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# A Review on Therapeutic Potential of *Justicia adhatoda* L.

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***Abstract*: *Justicia adhatoda* L. has been used in the indigenous system of medicine for more than 2000 years. It is distributed throughout tropical and sub-tropical parts of India. It is well-known for its beneficial properties. It is an exclusive herb that helps in improving the bronchial function with bronchodilatory, expectorant and mucolytic properties. The leaves, bark, fruits and flowers are used and considered safe and are recommended for usage and dosing. It possesses the most important bioactive phytochemicals with novel bioactivities that deliver a greater insight into its therapeutic use and also the medicinal value. The therapeutic potential of plant-based medicines to fight diseases is because of the presence of phytoconstituents in different parts of the plant. Medicinal plants possess a great ability to combat various ailments. Various phytoconstituents obtained from *Justicia adhatoda* L. viz., vasicine, vasicinone, flavonoids, phenols etc., play remarkable role in traditional medicinal system. Further, these compounds display several biological activities for instance, bronchodilatory, antitussive activity, anti-microbial activity, anti-oxidant activity, hepatoprotective activity, cardioprotective activity, anti-allergy activity etc.**

***Keywords*: Bronchodilatory, *Justicia adhatoda* L., medicinal, medicine, plants.**

## 1. Introduction

Plants are a vital constituent of the biodiversity as they function to maintain earth's environment and stability. Plants are an ideal source of medicine. Plants provide several medicines to the mankind, the fundamentals of typical traditional systems of medicines that have been beneficially used for thousands of years are copiously based on plants [1]. Plant derived drugs have revolutionized modern medicinal practice [2]. Medicinal plants are the most classical, extensive and preferred source of medication. Maximum drugs used to be made from plant or animal sources directly or indirectly up to the last century. Regardless of treatment through synthetic drugs, natural organic medicines are always endured as the "treatment of choice" and preferred over synthetic drugs [3]. Their knowledge has been spread over centuries among human populations and are fundamentally used in all the cultures. The documentation of traditional utilization of plants has given numerous essential drugs of modern day and 80 % of the human population is still dependent on plant derived products for healthcare in developing countries [4]. Notwithstanding the assumption that most of clinical drugs are synthetic in derivation, it is compelling to account that over 50 % of the top 20 drugs can be related to natural product research [5]. Utilizing medicinal plants is a deep-rooted practice of mankind, treatments with plants are disclosed in the holy Indian Vedas, ancient Chinese and German books. The oldest written documentation for utilization of medicinal plants for making drugs has been found on a 5000-year-old Sumerian clay slab in Nagpur [6]. Ayurvedic medicines are not merely used by the rural communities of developing nations but are also used in the modern medicine governing developed nations. Assessment and standardization of active plant compounds and plant-based drugs can lead to the advent of innovative era of healthcare system and medicaments. Isolation and documentation of plant compounds can lead to the uncovering of different therapeutic aids. Moreover, demands for plant-derived products are increasing throughout the globe [7]. The usage of medicinal plants in the industrialised societies has led to the expansion of various pharmaceuticals and chemotherapeutics, organic remedies have become more widespread in treating disorders and also on excuse of the increasing costs for maintaining health [8]. Whether in the custom of traditional preparations or in the form of pure active doctrines, plants form the foundation of curatives. Scientists are exploring indigenous plants that can substitute some pharmaceutical drugs and accept as true that such drug research may perhaps lead to industrial progress in developing countries where the flora is unexploited [9]. India is a broad reserve of natural resources. The literature of traditional remedies labels the inherent role of plants as a source of local therapy for several disorders like cancer, diabetes, arthritis and many others. They offer a cheaper source of treatment and available to the maximum population. There is a rise in demand for organic products both locally and internationally. Thus, boosting the usage of medicinal plants as a source of new drugs is needed [10]. The practice of using organic medications is cost effective and free from harmful side effects. India holds the position of a chief participant in the global medicinal plants market [11].

## 2. Plant Description

*Justicia adhatoda* L. is the medicinal plant of concern for this paper. It is commonly known as Vasaka or Adulsa. Its trade

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name Vasaka is indigenous to India, it grows all over India in lower Himalayan ranges [12]. It belongs to family acanthaceae and is widely known for its efficacy in curing respiratory problems. It is a perennial evergreen shrub and has been used in treating asthma, chronic bronchitis and other problems for centuries in Ayurveda [13]. It is a small evergreen perennial shrub reaching up to an average height of three metres with opposite and ascending branches. The leaves are broad, measuring about 10-15 centimetres in length and 4 centimetres in width approximately. Being pubescent, light green on top and darker green beneath, leaves grow in an opposite pattern and are entirely lanceolate, tapering towards both apex and base and shortly petiolate. The flowers are large, dense, terminal spikes with attractive white petals marked with purple lower lip. The fruit is small, clavate, longitudinally channelled capsule, containing four globular seeds [14].

*Classification:*

Kingdom : Plantae
Class : Magnoliopsida
Order : Lamiales
Family : Acanthaceae
Genus : *Justicia*
Species : *adhatoda*

Vernacular names: Malabar nut, Adulsa, Vasaka, Basak, Amalaka

Fig. 1. Image of *Justicia adhatoda* L.

*Ethnobotanical Uses:*

Plant parts of *Justicia adhatoda* L. are used in various ways for traditional medicine.

*Leaves:* Mature green leaves are used to heal fever, cough, asthma and dysentery. Inflorescence and mature leaves are also used as food. Mature leaves fried in mustard oil are eaten along with rice and other cuisine [15]. It is also consumed in tea form, herbal basak tea prepared with *Justicia adhatoda* L. leaves contain pharmacologically active vasicine alkaloids with antibacterial properties and helps in treating asthma [16]. The fresh leaves have stimulant effect on the respiratory tract, Yogis and Sadhus used to chew fresh leaves along with ginger [13].

