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REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF *Justicia adathoda*(L.)

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Abstract: For around 2500 years, the *Justicia adathoda*(L.), Nees have been used in indigenous medical systems all across the world. *Justicia adathoda*(L.) is commonly used in the Unani, an ayurvedic system of medicine. It was used traditionally to treat a variety of ailments and had strong pharmacological action, notably for bacterial infections, cough, bronchial infections, heart diseases reproductive abnormalities etc. *Justicia adathoda* (L.) contains a variety of constituents such as alkaloids, steroids, flavonoids, tannins, saponins, and so on. The plant's active constituents include maiontone, l-vasicinone, vasicinolone, deoxyvasicine, vasicine, and vasicinol among all other constituents. This review offers current information on the phytoconstituents found in *Justicia adathoda*(L.), their pharmacological activities, ethanomedicinal applications, numerous formulations and their indications, pharmacokinetic profile, precautions, and warnings while using this plant. According to the critical evaluation, it was determined that there is insufficient scientific data to explain how the extract may be detrimental to humans, particularly women while they are pregnant. Key information on conventional use, in addition to toxicological investigation was examined for accuracy, relevance, significance, and reliability in the overall assessment of the safety of *Justicia adathoda*(L.). Many clinical trials on *Justicia adathoda*(L.) herbal formulations are being undertaken all over the world (L.). This review offers significant evidence from phytochemical and pharmacological investigations that show *Justicia adathoda*(L.) is a distinctive indigenous plant of India with a commercialiazed reputation and may thus be encourage for diverse applications such as medicinal and other potential uses.

Keywords: *Justicia adathoda* (L.), active ingredients, pharmacological activities, versatile and safe native plant of India.

1] INTRODUCTION:

Justia adhatoda(L.) belongs to the family Acanthaceae and is also commonly known as vasaka, adhatodai, Bansa, and Basak. It is indigenous to India. It grows throughout India's plains and in the lower Himalayan peaks, at an altitude of 1,300 meters. It's a tiny evergreen, sub-herbaceous shrub that thrives on wide plains all throughout the world, particularly in the lower Himalayas up to 1300 metres above sea level (Global Herbal Supplies). Ranging from Punjab in the north through Bengal and Assam in the south-east, and then to Ceylon, Malaysia, and Singapore in the south[1]. Ayurvedic, siddha, and

allopathic systems of medicine have long employed, *Justicia adathoda* (L.) a prominent phytomedicinal plant of Indian country. The plant had discovered to have a wide range of pharmacological properties. The current study provides an update on its phytochemical and pharmacological activity. The study reveals the plant's diverse phytochemical constituents and therapeutic activities such as antibacterial, anti-inflammatory and antiulcer, hypoglycemic, cardiovascular protective activity, antitubercular, antiviral, hepatoprotective, antimutagenic, and antioxidant activity.

2] PLANT DESCRIPTION:

Fig:1 *Justicia adathoda* plant

2.1]ORGANOLEPTIC CHARACTERS:

Colour: Leaves are dark green, flowers are white.

Odour : Smell of the plant is unpleasant.

Taste : Bitter taste.

2.2] BOTANICAL DESCRIPTION OF *Justicia adathoda*(L.)

It is an Acanthaceae family tiny, compact, perennial, highly branching, evergreen shrub. This plant may reach heights of 3 to 6 metres. [4]

2.21] SEED: Each fruit contains four globular seeds.[**Fig:2]**

Fig:2 *Justicia adathoda* seeds

2.22] ROOT: A perennial shrub, with branched taproot system.[**Fig:3]**

Fig:3 *Justicia adathoda* root

2.23] STEM: It has ascending, opposing, long branches. The stem is herbaceous on the adaxial side and woody on the abaxial side (4). Stem of this plant are green to pale-green, herbaceous, erect, branching, cylindrical, solid, and with swelling nodes. This plant contains yellow coloured bark.[5] [**Fig:4]**

Fig:4 *Justicia adathoda* stem

2.24]LEAF: The plant's leaves are simple, dark green, tapering base, ramal and cauline; acute unicostate reticulate venation, exstipulate, hairy with breadth 4-7 cm and 7-19 cm long, elliptic-lanceolate or ovate-lanceolate, opposite, short peduncle [4,5].[**Fig:5]**

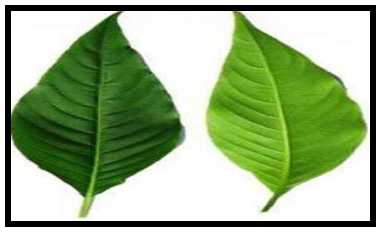


Fig:5 *Justicia adathoda* leaf

2.25]FLOWER:

- bracteolate (leafy bracteoles enclosing the bud), Bracteate (leafy bracts), zygomorphic, hermaphrodite, hypogynous, pentamerous,enormous, white.
- Calyx with quincuncial sepals, 5 polysepalous but slightly conate at the base and pale green colour.
- 5 petalled, , bilipped, gamopetalous 2/3 bilabiate personate flower with the anterior most middle petal of the anterior lip is raised and deeply nerved, an anterior lip of three petals, a posterior curving lip of two petals and white coronary outgrowths at the corolla's neck.
- Polyandrous, epipetalous, androecium with two stamens, outer anther lobe higher than inner, dithecous, introrse, basifixed, filaments long and robust.
- Gynoecium is syncarpous, bicarpellary, superior, bilocular, style is simple, long hairy, and stigma is somewhat bifid, carpels are medianly located, one or two ovules are present in each locule, axile placentation is present, an ovular disc is present below the ovary.[5] **[Fig:6]**

Fig:6 *Justicia adathoda* flower

2.26] FRUIT: This plant's fruit is tiny, clavate, and longitudinally capsulated. [4] **[Fig:7]**

Fig:7 *Justicia adathoda* fruit

2.3] VERNACULAR NAMES:

- ✓ English: Malabar nut
- ✓ Marathi: Adulsa
- ✓ Hindi: Adosa, Arusha, Rus, Bansa
- ✓ Tamil: Adathodai
- ✓ Telugu : Vasakam
- ✓ Malayalam: Adalodakam, Pothadalotakam, Vasica
- ✓ Sanskrit: vasaka
- ✓ Bengali : Basak
- ✓ Punjabi: Bansa, basuti, bhekkar
- ✓ Gujarati : Aradusi, adusa
- ✓ Manipuri : Nongmangkha-agouba
- ✓ Kannada: Adusoge
- ✓ Arabic : Adusha

2.4] SYNONYMS:[2]

- ✓ *Adeloda serrata Raf*
- ✓ *Adhatoda arborea Raf*
- ✓ *Adhatoda pubescens Moench*
- ✓ *Adhatoda vasica Nees*
- ✓ *Diantheralatifolia Salisb*
- ✓ *Ecbolium adhatoda (L.) Kuntze*
- ✓ *Adhatoda zeylanica Medik*
- ✓ *Gendaruss aadhadota (L.) Steud*

2.5] SCIENTIFIC CLASSIFICATION: [3]

- ✓ Kingdom: Plantae
- ✓ Clade: Tracheophytes
- ✓ Clade: Angiosperms
- ✓ Clade: Eudicots
- ✓ Clade: Asterids
- ✓ Order: Lamiales
- ✓ Family: Acanthaceae
- ✓ Genus: Justicia
- ✓ Species*: J. adhatoda*
- ✓ Binomial Name: *Justicia adhatoda* L.

2.6] SPECIES:[8]

- *Adhatoda aspera Nees*
- *Adhatoda gilliesii Nees*
- *Adhatoda auriculata Nees.*
- *Adhatoda martiana Nees*
- *Adhatoda bojeriana Nees.*
- *Adhatoda nuda Nees*
- *Adhatoda capensis Nees*
- *Adhatoda pilosa Nees*
- *Adhatoda ciliate Nees.*
- *Adhatoda spicata Nees*

3]*Justicia adathoda* PARTS USED FOR THERAPEUTIC PURPOSES:

- ✓ Root
- ✓ Stem
- ✓ Bark
- ✓ Leaves
- ✓ Flower
- ✓ Fruit
- ✓ Whole plant

4] PHYTOCHEMICALS PRESENT IN *Justicia adathoda*(L.)PLANT:

- Glycosides, alkaloids, polyphenolics, and phytosterols were discovered as a prominent class of chemicals in phytochemical investigations of various portions of *Justicia adathoda*(L.)[21]. The plant includes active quinazoline alkaloids such as adhatodine, vasicine, deoxyvasicinone and vasicinone[9].

