

Review

Ethnopharmacological uses, phytochemistry, pharmacological activities and toxicity of *Justicia adhatoda* L.: a review

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Abstract

Justicia adhatoda L. (*J. adhatoda* L.) belongs to the family of Acanthaceae and is a well-known medicinal plant in the South and Southeast Asia. The phytochemicals isolated from the plant include alkaloids, flavonoids, phenolic acids, triterpenoids, steroids and glycoside derivatives that are responsible for its diverse medicinal properties. The information was obtained from literature, sources including books, research papers, review papers and reports available online in accepted scientific databases such as Science Direct, Taylor and Francis, Frontiers, Scopus, Springer, MDPI, MEDLINE, Pubmed, Wiley. This review presents the up-to-date data information available on *J. adhatoda* L. After careful consideration, a total of 98 articles were used for this review. Herbal medicine is a form of healthcare that has been used for years in many countries. *Justicia adhatoda* L. is one such multipurpose plant with many uses, health benefits, and bioactivities. Several studies revealed the presence of approximately 233 phytochemical constituents. Abundance of these bioactive phytochemicals confer various pharmacological activities such as anti-microbial activity, antioxidant activity, anti-inflammatory activity, antipyretic activity, insecticidal properties, hepatoprotective activity, anti-diabetic activity, anti-tubercular activity, anti-cancer and radioprotective activity, anti-ulcer activity and activity against respiratory ailments. The review provides an overview of the traditional uses, phytochemistry, pharmacological activity and toxicology of *J. adhatoda* L. For future drug design and discovery from *J. adhatoda* L. more activity screening and structure–activity relationship studies are required to explore further. This present review brings forth the current findings on the pharmacological activities of *J. adhatoda* L. but there are still certain aspects of the plant that are limited, not reliable, or lacking in data. Also there need to be development of methods to isolate active compounds from other parts of the plant other than the leaves and to study their phytochemical potential.

Abbreviations

ABTS	2,2-azino-bis-3-ethylbenzothiazoline-6-sulphonic acid
BHT	Butylated hydroxytoluene
b.w.	Body weight
CFU	Colony-forming unit
DPPH	2,2-diphenyl-1-picrylhydrazyl
ED ₅₀	Effective dose 50

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FRAP	Ferric Reducing Antioxidant Power Assay or Ferric reducing ability of plasma
IC ₅₀	Lethal dose 50
IV	Intravenous
MRQ	Maharasnadhi Quathar
PG	Prostaglandins
p.o.	Per orally

1 Introduction

Justicia adhatoda L. also known as *Adhatoda vasica* is a plant that has been used in Ayurvedic and Unani medicine for many years. It belongs to the plant family Acanthaceae, and is well known as Malabar nut tree (in English) and Vasaka (in Sanskrit).

Justicia adhatoda L. is a dense, evergreen shrub that grows to a height of about 1–2.5 m with a herbaceous woody stem. The leaves are long and broad that are dark green on top and pale yellow below. The flowers are white, large and are densely arranged in a pedunculated spike with small and clavate fruit. *Justicia adhatoda* L. is widely distributed throughout the tropical regions of South and Southeast Asia (India, Pakistan, Sri Lanka, Malaysia, Singapore, Myanmar, Southern China, and Laos) [1–3].

Justicia adhatoda L. has many local names originating from various languages (Table 1).

Since past, *J. adhatoda* L. has been used for respiratory tract ailments including whooping cough, chronic bronchitis, asthma and also for the treatment of excessive phlegm. In Sri Lanka, the leaf extract is used for treatment of menorrhagia and related menstrual problems. It is also used for treatment of many other diseases or medical conditions such as impotence, sexual disorders, bleeding piles, leprosy, jaundice, diarrhea, dysentery, malaria, gonorrhea and vomiting [2–4].

2 Data collection

The data for the current article were obtained by searching scientific databases such as Science Direct, Taylor and Francis, Frontiers, Scopus, Springer, MDPI, MEDLINE, Pubmed, Wiley from 2000 to January 2024 using the following keywords: *Justicia adhatoda* L., *Adhatoda vasica*, phytochemicals of *J. adhatoda* L., the pharmacological properties and toxicity of *J. adhatoda* L., and ethnopharmacology of *J. adhatoda* L. A total of 160 published articles were studied, and 98 articles were used for this review.

3 Plant description

Justicia adhatoda L. belongs to the

Kingdom: Plantae,

Phylum: Tracheophyta,

Class: Magnoliopsida,

Order: Lamiales, and

Family: Acanthaceae

Genus: *Justicia*

Species: *Justicia adhatoda* L.

Justicia adhatoda L. grows into a small evergreen sub—herbaceous bush or to a small tree of about 4 m in height. The trunk is straight with a pretty smooth and ash-colored bark. The branches are long and opposite ascending with large (about 12–15 cm long and 3–4 cm broad), lance-shaped leaves. Leaves are opposite, taper-pointed and are smooth on both sides with a bitter taste. The whole end of the branchlet forms into a leafy panicle with a short flower bearing portion and is covered with large bracts. *Justicia adhatoda* L. has four seeded, small, capsular, shortly and bluntly pointed fruits with orbicular oblong, glabrous seeds. The flowering occurs in the cold season with opposite, large, white, pink or purple flowers [5–8].

Table 1 The local names for *J. adhatoda* L. in different languages [5, 6]

Arabic	Hashishatul-Sua'l
Bangla (Bengali)	Basak, Shada bashok
Burmese	Ma-ya-gyi
China	Ya-Zui-Hua
Darai	Asuro
Danish	Malabarnød
English	Malabar nut, coral-wood tree
Finnish	Valkopantterinkita
French	Carmantine en arbre, Carmantine de Ceylan, Noix de Malabar, Noyer des Indes
German	Malabarnußbaum
Gujarati	Alduso, Aduraspee, Aradusi, Bansa
Hindi	Arusha, Bansa, Baansa, Adulsa, Basuti
Kannada	Adusoge
Malay	Kacang malabar
Malayalam	Adalodakam, Ataloetakam
Manipuri	Nongmangkha-agouba
Nepali	Asuro, Kalo vasak
Newari	Aalcha
Persian	Bansa
Pashto	Bekar پکار
Raute/Doteli	Wasing
Sanskrit	Shwetavasa, Vasa, Vasaka
Sinhala	Adathoda, Pawatta, Agaladara
Swedish	Malabarnöt
Tamang	Vashak
Tamil	Adadodai
Telugu	Adasaramu
Thai	Sa niat
Tharu	Asur
Urdu	Arusa, Bansa, Bisonta

4 Chemical compounds and Nutritional value

The chemical compounds found in *J. adhatoda* L. plant includes proteins, amino acids, essential oils, gum, resins, fats, sugar and vitamin C. Leaves are rich in vitamin C, carotene, fats, resins and also yield a small amount of essential oil. Roots were reported to contain protein, fat, sugar, fibre, vitamin C and essential oil. Seeds contain fatty oil, linoleic, oleic, and cerotic [6–8]. An analysis showed the chemical composition of *J. adhatoda* L. seeds to be 25.8% of deep yellow oil composed of glycerides of 49.9% oleic, 12.3% linoleic acids, 11.2% behenic, 10.7% lignoceric, 5% cerotic, 3.1% arachidic, and (2–7%) β -sitosterol [9].

Macro and micro minerals present in *J. adhatoda* L. include Calcium (Ca), Copper (Cu), Potassium (K), Iron (Fe), Zinc (Zn), Manganese (Mn), Vanadium (V) and Chromium (Cr) [10, 11]. In a study conducted in India to determine the nutritional value and the mineral content present in *J. adhatoda* L. leaves, the mineral composition was found to be: Ca ($68,070 \pm 35.58$ ppm), K ($31,190 \pm 20.31$ ppm), Fe (705 ± 8.95 ppm), Mn (118 ± 6.03 ppm), Zn (67 ± 6.25 ppm), Cu (64 ± 5.86 ppm) and V (19 ± 1.11 ppm) [7, 12, 13]. In an elemental analysis of leaves and roots of *J. adhatoda* L. it was reported that Calcium (3.1%), Sodium (2.4%), Sulphur (1.2%), Iron (0.7%) and Zinc (0.5%) were found in the leaves. Whereas, in the leaves Calcium (1.5%), Sodium (1.4%), Sulphur (1.3%), Iron (1.2%) and Zinc (0.6%) were found [14].

5 Phytochemistry of *J. adhatoda* L.

Phytochemical screening of *J. adhatoda* L. has revealed the presence of approximately 233 phytochemical constituents (Table 2, 3, 4, 5). Among these are alkaloids, steroids, flavonoids, phenolic acids, organic acids and other chemical compounds such as hydrocarbon alkanes, alkenes, acetylene, alkylamine, fatty alcohol, naphthalene and naphthoquinone [11, 15, 16]. Abundance of these bioactive phytochemicals confer various pharmacological activities of *J. adhatoda* L. such as anti-microbial activity, antioxidant activity, anti-inflammatory activity, antipyretic activity, insecticidal properties, hepatoprotective activity, anti-diabetic activity, anti-tubercular activity, anti-cancer and radioprotective activity, anti-ulcer activity and activity against respiratory ailments [17]. Few of the bioactive components present in essential oil from *J. adhatoda* L. include octene, octanal, borneol, 1,2,3-trimethyl benzene, 2-tert-butyl-1,4-dimethoxy benzene, d-verbenone, undecanal, dodecane, d-verbenone, tetradecane, palmitic acid, [11, 18]. Some of the main phytochemicals of *J. adhatoda* L. are shown in Fig. 1.

5.1 Alkaloids

A total of 33 alkaloids were found in *J. adhatoda* L. so far. Pharmacologically most studied chemical component in *J. adhatoda* L. plant is vasicine, a bitter quinazoline alkaloid which is from the leaves, flowers and roots. Besides vasicine, leaves also contain several alkaloids such as vasicinone, vasicinol, adhatonine, adhatodine, adhvasinone, hydroxypeganine and anisotine (Table 2) [11]. It was reported in 2005, by Gulfranz et al. [14], that a higher concentration of vasicine was present in roots as compared to the leaves. Vasicine is responsible for most of the plant's phytochemical activities including antioxidant activity, bronchodilatory activity and anti-inflammatory activity.