*Flowers:* In Ayurveda, a preparation named gulkand is made from *Justicia adhatoda* L. flowers and is used in the treatment of tuberculosis. Flowers, fruits, leaves and bark are also known for removal of intestinal parasites [12].

*Bark and root:* The decoction of its root and bark have been given for consistent relief, especially in the acute stages of bronchitis. The root and bark decoction are given twice or thrice for 3 days to treat this problem in the doses of 30 grams. The juice from leaves is also given for the treatment of diarrhoea and dysentery in the doses of 2 to 4 grams [17].

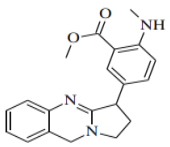
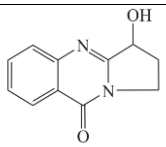
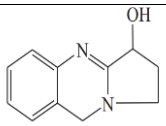
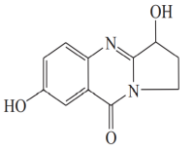
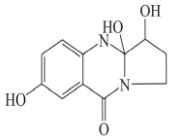
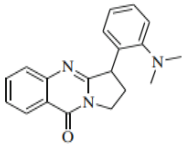
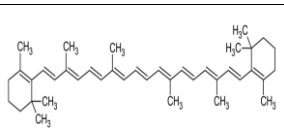
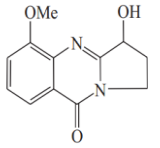
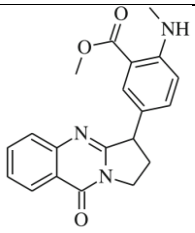
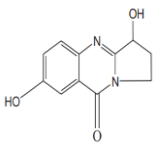
*Phytochemical Constituents:*

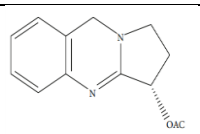
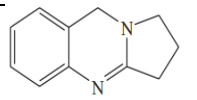
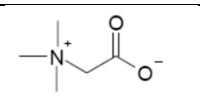
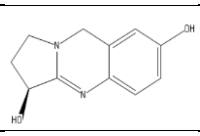
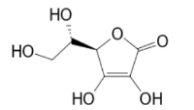
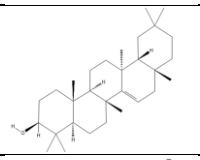
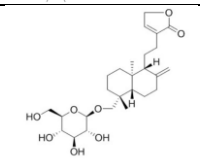
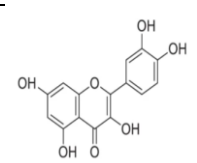
Medicinal plants vary extensively in terms of their structures, biological potential and modes of action. They have always been considered as important bases of natural products. Biologically active constituents are present in every part of the plants comprising leaves, flowers, fruit, stems and root. These constituents work as a defense response in order to cope up with stress for instance, polyphenols act as hydrogen donors and neutralize the free radicals generated in plants because of the oxidative stress and damage [20]. Phytochemicals have been considered as the centre for traditional herbal medicine. Various existing medicinal systems viz., ayurveda, homeopathy, naturopathy, unani, siddha as well as other substitute medicinal systems explore phytochemicals in order to utilize plants against various harmful ailments [21]. The various biological activities exhibited by plants such as hepatoprotective, anti-proliferation, cardioprotective, antimalarial, anti-inflammatory, oxidative DNA damage protection are ascribed to the occurrence of efficient bioactive complexes such as phytochemicals, vitamins, organic acids, minerals etc., [22].

Table 1
Ethnopharmacological and therapeutic uses of *Justicia adhatoda* L.

| S. No. | Part used | Administration | Treatment | References |
|---|---|---|---|---|
| 1 | Whole plant | Decoction | Asthma, cough, bronchitis, fever, Joint pain, malaria, rheumatism, lumber pain, eczema | [14] |
| 2 | Whole plant | Preparation of syrup along with Tulsi and ginger | Bleeding piles | [18] |
| 3 | Leaves | Mature leaves fried in mustard oil | Indigestion, cold, cough | [15] |
| 4 | Leaves | Chewing of leaf buds alone or in combination of ginger root | Clearing of respiratory passage | [14] |
| 5 | Leaves | Various preparations | Bleeding haemorrhage, wounds, skin diseases, headache | [14] |
| 6 | Leaves | Powder, decoction, juice | Relieve acidity, antipyretic | [18] |
| 7 | Leaves | Decoction, infusion, poultice | Rheumatic and painful inflammatory swellings | [19] |
| 8 | Roots | Paste, powder, decoction | Malarial fever, diphtheria, tuberculosis | [14] |
| 9 | Flowers | Various preparations | Phthisis, bronchitis, asthma, cough, cold, gonorrhoea, antiseptic | [14] |
| 10 | Fruits | Various preparations | Cold, jaundice, dysentery, diarrhoea | [18] |

Table 2
Important chemical compounds of *Justicia adhatoda* L.