- The presence of alkaloidal content in the plant, particularly vasicine (7.5%), is responsible for the plant's significant pharmacological activities.[22]

4.1]ROOT:

Table:1 The preliminary phytochemical screening of ethyl acetate ,chloroform and n-Hexane soluble fraction of methanol ,ethanol, aqueous extract of *Justicia adathoda*(L.)root [15][16]

S.NO.	**QUALITATIVE PHYTOCHEMICAL TESTS**	***Justicia adathoda* ROOT EXTRACT**
1	Alkaloids	+
2	Tannins (Phenolic Compounds)	+
3	Resins	+
4	Glycosides	+
5	Terpeniods	+
6	Reducing Sugar	+
7	Saponins	+

8	Gums and mucilage	+
9	Quinones	+
10	Flavonoids	+
11	Steroids	+
12	Volatile oils	-
13	Coumarins	-
14	Phenols	-

(+ indicates the presence of specific chemical group in extract and - indicates the specific chemical group is absent in extract)

- V. K. Sharma and M. P. Jam isolated two novel alkaloids such as **adhatonine[**13] **and vasicol**[14] and also reported the existence of a novel alkaloid known as **vasicinolone**,an oxidative product of vasicinol[10]. Root extract also contains alkaloids **vasicine, vasicinone and vasicinol**[11,12].

Table :2 Principal volatile compounds found in the extract of *Justicia adathoda*(L.) root using GC-MS analysis.[25].

S.No.	Retention Time	%Area	Chemical Compound	Chemical Formula	Mol.Wt.
1.	7.86	8.58	Ethanethioic acid, S-[2dimethylamino)ethyl]ester	$C_6H_{13}NOS$	147
2.	7.86	8.58	2-Aminononadecane	$C_{19}H_{41}N$	283
3.	9.87	9.64	Z,Z-2,5-Pentadecadien-1-ol	$C_{15}H_{28}O$	224
4.	11.62	7.16	3-Eicosyne	$C_{20}H_{38}$	278
5.	11.62	7.16	Z,Z-2,5-Pentadecadien-1-ol	$C_{15}H_{28}O$	224
6.	11.62	7.16	1,2-Benzenedicarboxylicacid, mono(2-ethylhexylester)	$C_{16}H_{22}O_4$	278
7.	13.44	19.44	Z,Z-2,5-Pentadecadien-1-ol	$C_{15}H_{28}O$	224
8.	15.41	3.42	trans-Z-à-Bisaboleneepoxide	$C_{15}H_{24}O$	220
9.	17.44	2.42	2-Cyclopentene-1-undecanoicacid	$C_{16}H_{28}O_2$	252
10.	24.78	12.00	Z,Z-2,5-Pentadecadien-1-ol	$C_{15}H_{28}O$	224
11.	25.33	5.62	VitaminE	$C_{29}H_{50}O_2$	430
12.	25.33	5.62	1,6,10-Dodecatrien-3-ol,3,7,11-trimethyl,[S-(Z)]-	$C_{15}H_{26}O$	222
13.	25.33	5.62	Pyrrolo[2,1-b]quinazolin-9(1H)-	$C_{19}H_{19}N_3$	351

			one,3-[2-(dimethylamino)phenyl] -2,3-dihydro-		
14.	33.36	2.06	β-Sitosterol	$C_{29}H_{50}O$	414
15.	33.36	2.06	Spiro[androst-5-ene-17,1'cyclobutan 2'one,3-	$C_{22}H_{32}O_2$	328
16.	34.67	1.46	Lupeol	$C_{30}H_{50}O$	426

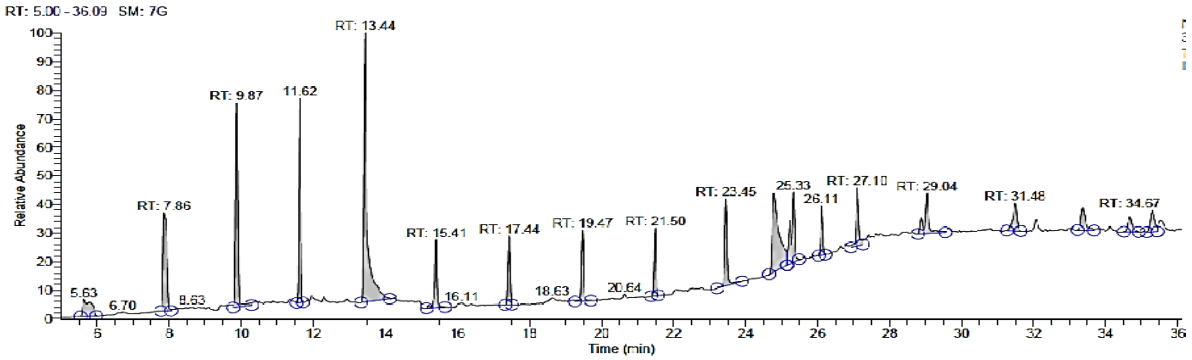


Fig.8 Spectrum of *Justicia adathoda*(L.) root extract by gas chromatography-mass spectrometry

4.2] STEM:

Table 3 summarises the preliminary phytochemical screening of ethyl acetate, n-Hexane, and chloroform soluble fractions of methanol, ethanol, and aqueous extract of *Justicia adathoda*(L.)stem. [16][17][18]

S.NO.	QUALITATIVE PHYTOCHEMICAL TESTS	*Justicia adathoda* STEM EXTRACT
1	Reducing Sugar	-
2	Flavonoids	+
3	Tannins (Phenolic Compounds)	+
4	Quinones	+
5	Terpeniods	+
6	Steroids	+
7	Resins	+
8	Alkaloids	+
9	Saponins	+
10	Glycosides	+

11	Gums and mucilage	+
12	Volatile oils	+
13	Coumarins	-
14	Phenols	-
15	Aldehyde and ketones	+

(+ indicates the presence of specific chemical group in extractand - indicates the specific chemical group is absent in extract).

- Stem extract of *Justicia adathoda*(L.) contains **monopalmitin, vanillic acid, daucosterol palmitate, β-sitosterol, , vasicinolone ,vasicinone and vanillin.**[19].

Table:4 Phytoconstituents identified in the methanolic extract of *Justicia adathoda(L.)* shoot using GC-MS analysis.[24]

S.No	Retention Time	Area	Area%	Compound name
1.	12.397	1142521	0.50	Methyl tetradecanoate
2.	12.705	1314765	0.57	Tetradecanoicacid
3.	12.898	1040958	0.45	Benzoicacid,4-hydroxy-3,5-dimethoxy-,hydrazide
4.	13.304	1174574	0.51	2-pentadecanone,6,10,14-trimethyl-
5.	13.395	2811456	1.22	2-propenoicacid,3-(4-hydroxy-3-methoxyphenyl)methylester
6.	14.116	59518139	25.86	n-hexadecanoicacid
7.	14.747	1107599	0.68	Heptadecanoicacid
8.	14.963	91112275	39.59	9,12-octadecadienoicacid,methyl ester
9.	15.915	3356623	1.46	1-dimethyl(3-chloropropyl)silyloxyoctane
10.	16.096	8375018	3.64	Methanone,[4-(dimethylamino)phenyl]phenyl-
11.	16.397	23919977	10.39	Tricyclo[20.8.0.0(7,16)]triacontane,1(22),7(16)-diepoxy-
12.	17.028	10679999	4.64	Mannitol,1,3,4,5-tetra-O-methyl-,diacetate,D-
13.	17.922	4643559	2.02	Undecane,6-cyclohexyl-
14.	18.464	3242496	1.41	Linoleic acid trimethylsilyl ester
15.	18.855	1462856	0.80	7-hexadecenoicacid,methylester,(Z)-
16.	25.185	997590	0.43	Octadecanoicacid,4-methoxy-,methylester

17.	25.518	1914437	0.83	Cholestane-3.beta.,5.beta.-diol
18.	26.523	1446286	0.63	5-Cholestene-3-ol,24-methyl-
19.	28.635	2693012	1.17	Gamma-sitosterol

4.3] LEAVES:

Table:5 shows the preliminary phytochemical screening of the soluble fractions of methanol, ethanol, and aqueous extract of *Justicia adathoda*(L.) leaf in n-Hexane, chloroform, and ethyl acetate. [16][17][20]

S.NO.	QUALITATIVE PHYTOCHEMICAL TESTS	*Justicia adathoda* LEAF EXTRACT
1	Flavonoids	+
2	Tannins (Phenolic Compounds)	+
3	Reducing Sugar	+
4	Gums and mucilage	+
5	Terpeniods	+
6	Resins	+
7	Glycosides	-
8	Phenols	+
9	Quinones	+
10	Alkaloids	+
11	Saponins	+
12	Volatile oils	+
13	Coumarins	+
14	Steroids	+
15	Aldehyde and ketones	+

(+ indicates the presence of specific chemical group in extractand - indicates the specific chemical group is absent in extract).

