

# Phytochemistry, pharmacology, and botanical aspects of *Stachytarpheta* species – A review

Priyanka D. Yadav, Karuna P. Modi, Mamta B. Shah\*

Department of Pharmacognosy and Phytochemistry, L. M. College of Pharmacy, Ahmedabad, Gujarat, India

## Abstract

**Introduction:** Globally, the use of traditional medicines is being encouraged for the treatment of chronic disorders, as synthetic drugs may cause untoward effects. The genus *Stachytarpheta* Vahl (Verbenaceae), known as “porter weed” [English], “gervao,” includes many species widely distributed in tropical and subtropical America and Africa with few members in tropical Asia and Oceania. It is valued traditionally for its different species that possess anticancer, anti-inflammatory, antidiabetic, antimicrobial, and antipyretic activities. Interestingly, current research on genus has revealed the presence of phenylethanoid with various pharmacological properties and multispectrum therapeutic applications. A relatively large number of studies cited here have adduced the possible areas where the important species of this genus can exhibit their therapeutic activities in the treatment of chronic ailments or diseases including ulcers, fever, renal disorders, and atherosclerosis. **Materials and Methods:** An extensive search in three electronic databases (Unbound Medline, PubMed, and Science Direct) and internet search engines (SciFinder and Google Scholar) was used to connote the studies on genus *Stachytarpheta*. **Results and Discussion:** This review amplifies the recent studies on phytochemical and pharmacological aspects, which alludes, these species have excogitated with noteworthy therapeutic activities. **Conclusion:** The present piece of write up will also draw the attention of scientists toward the issues and challenges associated with the probable approaches that may be reconnoitred to encourage people take the maximum benefit of these potentially useful species.

**Key words:** Pharmacology, Phenylethanoid glycoside, Phytochemistry, *Stachytarpheta*, Verbenaceae

## INTRODUCTION

The genus *Stachytarpheta* (Family – Verbenaceae) known as “gervao” or “orgevao” includes more than 100 species distributed in tropical and subtropical parts of America, Brazil, Asia, and Australia.<sup>[1-3]</sup> The genus name originated from the Greek stachy, meaning “spike” and tarpheta, meaning “thick.” Members of the genus are herbs, shrubs, and sometimes trees with leaves generally opposite or whorled, simple or palmately compound or exstipulated.<sup>[2,4,5]</sup> It is typified by small, intense blue, and pink-purple flowers brought together in dense showy inflorescences.<sup>[1]</sup> The whole plant and leaves of most species of *Stachytarpheta*, especially *Stachytarpheta jamaicensis*, *Stachytarpheta cayennensis*, *Stachytarpheta indica*, *Stachytarpheta urticifolia*, and *Stachytarpheta mutabilis* among others, have long been used in traditional medicine for the treatment of as purulent ulcers, skin lesions, and internally for inflammations, asthma, fever, renal

disorders, atherosclerosis, and venereal infectious diseases.<sup>[5-7]</sup> A search through the phytochemical literature revealed presence of the phenylethanoids, iridoids, and flavonoids that possess antiulcer, anticancer, hepatoprotective, anti-inflammatory, antipyretic, antidiabetic, analgesic, antimicrobial, antioxidant, antispasmodic, and anthelmintic activities the.<sup>[1,3,8,10-15]</sup> The present effort is to systematize encyclopedic review on the species of the genus *Stachytarpheta* Vahl with focus on their distribution, identification, traditional uses, and chemical and biological studies. It also focuses on need of future research on plants of this genus for their development as potential herbal drugs.

### Address for Correspondence:

Mamta B. Shah, Department of Pharmacognosy,  
L. M. College of Pharmacy, Navrangpura,  
Ahmedabad - 380 009, Gujarat, India.  
E-mail: mbshah2007@rediffmail.com

**Received:** 03-04-2021

**Revised:** 28-05-2021

**Accepted:** 09-06-2021

## MATERIALS AND METHODS

A literature search was conducted using the keywords “*Stachytarpheta*,” “phenylethanoid glycoside,” “Verbenaceae,” “phytochemicals,” and “biological activities” on electronic databases (Web of Science, PubMed, Scopus, Science Direct, Springer Link, and ACS Publications) in addition to free search in Google Scholar, to compile published research works till April 2021. The list of references of all the relevant articles was also studied and reviewed related to the subject. Inclusion criteria were papers reporting the botanical description, ethnobotanical aspects, isolated compounds, and biological activities related to the *Stachytarpheta* genus.

## RESULTS AND DISCUSSION

### Distribution and Habitat

*Stachytarpheta* Vahl is a monophyletic genus with 130 species distributed in the Americas, Africa, Asia, and Oceania, with abundant species in Brazil (81 spp.). They can be discriminated by the presence of androecium with two fertile stamens and two staminodes.<sup>[16]</sup>

Species of *Stachytarpheta* usually have four or five calyx lobes, but in *S. indica*, two of these lobes are enormously reduced giving 2-lobed appearance. Whereas other vegetative characters, along with the width of the rachis can be used to recognize introduced species of *Stachytarpheta* in Australia, *S. indica* can be discerned from these by means of its apparently bifid calyx and narrower, more lanceolate leaves. Moreover, *S. indica* can be substantiated by the presence of aborted guard cells from *S. cayennensis* which has contiguous stomata on the adaxial surface of the leaves.

As claimed by some botanists, there are five species of *Stachytarpheta* currently existing in India, but none of them is comparable to *S. indica*. The Flora of Java treatment differentiates *S. indica* and *S. jamaicensis* from *S. cayennensis* by presence of four teeth in the former two species in contrast to five teeth in the latter. If *S. indica* truly possess a clearly bifid calyx, then probably those authors have misinterpreted the name, in this case to *S. jamaicensis*.

The existence of several hybrids generates problems in the correct identification of the above species. Some phytologists suggested reduction of *S. urticifolia* to the synonymy of *S. cayennensis*, even though it is documented as a different species by others. It culminates in controversy regarding the authentication of various species, signifying the need of taxonomic revision of the genus.<sup>[17]</sup>

This genus has glabrous to densely hairy annual or perennial herbs or shrubs with quadrangular, or subquadrangular stem; sessile or petiolate, linear, elliptic, ovate leaves, and terminal spikes.<sup>[18]</sup>

### Taxonomy and Major *Stachytarpheta* Species

*Stachytarpheta* is an erect and branched half-woody plant, with slightly angled stem. Occasionally, the stem is hairy on opposite faces, while the other two faces are glabrous or hairy at the leaf nodes. Hairs can be simple, or uniseriate, and occasionally gland-tipped, and can be erect and pointing in all directions.<sup>[18]</sup> The leaves are elliptic to oblong-ovate, serrate and 2–10 cm long with decurrent base. The spikes are terminal, rather slender, 10–30 cm long and 3–4 mm thick. The calyx is small, oblique with four teeth on margin. The corolla is deep blue or blue-purple and 1 cm long. The fruit is enclosed in the calyx and oppressed to and somewhat sunk in the smooth and oblong rachis.<sup>[5]</sup> Different species of *Stachytarpheta* possess distinct pharmacognostical features depending on the geographical indication, as depicted in Table 1 and Figure 1.