| S.No. | Chemical constituent | Structure | Biological activities | References |
|---|---|---|---|---|
| 1. | Adhatodine |  | Antitubercular, antiallergic, hepatoprotective, cardioprotective. | [23,26] |
| 2. | Vasicinone |  | Immunostimulant, antiallergic, bronchodilator, hypotensive, cardial depressant effect. | [23] |
| 3. | Vasicine |  | Respiratory stimulant activity, thrombopoetic, abortifacient, uterotonic properties, bronchodilatory activity, cardial depressant effects, relaxation of tracheal muscles, antimicrobial, anthelmintic, antispasmodic, antihypertensive, gastric secretion promoter, oxytocic. | [23,18] |
| 4. | Vasicinolone |  | Respiratory stimulant activity, bronchodilatory activity. | [27] |
| 5. | Vasicol |  | Bronchodilatory effect. | [27] |
| 6. | Vasicoline |  | Bronchodilatory effect. | [27] |
| 7. | Carotene |  | Antioxidant, cardioprotective activity. | [27,26] |
| 8. | Adhavasinone |  | Antibacterial. | [27,34] |
| 9. | Anisotine |  | Promising inhibitory potential against novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). | [35] |
| 10. | Hydroxy vasicinone |  | Bronchodilatory. | [31] |

| | | | | |
|---|---|---|---|---|
| 11. | Vasicine acetate |  | Antimicrobial, antioxidant, cytotoxic. | [36] |
| 12. | Deoxy vasicine |  | Acetyl cholinesterase inhibitor, butyryl cholinesterase inhibitor. | [26,31] |
| 13. | Betaine |  | Antineoplastic, antihepatotoxin, antihypertensive. | [18] |
| 14. | Vasicinol |  | Antihistamine, insect antifeedant, antihypertensive, reduces fertility in insects. | [36] |
| 15. | Vitamin C |  | Antibacterial, antioxidant, dermatitis, vasodilation. | [17,37] |
| 16. | Taraxerol |  | Antiulcerative. | [18] |
| 17. | Neoandrogr-apholide |  | Antibacterial, antipyretic. | [18,26] |
| 18. | Quercetin |  | Antioxidant, cardioprotective, anti-inflammatory, neuroprotective, anti-cancer, anti-ulcer, antibacterial, antiviral, antiallergy activity. | [26,34] |

The main constituent of *Justicia adhatoda* L. are its various alkaloids. Vasicine, vasicoline, vasicinone, adhatodine, vasicolinone and anisotine are important quinazoline alkaloids found in *Justicia adhatoda* L. which are accountable for abundant pharmacological activities viz., anti-inflammatory, anti-oxidant, antibacterial, antidiabetic, anti-depressant, anti-cancerous, anti-fungal, anti-diabetic, anti-allergic etc., [23]. *Justicia adhatoda* L. is a rich source of polyphenolic compounds, which also accounts for its strong anti-oxidant activity. The phytochemical screening reveals the genuineness of the drugs and products obtained from *Justicia adhatoda* L. which are useful to the mankind [24]. *Justicia adhatoda* L. holds many biologically active compounds and its phytochemical profile can be exploited for the development of various plant-based drugs [25].

Thus, active compounds formed through secondary metabolism are typically accountable for the biological properties [30]. The important quinazoline alkaloids of *Justicia adhatoda* L. viz., vasicine and vasicinone form a quinazoline ring. This ring in their structure is biosynthetically synthesized through shikimic acid pathway by using up the primary metabolites like different amino acids viz., glutamic acid, ornithine, proline etc., [31]. *Justicia adhatoda* L. is rich in phytochemicals, its leaves and flowers contain high content of carbohydrates, high soluble proteins, phenols, flavonoids [32]. The analysis of *Justicia adhatoda* L. roots and fruits disclose the presence of various other important constituents also [33]. The leaves of *Justicia adhatoda* L. are rich in vitamin C, carotene, fats, resins etc., and elements viz., K, Na, Ca, Mg Zn, Cu, Cr, Ni, Co, Cd, Pd, Mn and Fe. The leaves also contain a small amount of essential oil [14].

## 3. Biological Activities

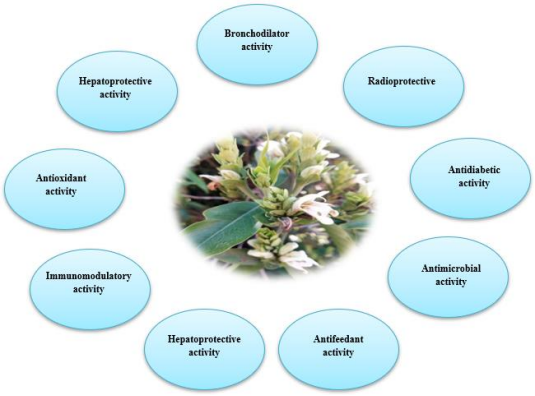



Fig. 2. Various pharmacological actions of *Justicia adhatoda* L.

Table 1
Phytoconstituents reported in *Justicia adhatoda* L.