- Alkaloids **(vasicine, adhatonine, hydroxypeganine, anisotine, vasicinol, adhvasinone, , vasicinone and adhatodine)** are found in the leaves of ***Justicia adathoda(L.)*,** as well as **betaine, steroids, alkanes, kaempferol, and quercetin [22].**
- carotene and vitamin C are abundant in the leaves, making it a source of essential oil [23]. It also posses amino acids and proteins.

Table :6 Phytocomponents identified in the methanolic extracts of *Justicia adathoda(L.)* leaf by Gas Chromatography-Mass Spectrum analysis [24]

S.No.	Retention Time	Area	Area%	Compound name
1.	11.933	1204336	0.59	2,4-heptadiene,2,4-dimethyl-
2.	12.739	1413434	0.69	2-propenoicacid,3-(4-hydroxyphenyl)-,methylester
3.	13.302	5517844	2.70	2-pentadecanone,6,10,14-trimethyl-
4.	13.838	34404595	16.86	Hexadecanoicacid,methylester
5.	15.015	54755840	26.82	9,12,15-octadecatrienoicacid,methylester,(Z,Z,Z)-
6.	15.284	39767291	19.49	9,12,15-octadecatrienoicacid,(Z,Z,Z)-,Linolenicacid
7.	16.401	19816699	9.69	Cyclopropaneoctanoicacid,2-[[2-[(2-ethylcyclopropyl)methyl]cyclopropyl]methyl]-,methylester
8.	16.722	12339833	6.03	Methyl(Z)-5,11,14,17-eicosatetraenoate
9.	17.352	4428361	2.16	Binaphthylsulfone
10.	17.685	2913202	1.42	5,5-dimethyl-1,3-dioxane-2-ethanol, tertbutyldimethylsilylether
11.	17.985	3525626	1.72	1,3-cyclohexanedione,5-isopropyl
12.	18.525	2155917	1.05	Cis-4,7,10,13,16,19 docosahexaenoicacid,trimethylsilylester
13.	18.765	1698100	0.83	Binaphthylsulfone
14.	19.250	1619081	0.79	Diazoprogesterone
15.	19.725	1079474	0.53	Pyrrolo[2,1-b]quinazolin-9(1H)-one,3-[2-(dimethylamino)phenyl]-2,3-dihydro-
16.	21.087	1017568	0.50	Dodecanoicacid,1,2,3-propanetriylester

17.	23.568	461550	0.35	Stigmasta-3,5-dien-7-one
18.	26.871	1834751	0.90	2-(6-Chloro-benzo[1,3]dioxol-5-ylmethylsulfanyl)-9H-1,3,4,9-tetraaza-fluorene
19.	28.675	2814052	1.38	Gamma-sitosterol

4.4] FLOWER:

Table:7 The preliminary phytochemical screening of methanolic flower extract of *Justicia adathoda(L.)* [17]

S.NO.	QUALITATIVE PHYTOCHEMICAL TESTS	*Justicia adathoda* FLOWER EXTRACT
1.	Flavonoids	+
2.	Glycosides	-
3.	Saponins	-
4.	Aldehyde and ketones	+
5.	Phenols	+
6.	Terpeniods	+
7.	Reducing Sugar	-
8.	Resins	+

(+ indicates the presence of specific chemical group in extractand - indicates the specific chemical group is absent in extract).

- **Flavonoids (Astragalin, Apigenin, Quercetin, Kaempferol,Vitexin) , triterpenes (α-amyrin), β-sitosterol-D-glucoside and alkanes have been found** in the flowers. [26]

Table:8 Phytocomponents identified in the methanolic extracts of *Justicia adathoda(L.)* flower by GC-MS analysis [24]

S.No.	Retention Time	Area	Area%	Compound name
1.	9.836	516043	2.21	Hydroquinone
2.	11.210	271287	1.16	Butylatedhydroxytoluene
3.	12.893	163495	0.70	Tetradecanoicacid
4.	13.973	1525337	6.53	Hexadecanoicacid, methylester
5.	14.329	6651477	28.47	n-hexadecanoicacid
6.	15.188	1558643	6.67	Dibutylphthalate
7.	15.323	1173754	5.02	9,12-octadecadienoicacid(Z,Z)-,methylester
8.	15.465	718923	3.08	9,12,15octadecatrienoicacid,Methylester

9.	15.633	2749691	11.77	Octadecanoicacid
10.	15.694	4130083	17.68	9,12-octadecadienoicacid(Z, Z)-
11.	15.834	3266777	13.98	9,12,15-octadecatrienoicacid (Z,Z, Z)-
12.	18.746	634285	2.72	Bis(2-ethylhexyl)phthalate

4.5] SEEDS:

Table:9 The preliminary phytochemical screening of *J. Adhatoda* seed extract table:9.[27,28]

S.NO.	QUALITATIVE PHYTOCHEMICAL TESTS	*Justicia adathoda* SEED EXTRACT
1.	Flavonoids	+
2.	Phenols	+
3.	Anthraquinones	-
4.	Steroids	+
5.	Glycosides	+
6.	Triterpenes	+
7.	Saponins	+
8.	Tannins	+
9.	Alkaloids	+
10.	Coumarins	+

(+ indicates the presence of specific chemical group in extractand - indicates the specific chemical group is absent in extract).

- Seeds contain 25.8% of deep yellow oil consists of 10.7% lignoceric acid, glycerides of 3.1% arachidic acid, 49.9%oleic acid, 12.3% linoleic acids, 5% cerotic, 2.6%β- sitosterol and 11.2% behenic.[32]

4.6] AERIAL PARTS:

- A novel triterpenoid, 3-hydroxy-D-fiiedoolean-5-ene, was isolated for the first time from the aerial portions of *Adhatoda vasica* Nees, together with two known chemicals, epitaraxerol and peganidine. [33]

4.7]WHOLE PLANT:

Table:10 Qualitative analysis of *Justicia adathoda* extract as well as powder [34]

Class of compounds	***A. vasica***
Phlobatanins	+
Tannins	+
Cardiac glycosides	+
Flavones, flavonols, chalcones	yellow
Terpenoids	-

Flavonoids	Dark yellow colour
Steroids	-
Anthraquinones	-
Coumarins	-
Alkaloids	+++
Saponins	+

+++ Strongly positive, ++ moderately positive, +weakly positive pink to purple – presence of terpenoids, - negative, dark yellow- presence of flavonoids, green- presence of steroids, yellow- presence of flavones, flavonols and chalcones.

