and as an expectorant, antispasmodial / anthelmintic agent [32].

**Leaves:** The various preparations of leaves has been used for curing bleeding, hemorrhage, skin diseases, wounds, headache and leprosy (chronic infection) while their infusion or the solvent extract has been observed to be an excellent agent for the destruction of white ants, flies, and mosquitoes [33]. The fresh juice of leaves mixed with honey and ginger juice cures all types of acute cough, chronic bronchitis, breathlessness and liquefies sputum and asthma [34]. The extract obtained by decoction of its leaves along with fruit of *Phyllanthus emblica*, mixed with honey has been effective against asthma [35]. The crushed fresh leaves of the plant have been used to treat snake bites (India and Sri lanka) [36]. Macerated extract from leaves/ Yellow leaves/smoke from dry leaves acts against cough and phlegm blockage during cold (Bangladesh) and an infusion protects from headache (Myanmar and Pakistan) [37-40]. The leaf powder boiled in sesame oil stops bleeding, earaches as well as pus from ears and jaundice [41]. Leaf juice has been used as the best medicine to enhance platelet count during dengue like viral fevers, postpartum hemorrhage, urinary trouble, acidity and belching and its mixture with jaggery reduces excessive mensutrual flow get cured [42,43]. Externally warmed leaves have been used for rheumatic pains and dislocation of joint, stomach catarrh with constipation, rheumatism, gout, fever and urinary stone [44,45,46]. Juice made from the bark and leaves help against vomiting [47].

**Flowers:** The flowers have been known to possess expectorant and antiasthmatic, antiseptic properties [48] and have been used against of opthalmia, cold, phthisis, asthma, bronchitis, cough, antispasmodic, high fever and gonorrhoea. Also the fowers improve blood circulation and hectic heet of blood [49, 50, 51].

**Fruits:** Fruits of the *Adhatoda vasica* are four seeded capsules. In Pakistan, fruits of the plant are used for cold, antispasmodic and bronchitis [51]. The fruit of the plant are also used for Diarrhea, Dysentery, Fever and as laxative [36,49,50].

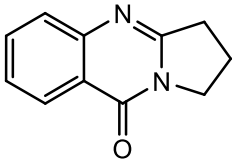
The some herbal preparation made from *Adhatoda vasica* which have been used for the treatment of different disorders are Kan Jang (used for alleviation of symptoms of cold, antitussive, mucolytic occasional and irritation of the respiratory track in Sweden), Spirote (used for alleviation of symptoms of colds, occasional cough in Sweden), Salus Tuss (used for dry cough, bronchitis, cold, smoker cough in Germany), Kada (used for Asthma in India) and Fermiforte (used for Leucorrhoea in India) [50]

**3. Phytochememical Composition**

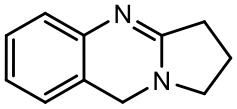
The chemical compounds found in *Adhatoda vasica* plant includes essential oils, fats, resins, sugar, gum, amino acids, proteins and vitamins 'C' etc [30]. The phytochemical analysis show that phenols, tannins, alkaloids, anthraquinone, saponins, flavonoids and reducing sugars were found in the leaves of plant [52]. But the pharmacologically most studied chemical component in plant is vasicine, a bitter quinazoline alkaloid, the novel alkaloid isolated leaves and characterized as 1, 2, 3, 9-tetrahydro- 5-methoxypyrrol [2, 1-b] quinazolin-3-ol [53]. It is present in the leaves, roots and flowers. Besides vasicine, the leaves contain several alkaloids (Vasicinone, Vasicinol, Adhatodine, Adhatonine, Adhvasinone, Anisotine and Hydroxypeganine), betaine, steroids and alkanes [54]. The leaves contain two major alkaloids called vasicine and vasicinone [19]. The pharmacological activities of vasicine and vasicinone are well known. Recent investigations on vasicine showed bronchodilatory activity comparable to theophylline, both in vitro and in vivo. Both the alkaloids in combination showed pronounced bronchodilatory activity. Vasicine also exhibits strong respiratory stimulant activity. There has also been a report of thrombopoetic4 (platelet increasing) activity with vasicine. Uterine stimulant activity and moderate hypotensive activity of the alkaloidshave been observed [53]. Vasicine is metabolized to vasicinone and analysis of plant