According to the recent investigations, bronchodilatory activity of vasicine and vasicinone is comparable to theophylline [17, 19]. A comparable study conducted using aqueous, methanol and petroleum ether extracts of *J. adhatoda* L. shoots. It was found that the water extracts contained more vasicine and vasicinone in contrast to the other two extracts. The water extracts achieved maximum antioxidant activity in comparison to the methanol and petroleum ether extracts. The alkaloids vasicine and vasicinone play a role in the antioxidant activity of *J. adhatoda* L. [20]. Bromhexine, a vasicine derivative, has demonstrated mucus-liquefying/expectorant properties. In a clinical trial with 30 patients suffering from different respiratory symptoms, significant change in the viscosity and acid mucopolysaccharide structure was found in the bromhexine-treated group as compared to the placebo group, and this was seen in both infected and noninfected patients. Ambroxol is a synthetic compound derived from bromhexine and it is a commonly used secretolytic agent. It has been found to suppress the secretion of IgE-dependent mediators from human mast cells and basophils, which are responsible for allergic inflammation. Compared to vasicine, ambroxol demonstrated a more significant reduction in the secretion of IL-4 and IL-13 from basophils. Additionally, it was reported to decrease IgE-dependent phosphorylation of p38 mitogen-activated protein kinase (MAPK) in basophils [21].

The anti-microbial activity of pure vasicine was compared with that of *J. adhatoda* L. leaves, standard antibiotics (Ofloxacin, Ciprofloxacin, Amphotericin B and Nystatin). The results showed that the *J. adhatoda* L. plant is a potential source for antimicrobial agents and that vasicine plays a major role in the antimicrobial activity [22].

Vasicine was reported as a potent natural ChE inhibitor suppressing both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). However, the metabolites of vasicine displayed weaker AChE and BChE inhibitory properties when compared to vasicine possibly due to metabolic inactivation in rats [23]. The potential anti-allergic properties of vasicine were assessed using passive cutaneous anaphylaxis (PCA) test which showed that oral administration improved the severity of atopic dermatitis-like lesional skin by decreasing histopathological changes and restoring epidermal thickness. Thus, there is therapeutic potential of vasicine for treatment of atopic dermatitis [24]. The chemical structure of few of the alkaloids extracted from *J. adhatoda* L. is given in Fig. 1.

5.2 Polyphenols

Polyphenols found in *J. adhatoda* L. includes 12 flavonoids such as kaempferol, apigenin, astragalin, luteolin, violanthin, vitexin, isovitexin, rhamnosyl vitexin, 2''-o-xylosylvitexin, quercetin, 2'-4-dihydroxychalcone-4-glucoside, anthocyanin and 14 phenolic acids including 3,4-dihydroxy benzoic acid, 4-hydroxybenzoic acid, p-coumaric acid and syringic acid. These compounds are found in the leaves and flowers of *J. adhatoda* L. and are mostly isolated from ether extracts [11]. Among the flavonoids there are several flavonols such as quercetin, kaempferol, astragalin

Table 2 Alkaloids extracted from *J. adhatoda* L. plant and their pharmacological properties

Alkaloid name	Source	Pharmacological properties	References
Vasicine (pegamine)	Leaves, roots, flowers	Antibacterial, antidiabetic, anti-tubular, antitubercular, antimalarial, anti-inflammatory, anti-carcinogenic	[2, 17, 19, 64–66]
Vasicoline	Inflorescence, young plants		
Vasicol	Inflorescence, roots		
Vasicinone	Aerial parts, roots		
Vasicinol	Roots, leaves		
Adhatodine	Inflorescence, roots, young plants		
Adhatonine	Leaves, roots		
Anisotine			
7-hydroxyvasicine			
Vasnetine	Leaves		
Betaine	Leaves, flowers		
9-acetamido-3,4-di-hydropyrido-(3,4-b)-indole	Roots		
Deoxyvasicine	Roots, leaves		
Deoxyvasicinone	Roots		
3-hydroxyanisotine	Leaves		

Table 3 Polyphenols extracted from *J. adhatoda* L. plant and their pharmacological properties

Bioactive compound	Source	Pharmacological properties	Reference
Flavonoids			
Kaempferol	Flowers	Antioxidant, anti-carcinogenic, anti-inflammatory, antibacterial, anthelmintic, hepatotoxicity	[11, 17, 66–68]
Astragalín			
Apigenin	Aerial parts		
Luteolin	Flowers, leaves		
Quercetin			
Vitexin			
Rhamnosylvitexin			
2''-o-xylosylvitexin			
Isovitexin			
Violanthin			
2'-4-dihydroxychalcone-4-glucoside	Flowers		
Anthocyanin	Leaves		
Phenolic acids			
3,4-dihydroxy benzoic acid	Leaves	Antioxidant, anti-inflammatory, antiproliferative, anti-microbial, antiangiogenic	[11, 65]
4-hydroxybenzoic acid	Flowers, leaves		
p-coumaric acid	Leaves		
Syringic acid			

Table 4 Terpenoids and Sterols extracted from *J. adhatoda* L. plant and their pharmacological properties

Bioactive compound	Source	Pharmacological properties	References
Steroids			
Sitosterol	Aerial parts, Roots	Anti-inflammatory, Anti-carcinogenic, Anti-microbial, anti-atherosclerotic	[17, 18] [66, 69]
Daucosterol	Roots		
β -sitosterol	Seeds, laves		
γ -sitosterol	Leaves		
Stigmasta-3,5-dien-7-one	Leaves		
Daucosterol	Roots	Antioxidant, anti-inflammatory, anti-microbial, hepatoprotective, antidiabetic, anticarcinogenic	[66, 70]
Epitaraxerol	Aerial parts		
Terpenoids			
β -carotene	Not available	Antioxidant, anti-inflammatory, anti-microbial, hepatoprotective, antidiabetic, anticarcinogenic	[66, 70]
Neandrographolide	Fresh leaves		
Triterpenoids			
α -amyrin	Flowers	Antioxidant, anti-inflammatory, anti-microbial, hepatoprotective, antidiabetic, anticarcinogenic	[66, 70]
Squalene	Leaves		
3- α -Hydroxy-D-friedolean-5-ene	Aerial parts	Antioxidant, anticarcinogenic, antidiabetic, anti-microbial	[66, 70]
Tetra-terpenoids			
Lycopene	Leaves		

Table 5 Other phytochemical compounds in *J. adhatoda* L. plant and their pharmacological properties

Bioactive Compound	Source	Pharmacological properties	References
Glycosides			
β-sitosterol-D-glucoside	Flowers, roots	Analgesic, anti-inflammatory, cardiotonic, anti-microbial, antiviral, anti-carcinogenic	[17, 66, 71]
β-glucoside-galactose	Roots		
Sitosterol-β-D-glucoside	Roots		
2'-4-dihydroxychalcone-4-glucoside	Flowers		
Organic acids			
Adhatodic acid	Leaves	Antioxidant	[70, 72]
Stictic acid			

(kaempferol-3-o-glucoside), and flavones such as violanthin, luteolin, agipenin, vitexin, isovitexin, rhamnosyl vitexin, 2''-o-xylosylvitexin. Phenolic acids are further subdivided into hydroxybenzoic acids (C1–C6 backbone) and hydroxycinnamic acids (C3–C6 backbone). Hydroxycinnamic acids include methylated (syringic acid), glycoside forms (p-coumaric acid) and hydroxybenzoic acids include 3,4-dihydroxy benzoic acid and 4-hydroxybenzoic acid from the *J. adhatoda* L. [11, 25, 26].

Polyphenols encompass a diverse range of molecules characterized by a classic phenol ring structure, featuring multiple hydroxyl groups attached to aromatic rings. These structures can range from simple molecules to complex polymers made up of highly polymerized compounds. Biological functions reported of polyphenols include several bioactivities including antioxidative, anti-carcinogenic, anti-inflammatory, anti-mutagenic and anti-aging activities. Quercetin is known to have anticancer, antioxidant, anti-inflammatory and anti-aging properties. Kaempferol is a potent antioxidant is also capable of directly inhibiting lipid peroxidation. It also has anti-microbial, anti-inflammatory, analgesic and anti-allergic effects. Furthermore, apigenin, luteolin, and syringic acid have antioxidant, anti-inflammatory, anti-microbial, cardio protective and anticancer activities [25–27]. For phenolic acids, p-coumaric acid, 3,4-dihydroxy benzoic acid and 4-hydroxybenzoic acid have lower antioxidant activity because they a mono hydroxylation structure (contains only one hydroxyl group) which limits the ability to scavenge free radicals or protect cells from oxidative stress. The polyphenols found in *J. adhatoda* L. is given in Table 3 and their chemical structure is shown in Fig. 1.

5.3 Terpenoids and sterols

A total of 23 terpenoids and sterols were identified in extracts of *J. adhatoda* L. which includes steroids (sitosterol, daucosterol, β-sitosterol, γ-sitosterol, stigmasta-3,5-dien-7-one, daucosterol and epitaraxerol), terpenoids (β-carotene, neoandrographolide), triterpenoids (α-amyrin, squalene, 3-α-Hydroxy-D-friedoolean-5-ene) and tetra-terpenoids (lycopene). These were found isolated mainly from leaves, shoot and roots. Sitosterol and β-sitosterol are commonly used in Chinese herbal medicines due to its anti-atherosclerotic and heart protection effects [11, 28]. Daucosterol has several potential pharmacological properties such as anti-inflammatory, antioxidant, antidiabetic, anti-cancer and neuroprotective [29]. The terpenoids and sterols found in *J. adhatoda* L. is given in Table 4 and their chemical structure is shown in Fig. 1.

6 Ethnopharmacology

J. adhatoda L. has been commonly used for treatment of respiratory ailments, asthma, cough and colds. The potential use of the plant for reproductive problems came to light in the 1994. The first field record was on the Neterhat people in Bihar. They used a decoction of the plant leaves before and after delivery to stimulate and heal. Later in 1997, it was observed that *J. adhatoda* L. was used as an abortifacient in Gora village, Lucknow [10].

Summarized in Table 6, is the various medicinal uses of *J. adhatoda* L. plant parts.