Table:11 Quantitative analysis of *Justicia adathoda* extract as well as powder [34]

Plant species	Flavonoids (%)	Saponin (%)	Phenols (%)	Tannins (%)	Alkaloids (%)
Adhatoda vasica	0.21±0.01	2.09±0.10	0.13±0.01	6.13±0.08	1.13±0.01

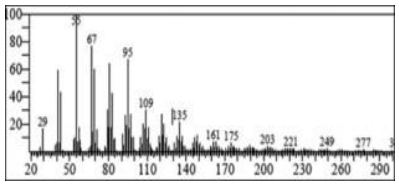
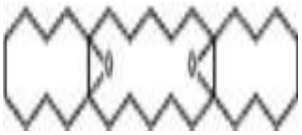
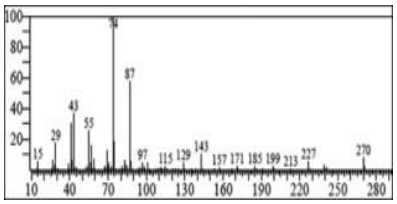
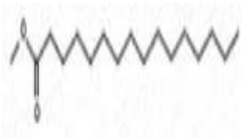
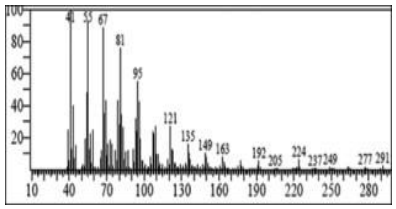
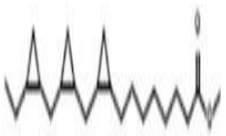
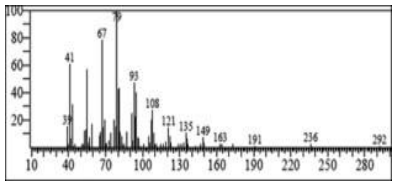
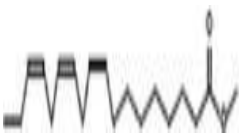
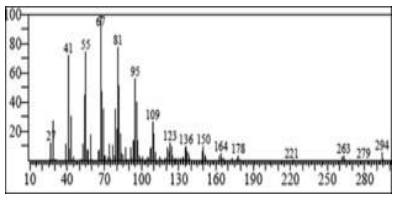
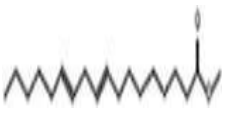
The data represents mean of three replicates

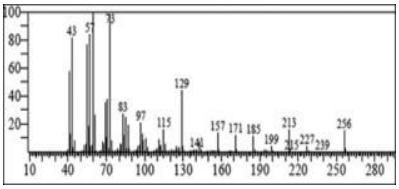
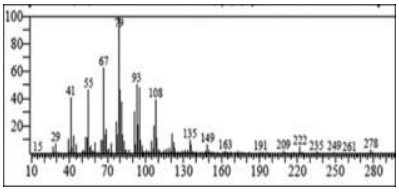
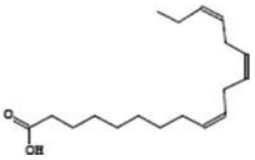
Table:12 Important phytoconstituents of *Adhatoda vasica* [29]

Major alkaloids	• Vasicinone • Peganine • Vasicine • Vasicol
Leaves	• Vasicolinine • Vasicoline • Anisotine • Adhatodine
Minor alkaloids	• Adhatonine • Vascinol • Vasicinolone
Flower content	• Quercetin • Kaempferol • 2,4dihydroxychalcone

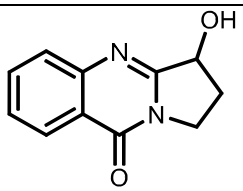
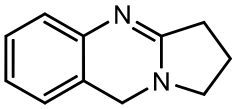
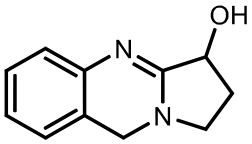
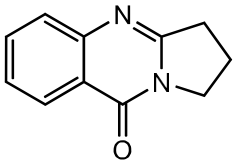
	and glucoside
Inflorescence	• Vasicol • Vasiconine

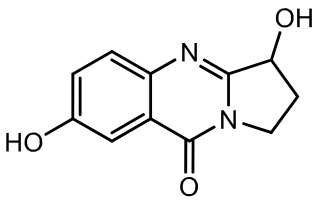
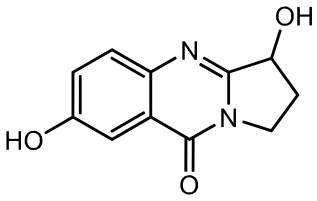
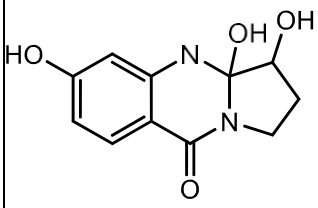
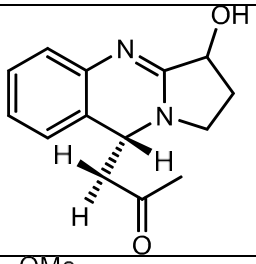
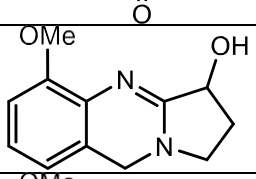
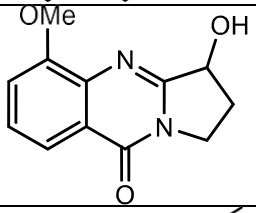
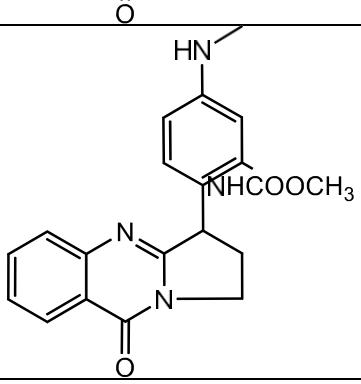
Table: 13 Major compound identified by GC-MS in *Justicia adathoda* [24]

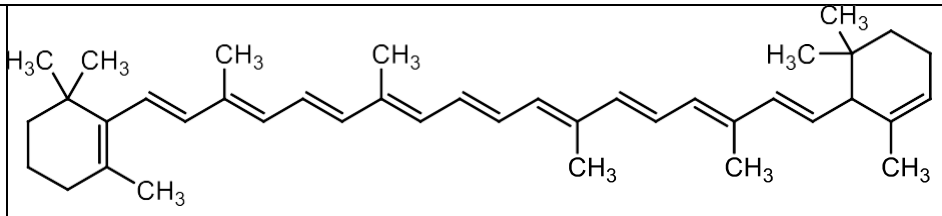
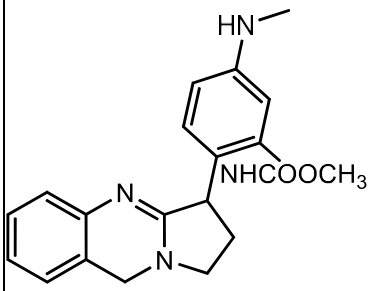
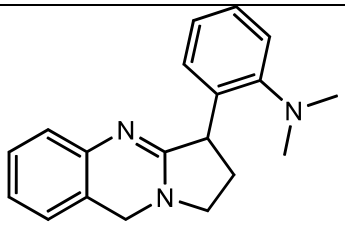
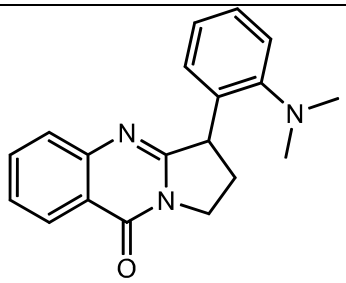
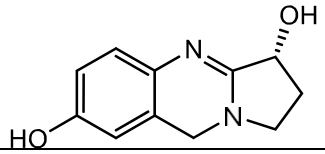
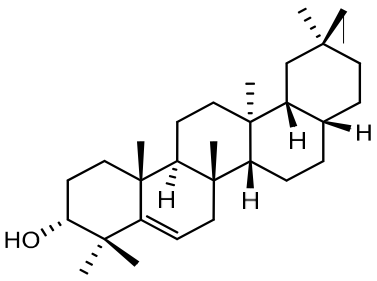
S. No	Name of compound	GC-MS chromatogram	Structure
1.	Tricyclo[20.8.0.0(7,16)]triacontane		
2.	Hexadecanoicacid		
3.	Cyclopropaneoctanoicacid		
4.	9,12,15-octadecatrienoicacid		
5.	9,12-octadecadienoicacid		