leaf extract showed that it contained 0.85% vasicine and 0.027% vasicinone. Sitosterol, β-glucoside-galactose and deoxyvasicine have been isolated from the roots of the plant [54]. 2'-4- dihydroxychalcone- 4-glucoside has also been recognized in the flowers [55]. Flowers of *Adhatoda vasica* mainly contain kaempferol and quercetin [56]. A new triterpenoid, 3 -hydroxy-D-friedoolean-5-ene, along with the known compounds, epitaraxerol and peganidine have been isolated from the aerial parts of *Adhatoda vasica Nees*. [57]. The leaves also contain a very small amount of an essential oil and a crystalline acid. An analysis published in India in 1956 showed the seeds as containing 25.8% of deep yellow oil composed of glycerides of arachidic 3.1%, be- henic 11.2%, lignoceric 10.7%, cerotic 5%, oleic 49.9% and linoleic acids 12.3% and β-sitosterol (2:6%) [58]. Elemental analysis using atomic absorption spectrophotometry revealed the presence of major (K, Na, Ca and Mg) and trace (Zn, Cu, Cr, Ni, Co, Cd, Pb, Mn and Fe) elements in *Adhatoda vasica* [59].

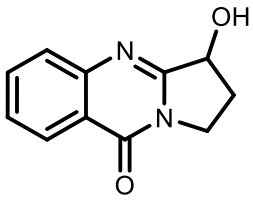
*Adhatoda vasica* mainly consists of alkaloids containing pyrroquinazoline ring derivatives like vasicine, vasicol, vasicinone along with other miner constituents. Vasicine is a major bioactive alkaloid of vasica which contain pyrroquinazoline ring.