Fig. 1 Phytochemical compounds isolated from *J. adhatoda* L. [11, 16]

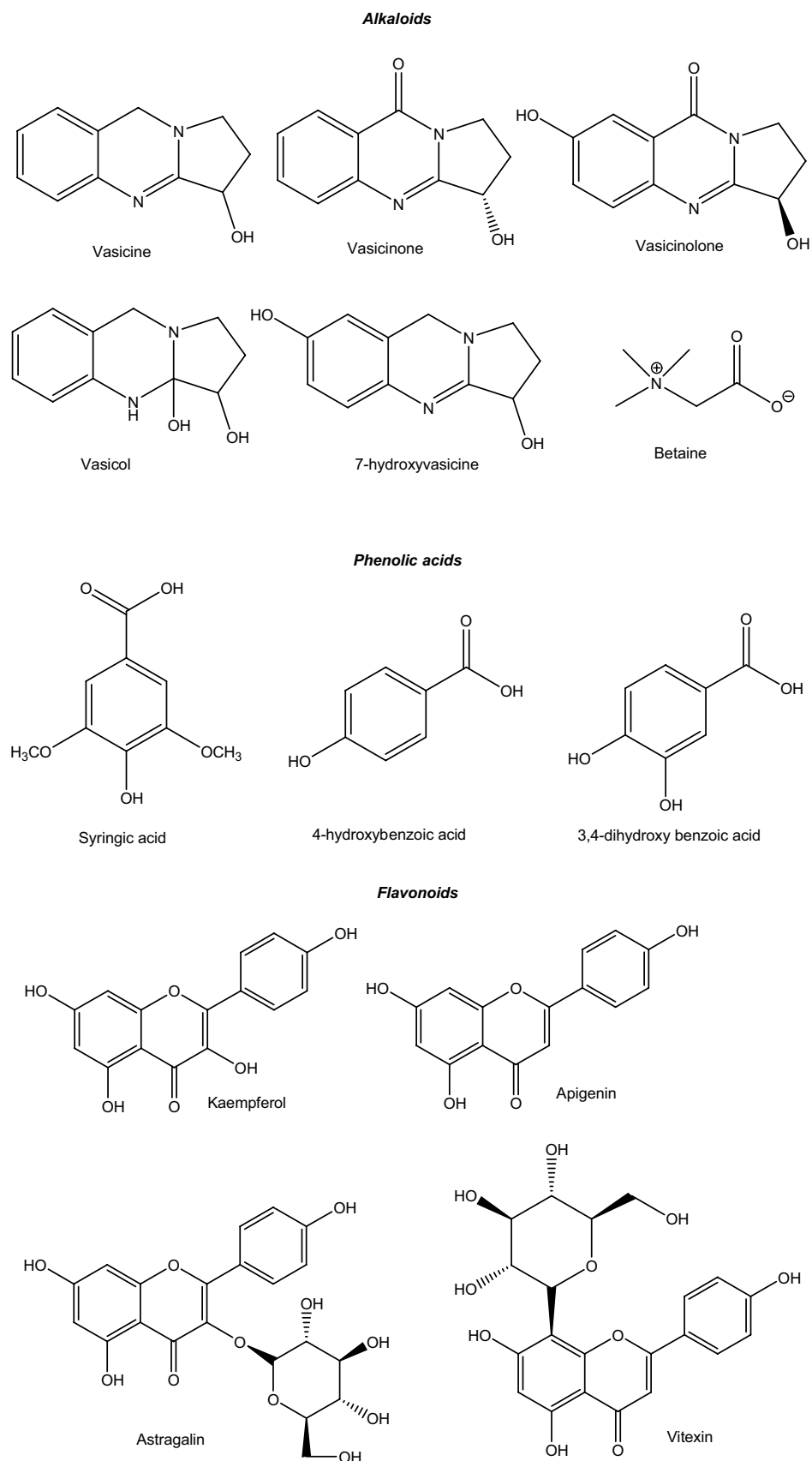
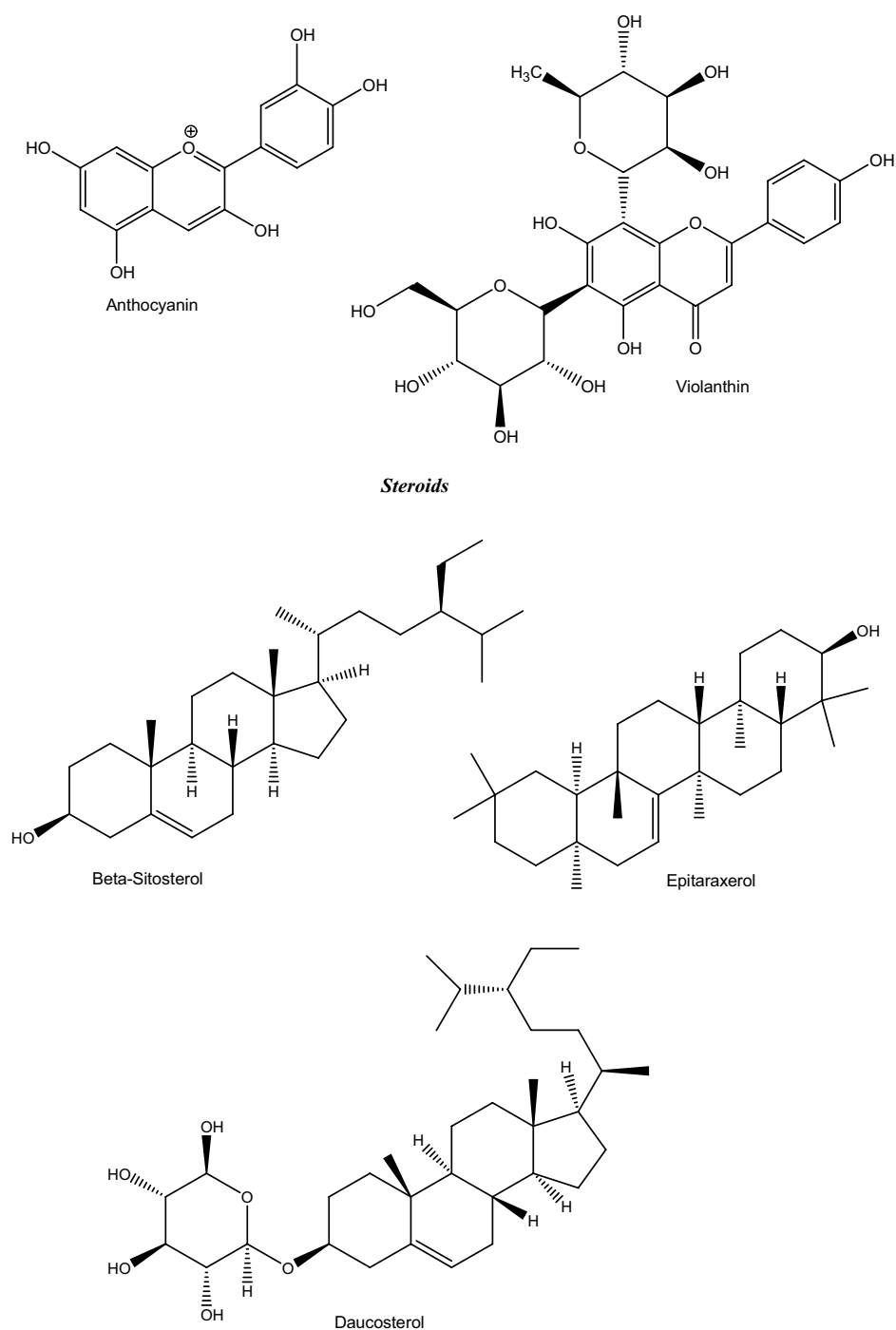


Fig. 1 (continued)

6.1 Bibliographical data

Around the world, for many years *J. adhatoda* L. plant has been used in traditional medicine. Various parts of the plant or the plant as a whole were used by Ayurvedic medicine practitioners, other Asian medicine practitioners and also by European medical practitioners.

Table 6 Medicinal use of various parts of *J. adhatoda* L.

Plant part	Use	References
Roots	<i>Paste</i> : easy child birth, tuberculosis, diphtheria, malarial fever, leucorrhea, eye diseases, acute nightfall <i>Extract</i> : diabetes, cough and certain liver disorders <i>Decoction</i> : gonorrhea <i>Syrup</i> : cough	[2, 64, 73]
Leaves	<i>Juice</i> : acute cough, chronic bronchitis, breathlessness, asthma, viral fevers, postpartum hemorrhage, urinary trouble, acidity, belching and vomiting <i>Crushed</i> : snake bites (India and Sri Lanka) <i>Infusion</i> : headache <i>Oil</i> : stops bleeding, ear aches, jaundice <i>Poultice</i> : fever, rheumatic pains and dislocation of joint, stomach catarrh with constipation, gout, and urinary stone	[2, 4, 64]
Flowers	<i>Syrup</i> : cough, chronic bronchitis and asthma <i>Infusion</i> : fever, gonorrhea, jaundice and rheumatism <i>Poultice</i> : ophthalmia	[2, 74]
Fruits	<i>Decoction</i> : cold, respiratory tract irritation, cough, bronchitis, asthma and intestinal worms	[2, 75]
Bark	<i>Decoction</i> : asthma, cough, expectorant, wound healing <i>Crushed</i> : wound healing <i>Powder</i> : chest diseases, asthma	[10]

6.1.1 Asia

By the year 1980, *J. adhatoda* L. was used as an expectorant and antispasmodic agent and the alkaloid 'vasicine' was identified. Over many different Asian countries, it is used for the treatment of various internal and external diseases and disorders. It is most frequently used for respiratory tract related diseases and disorders including colds, cough, bronchitis, asthma, and tuberculosis (phthisis). In the Ayurvedic medicine, it is also used for the treatment of joint pain, rheumatism, sprains, lumber pain, eczema, swelling, malaria and venereal diseases. In Sri Lanka, the whole plant is used for treatment of excessive phlegm and menorrhagia. For curing headaches, wounds, bleeding, haemorrhage, skin diseases, and leprosy, various leaf preparations are used in Southeast Asia. In the rural villages, the roots are used against diabetes, cough and certain liver disorders. The fresh flowers are used for ophthalmia in South-East Asia. Various preparations of flowers are also used for treatment of cough, cold, asthma, phthisis, bronchitis, fever, antispasmodic and gonorrhea in South-East Asia [30, 31]. In Table 7, the traditional uses of various parts of *J. adhatoda* L. plant and the preparation method used for ailments by country is summarized.

Leaves and roots are the most frequently used parts of the plant. Usually consumed in the form of a decoction or powder. In the Asian region, various extracts and syrups of *J. adhatoda* L. are available in the market such as Adulsa. These can be either consumed directly or required dilution.

Other than for its medicinal uses, the *J. adhatoda* L. is also consumed as food in various Asian countries. In the Meitei community of Manipur in India, mature leaves as well as inflorescence are used as food [32]. The flowers and tender leaves are used as a vegetable in Nepal [10].

6.1.2 Europe

J. adhatoda L. has also been used in the European medicine as well. It was said to be successfully used for treatment of influenza, cough, common cold, bronchitis, typhus fevers, and diphtheria [33]. Apart from that, *J. adhatoda* L. is also used for gastric catarrh, constipation, gout, rheumatism and urinary stones. There are many commercial products currently in the market containing *J. adhatoda* L. leaf powder such as Salus Tuss in Germany, and Kan Jang and Spirote in Sweden. In Sweden, *J. adhatoda* L. extract is used in cough syrup preparation and is classified as a natural remedy [34, 35]. In England, the fluid extract and tincture were used by medical practitioners as an expectorant, antispasmodic and febrifuge. It was said to be beneficial in treatment of intermittent diphtheria and typhus fever. In Germany, the leaves are used as an expectorant and spasmolytic agent [10, 36].