#### *S. jamaicensis* (L.) Vahl: [Figure 1A]

**Synonym:** *Abena jamaicensis*, *Stachytarpheta bogoriensis* Zoll. and Moritzi, and *Verbena jamaicensis*

It is commonly known as blue porter weed, blue snake weed, bastard vervain, Brazilian tea, Jamaica vervain, and light blue snakeweed (English) and kariartharani (Hindi). The plant has been widely used by the people throughout the world for the various medicinal purposes. It grows 0.6–1.2 m tall and has a smooth, dark green colored stem, which turns woody toward the base of the stem. This plant normally reproduces 5–7 mm long flowers in a mixture of

**Table 1:** Morphological comparison between different species of *Stachytarpheta*

Species	Plant height (m)	Leaf shape	Flower
<i>Stachytarpheta jamaicensis</i>	0.6–1.2	Ovate to elliptic, oblong	5–7 mm long mix of bluish and pinkish-purple to deep blue
<i>Stachytarpheta cayennensis</i>	1.5	Ovate to elliptic	4–5 mm dark blue/purple or violet-white center
<i>Stachytarpheta indica</i>	0.6–0.9	Lanceolate to oblong lanceolate or elliptic ovate	13 mm wide, deep blue with white center
<i>Stachytarpheta mutabilis</i>	0.1–0.2	Elliptic-oblong, lance shaped	13–18 mm long with bright rose-red-pink
<i>Stachytarpheta urticifolia</i>	0.5–1.5	Ovate to elliptic ovate	Purple-blue, or royal blue with a white throat

bluish and pinkish color or could bear flowers with a purple to deep blue color. Its leaves are grayish-green in color with smooth surface, ovate to elliptic shape, round apex, and distinct petioles.<sup>[19-22]</sup>

***S. cayennensis* (Rich.) Vahl: [Figure 1B]**

**Synonym: *S. guatemalensis* Moldenke**

It is locally known as blue rat's tail or rough-leaved false vervain in English. It is an erect, shrubby perennial plant up to 1.5 m high. The stem is slender, branched, quadrangular, pubescent, and woody at the base. The leaves are opposite or sometimes alternate having short, winged stalks. Flowers are dark blue, purple, or violet with white centers, sessile with two large and three small petals.<sup>[9,14,23]</sup>

***S. indica* Vahl: [Figure 1C]**

**Synonym: *Valerianoides indica* (L.) and *Verbena indica* L.**

It is popularly known as Indian snakeweed (English) and kariyartharani (Hindi). It is a well-branched annual herb about 0.6–0.9 m in height showing presence of long narrow

spikes. Leaves are elliptic, obtuse or acute, coarsely serrate, glabrous with tapering and decurrent base. The flowers are deep blue with white center, 5 lobed and 1.3 cm wide.<sup>[18,24-28]</sup>

***Stachytarpheta mutabilis* (Jacq.) Vahl: [Figure 1D]**

**Synonym: *Cymburus mutabilis* (Jacq.) Salisb, *Verbena mutabilis* Jacq., and *Valerianoides mutabilis* (Jacq.) Kuntze**

It is a species of flowering plant in the Verbenaceae family usually identified as changeable velvet berry, coral port weed, pink snakeweed, red snakeweed, and pink at red tail. It is cultivated as an ornamental plant. This species is a perennial herb or subshrub generally woody at base, up to 1.8 m high with branches covered with hairs. Leaves are 5–6 cm long, 4 cm wide, elliptic-oblong and lance-shaped, scabrous. Corolla is rose, slender, with pale pink stripes, bright rose-red-pink, whitish inside at mouth and bottom. The spike inflorescence is up to 60 cm long.<sup>[29-32]</sup>

***S. urticifolia* Vahl: [Figure 1E]**

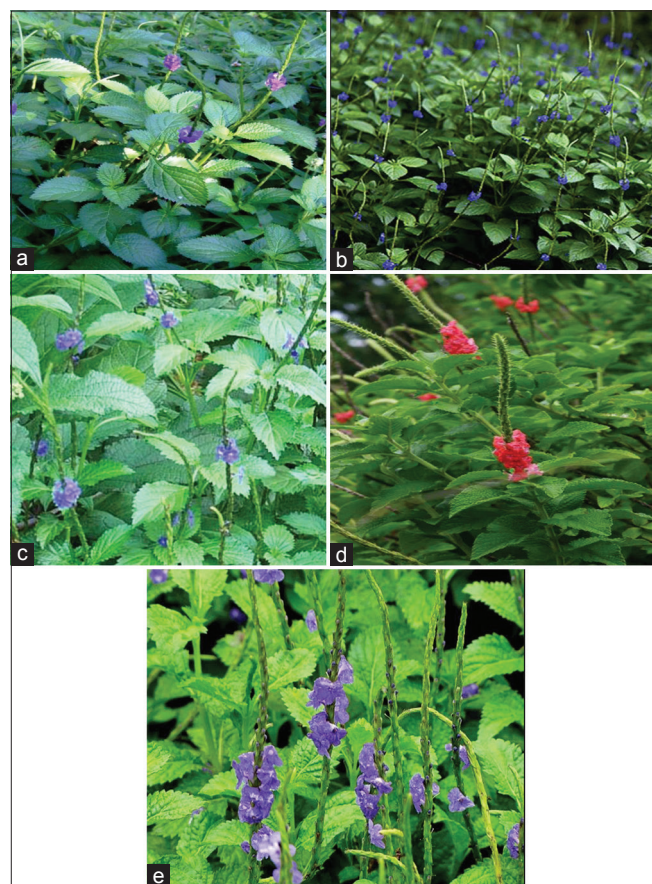
**Synonym: *Cymburus urticifolia* (Salisb) and *Zappania urticifolia* (Salisb)**

It is frequently named as blue snakeweed and nettle leaf velvet berry. It is a perennial herb growing wild in the Sylhet and Chittagong districts of Bangladesh and also cultivated as an ornamental weed. It is 0.5–1.5 m tall with ovate to elliptic ovate, or oblong, serrate leaves and 4 angled softly pubescent stems. Calyx lobes are shortly 5 toothed and corolla dark purple-blue, mauve or royal blue with a light or white throat.<sup>[33-36]</sup>

**Traditional Uses**

*Stachytarpheta* has been traditionally used as antibacterial, antispasmodic, antidiabetic, analgesic, anti-inflammatory, antipyretic, antifungal, anticancer, hepatoprotective, anxiolytic, hemolytic, laxative, larvicidal, anthelmintic, etc. Various parts of the plants of *Stachytarpheta* are used in Indian traditional medicine for the treatment of aforementioned conditions as well as for inhibition of gastric secretion and immunopathological diseases related to oxidative stress.