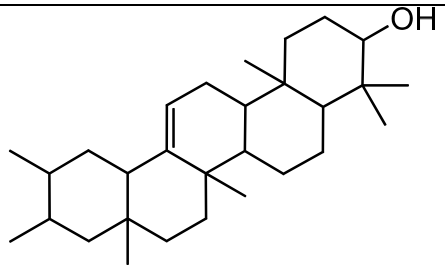
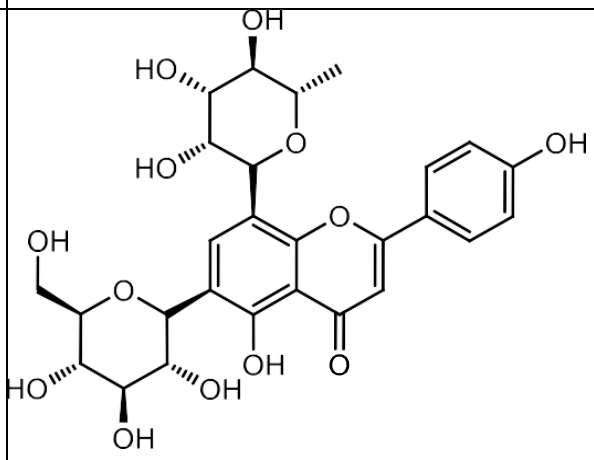
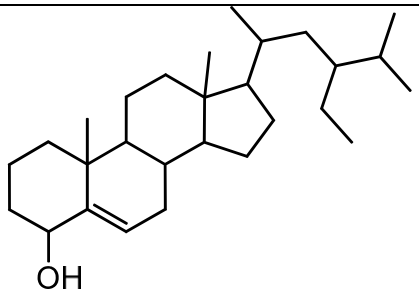
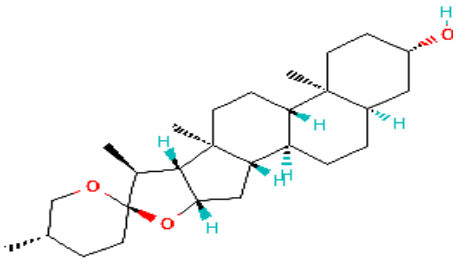
6.	n-hexadecanoicacid		
7.	9,12,15 octadecatrienoicacid, (Z,Z, Z)		

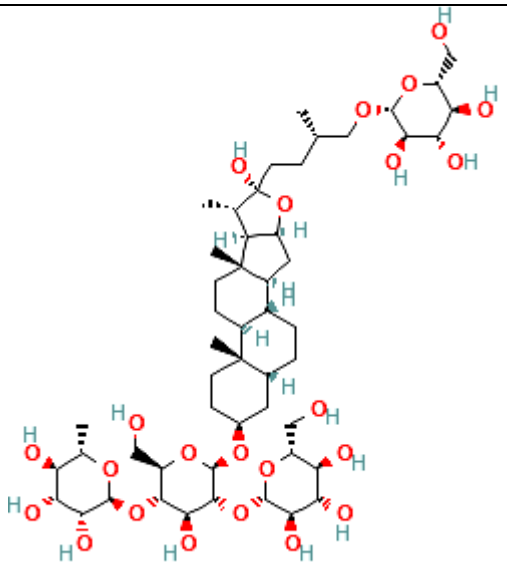
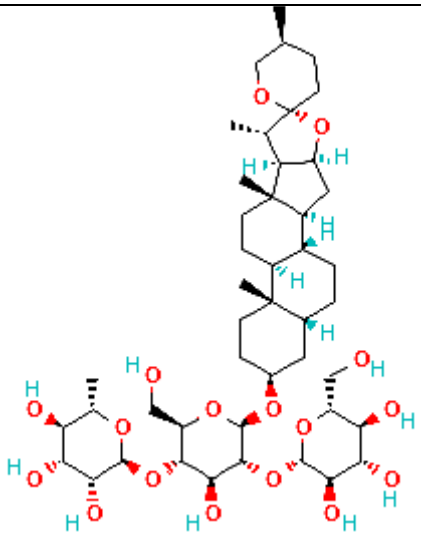
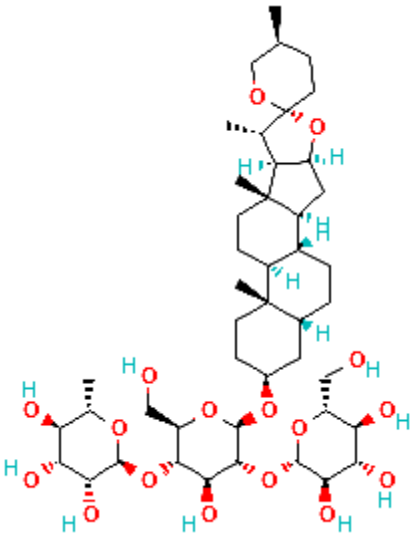
5] Table:14 STRUCTURES OF IMPORTANT PHYTOCONSTITUENTS OF *Justicia adathoda* [35][4]

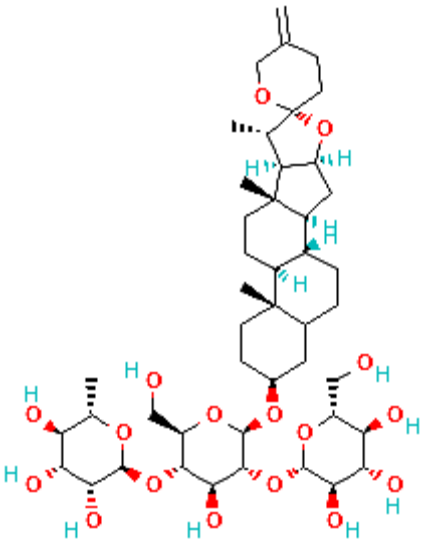
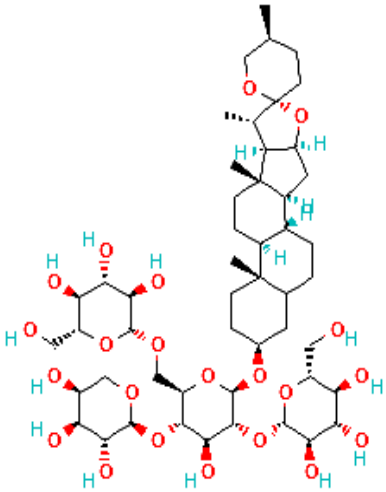
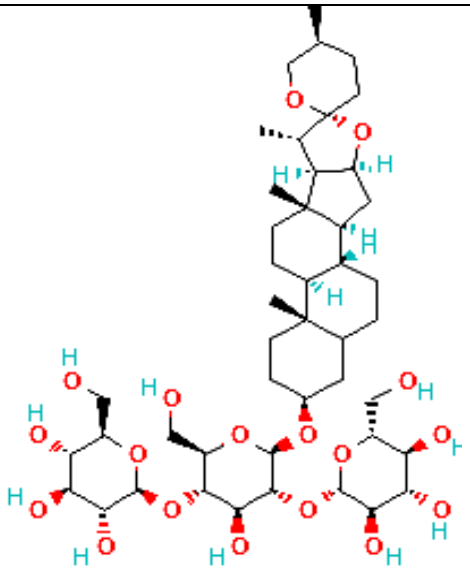
S.NO.	COMPOUND NAMES	STRUCTURES
1	Vasicine	
2	Deoxyvasicine	
3	Vasicinone	
4	Deoxyvasicinone	

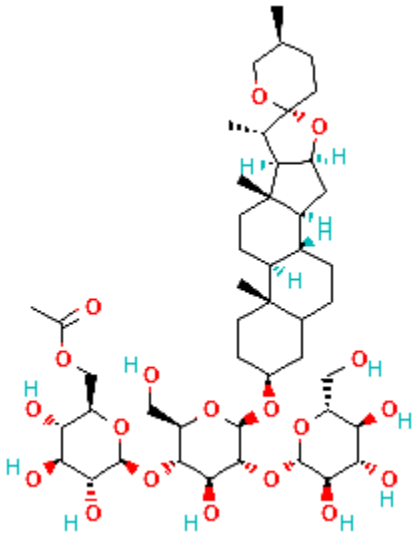
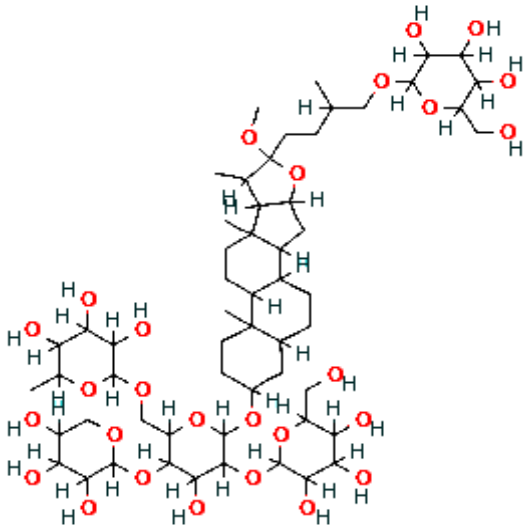
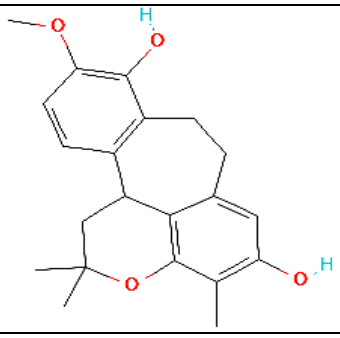
5	Vasicinolone	
6	6- Hydroxyl peganine	
7	Vasicol	
8	Peganidine	
9	Adhavasicine	
10	Adhavasinone	
11	Anisotine	