Table 7 Traditional uses of *J. adhatoda* L. in Asia

Major ailment category	Plant part	Preparation method	Country	References
Pulmonary (cough, cold, fever, bronchitis, malarial fever, asthma, tuberculosis, and pneumonia)	Leaves	Decoction	India, Bangladesh, Myanmar, Pakistan, Sri Lanka, Thailand	[76–81]
		Extract	India, Bangladesh	[82, 83]
	Bark	Juice	Myanmar	[80]
	Root	Powder	Bangladesh	[83]
		Powder	India	[77]
	Root bark	Decoction	India	[84]
	Roots and flowers	Raw	Bangladesh	[78]
	Roots and leaves	Juice	Myanmar	[80]
	Flowers	Extract	Pakistan	[31]
		Infusion	Sri Lanka	[74]
Diabetes	Whole plant		Sri Lanka	[30]
	Leaves	Extract	India	[85]
	Leaves	Powder	Bangladesh	[78]
Diarrhoea and dysentery		Juice	Bangladesh	[78, 79]
	Leaves	Extract	India, Myanmar	[82]
	Leaves	Powder	India	[77]
Skin diseases	Leaves	Paste	India	[77]
		Decoction	Pakistan	
Reproductive health (gonorrhoea, menorrhagia)	Flowers	Infusion	Sri Lanka	[74]
	Leaves		Myanmar	[80]
Jaundice	Flowers	Infusion	Sri Lanka	[74]
	Leaves	Poultice	India, Pakistan	
Rheumatism	Flowers	Infusion	Sri Lanka	[74]
	Flowers	Fresh flowers for ophthalmia	Sri Lanka, India	[10, 74]
Eye diseases	Leaves	Paste	Sri Lanka	[86, 87]
		Powder	Myanmar	[80]
Oral (gingival bleeding, oral hygiene, plaque)	Leaves	Poultice	India	
	Root bark		Pakistan	[6]
Wound healing	Leaves	Decoction	Myanmar	[80]
	Root bark	Juice	Myanmar	[80]
Urinary infections	Flowers and leaves	Raw	Myanmar	[80]
	Fruit	Juice	Bangladesh	[66]
Vomiting	Bark and leaves			

7 Pharmacology and toxicology

7.1 Anti-asthmatic and bronchodilator activity

The primary alkaloids of *J. adhatoda* L.; both vasicine and vasicinone are well established therapeutical respiratory agents [37]. The leaf and root extracts are useful in treatment of cough, cold, bronchitis and other lung and bronchiole disorders. Herbal tea prepared from the fresh leaves of *J. adhatoda* L. is a expectorant due to the presence of the alkaloid vasicine and its variations [38]. The antitussive activity of *J. adhatoda* L. extract was evaluated in anaesthetized rabbits and guinea pigs and in unanaesthetized guinea pigs. The results showed good antitussive activity [39]. The bronchodilating effect of *J. adhatoda* L. leaf ethanolic extract on acetylcholine and histamine aerosol induced broncho-constriction in guinea pigs was comparable to ketotifen. The possible mechanism of action may be due to the H₂ and Ach receptor blocking causing the inability of the smooth muscles to respond to histamine and Ach induced spasm leading to inhibition of bronchio-constriction [40].

7.2 Anti-microbial activity

Over the years, many studies were done on the anti-microbial activity of *J. adhatoda* L. plant (Table 8). The in-vitro anti-microbial activity of *J. adhatoda* L. of leaves were studied using the agar well diffusion method. Most activity was exhibited by the methanolic extract in comparison to the other solvents. Methanolic extract showed maximum activity against *Staphylococcus aureus* and was also effective against the other bacteria [41].

The anti-microbial activity of isolated compounds was evaluated by using the microdilution method. The pyrroloquinazoline alkaloids isolated from *J. adhatoda* L. exhibited most potential antibacterial activity against *Escherichia coli*. Similarly, maximum antifungal activity was against *Candida albicans* [42]. Vasicine acetate, obtained by acetylation of Vasicine has shown antibacterial activity. At 500 µg/ml, Vasicine acetate exhibited higher antibacterial activity in comparison to Vasicine. It was effective against, *Staphylococcus epidermidis*, *Enterobacter aerogenes*, and *Pseudomonas aeruginosa* [43].

The antibacterial properties of the non-polar (hexane) and polar (water and methanol) leaf extracts were investigated using the disc diffusion technique. The investigation concluded that when compared to Gram-positive strains, Gram-negative strains were more open to the extracts. Water extract exhibited highest inhibitory effect on *Staphylococcus simulans* and *Staphylococcus aureus* [44]. Antibacterial assay of vasicine from *J. adhatoda* L. leaf extract was carried out by two different strains (*Escherichia coli* and *Bacillus badius*) using colony forming units (CFU) assay. It was noted that with increase in vasicine concentration, the number of colonies reduced [45].

There have been comparative studies carried out with the standard antibiotic drug, Ampicillin. In 2009, the antibacterial activity of hexane, chloroform and methanol extracts of the leaves were compared with that of Ampicillin (positive control). The results showed that 400 µg/ml of the hexane extract showed results similar to that of the antibiotic [46]. Similarly, *J. adhatoda* L. leaf essential oil was also studied against that of ampicillin. However, there was significant effect from the drug in comparison to the essential oil [47].

7.3 Antioxidant activity

The antioxidant activity of hexane, chloroform and methanol *J. adhatoda* L. leaf extracts was studied against α -tocopherol (standard). The inhibitory activity of the methanol extract was the highest followed by chloroform and hexane extracts respectively. Thus, the results confirm the antioxidant potential of *J. adhatoda* L. leaves [46]. The radical scavenging activity of Vasicine acetate synthesized from Vasicine with Butylated hydroxytoluene (BHT) as standard showed increase in activity with increased concentration of the extract. The maximum radical scavenging activity was at 1000 µg/ml [43].

The antioxidant activity of vasicine from *J. adhatoda* L. leaf extracts was evaluated by Rudrapal et. al. using ABTS [2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid)] activity, DPPH radical scavenging activity, ferric reducing power (FRAP) assay, hydroxyl radical scavenging activity, and hydrogen peroxide assay. It showed antioxidant activity in ABTS scavenging assay (IC₅₀ = 11.5 µg/ml), FRAP assay (IC₅₀ = 15 µg/ml), DPPH radical scavenging assay (IC₅₀ = 18.2 µg/ml), hydroxyl radical scavenging assay (IC₅₀ = 22 µg/ml), and hydrogen peroxide assay (IC₅₀ = 27.8 µg/ml) [45]. The methanolic

Table 8 Studies on anti-microbial activity of *J. adhatoda* L.

Plant part	Method	Extracts	Organisms	Results ^a	References
Antibacterial activity					
Leaves	Agar well diffusion method	Ethanol	<i>Staphylococcus aureus</i>	19 mm	[1]
			<i>S. epidermidis</i>	18 mm	
			<i>B. subtilis</i>	14 mm	
			<i>P. aeruginosa</i>	15 mm	
			<i>P. vulgaris</i>	15 mm	
			<i>E. faecalis</i>	No activity	
			<i>E. coli</i>	No activity	
		Petroleum ether	<i>Klebsiella pneumoniae</i>	No activity	
			<i>Staphylococcus aureus</i>	16 mm	
			<i>S. epidermidis</i>	No activity	
			<i>B. subtilis</i>	No activity	
			<i>P. aeruginosa</i>	No activity	
			<i>P. vulgaris</i>	No activity	
			<i>E. faecalis</i>	No activity	
		Water	<i>E. coli</i>	No activity	
			<i>Klebsiella pneumoniae</i>	No activity	
			<i>Staphylococcus aureus</i>	No activity	
			<i>S. epidermidis</i>	No activity	
			<i>B. subtilis</i>	No activity	
			<i>P. aeruginosa</i>	No activity	
			<i>P. vulgaris</i>	No activity	
Leaves	Agar cup method	Water	<i>E. faecalis</i>	No activity	[88]
			<i>E. coli</i>	No activity	
			<i>Klebsiella pneumoniae</i>	No activity	
			<i>Staphylococcus aureus</i>	16 mm	
			<i>Shigella flexneri</i>	18 mm	
			<i>Bacillus licheniformis</i>	14 mm	
			<i>Brevibacillus brevis</i>	16 mm	
			<i>Vibrio cholerae</i>	16 mm	
			<i>P. aeruginosa</i>	14 mm	
			<i>Bacillus subtilis</i>	17 mm	
			<i>Staphylococcus epidermidis</i>	No activity	

Table 8 (continued)

Plant part	Method	Extracts	Organisms	Results ^a	References
Leaves	Agar disc diffusion method	Hot water	<i>Bacillus cereus</i>	3 mm	[38]
			<i>Bacillus subtilis</i>	8 mm	
			<i>Bacillus megaterium</i>	No activity	
			<i>Salmonella typhi</i>	No activity	
			<i>Staphylococcus aureus</i>	No activity	
			<i>Vibrio cholerae</i>	7 mm	
			<i>Escherichia coli</i>	2 mm	
		Alcohol	<i>Bacillus cereus</i>	6 mm	
			<i>Bacillus subtilis</i>	11 mm	
			<i>Bacillus megaterium</i>	No activity	
			<i>Salmonella typhi</i>	No activity	
			<i>Staphylococcus aureus</i>	No activity	
			<i>Vibrio cholerae</i>	13 mm	
			<i>Escherichia coli</i>	5 mm	
		Petroleum ether	<i>Bacillus cereus</i>	No activity	
			<i>Bacillus subtilis</i>	11 mm	
			<i>Bacillus megaterium</i>	No activity	
			<i>Salmonella typhi</i>	No activity	
			<i>Staphylococcus aureus</i>	No activity	
			<i>Vibrio cholerae</i>	15 mm	
			<i>Escherichia coli</i>	No activity	
Leaves	Agar disc diffusion method	Hexane	<i>Enterococcus faecalis</i>	18 mm	[46]
			<i>Staphylococcus epidermidis</i>	19 mm	
			<i>Vibriopara heamolysis</i>	17 mm	
			<i>Serraties masciens</i>	17 mm	
			<i>Staphylococcus heamophytenu</i>	27 mm	
			<i>Bactere maserins</i>	14 mm	
			<i>Vibrio cholerae</i>	17 mm	
		Chloroform	<i>Enterococcus faecalis</i>	18 mm	
			<i>Staphylococcus epidermidis</i>	15 mm	
			<i>Vibriopara heamolysis</i>	16 mm	
			<i>Serraties masciens</i>	20 mm	
			<i>Staphylococcus heamophytenu</i>	17 mm	
			<i>Bactere maserins</i>	16 mm	
			<i>Vibrio cholerae</i>	19 mm	
		Methanol	<i>Enterococcus faecalis</i>	16 mm	
			<i>Staphylococcus epidermidis</i>	18 mm	
			<i>Vibriopara heamolysis</i>	17 mm	
			<i>Serraties masciens</i>	16 mm	
			<i>Staphylococcus heamophytenu</i>	18 mm	
			<i>Bactere maserins</i>	16 mm	
			<i>Vibrio cholerae</i>	15 mm	