*S. jamaicensis* is utilized as medicine in Southeastern Asia and West Tropical Africa, it is considered to be aperient, as an important medicinal plant with great medicinal properties in the elderly as a cure for allergies and respiratory conditions, cough, cold, fever, constipation, digestive complications, and others. In Nigeria, the leaves are used for birth control, abortion, treatment of menstrual disorders, and as a galactagog. Whole plant of *S. jamaicensis* has been known to demonstrate antioxidant, hypoglycemic, antacid, analgesic, anti-inflammatory, hypotensive, anthelmintic, diuretic, laxative, purgative, sedative, spasmogenic, vasodilator



**Figure 1:** Different species of *Stachytarpheta*. (a) *Stachytarpheta jamaicensis*, (b) *Stachytarpheta cayennensis*, (c) *Stachytarpheta indica*, (d) *Stachytarpheta mutabilis*, (e) *Stachytarpheta urticifolia*



properties, and its infusion which have been used as a remedy for a headache it is used to treat sores in children's ears, heart trouble, and as anti-asthmatic, sedative, and anti-hypertensive.<sup>[7,8,19,37,38]</sup>

*S. cayennensis* is employed in traditional medicine for the management of mental illness and as an anti-inflammatory, analgesic, antipyretic, hepatoprotective, laxative agent, and in the treatment of gastric disorders. Ethnomedicinally in Nigeria and other parts of the world, the leaves are used for the management of insomnia and anxiety. Crushed leaves and roots have also been applied in the treatment of skin lesions and are used as folk medicine in Brazil and other countries to treat inflammation, varicose ulcers, fever, hepatic and renal disorders, hypertension, and diabetes.<sup>[6,37]</sup>

*S. indica* is being extensively used in the Indian traditional system of medicine for diabetes and liver liver complaints, and has been used as a folk medicine for the cure of allergies, respiratory conditions, cough, cold, fever, constipation, digestive complications, and dysentery and also reported to promote menstruation. Stem bark is valued in traditional medicine as analgesic, anti-inflammatory, and antipyretic drug.<sup>[38]</sup>

*S. mutabilis* leaves are used for adulterating tea. They are pounded with lime and applied to swollen wounds and sores. Plant is useful for the treatment of tumors also besides an ornamental, mainly in Amravati, India.<sup>[30]</sup>

*S. urticifolia* folklorically used as cure for fever, rheumatic inflammations, venereal diseases, dropsy, ulcer, and other stomach troubles. Infusion of the bark is advocated in the treatment of diarrhea and dysentery. It is used as an abortifacient agent by the tribal people of Bangladesh.<sup>[10]</sup>

## Phytochemistry

Preliminary phytochemical screening of the genus *Stachytarpheta* revealed the presence of alkaloids, flavonoids, tannins, saponins, glycosides, steroids, and phenols [Table 2 and Figure 2].

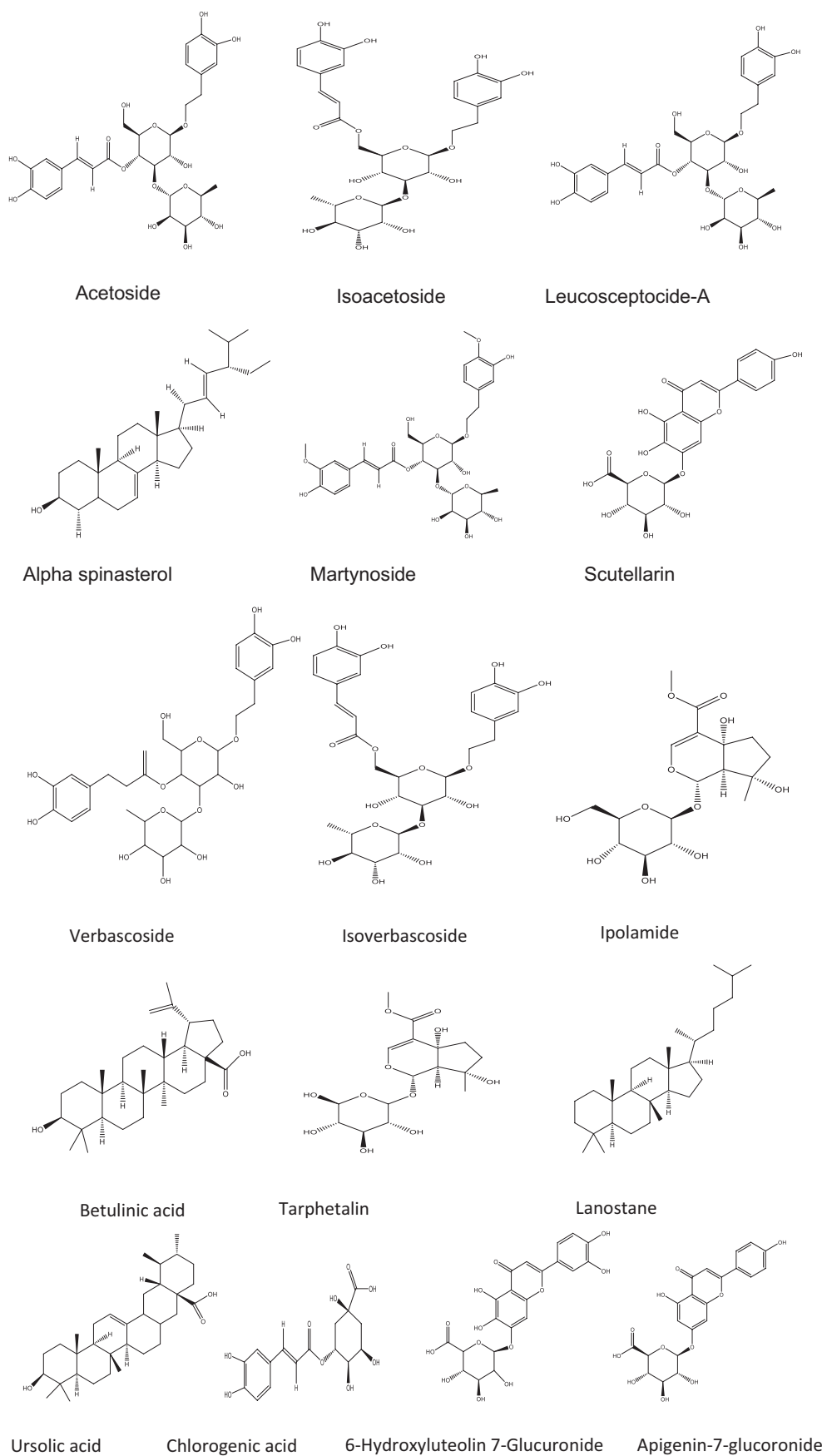
### *S. jamaicensis*

The active phytoconstituents from the leaves of *S. jamaicensis* are reported to have aforesaid major groups of secondary metabolites. Iridoid ipolamiide, phenylethanoid glycoside, and verbascoside are found to present in aqueous extract of leaves. The flavonoid, scutellarin has been isolated, with cardioprotective, anti-inflammatory, and antiviral actions and hispidulin to be bronchodilator, antispasmodic and anti-asthmatic. Study of leaves showed a new lanostane triterpenoid 16 $\beta$ -( $\beta$ -D-glucopyranosyl-3,8,22-trihydroxy)-cholestan-1  $\beta$ -yl-6-O-(3,4,5-trimethoxybenzoyl)- $\beta$ -D-glucopyranoside.