| S. No. | Plant part | Phytoconstituents | Quantity | References |
|---|---|---|---|---|
| 1. | Leaves | Vasicinone | 3.5 % | [33] |
| 2. | Leaves | Vasicine | 4.5 % | [33] |
| 3. | Leaves | Crude fat | 1.6 % | [38] |
| 4. | Leaves | Crude fiber | 6.4 % | [38] |
| 5. | Leaves | Carbohydrates | 16.4 % | [38] |
| 6. | Leaves | Potassium | 31190 mg/g | [39] |
| 7. | Leaves | Calcium | 68070 mg/g | [39] |
| 8. | Leaves | Iron | 705 mg/g | [39] |
| 9. | Leaves | Copper | 64 mg/g | [39] |
| 10. | Leaves | Zinc | 67 mg/g | [39] |
| 11. | Leaves | Chromium | 41 mg/g | [39] |
| 12. | Leaves | Vanadium | 19 mg/g | [39] |
| 13. | Leaves | Manganese | 118 mg/g | [39] |
| 14. | Leaves | Protein | 7.8 mg/g | [32] |
| 15. | Leaves | Phenols | 32.1 mg/g | [32] |
| 16. | Leaves | Flavonoids | 37.9 mg/g | [32] |
| 17. | Leaves | Alkaloids | 1.09 mg/g | [32] |
| 18. | Leaves | Water soluble ash | 12.85 % w/v | [40] |
| 19. | Leaves | Acid soluble ash | 3.17 % w/v | [40] |
| 20. | Leaves | Nickel | 1.47 ppm | [41] |
| 21. | Leaves | Cobalt | 1.5 ppm | [41] |
| 22. | Leaves | Organic matter | 0.53 % w/v | [40] |
| 23. | Leaves | Moisture content | 15.3 % | [38] |
| 24. | Flowers | Carbohydrate | 8.2 mg/g | [32] |
| 25. | Flowers | Protein | 2.5 mg/g | [32] |
| 26. | Flowers | Phenols | 22.8 mg/g | [32] |
| 27. | Flowers | Flavonoids | 29.2 mg/g | [32] |
| 28. | Flowers | Alkaloids | 1.08 mg/g | [32] |
| 29. | Roots | Dry matter | 66.4 % | [33] |
| 30. | Roots | Calcium | 3.1 % | [33] |
| 31. | Roots | Moisture | 24.6 % | [33] |
| 32. | Roots | Sodium | 2.4 % | [33] |
| 33. | Roots | Protein | 8.5 % | [33] |
| 34. | Roots | Sulphur | 1.2 % | [33] |
| 35. | Roots | Fat | 2.5 % | [33] |
| 36. | Roots | Iron | 0.7 % | [33] |
| 37. | Roots | Zinc | 0.5 % | [33] |
| 38. | Roots | Fiber | 5.2 % | [33] |
| 39. | Roots | Vitamin C | 5.2 % | [33] |
| 40. | Roots | Vasicine | 7.5 % | [33] |

*Justicia adhatoda* L. exhibits potent biological activities which justify the use of this plant as a traditional medicine.

*1) Hepatoprotective activity*

Playing major role in metabolism and excretion of xenobiotics from the body, liver is considered as a vital organ and the available synthetic drugs required to treat liver disorders also cause further damage to the liver henceforth herbal drugs have become progressively popular and their use is wide spread [42]. An attempt was made to investigate the proportional effect of ethanolic extracts of *Justicia adhatoda* L. on hepatoprotective activity against perchloroethylene induced liver damage in albino rats and compelling hepatoprotective activity was noticed which was equivalent to that of standard silymarin, with that antilipid peroxidative and free radical scavenging activities of extracts was also noticed, which vindicated the traditional use of *Justicia adhatoda* L. in treatment of liver disease as a propitious hepatoprotective agent [43]. The modulatory effect of ethanolic extract of *Justicia adhatoda* L. dosed Swiss albino mice was observed on extra-hepatic organs viz., lung, kidney and fore stomach for the activities of glutathione S-transferase, DT-diaphorase, superoxide dismutase and catalase. It operated as bifunctional inducer. A substantial reduction in malondialdehyde formation in liver was seen in treated groups which advised its role in defence against prooxidant induced membrane damage. *Justicia adhatoda* L. also stimulated other organs viz., lung kidney and fore stomach besides liver and enhanced the prospective associated with the detoxification of xenobiotic compounds [44]. The aqueous extracts of *Justicia adhatoda* L. were also tested for hepatoprotective activity after severe hepatotoxicity was brought in rats by means of intraperitoneal injection of D-galactosamine and subsequently the extracts showed noteworthy hepatoprotective effect on liver damage [45]. Carbontetrachloride administration in the body of model organism induces chronic hepatotoxicity by restricting the normal metabolic functions. Biotransformation of carbon tetrachloride into trichloromethyl radical carbon trichloride leads to joining of carbon tetrachloride with cellular proteins and membrane lipids which further raises lipid peroxidation and disintegrate them. Pre-treatment of carbon tetrachloride administered Swiss albino mice with methanolic, ethanolic and aqueous extracts of leaves and flowers of *Justicia adhatoda* L. was seen to lessen the toxic effects like increase in liver enzymes and decline in antioxidant activity of the body [46].

All of these studies support the use of plant as a hepatoprotective agent in traditional medicine.

*2) Bronchodilator activity*

*Justicia adhatoda* L. has been used for the treatment of many ailments and disorders predominantly for the respiratory tract ailments viz., breathlessness, cold, cough [19]. It is known for its chief elements which are its several alkaloids, the most essential being vasicine. Two main alkaloids called vasicine and vasicinone are well known for their functions, both in combination show prominent bronchodilatory activity [28]. Bronchodilatory activity of pure samples of vasicinone hydrochloride was examined in comparsion to isoperaline and aminophyllineo, where potentiating effect of vasicinone in bronchodilation was confirmed [29]. Several other alkaloids in combination with vasicine and vasicinone viz., vasicol, vasicinolone and adhatoda acid could play a potential role in bronchodilator effect of the bronchii. The leaf extract of *Justicia adhatoda* L. [30].