Table 8 (continued)

Plant part	Method	Extracts	Organisms	Results ^a	References
Leaves	Agar disc diffusion method	Essential oil and Ethanol	<i>Escherichia coli</i>	16 mm	[47]
			<i>Salmonella typhimurium</i>	7.5 mm	
			<i>Bacillus subtilis</i>	2 mm	
			<i>Staphylococcus aureus</i>	6 mm	
Leaves	Agar disc diffusion method	Methanol	<i>Klebsiella pneumoniae</i>	9.5 mm	[22]
			<i>Escherichia coli</i>	12 mm	
			<i>Pseudomonas aeruginosa</i>	5.0 mm	
			<i>Streptococcus pyogenes</i>	9.0 mm	
			<i>Staphylococcus aureus</i>	12.5 mm	
			<i>Serratia marcescens</i>	8.9 mm	
			<i>Bacillus subtilis</i>	15 mm	
Leaves	Agar well diffusion method	<i>n</i> -butanol	<i>Escherichia coli</i>	14 mm	
			<i>Klebsiella pneumoniae</i>	11 mm	
			<i>Proteus vulgaris</i>	13 mm	
			<i>Pseudomonas aeruginosa</i>	12 mm	
Leaves	Agar disc diffusion method	Methanol	<i>Staphylococcus aureus</i>	21 mm	[90]
			<i>Pseudomonas aeruginosa</i>	19 mm	
			<i>Escherichia coli</i>	18 mm	
Leaves	Agar disc diffusion method	Methanol	<i>Pseudomonas aeruginosa</i>	7.8 mm	[48]
			<i>Escherichia coli</i>	10 mm	
			<i>Listeria</i>	6 mm	
Antifungal activity					
Leaves	Agar well diffusion method	Ethanol	<i>C. albicans</i>	12 mm	[1]
	Agar disc diffusion method	Methanol	<i>Aspergillus flavus</i>	9.6 mm	[22]
			<i>Candida albicans</i>	14.8 mm	
			<i>Cryptococcus neoformans</i>	10.9 mm	

^aZone of inhibition (mm)

leaf extract of *J. adhatoda* L. showed a concentration-dependent increase in the antioxidants activity with 150 µl exhibiting maximum response [48].

7.4 Anti-cancer activity

There were several studies that reported the anti-cancer activity *J. adhatoda* L. Vasicine acetate synthesized by acetylation of Vasicine showed considerable anti-cytotoxic activity on A549 lung adenocarcinoma cancer cell lines with IC₅₀ value of 2000 µg/ml [43]. An alkaloid, 2-acetyl-benzylamine, isolated from *J. adhatoda* L. was studied for its potential anticancer activity against leukemia cells. For cytotoxic studies, various types of leukemia cells were used including CEM, NB-4, MOLM-14, Jurkat, IM-9, K562 and HL-60. The alkaloid exhibited the best cytotoxicity properties against MOLM-14 and NB-4 cells with IC₅₀ values of 0.40 mM and 0.39 mM [49].

The crude ethanolic extracts of *J. adhatoda* L. leaves showed that as the concentration of the extract increased for treatment, the percentage viability of PA1 ovarian cancer cells decreased linearly. The extract exhibited potential anti-cancer effect with a LC₅₀ value of 107.339 µg/ml. The gene expression studies for p53 and p21 genes showed increased expression in the extract treated cells in comparison to the untreated control cells. These p53 and p21 genes were found to have a potent role in the anticancer activity of *J. adhatoda* L. ethanol extracts [50]. The potential of *J. adhatoda* L. leaf methanolic extract on human breast cancer cells was studied by Kumar et al. [51]. A docking study was performed using the active compounds Vasicine, Vasicinone, Vasicinol, Vasicinolone and Deoxyvasicinone. The study showed that they had a good binding affinity towards the active site of NF-κB. The extract exhibited the highest cytotoxicity in MCF-7, a breast cancer cell line exhibiting potential anticancer activity.

7.5 Antidiabetic activity

In the literature, there were few studies done on the antidiabetic activity of *J. adhatoda* L. (Table 9). In the rural population, various parts of *J. adhatoda* L. plant is used in diabetes management and certain liver disorders. [52] demonstrated mammalian α -glucosidase inhibition by *J. adhatoda* L. leaves methanolic extract. The isolated vasicine and vasicinol showed high inhibitory activity against sucrase. However, the inhibitory activity against maltase, isomaltase and porcine pancreatic α -amylase was weak. Similarly, Vadivelan et al. [53], ethanolic extracts and fractions (chloroform and n-butanol) of *J. adhatoda* L. leaves to demonstrate in-vitro inhibition of α -amylase and α -glucosidase.

Flavonoids are known for their antidiabetic activity and are an important phytoconstituent of *J. adhatoda* L. flowers. The antidiabetic function of flavonoids have various mechanisms such as reducing apoptosis and regeneration of pancreatic β -cells, reducing insulin resistance and oxidative stress, enhancing insulin release, suppression of β -amylase and α -glucosidase, reduction of aldose reductase, enhanced uptake and utilization of glucose by peripheral tissues and increased hepatic glucokinase activity [54, 55].

A comparison study was done in 2009 with hexane, chloroform and methanolic extracts of *J. adhatoda* L. leaves and Glibenclamide, an antidiabetic medication used for treatment of type-2 diabetes, The results showed that 10 mg/kg of the antidiabetic drug displayed significant decrease in the serum glucose levels and similar effects were observed in the chloroform and methanolic extracts at 200 mg/kg dosage. It was concluded in the study that the antioxidant activity of the extracts attributed to the antidiabetic activity by means of scavenging the oxygen free radical [46].

7.6 Anti-inflammatory activity

The anti-inflammatory property of *J. adhatoda* L. is from the presence of its quinazoline alkaloid, vasicine. In 2001, the anti-inflammatory activity of the methanol extract, the non-alkaloid fraction, the saponins and the alkaloids was evaluated using the modified hen's egg chorioallantoic membrane test. The alkaloid mixture contained 80% vasicine, it showed a potent activity in the inhibition of membrane irritation. However, the methanol extract, the non-alkaloid fraction, and the saponins showed less activity [56].

An Ayurvedic polyherbal remedy Maharasnadhi Quathar (MRQ) has been used for treatment of arthritis. The effect of this polyherbal formula was investigated on Wistar rats via carrageenan-induced paw oedema. Results obtained concluded that MRQ significantly and dose-dependently inhibit carrageenan-induced rat paw oedema (the inhibition at third hour was greater than at first hour after induction of oedema) [57]. An evaluation of the anti-inflammatory activity of *J. adhatoda* L. leaves was done by Belemkar et al. in comparison to *Mentha piperita* Linn. leaves and Diclofenac sodium (reference drug). The methanolic extract of *J. adhatoda* L. at 400 mg/kg, *Mentha piperita* at 600 mg/kg were effective. The best effectiveness in comparison to the reference drug was achieved by combination of the plant extracts (*J. adhatoda* L. at 200 mg/kg and *Mentha piperita* at 300 mg/kg) [58].

The anti-inflammatory activity of different fractions of *J. adhatoda* L. leaf extract such as ethyl acetate, n-hexane, chloroform, and aqueous were observed via carrageenan-induced paw edema test. Chloroform fraction showed significant anti-inflammatory activity at the fourth hour at a higher concentration (300 mg/kg) followed by n-hexane, ethyl acetate, and aqueous fractions [59]. The anti-inflammatory effect of the *J. adhatoda* L. leaves methanol extract was investigated against the acute Carrageenan-induced inflammatory pain model in mice. The animals treated with the extract showed a marked reduction in paw edema and the 100 mg/kg showed a maximum response. A comparative analysis was carried out with the positive control group was treated with Dexamethasone, which also showed reduction in paw edema. The anti-inflammatory activity of *J. adhatoda* L. against Formalin-induced biphasic response showed a reduction in licking and nociceptive behavior in both early and late phases. The positive control group treated with Dexamethasone showed the best marked reduction in the painful reaction among all groups. The study also showed a dose-dependent increase in the protective antioxidants (GST, GSH and Catalase) when treated with *J. adhatoda* L. extract. However, Dexamethasone treated group also showed significant increase in the protective antioxidants enzymes [48].

7.7 Abortifacient activity

J. adhatoda L. has been used traditionally for inducing abortion and for stimulating uterine contractions in order to speed childbirth. There have been several studies that revealed vasicine, an alkaloid isolated from *J. adhatoda* L. is responsible

Table 9 Studies on antidiabetic effects of *J. adhatoda* L.

References	Part used	Purpose	Animals used and diabetic model	Antidiabetic drug used	Outcome
[4]	Leaves	Efficacy of crude extract on blood sugar levels	Human trial (male and female)	Not applicable	Significant decrease in blood sugar levels in both genders
[46]	Leaves	To investigate the effect of hexane, chloroform and methanolic extracts at 100 mg/kg and 200 mg/kg	Rats alloxan induced	Glibenclamide (10 mg/kg)	After 7 days, the chloroform and methanolic extract at dose of 200 mg/kg showed a significant reduction in blood glucose and cholesterol levels
[73]	Leaves and roots	To investigate the effect of ethanol extract on blood glucose levels at 50 mg/kg and 100 mg/kg	Rats alloxan induced	Glibenclamide (5 mg/kg)	From 2 to 6 days of treatment significant ($P < 0.05$) reduction in blood glucose levels
[53]	Leaves	Ethanolic extract, fractionated by chloroform and n-butanol to study their α -glucosidase and α -amylase inhibitory activity	In-vitro analysis	Not Applicable	Showed dose dependent inhibition of the α -amylase and α -glucosidase enzyme
[91]	Leaves and flowers	Effect of ethanolic extract on blood glucose levels and its antioxidant activity	Mice	Metformin/Glucophage (1 mg/kg)	Leaf extract is able to lower blood glucose levels
[64]	Leaves	Evaluate the effect of methanolic, ethanolic and ethyl acetate extract on diabetic mice	Mice alloxan monohydrate	Glibenclamide (10 mg/kg)	After 28 days, blood glucose level reduced in all extracts. 400 mg/kg, methanolic extract had the highest blood glucose reduction

for its abortifacient effects. In 1987, a survey was conducted in Farrukhabad and Lucknow of Uttar Pradesh and its anti-implantation efficacy was exhibited [60]. Oral administration of aqueous extract of *J. adhatoda* L. leaves in female albino rats after insemination with special reference to effects on fetal development showed successful abortion activity [60]. In both in-vitro and in-vivo studies the possible abortifacient activity of *J. adhatoda* L. has been investigated with rats, guinea pigs, hamsters, rabbits and human myometrial strips. An investigation was carried out on human volunteers with IV injection of vasicine. The results indicated that the uterus became firm and contracted after vasicine treatment which indicated its effectiveness as an oxytocic. Vasicine hydrochloride was deemed safe and promise as an effective abortifacient [61].