12	Carotene	
13	Adhatodine	
14	Vasicoline	
15	Vasicolinone	
16	Vasicinol	
17	Epitaraxerol	

18	Alpha-amyrin	
19	Violathin	
20	Sitosterol	
21	Sarsasapogenin	

22	Shatavarin I	
23	Shatavarin IV	
24	Shatavarin VI	

25	Shatavarin VII	
26	Shatavarin VIII	
27	Shatavarin IX	

28	Shatavarin X	
29	Asparosides C	
30	Racemosol	

6] PHARMACOLOGICAL PROFILE OF *Justicia adathoda:*

6.1] Ethanomedicinal uses:

From ancient times, the whole plant has been employed for its medicinal effect (36). It has been used to treat numerous respiratory tract illnesses in the ayurvedic system of medicine. In Indian traditional medicine, various portions of the plant are used to joint pain, cure asthma, sprains, lumber pain, cold, cough, venereal infections, rheumatism, malaria, swelling, and eczema (37). The extract of *Justicia adathoda* leaves can be utilised as an expectorant and spasmolytic drug (38).

6.2] Table:15 Parts of *Justicia adathoda* with their therapeutic uses

S.No.	Parts	Uses [21]	Country
1.	Leaves	Juice of leaves are recommened in malarial fever	Pakistan
2.	Leaves	Freshly prepared leaf extract blended with honey and ginger juice is indicated for coughs, chronic bronchitis, and asthma.	India
3.	Leaves	Infused extract of fruit and leaves of *Phyllanthus emblica* and mixing it with honey is used to treat asthma.	India
4.	Leaves	Extract by infusion is an effective repellent for flies, white ants and mosquitoes.	Nepal
5.	Leaves	Snake bites were treated with bruised fresh leaves.	India, Sri Lanka
6.	Leaves	Extract by maceration is used to cure cough, phlegm congestion together with cold orally.	Bangladesh
7.	Leaves	A infusion made from the leaves is used to treat headaches.	Myanmar, Pakistan
8.	Root	To aid birth, a fresh root paste is applied to the belly and vagina minutes before labour.	India
9.	Flower & Root	It is employed in apiculture. The root has expectorant and antispasmodic properties, and the infusion has antihelmintic properties. Fresh flowers can be used to treat high fever and gonorrhoea.	Pakistan
10.	Flowers& Leaves	Expectorant and antiasthmatic properties are found in the leaves and flowers.	India
11.	Bark & Leaves	The bark and leaves are used to treat nausea and as an anthelmintic.	Bangladesh
12.	Fruit	The fruits are used to treat colds, spasms, and bronchitis.	Pakistan

6.3] PHARMACOLOGICAL ACTIVITY:

Justicia adathoda's principle pharmacological actions are related to an alkaloid (vasicine) and its derivatives.

6.3.1] Wound healing activity:

G.Vinothapooshan and K.Sundar investigated the healing of wound ability of *Adhatoda vasica* plant extracts in the form of ointment in an excision wound model in albino rats. *Adhatoda vasica* methanolic extract ointment showed a significant effect in excision wound model as comparable to standard drug as well as other two extracts of ointment, by calculating the parameters, percentage closure of excision wound model(39) . A preclinical investigation found that the shoot portions of *Justicia adathoda* increase healing wound in mice. The methanolic extract of the leaf demonstrated remarkable wound healing activity and may be useful in treating various types of wounds and injuries in animals[40].

6.3.2] Anti-bacterial activity:

The use of Vasaka (*Justicia adhatoda* L.) leaf extract as a reducing and capping agent as a cost-effective and environmentally acceptable technique for green production of silver nanoparticles has been described. These nanoparticle's antibacterial activity against *Pseudomonas aeruginosa* MTCC

741 was assessed using an agar cup test , a serial dilution turbidity measurement assay, and the disc diffusion technique. The results demonstrate that green produced silver nanoparticles utilising Vasaka leaf extract have the capacity to suppress bacterial growth[47].

6.3.3] Anti-asthmatic activity:
The anti-asthmatic activity of ten azepino [2,1-b] quinazolone derivatives (R1 to R10) in a murine mouse asthma model was examined. In asthma-induced rats, the compounds R2, R4, R6, R7, and R8 significantly reduced eosinophilia and cytokine production. Yet, the decrease in asthma was generally substantial in R8-treated mice[48].

6.3.4] Anti-diabetic activity:
In alloxan-induced diabetic mice, the effects of *J. adhatoda* leaves and roots were investigated. The goal of this study was to investigate into the effects of the plant's leaves and roots on blood glucose and other diabetes-related indicators. Ethanolic root and leaf extracts of *J. adhatoda* have the ability to reduce sugar levels in blood, urine, and tissue lipids, which are actively raised in alloxan induced diabetic rats. These plant extracts have been demonstrated to enhance insulin levels in the blood. Additionally, its anti-hyperlipidaemic actions may constitute a preventive mechanism against atherosclerosis and other related diseases[49].

6.3.5] Insecticidal effect:
The insecticidal activity of *J. adhatoda* crude leaf extract (acetone, methanol, and water) against *Brevicoryne brassicae* was studied. Alcoholic extracts (5%) extracted with acetone and methanol showed 100 and 81.6% mortality of adult *B. brassicae*, respectively, and 100 and 90% mortality of *nymph B* respectively. The acetone and methanol crude leaf extract of *A. vasica* nees can cause a significant mortality percentage in *B. brassicae* (nymphs and adults), hence it can be utilised as an insecticide[50].

6.3.6]Anti-cancer activity:
2-acetyl-benzylamine, an alkaloid derived from *Adhatoda vasica*, was tested for anticancer activity against leukaemia cells. For cytotoxic experiments, seven distinct kinds of leukaemia cells were employed, including CEM, NB-4, MOLM-14, Jurkat, IM-9, K562, and HL-60. As compared to other studied cells, 2-acetyl-benzylamine shown strong cytotoxic activities against MOLM-14 and NB-4 cells, with IC50 values of 0.40 and 0.39 mM at 24 h, respectively. 2-acetyl-benzylamine caused cell cycle arrest in MOLM-14 cells at the G2/M phase and in NB-4 cells at the G0/G1 phase. RT-PCR and Western blot analyses evaluated the mechanism of apoptosis. In MOLM-14 and NB-4 cells, 2-acetyl-benzylamine lowered Bcl-2 activity while increasing Bax expression; cytochrome c was released, and caspases-3 was triggered. Moreover, 2-acetyl-benzylamine suppressed JAK2/STAT3 expression in MOLM-14 and NB-4 cells. In a xenograft mouse model, in vivo treatment of 2-acetyl-benzylamine reduced the development of MOLM-14 cells. A molecular docking research was carried out to analyse the binding manner and calculate the binding energy of 2-acetyl-benzylamine with the active sites of JAK-2, AKT1, FLT3, and Bcl-2. The study findings above demonstrated that 2-acetyl-benzylamine might be developed as a viable cancer treatment agent[51].

6.3.7] Anti-tussive activity: .
Adhatoda vasica (AV) extract was tested for antitussive activity in anaesthetized guinea pigs and rabbits, as well as unanaesthetized guinea pigs. In two different animal species, the antitussive efficacy of AV extract was compared to that of codeine against coughing induced by chemical, mechanical, and electrical stimulation. Oral administration of AV extract showed antitussive action equivalent to codeine against coughing generated by peripheral irritating stimuli. In cough triggered by electrical stimulation of tracheal mucosa, it was 1/4 as effective as codeine[52].

6.3.8] Thrombolytic activity:
The thrombolytic properties of Adhatoda vasica leaf extracts were evaluated using human erythrocytes, and the findings were compared with conventional streptokinase . Adhatoda vasica extracts can be employed to develop a variety of thrombolytic agents[53].