*3) Anti-microbial activity*

*Justicia adhatoda* L. shows a wide-ranging spectrum of antimicrobial activity and an impending source of antimicrobial agents that are considered advantageous for chemotherapy and controlling infectious diseases. Antimicrobial activity in methanolic leaf extracts of *Justicia adhatoda* L. in comparison to vasicine against various strains of microbes was determined. The study revealed inhibition of bacterial growth by plant extract and also plant-based antimicrobials do the work with lesser side effects [47]. Antimicrobial activity of *Justicia adhatoda* L. against different clinical pathogens with plant extracts prepared in different solvents was tested and subsequent antimicrobial activity against gram positive and negative bacteria was noticed [48]. The essential oil extracted through fresh leaves of *Justicia adhatoda* L. was investigated for its antimicrobial potential and displayed strong antimicrobial activity against methicillin resistant and sensitive *Staphylococcus aureus* along with its clinical isolates [49]. Ethyl actetate extract from *Justicia adhatoda* L. showed promising anti-fungal activity with MIC 80 ppm against the *Alternaria nidulans* and *Alternaria* sp. which suggests its use as fungicide against fungal plant diseases [50]. *Justicia adhatoda* L. has a potential to inhibit the growth of bacteria. The efficacy of green synthesized silver nanoparticles of *Justicia adhatoda* L. leaf extract was checked against the strains of pathogen *P.aeruginosa* MTCC 741 and the MIC values specified that vasaka leaf extract can stop the growth of pathogen. It was suggested that the alkaloids existing in the leaf extract can act as reducing or capping agent for Ag nanoparticles. The work presented a commercial, effectual and environment friendly way for green synthesis of Ag nanoparticles which demonstrated that Ag nanoparticles could be more reasonable and auspicious alternate antibacterial agent in the field of agriculture [51]. The antibacterial activity of *Justicia adhatoda* L. silver nanoparticles was witnessed against different strains i.e., *Bacillus subtilis*, *Klebsiella pneumonia*, *Pseudomonas putida*, *Escherichia coli*, *Staphylococcus aurous*. The essential oil extracted from leaves of *Justicia adhatoda* L. was tested against four bacterial strains though essential oil displayed high activity against *E. coli* which specified that the oil can be used for various health issues by comparing with the standard [52]. Various leaf extracts from *Justicia adhatoda* L. were screened for antibacterial activity against different microorganisms and the methanolic extract was seen to have maximum zone of inhibition ($18.17 \pm 0.44$ mm) for *Staphylococcus aureus* and the effect was found to be stronger than extracts based on the other solvents like hexane, chloroform respectively [53].

*4) Immunomodulatory activity*

Methanolic, chloroform and diethyl ether extracts of *Justicia adhatoda* L. leaves were pharmacologically tested for its immunomodulatory properties in adult wistar rats. Oral administration of extracts revealed noteworthy rise in adhesion of neutrophils to nylon fibers which simultaneously correlated to the margination of cells in blood vessels. The extracts were also seen to bring delayed type hypersensitivity reaction by sheep erythrocytes and the perceived results at different doses were found to be substantial when compared to control groups which acclaimed that the extracts certainly modulated immunity of the host [54].

*5) Anti-tussive effect*

Coughing is a usual physiological response resulted due to mechanical or chemical stimulation of the laryngo-tracheo-bronchial system caused due to an irritation which could be achy and fatiguing and thus needs suppression by antitussive drugs. The efficacy of *Justicia adhatoda* L. extract as an antitussive drug was tested in anaesthetized guinea pigs and rabbits as well as in unanaesthetized guinea pigs and the extracts were found to exhibit a good antitussive activity. The antitussive activity was found to be comparable to that of control codeine in orally administered animal models in response to induced coughing caused by irritant aerosols [55]. A branched polysaccharide named arabinogalactan was isolated from the aqueous ethanol precipitated extracts of *Justicia adhatoda* L. and an oral administration of extract containing this polysaccharide in guinea pigs was seen to prevent and supress the number of coughs which were induced to the model animals by aerosol of citric acid through jet nebulizer. This study specified that the arabinogalactan isolated from *Justicia adhatoda* L. demonstrated very promising cough suppressive effect in the antitussive assays additionally isolation of such polysaccharides are advantageous in being inexpensive moreover such antitussive drugs isolated without toxic chemical reagents can be considered safe for industrial use [56]. The antitussive activity of *Justicia adhatoda* L. was evaluated in cough model induced by sulphur dioxide gas. The administration of ethanolic extracts of *Justicia adhatoda* L. in experimental animals witnessed very significant effects in preventing the cough reflex at the dose of 800 mg/kg and 200 mg/kg at the level of $p < 0.01$ in comparison to that of control group. The antitussive activity of the extract was found to be comparable to that of standard antitussive drug codeine sulphate [57]. Antitussive effect of a fixed combination of extracts of leaves of *Justicia adhatoda* L., roots of *Echinacea purpurea* and roots of *Eleutherococcus senticosus* were administered in patients with acute upper respiratory tract infection in the form of an oral solution Kan Jang (KJ). Kan

Jang being a brand of herbal medicinal products displayed a greater reduction in the cough intensity as compared to other groups i.e., placebo and bromhexine. Overall, the Kan Jang group put forth significant and more fast antitussive effect and a noble tolerability profile [58]. KanJhang oral solution was compared with the combined extracts of *Echinacea purpurea* and *Eleutherococcus senticosus*. Better recovery was witnessed in patients treated with KanJang oral solution in comparison to those receiving standard treatment. The reason behind was lack of *Justicia adhatoda* L. in the treatment which reduced its potential with comparison to the complete KanJang oral solution [59].

*6) Anti-diabetic activity*

The effects of ethanolic extracts of leaves and roots of *Justicia adhatoda* L. was studied in alloxan induced diabetic animals. Oral administration of *Justicia adhatoda* L. leaves extract made a substantial drop in blood glucose levels as compared to the root extracts. Also noteworthy improvement was observed on the glucose tolerance, serum lipid profiles, glycosylated haemoglobin and bodyweight of experimental animals which recommended defensive mechanism of *Justicia adhatoda* L. against the development of other similar diseases also [60].