Some secondary metabolites that have been found include lanostane phenylacetate (1,3,16 $\beta$ -yl-phenylpropylacetate-lanostan-5,11,14,16,23,25-hexen-22-one), two steroidal glucosides 16  $\beta$ -(glucopyranosyl  $\beta$ -D, 3,8,22-trihydroxy) cholestan-1  $\beta$ -yl-6-O-(3,4,5-trimethoxy benzoyl)  $\beta$ -D and 16- $\beta$  ( $\beta$ -D-glucopyranosyl

**Table 2: Phytochemistry of genus *Stachytarpheta***

Component	Sub-type	References
Phenyl propanoid glycoside	Acetoside	[9,14,41,46]
	Iso-acetoside	[9,41,46]
	Leucosceptoside A	[9]
	Martynoside	[9,46]
Steroidal glycosides	Jinoside D	[9]
	Spinasterol	[10,11]
	$\alpha$ -spinasterol	[8,10,11]
	16 $\beta$ -( $\beta$ -D-glucopyranosyl-3,8,22-trihydroxy)-cholestan-1 $\beta$ -yl-6-O-(3,4,5-trimethoxy benzoyl) $\beta$ -D-glucopyranoside	[8,36,40,41]
	16- $\beta$ ( $\beta$ -D-glucopyranosyl 2) 3,8,22-tri-hydroxy cholest 5, 14, 16,23 tetraene-1 $\beta$ -yl-6-O-(3, 4, 5-trimethoxybenzoyl) $\beta$ -D, glucopyranoside	[8,36,40,41]
Flavonoids	Scutellarin	[36,41]
	Hispidulin	[36,41,42]
Phenylethanoid glycosides	Verbascoside	[41,46]
	Isoverbascoside	[43,46]
Iridoid glycosides	Ipolamiide	[3,10,14,44]
	Ipolamiide	[14,44]
	6 $\beta$ -hydroxy ipolamide	[40]
	Betulonic acid	[46]
	Tarphetalin	[8]
Terpene glycoside	Lanostane terpenoids	[36,40,41,42]
	Lanostane phenylacetate	[36,40,41,42]
Phenolic acid	Ursolic acid	[41]
	Chlorogenic acid	[8]
	Catechin tannins	[8]
	6-Hydroxy luteolin 7-glucuronide	[8]
	Luteolin 7-glucuronide	[8]
	Apigenin	[41]
Alkaloids	N-nenoside B	[23]



**Figure 2:** Chemical structures of some important constituents of *Stachytarpheta*

3,8,22-trihydroxy-cholest-5,14,16,23-tetraene, 1 $\beta$ -yl,6-O-(3,4,5-trimethoxybenzoyl)  $\beta$ -D-glucopyranoside.<sup>[8,36,39-42]</sup>

### *S. cayennensis*

The Nnenoside-B isolated from the leaves of *S. cayennensis* showed absorption peaks characteristic bands at  $V_{\max}$  2980  $\text{cm}^{-1}$  and 2750  $\text{cm}^{-1}$ . It is also considered to be most rich in iridoids glycosides, mainly ipolamiide, lamiide; phenylethanoid glycosides such as, jinoside-D, martiniside (martynoside), acetoside, iso-acetoside, leucosceptoside-A. Arylpropanoid glycosides found are verbascoside and isoverbascoside.<sup>[9,23,37,43]</sup>

### *S. indica*

The active constituents include sterols,  $\beta$ -sitosterol, lupeol, and stigmasterol together with triterpenic acid, ursolic acid, and flavone apigenin, iridoids ipolamide, phenylethanoid glycosides, and verbascoside in entire plant of *S. indica*. Sulfurous acid, 2-ethylhexyl hexyl ester, N-t-butylpyrrole, pantanoic acid, 5-decyne 11,14,17-eicosatrienoic acid, methyl ester, phytol 2-methylheptanoic acid, norpiperone, 1,5,9-undecatriene, 2,6,10-trimethyl-, vitamin E, 1,3-benzenediol, o-(2-methoxybenzoyl)-o'-ethoxycarbonyl- 4-methyl-2,4-bis (4'-trimethylsilyloxyphenyl) pentene-1, phthalic acid, and di (2,3-dimethylphenyl) ester are found to be present in the leaves.<sup>[1,38,44]</sup>

### *S. mutabilis*

*S. mutabilis* showed the presence of iridoid glycoside, 6  $\beta$ -hydroxy ipolamide, lamiide, and saponin. Essential oil of *S. mutabilis* analyzed by GC/MS demonstrated major components 1-octen-3-ol, (Z)-3-hexen-1-ol, (Z)-4-hexen-1-ol, linolenic acid, palmitic acid, octan-3-ol, and rosifoliol.<sup>[29]</sup>

### *S. urticifolia*

Phytochemical analysis of *S. urticifolia* revealed the presence of saponins, flavonoids, terpenoids, steroids, glycosides, quinines, alkaloids, tannins, and phenols in various extracts of root, stem, leaf, and inflorescence. The methanolic extract of the leaves is found to contain iridoid glycoside, ipolamiide whereas the n-hexane extract of the root yielded the sterol,  $\alpha$ -spinasterol.<sup>[11,45]</sup>

## Pharmacological Activities

A variety of species of *Stachytarpheta* is prescribed since a longer time for their medicinal use in treatment of ulcers, skin lesions, allergies, cough, cold, insomnia, anxiety, internally for inflammations, fever, renal disorders, atherosclerosis,

also as antimicrobial, antispasmodic, antidiabetic, analgesic, anticancer, and hepatoprotective and many of these claims have been proved through scientific studies [Table 3].

## Antibacterial and Antimicrobial Activity

In a study, targeting antimicrobial activity mixture of verbascoside, martynoside, and iso-verbascoside of the ethyl acetate fraction is shown to exhibit greater antibacterial inhibition when compared to other fractions of *S. cayennensis*. The aqueous extract of *S. indica* root and methanolic extract of *S. urticifolia* leaf showed significant activity against various species of bacteria which is comparable with standard antibiotic streptomycin and ampicillin, respectively. Several studies have demonstrated the antimicrobial potential of *S. jamaicensis* extracts toward pathogenic microorganisms, including bacteria and fungi.<sup>[8,10,46-48]</sup>

## Antioxidant Activity

The methanol and ethyl acetate extract of *S. jamaicensis* leaf showed 59.53 and 60.20% percentage free radical scavenging activity at 100  $\mu\text{g/mL}$ . The  $\text{IC}_{50}$  for the methanol extract (16.95  $\mu\text{g/mL}$ ) was lower than the ethyl acetate extract (33.12  $\mu\text{g/mL}$ ). The 75% methanolic extract of *S. indica* leaf was found to have the highest antioxidant activity in both fresh and dry samples compared to the aqueous and 50% methanolic extract. Verbascoside and betulinic acid isolated from *S. cayennensis* increased the tolerance and decreased the lipid peroxidation of *S. cerevisiae* to reactive oxygen species. Moreover, the methanolic leaf and inflorescence extracts of *S. urticifolia* also showed significant antioxidant activity.<sup>[8,42,47,49-51]</sup>