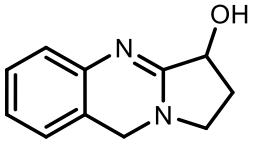
Deoxyvasicinone



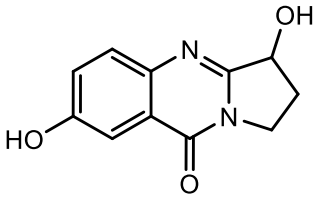
Deoxyvasicine



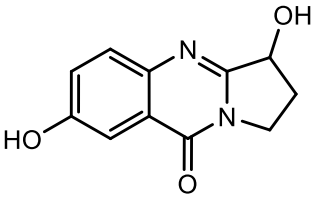
Vasicine



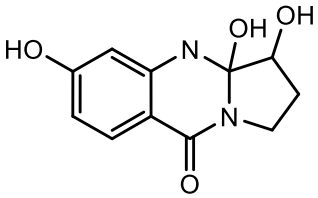
Vasicinone



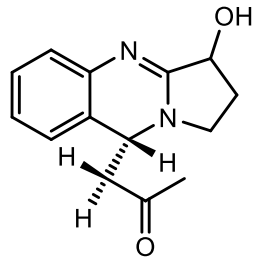
Vasicinolone



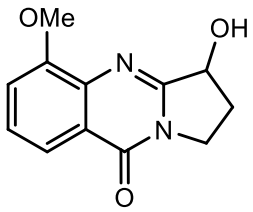
6- Hydroxyl peganine



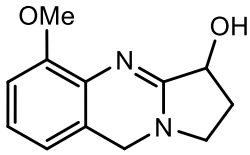
Vasicol



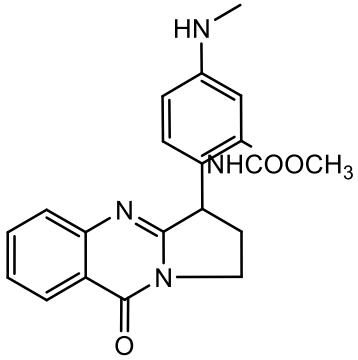
Peganidine



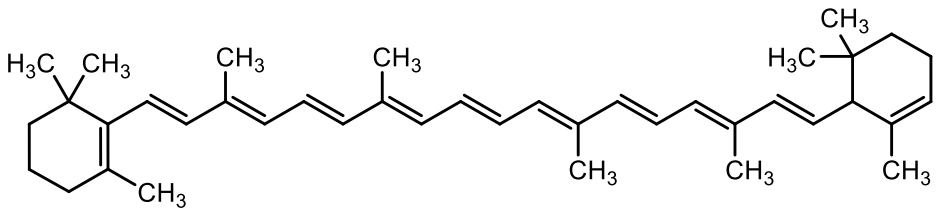
Adhavasinone



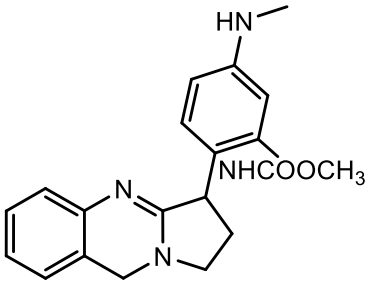
Adhavasicine



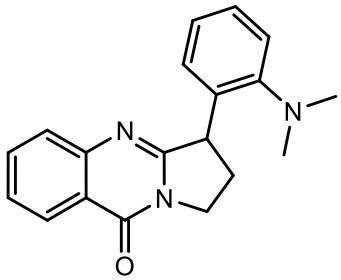
Anisotine



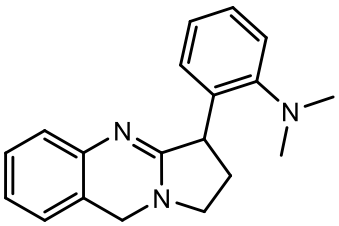
Carotene



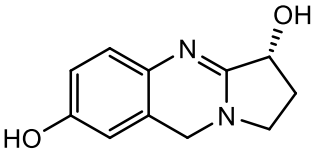
Adhatodine



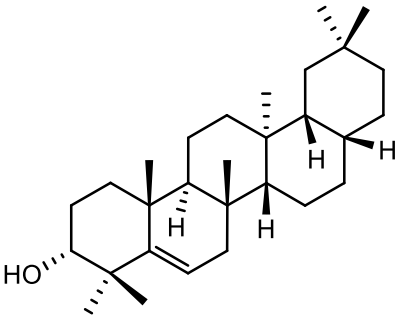
Vasicolinone



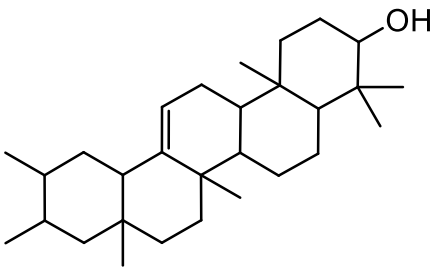
Vasicoline



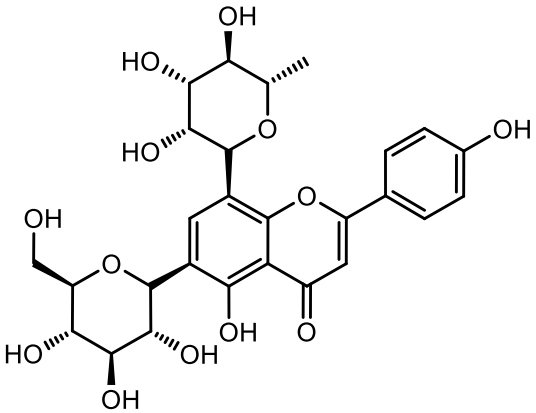
Vasicinol

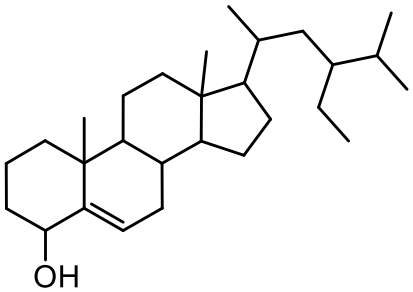


Epitaraxerol



Alpha-amyrin





Violathin Sitosterol

**Fig.-1: Structure of major chemical constituents of *Adhatoda vasica Nees***

**4. Biological activity (pharmacology)**

The medicinal properties of *Adathoda Vasica Nees* (Natural Order: Acanthaceae) have been known in India and several other countries for thousands of years. A few of the biological activities of the plant has been enumerated.

**Antibacterial Activity:** Water, ethanolic and petroleum ether extracts of Adhatoda leaves enriched with alkaloids, phenols, tannins and reducing sugars, main constituent vasicine etc. have been found to possess antibacterial activity (singularly or in combination) *against S. epidermidis, S. aureus B. subtilis, E. faecalis, E. coli, P aeroginosa, P. vulgaris, K. pneumoniae and C. Albicans* [68,63].

**Abortifacient Activity**: *Adhatoda* vasica possesses abortifacient and uterotonic properties (tested for different species including human beings), due to the presence of vasicine in its extracts.[69] The compound initiated rhythmic contractions of human myometrial strips from both non-pregnant and pregnant uteri with the effect which was comparable with that of oxytocin and mathergin [11]. The abortifacient effect on guinea pigs were more marked when estrogens were used as a priming influence, indicating that the actions of vasicine was probably enhanced by the synthesis and release of prostogladins [70].