*7) Anti-typhoid activity*

The methanolic extracts of leaves of *Justicia adhatoda* L. were screened for antityphoid activity against the strains of *Salmonella typhi* and further extracts were seen to inhibit the growth of *Salmonella typhi* which suggested that it is an effective antityphoid agent and its application can be an inspiring development in the field of antibiotics which can help to develop new chemical classes of medicines that exhibit multi drug resistance [61].

*8) Anti-oxidant activity*

The antioxidant activity of *Justicia adhatoda* L. was observed and compared with BHA, subsequently reducing power was determined by comparing with Ascorbic acid. High antioxidant and reducing power activity was observed in the leaf samples and it was suggested that *Justicia adhatoda* L. can be utilised as medicine against antioxidant system failure and compelling antioxidant supplement for typhoid patients [61]. The leaves of *Justicia adhatoda* L. are good sources of antioxidants and might be beneficial in tackling diseases linked with treating oxidative stress. The aqueous leaf extracts from *Justicia adhatoda* L. were investigated for chelating activity and seen to possess $Fe^{2+}$ chelating activity which could play a protective role against oxidative damage. *Justicia adhatoda* L. possessed higher chelating power (51.91 ± 1.235 %), which could be attributed to high concentration of phenolic compounds present in it that can chelate metal ions [62]. Vasicine extracted through n-butanol fraction of *Justicia adhatoda* L. leaves was found to be a strong scavenger of $O_2^{*-}$ radical with the maximum percentage inhibition of superoxide radical generation at 1000 µg/ml with $IC_{50}$ 539.64 µg/ml [63]. Analysis of the effect of gamma irradiation on the natural antioxidants of *Justicia adhatoda* L. was done in a study where the consequence of radiation was inspected on the methanol extract by different assays and it was concluded that irradiation dose improved the antioxidant activity, noteworthy scavenging activity was seen at the dose of 5 kGy for DPPH assay and also the FRAP value and absorbance was found to be maximum at 5 kGy dose in case of FRAP and reducing power assay [64]. Evaluation and comparison of radical scavenging properties of leaf extracts of *Justicia adhatoda* L. using 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay was done and the results of antioxidant activity and phenolic content of cold and Soxhlet methanolic extracts confirmed the major contribution of phenolic compounds towards antioxidant capacities of these extracts [65].

*9) Anti-inflammatory activity*

The methanolic extract, saponins, non-alkaloid fraction and alkaloids of *Justicia adhatoda* L. were examined for anti-inflammatory activity through modified hen's egg chorioallantoic membrane test. Effective anti-inflammatory activity was noticed in the alkaloidal fraction which was equivalent to that of hydrocortisone [66]. The chloroform fractionated extracts of *Justicia adhatoda* L. were tested for anti-inflammatory activity by using carrageenan and CFA-model induced paw oedema, oedema was subcutaneously induced in left hind paw in rats by injecting 0.05 ml of 1.0 % (w/v) carrageenan. The results exposed that vasicine exhibited most remarkable anti-inflammatory activity (59.51 %) at the dose of 20.0 mg/kg at 6 h after carrageenan injection [67].

*10) Radioprotective effect*

Radiation-induced alterations in model organisms are widely studied now a days, radiation exposure to entire body can cause serious complications. In a study, it was observed that Gamma radiation induced sickness brought in mice consequently marked changes in histology of testis and chromosomal aberrations in bone marrow cells. *Justicia adhatoda* L. pretreated irradiated mice was seen to significantly prevent the radiation-induced chromosomal damage in bone marrow cells. Subsequently death of irradiated mice pretreated with *Justicia adhatoda* L. was reduced to 70 % in 30 days. There was significantly lesser degree of damage to testis tissue architecture and various cell populations including spermatogonia, spermatids and Leydig cells [68]. Furthermore, protective effect of *Justicia adhatoda* L. against radiation induced damage at cellular, biochemical and chromosomal levels in model organism was investigated where *Justicia adhatoda* L. leaf extracts reduced the stickiness of chromosomes and the chromosomal aberrations that happened because of the effect of radiation [69].

*11) Anti-tuberculosis activity*

The alkaloids of *Justicia adhatoda* L. were tested for their efficacy as anti-tuberculosis agent. Docking simulations were conducted on *Justicia adhatoda* L. derived alkaloids which provided remarkable insights into the binding of different inhibitors and their activity. Conclusion was made that the extensive studies on the compound formulated from the potent inhibitor (Vasicoline) might result in a good anti-tuberculosis compound suggesting that the outcomes will be beneficial for designing inhibitors for *Mycobacterium tuberculosis* and in turn a well-intentioned beginning for natural plant-based pharmaceutical chemistry [23]. The in-vitro inhibitory effect of

semi-synthetic derivatives of vasicine from *Justicia adhatoda* L. was investigated and the results suggested that bromhexine and its principle metabolite ambroxol show inhibitory activity against *Mycobacterium tuberculosis* though benzylamines, bromhexine and ambroxol are known to have a pH-dependent growth-inhibitory effect on *Mycobacterium tuberculosis* and can act as an anti-tuberculosis drug [70].

*12) Anti-cestodial activity*

*Justicia adhatoda* L. retains substantial anticestodal efficacy. The methanol leaf extract treated *Hymenolepis diminuta*-rat experimental model in the double dose of 800 mg/kg showed extensive potency against mature worms where the anticestodial worth was evaluated by monitoring the eggs per gram (EPG) of faeces counts and percentage worm recovery rates and *Justicia adhatoda* L. extract was found to reduce the EPG count by 79.57 % and percentage worm recovery rate by 16.6 %. The effects were even found to be better than treatment with standard drug praziquantel [71].