6.3.9] Anti-inflammatory and Analgesic effect:
The anti-inflammatory and analgesic effects of an ethanolic extract of *Adhatoda vasica* Linn. (Acanthaceae) roots were investigated. The anti-inflammatory efficacy of ethanolic extract was tested in albino rats using carrageenan-induced paw edoema assay and formalin-induced paw edoema assay. In albino rats, analgesic activity was assessed using the acetic acid-induced writhing reaction, the hot plate method, and the tail flick method. Oral treatment of extract at dosages of 200 and 400 mg/kg decreased both carrageenan- and formalin-induced inflammation considerably (P 0.05-0.01). In addition, acute extract administration resulted in a substantial (P 0.05-0.01) antinociceptive impact in acetic acid-induced writhing, formalin-induced pain licking, and hot-plate-induced pain. The results of the experiments proved that an ethanolic extract of the roots of *Adhatoda vasica* Linn. has significant anti-inflammatory and analgesic properties [54].

6.3.10] Hepatoprotective activity:
The low expression levels of the CYP2E1 gene in H-R-Z exposed rats might be attributable to the fact that females display somewhat distinct toxic responses to HR-Z co-treatment throughout the anti-TB medication regimen, as documented in this investigation. Acetylation of H (a stage in isoniazid metabolism) was discovered to be a critical factor in NAT gene up-regulation in all treated groups. The presence of cholesterol may impact the up-regulation of CYP7A1 gene expression in the toxicant group, and their differential expression in various treatment groups may be due to the presence of cholesterol in their metabolic system. The upregulation of CYP2E1, UGT1A1, and downregulation of CYP7A1 gene expression in the *A. vasica* treatment group might be attributed to a fatty acid-induced feedback loop. They stated that the usage of this plant and its beneficial phytoconstituents might successfully eliminate drug-mediated hepatic impairments based on their study findings that *A. vasica* could be an effective bi-functional inducer of both phase I and phase II metabolising enzyme systems[55].

6.3.11] Anti-tubecular activity:
The oil extracted from the leaves, flowers, and roots of vasica plants has a substantial antitubercle bacilli action. According to "Indian Materia Medica," under phase-transfer catalysis, alkylhalides from quinazoline present in the plant synthesise compounds with antimycobacterial activity against strains of Mycobacterium tuberculosis, Mycobacterium avium, 4-(S-Butylthio)quinazoline (3c) was even more active against atypical strains of mycobacteria[56].

6.3.12] Aborfacient effect:
Vasicine, one of the most significant alkaloids, has an oxytocic activity by secreting prostaglandins, which stimulates uterine contractions and aids in the passage of delivery during parturition, as well as acting as an abortifacient like oxytocin (57). Several tests were conducted to confirm the oxytocic action of Adhatoda vasica. Rassins, hamsters, and guinea pigs were administered vasicine, which proved to be an abortifacient owing to the secretion of prostaglandin. The effective concentration of alkaloid in this trial ranged from 2.5 to 10mg/kg[58]

6.3.13] Immunomodulatory activity:
In male Swiss albino mice, the immunomodulatory potential of AV was studied. The impact of a 500mg/kg *p.o.* AV leaf alcoholic extract on haematological profile, splenic lymphocytes, and peritoneal

macrophages was assessed 5, 10, 15, and 20 days following therapy. It was also investigated for its impact on macrophage phagocytic index, E.coli-induced abdominal peritonitis, and SRBC-induced delayed type hypersensitivity. AV substantially increased total WBC, blood lymphocytes, splenic lymphocytes, and peritoneal macrophages. It also showed significant resistance to E.coli-induced abdominal peritonitis. *Adathoda vasica* leaf extract may have immunoprophylactic and immunopotentiating activity[59].

6.3.14] Radioprotective effect:
After 22 days, radiation-exposed rats exhibited diseases such as substantial abnormalities in testicular histology and chromosomal abnormalities in bone marrow cells, as well as death. Each mouse was given an ethanolic extract of A. vasica leaf orally for 15 days at 800 mg/kg before being exposed to radiation, and it reduced mortality by 70% in 30 days. Radiation-induced chromosomal damage was decreased in bone marrow cells by the plant extract, showing that it has radioprotective capabilities in the testis. [60].

6.3.15] Anticholinesterase activity:
Vasicinone (an alkaloid isolated from A. vasica roots) induces hypotension in a cat model. It also produces contraction of the isolated intestine and depression of the isolated frog heart in a guinea pig model[61].

6.3.16]Antihelmintic activity:
Adhatoda vasica's anthelmintic activity was investigated using Pheretima pothuma as an experimental model. The normal reference was albendazole. All extracts of *Adhatoda vasica* were evaluated at different concentrations (16.6, 33.3, and 83.3 mg/ml), and observations were represented in terms of time at which worm paralysis and time at which the worms dead. As compared to other extracts such as hexane, chloroform, ethyl acetate, aqueous, and standard albendazole, ethanolic leaf extract of *Adhatoda vasica* showed reduced duration of paralysis and death of the earthworm. The wormicidal activity of different extracts of *Adhatoda vasica* leaf implies that it is beneficial against human parasitic infections[16].

6.3.17] Anti-Ulcer Activity:
The anti-ulcer effect of Adhatoda vasica leaves was investigated utilising two ulcer models: (1) Ethanol-induced and (2) Pylorus ligation with aspirin-induced. In comparison to a control, Adhatoda vasica leaf powder shown considerable anti-ulcer effectiveness in experimental rats. The ethanol-induced ulceration model had the highest level of activity (80%). The study's findings show that, in addition to its known pharmacological properties, the plant has enormous potential as an anti-ulcer drug. [62]

6.3.18] Anti Pyorrhoeal activity:
Twenty-five individuals with pyorrhoea symptoms who consulted dental clinics were chosen at random. The patients were directed to use Adhatoda vasica leaf extract to massage the swollen gums. The application was recommended twice a day for three weeks. The G.I. index of each patient was recorded before starting therapy with Adhatoda vasica extract and at the end of each week for three weeks. Gum irritation and bleeding decreased consistently from day to day and week to week[63].

6.3.19] Antigingival effect :
The benefits of toothpaste made using a combination of herbs, one of which is *A.vasica*, for oral hygiene and gingival health. One ml of resting saliva was collected at the start of the study to measure anaerobic and aerobic bacterial counts, plaque index, proportion of sites with bleeding on probing, and pocket depth at six locations per tooth. A significant reduction was seen in the test sample treatment

group, suggesting that this herbal toothpaste containing AV has beneficial effects on dental hygiene and gingival health. [7].

6.3.20] Action On Reproductive System:

A.vasica, along with a few other medical plants, is used to treat infertility. From March to July 1987, a survey conducted in Lucknow and Farrukhabad, two cities in Uttar Pradesh, India, discovered that *AV* was a well-known herb taken by women for its anti-reproductive ability. An experimental investigation was carried out in support of the survey. Aqueous and 90% ethanol extracts of *AV* were given orally for 10 days after insemination to see how they affected foetal development. At dosages of 175 mg/kg, *AV* leaf extracts were proven to be 100% abortive[64]. In another study, many extracts of 108 medicinal herbs were tested for anti-implantation efficacy in female albino rats. An ethanolic extract of *AV* displayed anti-implantation effectiveness of 60-70%.[65]

6.3.21] Alleopatic effect:

Adhatoda vasica's allelopatic activity was investigated. Turnip seed germination and seedling survival were inhibited by aqueous leaf and flower extracts. The floral extract had a noticeably decreased inhibitory impact at all dosages. In contrast, both extracts had a stimulating impact on turnip seed weight, especially at lower and moderate dosages[66].

6.3.22] Muscle relaxant activity:

An essential oil extracted from the leaves of vasica revealed smooth muscle relaxant activity in the isolated guinea-pig tracheal chain. Vasicine derived from *Adhatoda vasica* stimulates uterine and tracheal muscle in rats and guinea pigs, as well as other tissues. [67].