Animal model study using rats, hamsters, rabbits and guinea pigs revealed vasicine operates similar to oxytocin and ergometrine in animal models. It was discovered that the potential of vasicine as uterotonic and abortifacient is probably due to the synthesis and release of PG (prostaglandins) [62]. The dosage and the action are dependent on the stage of pregnancy. When estrogens were utilized as priming agents, the effects of vasicine were stronger. This suggests that it acts via prostaglandin release [19, 60].

7.8 Other pharmacological activities

Other than the above-mentioned activities, *J. adhatoda* L. plant has been investigated for its other pharmacological properties such as analgesic activity, hepatoprotective activity, antitussive activity and wound healing (Table 10). Maharasnadi Quathar (MRQ) is an Ayurvedic polyherbal remedy that has been used for treatment of arthritic conditions. One of the ingredients of MRQ is *J. adhatoda* L. roots. The investigation concluded that the formulation had powerful dosage-dependent analgesic and anti-inflammatory activity [57].

7.9 Toxicology of *J. adhatoda* L.

Few investigations have been done on toxicological aspects of *J. adhatoda* L. However, there has been no record of acute adverse or serious side effects of the plant. There are some minor effects observed due to use of higher than recommended dose such as diarrhea or vomiting. The leaves show prominent abortifacient activity, which is from the presence of vasicine. Vasicine and vasicine hydrochloride is known for potential toxicities. However, it is reported to be non-poisonous to mammals. Therefore, it can be concluded that *J. adhatoda* L. is non-toxic in dose-dependent manner [11, 19].

Acute toxicity studies were performed on Wistar rats and it was found to be safe up to a maximum dose of 2000 mg/kg body weight in rats. There were no changes in normal behavioral pattern, no signs and symptoms of toxicity and mortality were observed [22, 63]. Similarly, as per acute toxicity studies carried out for vasicine, the LD50 value for various animal models are shown in Table 11 [10, 19].

8 Conclusion

J. adhatoda L. is an ethnomedicinal herb that is widely used by medical practitioners in South Asia, Southeast Asia, and Europe. The wide range of pharmacological properties includes anti-microbial, antioxidant, anti-inflammatory, anti-diabetic, anti-tubercular, antipyretic, hepatoprotective, insecticidal properties, activity against respiratory ailments, anti-cancer and radioprotective activity. Given its multiple uses, more activity screening and structure–activity relationship studies are required to explore further. This present review brings forth the current findings on the pharmacological activities of *J. adhatoda* L. but there are still certain aspects of the plant that are limited, not reliable, or lacking in data. Leaves are the most utilized part of the plant and there is a lack of studies undertaken in regards to the other parts of the plant. This also includes the toxicological aspects of the plant whole plant. There is room for further experiments on developing methods to isolate active compounds from other parts of the plants and to study their phytochemical potential.

Table 10 Studies on various other pharmacological activities of *J. adhatoda* L.

Plant part	Extract	Methods used	Species	Outcome	References
Analgesic activity	Leaves	Ethanol and methanol	Writhing test, tail immersion test, hot plate test	Wistar rats	Significant results were obtained when the writhing response induced by the acetic acid was treated with the alcoholic extracts [92]
		Methanol	Tail immersion test, hot plate test		Oral administration of extract and significantly inhibits the pain and also raised the pain threshold. The extracts showed less pain threshold in comparison to the reference drug, diclofenac sodium [58]
		Ethyl acetate, n-hexane, chloroform and aqueous	Writhing test, licking paw test, tail immersion test	Swiss albino mice	Ethyl acetate fraction was most effective in writhing and licking paw test. Chloroform and aqueous fractions showed preferred results against reference drug in tail immersion test [59]
Hepatoprotective activity	Leaves	Ethanol	Carbon tetrachloride (CCl ₄) induced	Wistar rats	Significant hepatoprotective effect at doses of 100–200 mg/kg, p.o [93]
		Aqueous	D-galactosamine induced		Significant hepatoprotective effect at doses of 50–100 mg/kg, p.o [94]
		Methanol, chloroform, and diethyl ether	Carbon tetrachloride (CCl ₄) induced		Methanolic extract showed significant effect at the dose of 200 mg/kg b.w. compared to other extracts [63]
		Ethyl acetate	Carbon tetrachloride (CCl ₄) induced	Swiss albino mice	200 mg/kg b.w. dose has prominent hepatoprotective activity [95]
Antitussive activity	Leaves and flowers	Ethanol	5% citric acid induced 2.8% NH ₄ OH induced 0.5N H ₂ SO ₄ induced	Guinea-pigs	ED ₅₀ = 75.6 mg/kg p.o ED ₅₀ = 200.0 mg/kg p.o ED ₅₀ = 125.8 mg/kg p.o [39]
	Leaves	Ethanol	Sulphur dioxide induced	Swiss albino mice	Significant effect with inhibition of 43.02% compared to standard drug [96]
Wound healing	Leaves	Methanol, chloroform, and diethyl ether	Excision wound model	Wistar rats	Methanolic extract showed significant effect compared to standard drug and other two extracts [97]
		Methanol, ethanol, ethyl acetate, chloroform and hexane	Excision wound model	Swiss albino mice	Methanolic extract of the leaf showed remarkable wound healing activity [98]

p.o.: per orally; ED₅₀: effective dose; b.w.: body weight

Table 11 LD50 values for vasicine in various animal models

Animal	LD50 values (mg/kg)			
	Oral	Intravenous	Intraperitoneal	Subcutaneous
Rats	700–1200	40–80	500	500–800
Mice	300–800	30–50	250	250–400
Rabbits	1200	Not available	Not available	Not available

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Declarations

Competing interests The authors declare no competing interests.

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References

- Karthikeyan A, Shanthi V, Nagasathaya A. Preliminary phytochemical and antibacterial screening of crude extract of the leaf of *Adhatoda vasica* L. Int J Green Pharm. 2009;3(1):78. <https://doi.org/10.4103/0973-8258.49381>.
- Sharma A, Bhardwaj G, Cannoo DS. Overview of phytochemistry and pharmacology of *Adhatoda vasica*. Int J Adv Manag Technol Eng Sci. 2018;8(3):1286–302.
- Shrestha RK, Dongol Y, Lakkappa B, Rai A, Aryal G. Chapter 16: Pharmaceutical potential of *Adhatoda vasica* (Acanthaceae) in management of diabetes mellitus and its complications. In: Recent progress in medicinal plants, metabolic disorders: diabetes I, recent progress in medicinal plants, vol. 45. USA: Studium Press. 2017; pp. 300–14.
- Talib M, Gulfranz M, Mussaddeq Y. Effect of crude extract of *Adhatoda vasica* Nees on diabetic patients. J Biol Sci. 2002;02(07):436–7. <https://doi.org/10.3923/jbs.2002.436.437>.
- Akbar S. Handbook of 200 medicinal plants: a comprehensive review of their traditional medical uses and scientific justifications. Cham: Springer International Publishing; 2020. <https://doi.org/10.1007/978-3-030-16807-0>.
- Joshi LR, et al. *Justicia adhatoda* L. Acanthaceae. In: Kunwar RM, Sher H, Bussmann RW, editors., et al., Ethnobotany of the Himalayas. Ethnobotany of Mountain Regions. Cham: Springer International Publishing; 2021. p. 1–9.
- Yadav S, Yadav VK, Water Lab, Central Pollution Control Board. Ethnomedicinal value and pharmacognosy of the member of Acanthaceae: *Adhatoda vasica*. (Linn). Asian Pac J Health Sci. 2018;5(2):40–3. <https://doi.org/10.21276/apjhs.2018.5.2.10>.
- Dhankhar S, Kaur R, Ruhil S, Balhara M, Dhankhar S, Chhillar AK. A review on *Justicia adhatoda*: a potential source of natural medicine. Afr J Plant Sci. 2011;5(11):620–7.
- Dweck AC. The William garden collection of Chinese medicinal plants, China. 1995. p. 31.
- Claeson UP, Bruhn JG. *Adhatoda vasica*: a critical review of ethnopharmacological and toxicological data. J Ethnopharmacol. 2000;72:1–20.
- Shamsuddin T, et al. *Adhatoda vasica* (Nees.): a review on its botany, traditional uses, phytochemistry, pharmacological activities and toxicity. Mini-Rev Med Chem. 2021;21(14):1925–64. <https://doi.org/10.2174/1389557521666210226152238>.
- Kumar M, Dandapat S, Kumar A, Sinha MP. Pharmacological screening of leaf extract of *Adhatoda vasica* for therapeutic efficacy. Glob J Pharmacol. 2014;08(04):494–500. <https://doi.org/10.5829/idosi.gjp.2014.8.4.8419>.
- Kumar M, Dandapat S, Kumar A, Sinha MP. Determination of nutritive value and mineral elements of five-leaf chaste tree (*Vitex negundo* L.) and Malabar nut (*Adhatoda vasica* Nees). Acad J Plant Sci. 2013;06(03):103–8.
- Gulfranz M. Investigation for bioactive compounds of *Berberis lyceum* Royle and *Justicia adhatoda* L. Ethnobot Leaflet. 2005;1(22):5.