**Anti- inflammatory Activity:** A dose of 50 μg/pellet alkaloid fraction (methanol extract), has been reported to be potent anti-inflammatory agent as was shown in modified hen's egg chorioallantoic membrane test [71].

**Antitussive and bronchodilatory Activity**: The leaves of *Adhatoda vasica* are mostly used in the treatment of respiratory ailments in Ayurveda. The two main alkaloids, vasicine and vasicinone present in the leaves, possess respiratory stimulant activity [72]. Vasicine, at low concentrations induces bronchodilation and relaxation of the tracheal muscle. However, at high concentrations, vasicine presented a significant protection against histamine-induced

broncho-spasm in guinea pigs. Leaf of *Adhatoda vasica* is an important drug of Ayurveda, prescribed as an expectorant. The plant extract shows the Antitussive activity against guinea-pig similar to that of codeine against coughing induced by irritant aerosols [73]. An herbal tea of an expectorant action was prepared with *Adhatoda vasica* leaves [74].

**Antiulcer Activity**: *Adhatoda vasica* also has immense potential as an anti-ulcer agent which is used to treat or ameliorate peptic ulcer or irritation of the gastrointestinal track of great therapeutic relevance. *Adhatoda vasica* leaf powder showed a considerable degree of anti-ulcer activity in rats with the highest degree of activity (80%) observed in the ulceration model induced by enthanol in comparison to pylorus and aspirin indiuced peptic ulcer (41%) [75].

**Anti-diabetic Activity:** The extracts of roots and leaves of *A. vasica* are commonly used by rural population against diabetes and certain liver disorders [76]. The methanolic extract from the leaves of *A. vasica* (Acanthaceae) showed excellent sucrase inhibitory activity with sucrose as a substrate [63]. A different study by highlights the role of vasicine which is the main constituent of the plant, in sucrose metabolism. Epidemiological studies and clinical trials strongly support that, control of hyperglycemia is critical in treatment of not only, diabetic patients but also, persons with impaired glucose acceptance. This current report explains that, vasicine can also act as irreversible α-glucosidase (sucrose). Thus, *A. vasica* can be explored as a potent natural antidiabetic agent.