## Hypoglycemic Activity

The ethanolic extract of *S. jamaicensis* leaf as well as *S. indica* plant when used continuously for a period of 15 days, they produced a significant reduction in the blood glucose level in streptozotocin-induced diabetic rats. The effect of the extract at 600 was almost equal to that of the standard metformin (500 mg/kg) used for the control of diabetes.<sup>[49,52]</sup>

## Antihypertensive Activity

The aqueous leaf extract of *S. jamaicensis* demonstrated a significant dose-dependent antihypertensive effect. The extract reduced blood pressure and heart rates of anesthetized rabbits, gradually in increasing doses, and the maximum effect was observed at 80 mg/kg dose.<sup>[53]</sup>

## Sedative and Anxiolytic Activity

The methanolic leaf extract of *S. cayennensis*, its butanol and aqueous fractions, inhibited rearing and spontaneous locomotion and prolonged pentobarbitone-induced sleep time in mice. The

anxiolytic effect was observed in both the aqueous and *n* butanol fraction at dose 20 and 5 mg/kg, by elevated plus maze test.<sup>[6]</sup>

### Anti-inflammatory and antinociceptive activity

The ethanolic leaf extract of *S. jamaicensis* exhibited antinociceptive activity against chemically and thermally induced nociception and against both inflammation and non-inflammation-mediated nociception through suppression of both peripheral and central levels. It also showed anti-inflammatory activity through inhibition of arachidonate COX. The alcoholic and *n*-butanolic extracts of dried leaves of *S. cayennensis* significantly inhibited carrageenan induced edema formation at doses ranging from 100 to 200 mg/kg. The iridoid ipolamiide and the phenylethanoid glycoside acetoside isolated from the active fraction, demonstrated inhibitory effect on histamine and bradykinin-induced contractions of guinea-pig ileum. These compounds also found to have *in vivo* anti-inflammatory activity when administered orally to rats mainly in the 4<sup>th</sup> h after the administration of the phlogistic agent (70.22% and 93.99%, respectively). The extracts also exhibited antinociceptive activity measured by the hot plate test in doses ranging from 100 to 300 mg/kg. An infusion of the methanol leaf extract of *S. indica* showed significant anti-inflammatory activity in a dose-dependent manner comparable to that of standard indomethacin.<sup>[8,24,54]</sup>

### Hepatoprotective Activity

The alcoholic extract of *S. indica* whole plant significantly improved the biochemical profiles in various liver functions tests at the dose 600 mg/kg in rats. The protective action was further confirmed by histopathological study and found to be equal to that of silymarin (100 mg/kg).<sup>[55]</sup>

### Wound healing Activity

The ethanolic leaf extract of *S. jamaicensis* exhibited significant wound healing in albino rats when applied externally. It showed better wound contraction and promoted faster wound closure.<sup>[56,57]</sup>

### Immunomodulatory Activity

Methanolic extract of *S. cayennensis* exhibited 64.21% inhibition of determination of delayed type hypersensitivity response at 500 mg/kg and evoked 139.64% of phagocytic stimulation at 100 µg/ml dose. It also showed dose-related stimulation of humoral immunity and leucocyte mobilization of 10.15% at 250 mg/kg dose.<sup>[58]</sup>

### Antimalarial Activity

The methanolic extract of *S. cayennensis* leaf (90–270 mg/kg/day) showed significant ( $P < 0.05$ ) blood schizonticidal

activity against chloroquine sensitive *Plasmodium berghei berghei* in mice with a considerable mean survival time comparable to that of the standard drug, chloroquine, 5 mg/kg/day. The extract also showed anti-plasmodium activity against chloroquine sensitive strain poW and multiresistant clone Dd2 of *Plasmodium falciparum*.<sup>[58,59]</sup>

### Gastric Acid Secretion and Antiulcer Activity

The aqueous extract of *S. cayennensis* the whole at dose 2 g/kg increased the intestinal motility and protected mice against ulcers induced by ethanol, indomethacin and stress (cold restrained). It also inhibited the basal acid secretion as well as that induced by histamine and bethanechol in pylorus-ligated mice when injected into the duodenal lumen. The purified active fraction (benzene fraction of the butanolic phase of water extract and its ethanol fraction) reduced gastric acid secretion 5–10 times higher compared to the original extract.<sup>[3,60]</sup>

### Cytotoxic Activity

The dichloromethane extract of *S. jamaicensis* aerial parts exhibited a potent cytotoxicity against human oral squamous cell carcinoma cell lines CLS-354/WT and CLS-354/DX. In another study, the dichloro from same plant was found to have cytotoxic activities in HeLa and T47D cell line with IC<sub>50</sub> values of 84,198 µg/ml and 64,167 µg/ml respectively. Furthermore, the *n*-hexane and the methanol extract of *S. urticifolia* leaf and root bark as well as isolated compounds ipolamiide and  $\alpha$ -spinasterol also demonstrated moderate cytotoxic activities against brine shrimp nauplii (*Artemia salina*) where vincristine sulfate was taken as a standard.<sup>[10,61,62]</sup>

### Antidyslipidemia Activity

The aqueous infusion (tea) of *S. jamaicensis* significantly reduced the plasma levels of triglycerides, total cholesterol, low-density lipoprotein (LDL), and and VLDL but but increased high-density lipoprotein cholesterol levels in the treated animal models.<sup>[63]</sup>

### Miscellaneous

Zinc oxide (ZnO) and Cu-doped ZnO nanoparticles synthesized from aqueous leaf extract of *S. jamaicensis* showed antibacterial activity against *Bacillus subtilis* and *Staphylococcus aureus* at the concentration 500 mg/mL. Its silver nanoparticles demonstrated highest activity against *Escherichia coli*, *S. epidermis*, and fungal strain *Candida*. pH-Sensitive biopolymeric hydrogel based on indole-3-acetic acid extracted from *S. jamaicensis* leaf showed good surface morphology and thermal stability, and is proposed for wound healing and anti-cancer applications. *S. cayennensis*-mediated copper nanoparticles showed anticancer effect in