*13) Anti-cancer activity*

Methanol extract of *Justicia adhatoda* L. showed significant inhibition of cancer cells. The MTT assay was applied to investigate the cytotoxic effect of the methanolic and ethanolic extracts of *Justicia adhatoda* L. on cancer cell-line where MCF-7 cell line exposed the cytoxicity of extracts in a dose dependent manner, cytotoxicity was seen to increase with increase the concentrations of doses. Subsequently, the compound ''vasicine'' isolated from n-butanol fraction of *Justicia adhatoda* L. was found compelling in preventing proliferation of prostate cancer cells [72]. Cytotoxicity of the *Justicia adhatoda* L. silver nanoparticles on human epitheloid carcinoma cells was estimated in a dose dependent manner at different concentrations and the in-vitro screening of nanoparticles displayed a potential cytotoxicity against the cancer cell lines. A complete mortality rate (82.15 % cell death) was witnessed in 80 µg/µl concentration of the silver nanoparticles and cisplatin (45 µg/ml) was used as the standard anticancer drug to confirm and correlate the anti-cancer activity [73]. Efficacy of gold nanoparticles (AuNPs) for the anti-cancer activity was explored on human lung cancer cell line (A549) through measuring cytoxicity by MTT assay and apoptosis by propidium iodide staining. An apoptotic mechanism was observed in the cytomorphology of treated cells leading to cell death and other alterations including cell shrinkage, inhibition of cell growth membrane integrity and distinctive morphological changes comprising constant detachments of cells. The results directed anti-proliferation effect of synthesized AuNPs on the A549 lung cancer cells concluding biosynthesized AuNPs treated A549 cells underwent cell death [74]. Anti-carcinogenic potential of vasicine was estimated at various concentrations (30, 50 and 100 µg/ml) to prevent the growth of human prostate cancer (PC-3) cells in comparison to cell growth inhibitor i.e., camptothecin. Vasicine was seen to inhibit 50 % cell growth with 81.11 µg/ml $IC_{50}$ concentration in a dose dependent manner [63]. Green synthesized cerium oxide ($CeO_2$), silver loaded cerium oxide ($Ag/CeO_2$), gold loaded cerium oxide ($Au/CeO_2$) and silver-gold loaded cerium oxide ($Ag\text{-}Au/CeO_2$) nanoparticles prepared through *Justicia adhatoda* L. extract were examined for anticancer activity among which $Ag\text{-}Au/CeO_2$ nanoparticles displayed outstanding anticancer activities in comparison to $Ag/CeO_2$, $CeO_2$ and $Au/CeO_2$ nanoparticles [75].

*14) Anti-viral activity*

The crude extracts of *Justicia adhatoda* L. reported antiviral effect against influenza virus by Hemagglutination (HA) reduction in two different layouts of instantaneous and post treatment assay. Methanolic and aqueous extracts were used for investigation in the non-cytotoxic range where 100 % reduction was shown in hemagglutination at the concentration of 10 mg/ml simultaneously aqueous extracts also reduced the hemagglutination to 33 % and 16.67 %, respectively. The study suggested strong anti-influenza virus activity of the *Justicia adhatoda* L. extracts [76].

*15) Anti-plasmodial activity*

Anti-plasmodial activity was investigated in *Justicia adhatoda* L. Vasicinone, vasicine and the novel compound VA-1 synthesized from alkaloid vasicine (VA-1) 9-oxo-1,2,3,9-tetrahydropyrrolo[2,1-b]quinazolin-3-yl acetate extracted through the leaves of *Justicia adhatoda* L. were tested in-vitro for anti-plasmodial activity. Both vasicine and vasicinone exhibited moderate antiplasmodial activity with $IC_{50}$ values 89.8 µg/ml and 38.9 µg/ml, comparatively excellent antiplasmodial activity with $IC_{50}$ = 06.0 µg/ml was observed in the compound VA-1 in comparison to the standard drug i.e., chloroquine ($IC_{50}$= 12.6 µg/ml). Outcomes proposed that isolated semi-synthetic compounds can serve as a chief antiplasmodial agent [77].

*16) Thrombolytic activity*

Natural extractives from *Justicia adhatoda* L. were assessed for thrombolytic activity in order to discover cardioprotective drugs. Different fractions of *Justicia adhatoda* L. were tested for thrombolytic activity. Methanolic fraction exhibited highest thrombolytic activity (53.23 %) among other fractions i.e., n-Hexane soluble fraction (44.18 %) and carbon tetrachloride soluble fraction (38.17 %) in comparison to the standard drug Streptokinase (80.65 %) which suggested that *Justicia adhatoda* L. extracts can be designed as a thrombolytic agent [78]. The chloroform and ethyl acetate soluble fractions of stem and root of *Justicia adhatoda* L. were assessed for thrombolytic activity by determining the ability of clot lysis, the highest clot lysis values were observed in ethyl acetate soluble fractions i.e., 42.63 % (stem) and 46.48 % (root) in comparison to standard streptokinase enzyme i.e., 63.52 % (control) [79].

*17) Non-abortifacient activity*

*Justicia adhatoda* L. leaf extract was examined for abortive effect in rats. The extract was administered at the dose of 325 mg/kg/day with a gastric cannula to a group of 5 pregnant females. No significant differences witnessed in maternal and fetal parameters amongst control and treated rats which concluded that the administration of *Justicia adhatoda* L. did not create abortion in any of the treated groups [80].

*18) Anti-mutagenic activity*

*Justicia adhatoda* L. leaf extract was assessed for anti-mutagenic activity against sodium azide and 4-nitro-O-phenylenediamine by using two strains of *Salmonella*

*typhimurium* i.e., TA100 and TA98. The alkaloid-vasicine was isolated from the bioactive n-butanol fraction of *Justicia adhatoda* L. and further analysed. Though a significant inhibitory activity was not observed by isolated compound vasicine against direct acting mutagens viz., sodium azide and 4-nitro-O-phenylenediamine in both the tester strains of *Salmonella typhimurium*. In both strains, the percent inhibiton against the direct acting mutagen was found to be in the range of 17-43 % [63].