15. Jayapriya G, Shoba FG. GC-MS analysis of bio-active compounds in methanolic leaf extracts of *Justicia adhatoda* (Linn.). J Pharmacogn Phytochem. 2015;04(01):113–7.
16. Singh SK, Patel JR, Dubey PK, Dangi A. Pharmacognostic study and phytochemical screening of leaf of *Adhatoda vasica* (Acanthaceae). J Med Plants Stud. 2014;2:29–31.
17. Lone SA, Yadav AS, Sharma AK, Tafazul M, Yogesh B, Raghuwanshi DK. A review on *Adhatoda vasica* Nees—an important and high demanded medicinal plant. Indo Am J Pharm Res. 2013;3:2600–15.
18. Masyita A, et al. Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives. Food Chem X. 2022;13:100217. <https://doi.org/10.1016/j.fochx.2022.100217>.
19. Shoaib A. A systematic ethnobotanical review of *Adhatoda vasica* (L.), Nees. Cell Mol Biol. 2022;67(4):248–63. <https://doi.org/10.14715/cmb/2021.67.4.28>.
20. Roja G, Vikrant BH, Sandur SK, Sharma A, Pushpa KK. Accumulation of vasicine and vasicinone in tissue cultures of *Adhatoda vasica* and evaluation of the free radical-scavenging activities of the various crude extracts. Food Chem. 2011;126(3):1033–8. <https://doi.org/10.1016/j.foodchem.2010.11.115>.
21. Gulati K, Verma P, Rai N, Ray A. Chapter 7-Role of nutraceuticals in respiratory and allied diseases. In: Gupta RC, Lall R, Srivastava A, editors. Nutraceuticals. 2nd ed. Cambridge: Academic Press; 2021. p. 101–15. <https://doi.org/10.1016/B978-0-12-821038-3.00007-0>.
22. Pa R, Mathew L. Antimicrobial activity of leaf extracts of *Justicia adhatoda* L. in comparison with vasicine. Asian Pac J Trop Biomed. 2012;2(3):S1556–60. [https://doi.org/10.1016/S2221-1691\(12\)60452-3](https://doi.org/10.1016/S2221-1691(12)60452-3).
23. Liu W, et al. In vitro and in vivo metabolism and inhibitory activities of vasicine, a potent acetylcholinesterase and butyrylcholinesterase inhibitor. PLoS ONE. 2015;10(4):e0122366. <https://doi.org/10.1371/journal.pone.0122366>.
24. Zhang Y, et al. Vasicine alleviates 2,4-dinitrochlorobenzene-induced atopic dermatitis and passive cutaneous anaphylaxis in BALB/c mice. Clin Immunol. 2022;244:109102. <https://doi.org/10.1016/j.clim.2022.109102>.
25. Zoltán P, et al. *Agrimonia eupatoria* L. and wound healing. J Herb Med. 2023;42:100765. <https://doi.org/10.1016/j.hermed.2023.100765>.
26. Wang Y, Wang C, Shi J, Zhang Y. Effects of derivatization and probiotic transformation on the antioxidative activity of fruit polyphenols. Food Chem X. 2024;23:101776. <https://doi.org/10.1016/j.fochx.2024.101776>.
27. Maurya S, Singh D. Quantitative analysis of total phenolic content in *Adhatoda vasica* Nees extracts. Int J Pharmtech Res. 2009;2(4):2403–6.
28. Jiang S, Gao K, Zhang F, Wang Y, He X, Yang J. β -sitosterol alleviates atherosclerosis by regulating catalase. Heliyon. 2024;10(15):e35639. <https://doi.org/10.1016/j.heliyon.2024.e35639>.
29. El Omari N, et al. Natural sources, pharmacological properties, and health benefits of daucosterol: versatility of actions. Appl Sci. 2022;12(12):5779. <https://doi.org/10.3390/app12125779>.
30. Hossain MT, Hoq MO. Therapeutic use of *Adhatoda vasica*. Asian J Med Biol Res. 2016;2(2):156–63. <https://doi.org/10.3329/ajmbr.v2i2.29005>.
31. Murali RSS, Nageswara Rao G, Basavaraju R. Ethnomedicinal importance of *Adhatoda vasica* in the south east Asian countries: review and perspectives. Stud ETHNO Med. 2018;12(02):120–31. <https://doi.org/10.31901/24566772.2018/12.02.526>.
32. Singh KJ, Huidrom D. Ethnobotanical uses of medicinal plant, *Justicia adhatoda* L. by Meitei community of Manipur, India. J Coast Life Med. 2013;1(4):322–5. <https://doi.org/10.12980/JCLM.1.2013C895>.
33. Roberts M. Potter's new cyclopaedia of botanical drugs and preparations. R. C. Wren; completely revised by Elizabeth M. Williamson and Fred J. Evans. C. W. Daniel Company, Ltd, Saffron Walden. 1988. £14.25. Phytotherapy Research. 1989;3. Available from: <https://api.semanticscholar.org/CorpusID:86113412>.
34. Velichkova S, Theunis M, Naessens T, Pieters L, Foubert K. Development and validation of an HPLC-DAD method for Rapid quantification of vasicine in *Adhatoda vasica* leaves and commercial products. Heliyon. 2022;8(8):e10226. <https://doi.org/10.1016/j.heliyon.2022.e10226>.
35. Wikman GPA. The efficacy of multi-drug therapy for the common cold with particular reference to Kan Jang fixed combination. Planta Med. 2007;73(09):P_596. <https://doi.org/10.1055/s-2007-987376>.
36. Ali M, Hakeem KR. Scientific explorations of *Adhatoda vasica*: an Asian health remedy. Cham: Springer International Publishing; 2020. <https://doi.org/10.1007/978-3-030-56715-6>.
37. Dorsch W, Wagner H. New antiasthmatic drugs from traditional medicine? Int Arch Allergy Appl Immunol. 1991;94(1–4):262–5. <https://doi.org/10.1159/000235378>.
38. Sarker AK, Ahamed K, Chowdhury JU, Begum J. Characterization of an expectorant herbal basak tea prepared with *Adhatoda vasica* leaves, Bangladesh. J Sci Ind Res. 2009;44(2):211–4. <https://doi.org/10.3329/bjsir.v44i2.3674>.
39. Dhuley JN. Antitussive effect of *Adhatoda vasica* extract on mechanical or chemical stimulation-induced coughing in animals. J Ethnopharmacol. 1999;67(3):361–5. [https://doi.org/10.1016/S0378-8741\(99\)00074-4](https://doi.org/10.1016/S0378-8741(99)00074-4).
40. Dangi A, Patel S, Yaduvanshi PS. Phytochemical screening and assessment of *adhatoda vasica* (leaf) for antiasthmatic activity. Int J Pharm Pharm Sci. 2015;4(3):680–704.
41. Ramachandra YL, Ashajyothi C, Padmalatha S, Thanekar SKS, Shruthi SD. Antibacterial activity of leaf extracts of *Adhatoda vasica*. Int J Biomed Pharm Sci. 2012;7(1):45–7.
42. Singh B, Sharma RA. Anti-inflammatory and antimicrobial properties of pyrroloquinazoline alkaloids from *Adhatoda vasica* Nees. Phytomedicine. 2013;20(5):441–5. <https://doi.org/10.1016/j.phymed.2012.12.015>.
43. Duraipandian V, Al-Dhabi NA, Balachandran C, Ignacimuthu S, Sankar C, Balakrishna K. Antimicrobial, antioxidant, and cytotoxic properties of vasicine acetate synthesized from vasicine isolated from *Adhatoda vasica* L. BioMed Res Int. 2015;2015:1–7. <https://doi.org/10.1155/2015/727304>.
44. Fatima M, et al. Multifunctional analysis and antimicrobial activity of *Adhatoda vasica*: a traditional medicinal plant. Drug Metab Pers Ther. 2023. <https://doi.org/10.1515/dmpt-2023-0012>.
45. Rudrapal M, et al. Valorization of *Adhatoda vasica* leaves: extraction, in vitro analyses and in silico approaches. Front Nutr. 2023;10:1161471. <https://doi.org/10.3389/fnut.2023.1161471>.
46. Ilango K, Chitra V, Kanimozhi P, Balaji G. Antidiabetic, antioxidant and antibacterial activities of leaf extracts of *Adhatoda zeylanica*. Medic (Acanthaceae). J Pharm Sci Res. 2009;1(2):67–73.