**Table 3:** Pharmacological activity of different species of *Stachytarpheta*

Plant part	Component responsible	Mechanism of action	Activity	References
Leaves ( <i>Stachytarpheta jamaicensis</i> )	Scutellarin	Protein-protein interaction	Cardioprotective	[64]
Leaves ( <i>Stachytarpheta jamaicensis</i> )	Hispidulin	Targeting $\beta$ -2 receptor	Antiasthmatic, bronchiodilator	[36,41]
Leaves ( <i>Stachytarpheta jamaicensis</i> )	Verbascoside, acetoside	-	Antioxidant, neuroprotective, antibacterial	[41]
Whole plant ( <i>Stachytarpheta indica</i> )	Flavonoids scutellarin	Ability to moderate some cell signaling	Antidiabetic, and hypolipidemic	[52,65]
Leaves ( <i>Stachytarpheta urticifolia</i> )	Polyphenols	1,1-diphenyl-2-picrylhydrazyl radical scavenging activity	Antioxidant activity	[15]
Whole plant ( <i>Stachytarpheta indica</i> )	Ipolamiide	Locally	Anti-inflammatory	[44,54]
Leaves ( <i>Stachytarpheta indica</i> )	-	Agar well diffusion method	Antibacterial and antifungal activity	[1,27]
Leaves ( <i>Stachytarpheta cayennensis</i> )	Ipolamiide and verbascoside	Inhibition of leukocyte accumulation, neutrophil, and mononuclear cell influx	Gastric acid secretion and antiulcer activity	[3,48,66]
Leaves ( <i>Stachytarpheta cayennensis</i> )	Ipolamiide and verbascoside	-	Anti-inflammatory activity	[66]
Leaves ( <i>Stachytarpheta indica</i> )	Flavonoids and tannins	-	Hypoglycemic activity	[67]
Leaves ( <i>Stachytarpheta jamaicensis</i> )	Flavonoids, triterpenes, and sterols	Excision and dead space model	Wound healing activity	[56,57]
Whole plant ( <i>Stachytarpheta jamaicensis</i> )	Ipolamiide, acetoside	Inhibition of histamine, and bradykinin receptor	Antihistamine, other respiratory conditions	[8,30,33]
Whole plant ( <i>Stachytarpheta jamaicensis</i> )	-	-	Antimicrobial activity	[68]
Leaves ( <i>Stachytarpheta cayennensis</i> )	-	Delayed-type hypersensitivity response, humoral immune responses, and in the <i>in vivo</i> leukocyte immobilization tests	Immunomodulatory effects	[58]
Leaves ( <i>Stachytarpheta indica</i> )	-	CCl <sub>4</sub> -induced toxicity with standard drug Liv-52	Hepatoprotective activity	[52]
Leaves ( <i>Stachytarpheta cayennensis</i> )	-	GABAergic and opioid	Sedative and anxiolytic	[6]
Whole plant ( <i>Stachytarpheta mutabilis</i> )	-	-	Treatment of tumor	[30]

skin melanoma cancer. Silver nanoparticles of this species moderately inhibited the denaturation of egg albumin,

suggesting their anti-inflammatory and moderate pro-regenerative action.<sup>[69-73]</sup>



## CONCLUSION

The present piece of writing is a result of in-depth studies of the documented literature on the genus *Stachytarpheta*. It highlights the knowledge about botanical description that would be useful in identification, phytochemistry, and pharmacology acknowledging the traditional medicinal uses. Further, it also has been noted that the majority of the species remain unknown or scantily studied for the chemical composition and biological activities. The combined efforts of ethnobotanists, pharmacognosists, and pharmacologist could be a practical approach to evaluate and validate the usage of the species of the genus *Stachytarpheta* with the modern scientific methods and innovative techniques.

## REFEREWNCS

- Princely S, Basha NS, Kirubakaran JJ, Dhanaraju MD. Preliminary phytochemical screening and antimicrobial activity of aerial parts of *Stachytarpheta indica* L. (Vahl.). *Med Plants* 2013;5:96-101.
- Adedeji O. Palynology of the genus *Stachytarpheta* Vahl. (*Verbenaceae*). *Not Sci Biol* 2010;2:27-33.
- Vela SM, Souccar C, Lima-Landman MT, Lapa AJ. Inhibition of gastric acid secretion by the aqueous extract and purified extracts of *Stachytarpheta cayennensis*. *Planta Med* 1997;63:36-9.
- Idu M, Erhabor JO, Odia EA. Morphological and anatomical studies of the leaf and stem of some medicinal plants: *Stachytarpheta jamaicensis* (L.) Vahl. and *S. cayennensis* (L.C.Rich) Schau. *Ethnobot Leaflets* 2009;13:1417-25.
- Iroka FC, Okeke CU, Okereke CN. Taxonomic significance of alkaloids and phenols in the species of *Stachytarpheta* found in Awka, Nigeria. *J Glob Biosci* 2015;4:1961-5.
- Olayiwola G, Ukponmwan O, Olawode D. Sedative and anxiolytic effects of the extracts of the leaves of *Stachytarpheta cayennensis* in mice. *Afr J Tradit Complement Altern Med* 2013;10:568-79.
- Solanke DG, Oziegbe M, Azeez SO. Interspecific hybridization studies of three *Stachytarpheta* species from Nigeria. *Jordan J Biol Sci* 2019;12:435-40.
- Liew PM, Yong YK. *Stachytarpheta jamaicensis* (L.) Vahl: From traditional usage to pharmacological evidence. *Evid Based Complement Altern Med* 2016;16:1-7.
- Froelich S, Gupta MP, Siems K, Jenett-Siems K. Phenylethanoid glycosides from *Stachytarpheta cayennensis* (Rich.) Vahl, *Verbenaceae*, a traditional antimalarial medicinal plant. *Rev Bras Farmacogn* 2008;18:517-20.
- Chowdhury R, Rashid MU, Khan OF, Choudhury MH. Bioactivity of extractives from *Stachytarpheta urticaefolia*. *Pharm Biol* 2004;42:262-7.
- Chowdhury R, Rashid MU, Khan OF, Hasan CM. Ipolamiide and  $\alpha$ -spinasterol from *Stachytarpheta urticaefolia*. *Biochem Syst Ecol* 2003;31:1209-11.
- Akuodor GC, Essien AD, Udia PM, David-Oku E, Chilaka KC, Asika EC, *et al.* Analgesic, anti-inflammatory and antipyretic potential of the stem bark extract of *Stachytarpheta indica*. *Br J Pharmacol Toxicol* 2015;6:16-21.
- Okoye TC, Akah PA, Okoli CO, Ezike AC, Mbaaji FN. Antimicrobial and antispasmodic activity of leaf extract and fractions of *Stachytarpheta cayennensis*. *Asian Pac J Trop Med* 2010;3:189-92.
- Schapoval EE, Vargas MR, Chaves CG, Bridi R, Zuanazzi JA, Henriques AT. Antiinflammatory and antinociceptive activities of extracts and isolated compounds from *Stachytarpheta cayennensis*. *J Ethnopharmacol* 1998;60:53-9.
- Sreelatha R, Kasturi A, Kumar S, Challa M. *In vitro* antimicrobial activity of different parts of *stachytarpheta urticifolia* (Salisb) Sims. *Int J Pham Pharm Sci* 2013;6:340-3.
- Cardoso PH, Lima LV, Dittrich VA, Salimena FR. Typifications and additional taxonomic notes in Brazilian *Stachytarpheta* (*Verbenaceae*). *Phytotaxa* 2019;411:223-9.
- Chandler GT, Westaway JO, Conn BJ. Taxonomic uncertainty of *Stachytarpheta* (*Verbenaceae*) in the Asia-Pacific and implications for invasive weed recognition and management. *Telopea* 2014;16:83-8.
- Atkins S. The genus *Stachytarpheta* (*Verbenaceae*) in Brazil. *Kew Bull* 2005;60:161-272.
- Thangiah AS. Phytochemical screening and antimicrobial evaluation of ethanolic-aqua extract of *Stachytarpheta jamaicensis* (L.) vahl leaves against some selected human pathogenic bacteria. *Rasayan J Chem* 2019;12:300-7.
- Stachytarpheta jamaicensis* (L.) Vahl-The Plant List; 2021. Available from: <http://www.theplantlist.org/tpl1.1/record/kew-195911>. [Last accessed on 2021 May 27].
- Stachytarpheta jamaicensis* (L.) Vahl, Species, India Biodiversity Portal; 2021. Available from: <https://www.indiabiodiversity.org/species/show/33308>. [Last accessed on 2021 May 26].
- Stachytarpheta jamaicensis*-Wikipedia; 2020. Available from: [https://www.en.wikipedia.org/wiki/stachytarpheta\\_jamaicensis](https://www.en.wikipedia.org/wiki/stachytarpheta_jamaicensis). [Last accessed on 2021 May 26].
- Okoronkwo NE, Echeme JO. Isolation and characterisation of compound from *Stachytarpheta cayennensis* (Rich.) Vahl leaves. *Chem J* 2015;1:74-80.
- Joshi VG, Sutar PS, Karigar AA, Patil SA, Gopalakrishna B, Sureban RR. Screening of ethanolic extract of *Stachytarpheta indica* L. (Vahl) leaves for hepatoprotective activity. *Int J Res Ayurveda Pharm* 2010;1:174-9.
- Stachytarpheta indica*-Indian Snakeweed; 2021. Available from: <http://www.flowersofindia.net/catalog/slides/indiansnakeweed.html>. [Last accessed on 2021 May 26].