6.3.23] Antimicrobial, Antiquorum-Sensing And *Ex-Vivo* Antispasmodic Activity Of *Adhatoda Vasica*

Adhatoda vasica stem extract contains β-sitosterol, daucosterol palmitate, monopalmitin, vanillin, vanillic acid, vasicinolone, and vasicinone. The petroleum ether fraction, daucosterol palmitate, monopalmitin, vanillin, and vanillic acid all shown antibacterial activity against E. coli and S. aureus. Whereas both daucosterol palmitate and vanillic acid were effective antifungal agents against *Candida albicans*. In the antiquorum-sensing experiment, the most active compounds were -sitosterol, vanillin, and vanillic acid. While petroleum ether and methylene chloride fractions showed some antiquorum-sensing effect, vasicinolone and daucosterol palmitate did not. For antispasmodic activities, petroleum ether fraction reduced Ach-induced contraction at 200 and 250 g/mL (89.5 and 95.2%, respectively). The methylene chloride fraction likewise demonstrated high inhibition (97.6%) at 150 g/mL. At 150 g/mL, vasicinone and vasicinolone inhibited significantly (89.9% and 84.8%, respectively). The extracted compounds and extracts from the plant's stem demonstrated remarkable action. This study adds to the body of data supporting *A. vasica's* traditional medicinal use in the treatment of a wide range of ailments. [19].

6.3.24] Cholagouge activity

Several studies have shown that a 5mg/kg IV dosage of Adhatoda vasica in pharmaceuticals in dogs and cats stimulates bile activity by excreting up to 40- 100% of the bile. Bilirubin excretion in animals increased [68].

6.3.25]Effect on gastric system:

In vitro investigations revealed that Adhatoda vasica stimulates digestion by activating the trypsin enzyme when the decoction of leaves were given [69].

7] Table:16 VARIOUS FORMULATIONS AND THEIR INDICATIONS OF *Justicia adathoda* PLANT[41-44,45,46]

PLANT PART USED	FORMULATIONS	INDICATIONS
Leaves	Vasa Swarasa (juice of *Justicia adthoda* leaves)[42]	Schizophrenia and Convulsive disorders
Leaves	Vasa Avaleha (sugar formulation of *Justicia adthoda* leaves)[43]	Various respiratory diseases- Asthma And Tuberculosis
Leaves	Vasa Ghrita (clarified butter of *Justicia adthoda* leaves) [44]	Bronchitis, Haemoptysis, Dysfunctional uterine bleeding, Thrombocytopenia, Idiopathic Thrombocytic purpura, Malena, haemoptysis, Bilious head ache Etc.
Leaves	Vasa Asava/Arista (Alcoholic preparation *Justicia adthoda* leaves)[45]	lung infections and Asthma
Leaves	Puff preparation[46]	Respiratory disorders, Asthma, Bronchodilator, Antitussive, Antimicrobial(46)
Leaves	Infusion, alcoholic extract	Insecticide..
Leaves	Decoction, infusion, poultice	Rheumatic and inflammatory swellings, Neuralgias and Rheumatism.
Leaves	Leave extract	Antiseptic
Leaves	NS	Emmenagogue
Leaves	Bruised fresh leaves	Snake-Bites
Leaves	Infusion	Vomiting, Leprosy, Gonorrhoea, Headache
Roots	Powder, decoction, infusion electuary, powder, paste	Bronchitis, Colds, Expectorant, Asthma, Antispasmodic, Respiratory Diseases,Tuberculosis, Phthisis, Cough, Lung Tonic, Diphtheria, Liquefy Sputum.
Roots	powder	Gonorrhoea,Antiseptic., Antiperiodic, Anthelmintic,
Roots	NS	Bilious vomiting, rheumatism, Leucorrhoea, Eye diseases, helps in foetus expulsion, Diuretic, Strangury.
Roots	Decoction, bruised	Wounds
Roots	Macerated roots	Abnormal labour
Root-bark	NS	Abdominal tumour, Haemoptysis, Heart diseases Cataract.
Bark	Decoction, powder, cigarettes	Asthma, expectorant, Chest diseases, phthisis, antispasmodic
Bark	Bruised, decoction	Wounds
Flowers	Fresh flowers	Opthalmia

Flowers	Infusion, electuary	Fever
Flowers	NS	Gonorrhoea, Jaundice, Abdominal tumour, Antiseptic, Hectic heat of blood, Rheumatism, Improve blood circulation
Fruit	hung round the children neck	Colds, antispasmodic, bronchitis
Fruit	Unriped fruit boiled with milk	Diarrhoea, dysentery
Fruit	NS	Fever, Laxative
Whole plant	NS	Excessive phlegm, Menorrhagia

NS -not stated.

8] SAFETY PROFILE:[6]

As we looked at the safety profile of A. vasaka, we couldn't uncover any evidence of significant sideeffects or mortality. Some minor adverse effects, such as diarrhoea and vomiting, do occur when the medicine is used in greater quantities than recommended. Apart from the viable and hepatotoxic effects, the plant's leaves have a strong impact on the uterus, causing greater contraction and perhaps leading to termination [7]. All of the studies under toxicity are related to reproductive toxicity, either from the plant as a whole or from the active components, such as vasicine. As a consequence, we may be able to ascertain that this plant is safe in a dose-dependent manner (5, 105, 106). The acute toxicity studies for vasicine were carried out after a single dose, and the LD50 was calculated for each species, as indicated in the table.

Table:17 Doses of vasicine at which it causes toxicity in different animals

Animals	Intraperitoneal	Oral	Intravenous	hypodermoclysis
Mice	125	290	79	200
Rats	115	640	nil	335

9] METHODS FOR USES AND DOSAGES:

Vasaka is often used in doses ranging from 15 to 30 in the form of extract obtained from its leaves, mixed with ginger or honey. The dried leaves can be taken in powder form in doses of 2 mg or made into a decoction. Both the decoction and powder are utilised in several Ayurvedic treatments for respiratory problems. The roots and bark, like the leaves, offer medicinal effects. The bark decoction is taken in dosages of 30 to 60 mL, and the powdered root-bark is given in doses of 0.75 to 2 gm[29].

10] PHARMACOKINETICS:

The results from investigations on vasicine absorption and distribution in mice after intramuscular, intravenous, and subcutaneous administration are identical to those reported in rats. Vasicine (20 mg/kg) was effectively absorbed, with a maximal blood level of roughly 56 g/ml in both pregnant and non-pregnant rats, and up to 10 g/ml in amniotic fluid (36). Within 5 minutes of intravenous therapy, high levels of vasicine were identified in the uterus of rats and mice, with the highest level attained after 10 minutes. After intravenous treatment, the half-life was 5 to 7 minutes, and 1.5 and 2 hours after intramuscular and subcutaneous doses, respectivel. The most of vasicine and its metabolites are eliminated in the urine, according to study. Around 55% of the excreted product was vasicine during

the first 18 and 22 hours after intravenous and intramuscular treatment, respectively, but approximately 18% was vasicine during the first 24 hours after oral dosing (36). The uterus showed a very low concentration of vasicine after oral medication. Vasicine is metabolised in the liver to vasicinone and other metabolites, which contribute to first-pass effects and are an important mechanism of Vasicine clearance[31].

11] SPECIAL PRECAUTIONS AND WARNINGS:

When used orally: There isn't enough relevant evidence to say whether Malabar nut is safe or what the potential side effects are. Those who are pregnant or breastfeeding should avoid taking Malabar nut. It is also advised not to use it if women are breastfeeding. The effects of Malabar nut on a nursing newborn are unclear till now.[30]

12] GLOBAL PERSPECTIVES AND FUTURE ASPECTS;

According to the information presented above, the plant *Justicia adathoda* is widely used for the treatment of a wide range of illnesses, many of which are well documented and detailed in pharmaceutical applications. The plant's various components and chemical constituents guarantee that it may be utilised to treat a wide range of diseases. Ultimately, it may be used as a therapy strategy and to create a unique, innovative drug delivery system. To examine its possible further actions, screening and bioassay are required, as well as sufficient information about the compounds and their structure-activity connection investigations. The existing data will be used to provide the groundwork for the development of a completely novel natural product with fewer or no adverse actions in compare with the synthetic drugs. It also promotes agricultural researchers who primarily work with herbal goods. Better resolution with the several bioactive components extracted from the *Justicia adathoda* is in the future. Furthermore, because relatively few studies have been undertaken with the fruit, stem bark extract of *Justica adathoda*, this review can assist researchers in focusing on these parts of the plant with great pharmacological benefits.

13] CONCLUSION

In accordance with a literature study, *Justicia adathoda* has been extensively researched for its pharmacological activities. It includes a number of therapeutically important phytoconstituents, including vasicine, vasicinone, vasicoline, and minor alkaloids. When researchers embrace a global approach for drug discovery from plant sources, the development of therapeutically active molecules from *Justicia adathoda* should be prioritised.

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