47. Sarker A, Chowdhury J, Bhuiyan H. Chemical composition and antimicrobial activity of essential oil collected from *Adhatoda vasica* leaves, Bangladesh. J Sci Ind Res. 2011;46(2):191–4. <https://doi.org/10.3329/bjsir.v46i2.8185>.
48. Basit A, et al. Anti-inflammatory and analgesic potential of leaf extract of *Justicia adhatoda* L. (Acanthaceae) in Carrageenan and Formalin-induced models by targeting oxidative stress. Biomed Pharmacother. 2022;153:113322. <https://doi.org/10.1016/j.biopha.2022.113322>.
49. Balachandran C, et al. In vitro and in vivo anticancer activity of 2-acetyl-benzylamine isolated from *Adhatoda vasica* L. leaves. Biomed Pharmacother. 2017;93:796–806. <https://doi.org/10.1016/j.biopha.2017.06.096>.
50. Nikhitha JN, Swathy KS, Chandran RP. In vitro anticancer activity of ethanol extract of *Adhatoda vasica* Nees on human ovarian cancer cell lines. J Genet Eng Biotechnol. 2021;19(1):116. <https://doi.org/10.1186/s43141-021-00215-1>.
51. Kumar S, et al. In vitro anticancer activity of methanolic extract of *Justicia adhatoda* leaves with special emphasis on human breast cancer cell line. Molecules. 2022;27(23):8222. <https://doi.org/10.3390/molecules27238222>.
52. Gao H, Huang Y-N, Gao B, Li P, Inagaki C, Kawabata J. Inhibitory effect on α -glucosidase by *Adhatoda vasica* Nees. Food Chem. 2008;108(3):965–72. <https://doi.org/10.1016/j.foodchem.2007.12.002>.
53. Vadivelan R, Dhanabal SP, Santilna KP, Shirisha S. Inhibitory effect of α -glucosidase and α -amylase enzyme activities of *Adhatoda vasica*. Eur J Pharm Med Res. 2015;02(02):375–80.
54. Babu PVA, Liu D, Gilbert ER. Recent advances in understanding the anti-diabetic actions of dietary flavonoids. J Nutr Biochem. 2013;24(11):1777–89. <https://doi.org/10.1016/j.jnutbio.2013.06.003>.
55. Mohan S, Nandhakumar L. Role of various flavonoids: hypotheses on novel approach to treat diabetes. J Med Hypotheses Ideas. 2014;8(1):1–6. <https://doi.org/10.1016/j.jmhi.2013.06.001>.
56. Chakraborty A, Brantner AH. Study of alkaloids from *Adhatoda vasica* Nees on their antiinflammatory activity. Phytother Res. 2001;15(6):532–4. <https://doi.org/10.1002/ptr.737>.
57. Thabrew MI, Dharmasiri MG, Senaratne L. Anti-inflammatory and analgesic activity in the polyherbal formulation Maharasnadhi Quathar. J Ethnopharmacol. 2003;85(2–3):261–7. [https://doi.org/10.1016/S0378-8741\(03\)00016-3](https://doi.org/10.1016/S0378-8741(03)00016-3).
58. Belemkar S, Thakre SA, Pata MK. Evaluation of anti-inflammatory and analgesic activities of methanolic extract of *Adhatoda vasica* Nees and *Mentha piperita* Linn. Inven Rapid Ethnopharmacol. 2013;2013(2):1–6.
59. Musa M, et al. Pharmacological activities and gas chromatography–mass spectrometry analysis for the identification of bioactive compounds from *Justicia adhatoda* L. Front Pharmacol. 2022;13:922388. <https://doi.org/10.3389/fphar.2022.922388>.
60. Nath D, Sethi N, Singh RK, Jain AK. Commonly used Indian abortifacient plants with special reference to their teratologic effects in rats. J Ethnopharmacol. 1992;36(2):147–54. [https://doi.org/10.1016/0378-8741\(92\)90015-J](https://doi.org/10.1016/0378-8741(92)90015-J).
61. Wakhloo RL, Kaul G, Gupta OP, Atal CK. Safety of vasicine hydrochloride in human volunteers. Indian J Pharmacol. 1980;12(2):129–31.
62. Gupta OP, Anand KK, Ghatak BJ, Atal CK. Vasicine, alkaloid of *Adhatoda vasica*, a promising uterotonic abortifacient. Indian J Exp Biol. 1978;16(10):1075–7.
63. Vinothapooshan G, Sundar K. Hepatoprotective activity of *Adhatoda vasica* leaves against carbontetrachloride induced toxicity. Pharmacologyonline. 2010;2:551–8.
64. Ameer MR, Khalid ZM, Shinwari MI, Ali H. Correlation among antidiabetic potential, biochemical parameters and GC-MS analysis of the crude extracts of *Justicia adhatoda* L. Pak J Bot. 2021;53(6):2111–25. [https://doi.org/10.30848/PJB2021-6\(30\)](https://doi.org/10.30848/PJB2021-6(30)).
65. Khan AM, Bhadauria S, Yadav R. Phytochemical screening and antioxidant activity of extract of different parts of *Adhatoda vasica*. Res J Pharm Technol. 2019;12(12):5699–705. <https://doi.org/10.5958/0974-360X.2019.00986.7>.
66. Singh TP, Singh OM, Singh HB. *Adhatoda vasica* Nees: phytochemical and pharmacological profile. Nat Prod J. 2011;1:29–39.
67. Chen J, Mangelinckx S, Adams A, Wang ZT, Li WL, De Kimpe N. Natural flavonoids as potential herbal medication for the treatment of diabetes mellitus and its complications. Nat Prod Commun. 2015;10(1):187–200. <https://doi.org/10.1177/1934578x1501000140>.
68. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. Sci World J. 2013;2013:162750. <https://doi.org/10.1155/2013/162750>.
69. Jain MP, Koul SK, Dhar KL, Atal CK. Novel nor-harmal alkaloid from *Adhatoda vasica*. Phytochemistry. 1980;19(8):1880–2. [https://doi.org/10.1016/S0031-9422\(00\)83845-5](https://doi.org/10.1016/S0031-9422(00)83845-5).
70. Venkata Narasimhaji C, et al. *Justicia adhatoda* L. vasicin and vasicinone as bioactive phytochemical compounds: isolation, characterization, and computational studies. Results Chem. 2023;6:101127. <https://doi.org/10.1016/j.rechem.2023.101127>.
71. Bhartiya HP, Gupta PC. A chalcone glycoside from the flowers of *Adhatoda vasica*. Phytochemistry. 1982;21(1):247. [https://doi.org/10.1016/0031-9422\(82\)80064-2](https://doi.org/10.1016/0031-9422(82)80064-2).
72. Ahmed W, et al. Pharmacological studies of isolated compounds from *Adhatoda vasica* and *calotropis procera* as an antioxidant and antimicrobial bioactive sources. Pak J Bot. 2018;50(6):2363–7.
73. Gulfraz M, et al. Antidiabetic activities of leaves and root extracts of *Justicia adhatoda* Linn against alloxan induced diabetes in rats. Afr J Biotechnol. 2011;10(32):6101–6. <https://doi.org/10.5897/AJB10.1186>.
74. Gunawardana SLA, Jayasuriya WJ. Medicinally important herbal flowers in Sri Lanka. Evid Based Complement Altern Med. 2019;2019:2321961. <https://doi.org/10.1155/2019/2321961>.
75. Kumar KPS, Bhowmik D, Tiwari P, Kharel R. Indian traditional herbs *Adhatoda vasica* and its medicinal application. J Chem Pharm Res. 2010;02(01):240–5.
76. Arjariya A, Chaurasia K. Some medicinal plants among the tribes of Chhatarpur district (M.P.) India. Ecoprint Int J Ecol. 2009;16:43–50. <https://doi.org/10.3126/eco.v16i0.3472>.
77. Poonam K, Singh GS. Ethnobotanical study of medicinal plants used by the Taungya community in Terai Arc Landscape, India. J Ethnopharmacol. 2009;123(1):167–76. <https://doi.org/10.1016/j.jep.2009.02.037>.
78. Goswami H, et al. Ethnomedicinal wisdom of the Tripura tribe of Comilla district, Bangladesh: a combination of medicinal plant knowledge and folk beliefs. 2013.
79. Mannaf M, et al. A randomized survey of differences in medicinal plant selection as well as diseases treated among folk medicinal practitioners and between folk and tribal medicinal practitioners in Bangladesh. Am Eurasian J Sustain Agric. 2013;7:196–209.
80. DeFilipps RA, Krupnick GA. The medicinal plants of Myanmar. PhytoKeys. 2018;102:1–341. <https://doi.org/10.3897/phytokeys.102.24380>.

81. Iqbal Chowdhury I, et al. Supplements of an aqueous combination of *Justicia adhatoda* and *Ocimum tenuiflorum* boost antioxidative effects and impede hyperlipidemia. *Anim Models Exp Med*. 2020;3(2):140–51. <https://doi.org/10.1002/ame2.12115>.
82. Shiddamallayya N, Yasmeen A, Gopakumar K. Hundred common forest medicinal plants of Karnataka in primary healthcare. *Indian J Tradit Knowl*. 2010;9(1):90–5.
83. Tuhin IH, Islam E, Khatun Z. Medicinal plants used by folk medicinal herbalists in seven villages of Bhola district, Bangladesh. *Am Eurasian J Sustain Agric*. 2013;7(3):210–8.
84. Shadangi A, Panda RP, Patra AK. Ethnobotanical studies of wild flora at G. Udayagiri forest in eastern Ghat, Odisha. *IOSR J Environ Sci Toxicol Food Technol*. 2012;2(2):25–37. <https://doi.org/10.9790/2402-022537>.
85. Khan MH, Yadava P. Antidiabetic plants used in Thoubal district of Manipur, Northeast India. *Indian J Tradit Knowl*. 2010;9(3):510–4.
86. Jayashankar S, Panagoda G, Amaratunga E, Perera K, Rajapakse P. A randomised double-blind placebo-controlled study on the effects of a herbal toothpaste on gingival bleeding, oral hygiene and microbial variables. *Ceylon Med J*. 2011;56(1):5. <https://doi.org/10.4038/cmj.v56i1.2887>.
87. Gamage DGND, Dharmadasa RM, Abeysinghe DC, Wijesekara RGS, Prathapasinghe GA, Someya T. Ethnopharmacological survey on medicinal plants used for cosmetic treatments in traditional and ayurveda systems of medicine in Sri Lanka. *Evid Based Complement Alternat Med*. 2021;2021:1–15. <https://doi.org/10.1155/2021/5599654>.
88. Thatoi HN, Panda SK, Rath SK, Dutta SK. Antimicrobial activity and ethnomedicinal uses of some medicinal plants from Similipal Biosphere Reserve, Orissa. *Asian J Plant Sci*. 2008;7(3):260–7. <https://doi.org/10.3923/ajps.2008.260.267>.
89. Prasad MV, Sudha GS, Khadri CH, Riazunnisa DK. In vitro antibacterial activity and phytochemical studies of leaf extracts of *Adhatoda vasica* and *Crotalaria verrucosa*. *World J Pharm Pharm Sci*. 2015;4(06):506–13.
90. Mehreen A, Waheed M, Liaqat I, Arshad N. Phytochemical, antimicrobial, and toxicological evaluation of traditional herbs used to treat sore throat. *BioMed Res Int*. 2016;2016:1–9. <https://doi.org/10.1155/2016/8503426>.
91. Ahmad B, Ahmed A, Irshad G, Aslam HR, Khaliq N. Anti-diabetic and anti-oxidative role of a local medicinal plant *Justicia adhatoda* L in diabetes mellitus. *Pak J Med Health Sci*. 2019;13(01):91–5.
92. Mulla WA, More SD, Jamge SB, Pawar AM, Kazi MS, Varde MR. Evaluation of antiinflammatory and analgesic activities of ethanolic extract of roots *Adhatoda vasica* Linn. *Int J PharmTech Res*. 2010;2(2):1364–8.
93. Pandit S, Sur TK, Jana U, Debnath PK, Sen S, Bhattacharyya D. Prevention of carbon tetrachloride induced hepatotoxicity in rats by *Adhatoda vasica* leaves. *Indian J Pharmacol*. 2004;36(5):312–20.
94. Bhattacharyya D, Pandit S, Jana U, Sen S, Sur TK. Hepatoprotective activity of *Adhatoda vasica* aqueous leaf extract on D-galactosamine-induced liver damage in rats. *Fitoterapia*. 2005;76(2):223–5. <https://doi.org/10.1016/j.fitote.2004.10.014>.
95. Ahmad R, Raja V, Sharma M. Hepatoprotective activity of ethyl acetate extract of *Adhatoda vasica* in swiss albino rats. *Int J Curr Res Rev*. 2013;05(06):16–21.
96. Jahan Y, Siddiqui HH. Study of antitussive potential of *Glycyrrhiza glabra* and *Adhatoda vasica* using a cough model induced by sulphur dioxide gas in mice. *Int J Pharm Sci Res*. 2012;3(6):1668–74. [https://doi.org/10.13040/IJPSR.0975-8232.3\(6\).1668-74](https://doi.org/10.13040/IJPSR.0975-8232.3(6).1668-74).
97. Vinothapooshan G, Sundar K. Wound healing effect of various extracts of *Adhatoda vasica*. *Int J Pharma Bio Sci*. 2010;1(4):530–6.
98. Subhashini S, Arunachalam KD. Investigations on the phytochemical activities and wound healing properties of *Adhatoda vasica* leave in Swiss albino mice. *Afr J Plant Sci*. 2011;5(2):133–45.

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