26. Plant Details for a *Stachytarpheta indica* (L.) Vahl; 2021. Available from: <http://www.envis.frlht.org/plantdetails/35d71e19166093f74f18f0df8d53c868/7c6a34fad6eea9aec562c6a4451c8909>. [Last accessed on 2021 May 25].
27. Musa AD, Ogbiko C, Dabai MU, Ali IJ, Yelwa AS, Buhari HB. *Stachytarpheta indica* leaf extract: Oral acute toxicity, *in vitro* phytochemical and antimicrobial potentials. *Earthline J Chem Sci* 2019;2:163-73.
28. National Parks, Flora and Fauna Web of *Stachytarpheta indica* (L.) Vahl; 2021. Available from: <https://www.nparks.gov.sg/florafaunaweb/flora/2/4/2475>. [Last accessed on 2021 May 24].
29. Osorio DV, González IR, Fermín LR, Silva BS, Arzola JC, Meza MA. Composición del aceite esencial y caracterización fisicoquímica de las hojas de *Stachytarpheta mutabilis* (Jacq.) Vahl. *Avances Quim* 2014;9:15-9.
30. Ingle SN. Diversity and useful products in some verbenaceous member of Melghat and Amravati regions, Maharashtra, India. *Biodiversitas* 2011;12:146-63.
31. *Stachytarpheta mutabilis*-Pink Snakeweed; 2021. Available from: [http://www.flowersofindia.net/catalog/slides/pink\\_snakeweed.html](http://www.flowersofindia.net/catalog/slides/pink_snakeweed.html). [Last accessed on 2021 May 23].
32. Plant Details-Information about *Stachytarpheta mutabilis* Plant. Available from: <http://www.efloraofgandhinagar.in/herb/stachytarpheta-mutabilis>. [Last accessed on 2021 May 23].
33. *Stachytarpheta urticifolia* (Salisb.) Sims-The Plant List; 2021. Available from: <http://www.theplantlist.org/tpl1.1/record/kew-196016>. [Last accessed on 2021 May 24].
34. *Stachytarpheta urticifolia* (Salisb.) Sims-The Plant List; 2021. Available from: <http://www.theplantlist.org/tpl/record/kew-196016>. [Last accessed on 2021 May 24].
35. Daniel P, Rajendran A. Lectotypification of *Stachytarpheta urticifolia* Sims (*Verbenaceae*). *Taxon* 1992;41:751.
36. Udodeme HO, Odoh UE, Ugwu PN, Diovu EO, Okonta EO, Onyekere PF, *et al.* Pharmacognostic studies of the leaves of *Stachytarpheta jamaicensis* Linn. (Vahl) (*Verbenaceae*). *Int J Pharmacogn Phytochem Res* 2016;8:1503-8.
37. Sideney BO, Francini YK, Shaiana PM. Antioxidant activity, total phenolic and flavonoids contents in *Stachytarpheta cayennensis*, (Rich.) Vahl. (*Verbenaceae*). *J Med Plants Res* 2015;9:569-75.
38. Yuvaraj R, Rao MR, Prabhu K, Sundram RL, Shil S, Kumar MS, *et al.* The gas chromatography-mass spectrometry study of one medicinal plant, *Stachytarpheta indica*. *Drug Invent Today* 2019;12:1665-9.
39. Melita RS, Castro O. Pharmacological and chemical evaluation of *Stachytarpheta jamaicensis* (*Verbenaceae*). *Rev Biol Trop* 1996;44:353-9.
40. Yuliana, Auwaliah F, Fatmawati S. 6 $\beta$ -hydroxyipolamiide of *Stachytarpheta jamaicensis* leaves. *J Technol Sci* 2019;30:68-72.
41. Okwu DE, Ohenhen ON. Isolation and characterization of steroidal glycosides from the leaves of *Stachytarpheta jamaicensis* Linn Vahl. *Chem Sin* 2010;1:6-14.
42. Okwu DE, Ohenhen ON. Isolation, characterization and antibacterial activity of lanostane triterpenoid from the leaves of *Stachytarpheta jamaicensis* Linn Vahl. *Pharma Chem* 2009;1:32-9.
43. Leitao GG, de Souza PA, Moraes AA, Brown L. Step-gradient CCC separation of phenylpropanoid and iridoid glycosides from roots of *Stachytarpheta cayennensis* (Rich.) Vahl. *J Liq Chromatogr Relat Technol* 2005;28:2053-60.
44. Roengsumran S, Sookkongwaree K, Jaiboon N, Chaichit N, Petsom A. Crystal structure of ipolamiide monohydrate from *Stachytarpheta indica*. *Anal Sci* 2002;18:1063-4.
45. Sreelatha R, Challa M, Kasturi A, Edavana SK, Sanivada SK. Phytochemical screening, total phenol content and antioxidant activity of different parts of *Stachytarpheta urticifolia* (Salisb) Sims. *JPR* 2013;1:718-23.
46. de Souza PA, Silva CG, Machado BR, de Lucas NC, Leitão GG, Eleutherio EC, *et al.* Evaluation of antimicrobial, antioxidant and phototoxic activities of extracts and isolated compounds from *Stachytarpheta cayennensis* (Rich.) Vahl, *Verbenaceae*. *Rev Bras Farmacogn* 2010;20:922-8.
47. Subbaiah SGP, Dakappa SS, Lakshmikan RY. Antibacterial and molecular docking studies of bioactive component from leaves of *Stachytarpheta cayennensis* (Rich.) Vahl. *Res J Phytochem* 2016;11:28-34.
48. Krishna Kumar HN, Preethi SD, Chandana E, Chauhan JB. Phytochemical screening and antibacterial activity of *Stachytarpheta indica*. *Int J Pharm Sci Res* 2012;3:1684-7.
49. Egharevba E, Chukwuemeke-Nwani P, Eboh U, Okoye E, Bolanle IO, Oseghale IO, *et al.* Evaluation of the antioxidant and hypoglycaemic potentials of the leaf extracts of *Stachytarphyta jamaicensis* (*Verbenaceae*). *Trop J Nat Prod Res* 2019;3:170-4.
50. Maisuthisakul P. Phenolic constituents and antioxidant properties of some Thai plants. In: Rao V, editor. *Phytochemicals-A Global Perspective of Their Role in Nutrition and Health*. Rijeka: Intech; 2012. p. 187-212.
51. Sahoo SR, Dash RR, Bhatnagar S. Phytochemical screening and bioevaluation of medicinal plant *Stachytarpheta indica* (L.) Vahl. *Pharmacol Toxicol Res* 2014;1:1-5.
52. Silambujanaki P, Chitra V, Soni D, Raju D, Sankari M. Hypoglycemic activity of *Stachytarpheta indica* on streptozotocin induced wistar strain rats. *Int J Pharmtech Res* 2009;1:1564-7.
53. Idu M, Omogbai EK, Amaechina F, Ataman JE. Some cardiovascular effects of the aqueous extract of the leaves of *Stachytarpheta jamaicensis* L. Vahl. *Int J Pharmacol* 2006;2:163-5.
54. Ogbiko C, Musa DA, Dabai MU, Ali IJ, Yelwa AS,