**Antioxidant Activity**: The significant characteristic of an antioxidant is its potential to trap free radicals generated in the body. These free radicals may oxidize proteins, lipids or nucleic acids and can initiate verious degenerative disease. All *A. vasica* plant extracts showed antioxidant potential (337µg/ml). Besides this, the antioxidant, antidiabetic and antibacterial activity of various extracts of *Adhatoda vasica* has also been investigated. Among hexane, chloroform and methanolic extracts of the plant, the methanolic extract had shown to have maximum antioxidant activity and blood cholesterol lowering activity. *Adhatoda vasica* also

shows the antioxidant and anti-clastogenic efficacy against cadmium chloride ($CdCl_2$) induced renal oxidative stress and genotoxicity induced by cadmium chloride ($CdCl_2$) in Swiss albino mice supports its anti-mutagenic efficacy [72].

**Muscle relaxant activity:** An essential oil from the leaves of vasica showed smooth muscle relaxant activity in the isolated guinea-pig tracheal chain. Vasicine from the plant *Adhatoda vasica* has stimulatory effects on rat/guinea pig uterus and tracheal muscle as well as, on other tissues [78].

**Anti-allergic Activity:** A methanolic extract from the entire plant has been shown to possess anti-allergic activities in the guinea- pig after inhalation or intragastric administration at doses of 6 mg per animal or 2.5 gm/kg, respectively [67]. A structural analogue of vasicinone, an alkaloid present in the leaves and roots of Adhatoda vasica (Acanthaceae) possesses potent anti-allergic activity in mice, rats and guinea pigs. A plant extract containing the alkaloid vascinol and 20% vasicine inhibited allergic reactions induced by oval bumin about 37% at a concentration of 5 mg [79]. Vasicinone has been shown to be a potent anti-allergen in tests on mice, rats and guinea pigs [80].

**HIV-Protease inhibitor activity**: The crude extracts of *Adhatoda vasica* plant exhibited powerful inhibitory activity of pepsin enzyme thus it might be a effective inhibitor of HIV-Protease which belongs to same family of enzyme aspartate and sharing same signature group at the active site [76].

**Heptoprotective Activity**: *Adhatoda vasica* was reported to be hepatoprotective and, it is believed to be based on its antioxidant property [82]. Various leaf extracts of the plant *Adhatoda vasica* contains biologically active phytoconstituents such as Alkaloids-Quinazoline, Flavonoids, Tannins, Vasicinone, Essential oil which are accountable for the significant hepatoprotective activity [83].

**Cardioprotective Activity**: Combination of vasicine and vasicinone from the leaf extract of the plant significant reduction in cardial depressant effects was observed. No effect was

shown by DL-form of vasicinone, however L- form was found to be effective stimulating cardiac muscles weakly [11].

**Toxicity:** *Adhatoda* is said to be non-poisonous to mammals, but to kill all forms of lower life like fish, insects, and lower organisms [49, 84, 85].

Apart from above activities, Anti-cancer Activity, Radio protecter activity [86, 87], Anti-mutagenic activity [77], Anti-Tubercular Activity [88, 79], Antipyretic Activity [89, 90] and Anticholinesterase [91] were also shown by the plant *A. vasica*.

## 5. Conclusion

It has been revealed from the literature that the quinazoline based alkaloids have been the major constituents present in the different parts of *A. vasica*, which have been mainly responsible for their wide range of pharmacological potential. *A. vasica* has been an important medicinal herb well known for its applications in different traditional medicinal system such as Ayurveda, Siddha and Unani etc. *A. vasica* also showed many pharmacological activities *Viz.* hepatoprotective, antiulcer, abortifacient, antiviral, anti-inflammatory, thrombolytic, antibacterial, antifungal, radiomodulation, hypoglycaemic, antitubercular, antioxidant and antitussive. Owing to its wide range of biological activities it may act as an important source for the discovery of new and potent drug molecules.

Thus, the current review would be helpful in the advancement of today's research in the development of new novel bioactive compounds derived from medicinal plants which would find a large number of applications in pharmaceuitical, cosmatics and agricultural fields.

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