*19) Anti-depressant activity*

The impact of *Justicia adhatoda L.* leaf extract was examined in alloxan-induced diabetes and co-morbid depression in mice. Depression is predominant as a neurological complication in the diabetic patients, increased levels of neuronal oxidative stress being a consequence of diabetes may cause neuropsychological complications such as depression. Mice was administered a dosage of alloxan at 200 mg/kg intraperitoneally to retain diabetes after that the mice were given ethanolic leaf extracts of *Justicia adhatoda* L. After 3 weeks of developing chronic diabetic state, anti-depressant effect was assessed by behavioural despair tests, followed by oxidative stress analysis and monoamine oxidase (MAO) activity. The results displayed that extract treatment was effective in dropping the raised blood glucose and reversed co-morbid depressive behaviour and established the potential protective action [81].

*20) Anti-ulcer activity*

*Justicia adhatoda* L. has enormous potential as an anti-ulcer agent of pronounced therapeutic application. The investigation was carried out to explore the anti-ulcer activity of *Justicia adhatoda* L. leaves using two ulcer models viz., Ethanol-induced and Pylorus ligation plus aspirin-induced rat models. Acute gastric ulcers were induced in both the experimental animals. *Justicia adhatoda* L. leaf powder displayed substantial degree of anti-ulcer activity in the experimental rats with comparison to control. The highest degree of anti-ulcer activity (80 %) was witnessed in the ethanol-induced ulceration model [82].

*21) Anti-feedant activity*

Antifeedants can be used effectively in integrated pest control program The crude methanolic extracts of leaves of *Justicia adhatoda* L. were investigated in the laboratory on *Spodoptera litterolis* larvae for its feeding and performance and it was found to have conspicuous antifeedant and toxic properties. The extract unveiled strong antifeedant and toxic activity against the larvae. 100 % mortality was observed in larvae feeding on fresh leaves after 26 days of unsubstantial growth. High mortality, reduced growth rates and low weight gain was observed in larvae nurtured on diets comprising 20-2000 ppm of the extract predicting the toxicity of extract. The animals nurtured on extract-free diet displayed considerably higher growth efficiency in contrary to the animals fed on extract-containing diets, signifying its antifeedant, toxic, suppressant and deterrent properties [83]. Various alkaloids from *Justicia adhatoda* L. were found to be accountable for the antifertility and antifeedant activity of plant extracts and seemed to play a chief role for the non-selection of plant by insects because of their antifertility and antifeedant characteristics [84].

*22) Anti-pathogenic activity*

*Justicia adhatoda* L. extract was investigated to suppress the *Aedes aegypti* population. *Aedes agypti* being a mosquito species, is a vector of deadly pathogens. Strong negative effects on *Aedes agypti* were seen, extract directed reduction in fecundity and increase in oviposition deterrence of gravid females in comparison to that of controls. Strong deleterious effects in survival with respect to extensive damage in midgut epithelial cells and peritrophic matrix were observed in the larvae exposed to dietary leaf extracts. The extract exposure reduced survival rate sharply and approached zero within 15 days. Also, fasted adult females were repelled by the essence of leaf extracts present on human arms, with optimal repellency at 50 ppm [85].

*23) Anti-allergic activity*

Compound 73/602 (AA) being a structural analogue of vasicinone, present in the leaves and roots of *Justicia adhatoda* L. possesses potent antiallergic activity in mice, rats and guinea pigs [86]. *Justicia adhatoda* L. in combination with *Glycyrrhiza glabra* and *Solanum xanthocarpum* was investigated to explore their interaction potential on egg albumin induced degranulation and mast cell stabilization compound 48/80. Mast cells are the chief manufacturers of mediators of inflammatory reactions resulting in allergy and instantaneous allergic responses. Various combinations of extracts treated mast cells validated significant protection of mast cells against compound 48/80 and egg albumin induced mast cell degranulation in a dose dependent manner and suggested the synergistic effects of liquorice extract with *Justicia adhatoda* L. and *Solanum xanthocarpum* [87].

*24) Anti-diarrheal activity*

The methanolic extract of roots of *Justicia adhatoda* L. was screened for anti-diarrheal property by administering castor oil in Swiss-albino mice of either sex. *Justicia adhatoda* L. displayed 29.31 % inhibition in defecation comparison to standard loperamide which exhibited 58.62 % inhibition of defecation [88].

*25) Rheumatoid arthritis*

Protective effect of methanolic extract of *Justicia adhatoda* L. leaf was assessed on collagen-induced arthritis in male Swiss albino mice. Post oral administration of leaf extract dosages reduced the arthritic manifestation and footpad inflammation which suggested that it could be used for forthcoming drug innovations and progresses in the arenas of rheumatology as it was found to recover chronic inflammation throughout deleterious growth of rheumatoid arthritis and pro-inflammatory mediator release [89].

## 4. Conclusion

The literature survey of *Justicia adhatoda* L. explores a broad spectrum of medicinal properties. The major biochemicals present in *Justicia adhatoda* L. build up its strong pharmacological profile viz., hepatoprotective, anti-fungal, anti-depressant, anti-bacterial, anti-diabetic, anti-allergic, anti-diarrheal, anti-pathogenic etc., which makes it a potent drug

source and helpful to the mankind. *Justicia adhatoda* L. is a plant of great importance and it should be explored for further studies.

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