- Bature HB. Phytochemical, quantitative proximate and *in vitro* anti-inflammatory study of the crude methanol extract of *Stachytarpheta indica* leaves (*Verbenaceae*). *Earthline J Chem Sci* 2019;2:153-62.
55. Gayatri G, Babu JR, Sumalatha N, Venkateswarao J, Vidyadhara S. Hepatoprotective activity of ethanolic extract of *Stachytarpheta indica* on wistar rats. *Int J Compr Pharm* 2011;1:1-4.
  56. Pandian C, Srinivasan A, Pelapolu IC. Evaluation of wound healing activity of hydroalcoholic extract of leaves of *Stachytarpheta jamaicensis* in streptozotocin induced diabetic rats. *Pharm Lett* 2013;5:193-200.
  57. Caluya ED. Wound healing potential of the crude leaf extract of *Stachytarpheta jamaicensis* Linn. Vahl (Kandikandilaan) on induced wounds in rats. *J Med Plants Stud* 2017;5:375-81.
  58. Okoye TC, Akah PA, Ezike AC, Uzor PF, Odoh UE, Igboeme SO, *et al.* Immunomodulatory effects of *Stachytarpheta cayennensis* leaf extract and its synergistic effect with artesunate. *BMC Complement Altern Med* 2014;14:376.
  59. Okokon JE, Ettebong E, Antia BS. *In vivo* antimalarial activity of ethanolic leaf extract of *Stachytarpheta cayennensis*. *Indian J Pharmacol* 2008;40:111-3.
  60. Mesia-Vela S, Souccar C, Lima-Landman MTR, Lapa AJ. Pharmacological study of *Stachytarpheta cayennensis* Vahl in rodents. *Phytomedicine* 2004;11:616-24.
  61. Khummueng W, Rakhman SA, Utaipan T, Pakhathirathien C, Boonyanuphong P, Chunglok W. Phytochemicals, antioxidant and cytotoxicity of *Stachytarpheta jamaicensis* (L.) Vahl extracts. *Asian J Sci Technol Rep* 2020;23:45-54.
  62. Widiyastuti Y, Sholikhah IY, Haryanti S. Cytotoxic activities of ethanolic and dichloromethane extract of leaves, stems, and flowers of Jarong [*Stachytarpheta jamaicensis* (L.) Vahl.] on HeLa and T47D cancer cell line. *AIP Conf Proc* 2019;2202:020101.
  63. Ikewuchi CJ, Ikewuchi CC. Alteration of plasma lipid profiles and atherogenic indices by *Stachytarpheta jamaicensis* L. (Vahl). *Biochemistry* 2009;21:71-7.
  64. Meng ZQ, Wu JR, Zhu YL, Zhou W, Fu CG, Liu XK, *et al.* Revealing the common mechanisms of scutellarin in angina pectoris and ischemic stroke treatment via a network pharmacology approach. *Chin J Integr Med* 2020;27:62-9.
  65. Aba PE, Asuzu IU. Mechanisms of actions of some bioactive anti-diabetic principles from phytochemicals of medicinal plants: A review. *Indian J Nat Prod Resour* 2018;9:85-96.
  66. Penido C, Costa KA, Futuro DO, Paiva SR, Kaplan MA, Figueiredo MR, *et al.* Anti-inflammatory and anti-ulcerogenic properties of *Stachytarpheta cayennensis* (L.C. Rich) Vahl. *J Ethnopharmacol* 2006;104:225-33.
  67. Kasali FM, Wendo FM, Muyisa SK, Kadima JN. Comparative hypoglycemic activity of flavonoids and tannins fractions of *Stachytarpheta indica* (L.) Vahl leaves extracts in guinea-pigs and rabbits. *Int J Pharm Pharm Res* 2016;5:48-57.
  68. Rampratap M, Pitchai R. Evaluation of antimicrobial activity and preliminary phytochemical studies on whole plant of *Stachytarpheta jamaicensis* (L.) Vahl. *Int Res J Pharm* 2011;2:234-9.
  69. Khan MM, Harunsani MH, Tan AL, Hojamberdiev M, Poi YA, Ahmad N. Antibacterial studies of ZnO and Cu-Doped ZnO nanoparticles synthesized using aqueous leaf extract of *Stachytarpheta jamaicensis*. *Bionanoscience* 2020;10:1037-48.
  70. Jenin GA, Sajitha SS, Muthumariappan S, Metilda SP. SEM/EDAX and antimicrobial analysis of *Stachytarpheta jamaicensis* in silver nano particles. *Compliance Eng J* 2019;10:1-8.
  71. Chitra G, Selvi MS, Franklin DS, Sudarsan S, Sakthivel M, Guhanathan S. pH-sensitive biopolymeric hydrogel-based on indole-3-acetic acid for wound healing and anti-cancer applications. *SN Appl Sci* 2019;1:1641.
  72. Seshadri VD. Amalgamation and Characterization of Copper Nanoparticles Alleviated with *Stachytarpheta cayennensis* and its Anti-Cancer Activity in Both *In vitro* and *In vivo* Animal Model. Version: 1. Research Square; 2021. Available from: <https://www.researchsquare.com/article/rs-161215/v1>. [Last accessed on 2021 Feb 03].
  73. Meva FE, Mbeng JO, Ebongue CO, Schlüsener C, K  k  am-Demir   , Ntumba AA, *et al.* *Stachytarpheta cayennensis* aqueous extract, a new bioreactor towards silver nanoparticles for biomedical applications. *J Biomater Nanobiotechnol* 2019;10:102-19.

**Source of Support:** Nil. **Conflicts of Interest:** None declared.