Review Paper:

A Comprehensive Review of Phytochemical Findings, Therapeutic Potential and Toxicological Studies of *Stachytarpheta jamaicensis*

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Abstract

Stachytarpheta jamaicensis (L.) Vahl, one of the hidden assets among traditional medicine, is well-known among native people and is being used for decades but its medicinal values are unrecognised and underutilized. The plant is distributed across the tropical Asia, North and South America, Africa, Madagascar, Indonesia, Brazil and other tropical and subtropical regions. The aim is to identify and list out phytoconstituents, therapeutic properties and toxicological findings of Stachytarpheta jamaicensis reported so far.

Anti-oxidant, anti-diabetic, anti-microbial, anti-inflammatory, anti-nociceptive, wound healing, hypotensive, parasiticidal, anti-dyslipidemic and anti-diarrheal properties of Stachytarpheta jamaicensis have been reported. The extracts of Stachytarpheta jamaicensis do not affect biological profile indicating absence of toxicity of the extracts and compounds obtained from Stachytarpheta jamaicensis. Several compounds including flavonoids, Iridoid glucosides, Lanostane triterpenoids, Sterol glycosides and coumarins were reported. The present review summarises the compounds identified along with chemical and pharmaceutical importance of Stachytarpheta jamaicensis (L.) Vahl.

Keywords: *Stachytarpheta jamaicensis* extract, Phytochemicals, Therapeutical properties, Anti-oxidant activity, Anti-microbial activity, Anti-inflammatory.

Introduction

Medicinal plants have compounds which can be used for therapeutic purposes or developing drugs with therapeutic potential. Natural medicines play a pivotal role in people's health needs all over the world, undeniable from the past and will continue to grow important in future as well[53,62]. World Health Organization (WHO)[78] summarizes traditional medicine as "The sum total of the knowledge, skill and practices based on the theories, beliefs and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness".

From the beginning of human history, many drugs have been found through the use of traditional medicine. In India, people from all sectors have been utilizing medicinal plants for a long time through conventional medicinal practices or distinct native medicinal practices or pharmaceutical preparations[11]. Studies are still being conducted on the potential of natural medications such as pepper, ginger, neem and turmeric to treat a variety of severe illnesses including more recent ones like the Covid-19[48].

More than 100 species constitute the genus *Stachytarpheta* under the family Verbenaceae, which were distributed across the tropical regions of Australia, America and Asia. The Greek words *spike* (stachy) and *thick* (tarpheta) are the source of the genus name. It can be identified by tiny, vivid purple to pale rose blossoms arranged in dense, eye-catching inflorescences. Several species including *Stachytarpheta jamaicensis*, *Stachytarpheta cayennensis, Stachytarpheta indica, Stachytarpheta urticifolia* and *Stachytarpheta mutabilis*, were successfully utilized for a long time in traditional medicine. Various ailments such as inflammations, asthma, fever, renal disorders, atherosclerosis, skin lesions and infections affecting reproductive system were treated with them. *Stachytarpheta jamaicensis (L.)* Vahl (Figure 1), known as Seemai naayuruvi in Tamil, is one among them[11,58].

Botanical description of *Stachytarpheta jamaicensis*: The taxonomical classification of *Stachytarpheta jamaicensis* is summarised in table 1.

Plant morphology

Stem: The stalk is woody around the base and delicate on the top.

Leaves: The leaves are arranged alternatively, glabrous on both sides, curved with sharp tip and short leafstalks.

Inflorescence: The inflorescence consists of flowers arranged in thin spikes on a long, inflated rachis which ranges between 30 - 40 cm.

Flowers: The flowers have a white corolla tube and a bluish colour ranging from deep blue to reddish purple. Its lobes are roughly 3 mm long and its tubular corolla is around 10 mm long. The flowers reside in the inflorescence's axis and are arranged along it.

Table 1
Taxonomical classification of *Stachytarpheta jamaicensis*

Domain	Eukaryota
Kingdom	Plantae
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Dicotyledonae
Order	Lamiales
Family	Verbenaceae
Genus	*Stachytarpheta*
Species	*Stachytarpheta jamaicensis*

Dispersal: *S. jamaicensis* is a perennial herbaceous plant that grows around 60-120 cm and spreads by seeds.

Geographical range:
Distribution: *S. jamaicensis* can be found across Central America, the Caribbean, the Pacific Islands, parts of Africa and parts of East and Southeast Asia.

Habitat: It is commonly grown in grasslands, fields, young forest and watersides.

Other names: Gervao, Brazilian tea, Bastard vervain, Jamaica vervain, Verbena cimarrona and Blue porter weed.

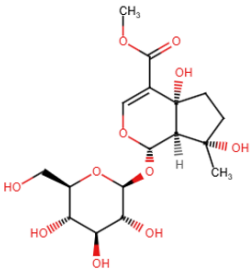
In both traditional and folk medicinal practices, *S. jamaicensis* plays a significant role with its great medicinal properties[5,36,50,58,60,61]. *Stachytarpheta Jamaicensis* is used as remedy in folk medicine since immemorial. In this study, phytochemical studies, therapeutical properties and toxicological studies of this Indian traditional medicine have been discussed.

Figure 1: *Stachytarpheta jamaicensis (L.)* Vahl

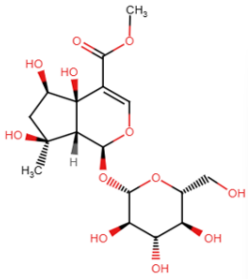
Phytochemical studies: The various phytochemical investigation of *S. jamaicensis* revealed the presence of numerous compounds. The aqueous, alcoholic, ethyl acetate, petroleum ether and chloroform extracts of leaves, root, stem, aerial parts and whole plant had been studied.

Table 2
Phytochemicals reported from *Stachytarpheta jamaicensis*

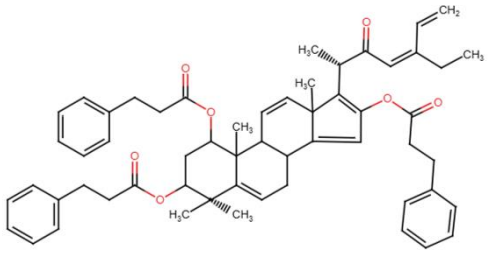
Name of the compound	**Nature of the compound**
Ipolamiide (Tarphetalin)	Iridoid glucoside[10,28,36,80]
6β-Hydroxyipolamiide	
1,3,16β-yl-phenypropylacetate-lanostan-5,11,14,16,23,25- hexen-22-one	Lanostane triterpenoid[43]
16 β- (β-D glucopyranosyl, 3, 8, 22–trihydroxy) Cholestan–1 β-yl–6–O-(3, 4, 5 –trimethoxybenzoyl) β-D, glucopyranoside	Sterol glycoside[42]
16-β (β-D–glucopyranosyl 3,8,22-trihydroxy-cholest-5,14,16,23 tetraiene 1β-yl, 6-O-(3,4,5-trimethoxybenzonyl) β-D glucopyranoside	
Apigenin	Flavonoid[9,14,16,21,41,47]
Hispidulin	
Scutellarein	
Luteolin	
Vitexin	
Isovitexin	
Apigenin 7,4'-dimethyl ether	
5,7,2'-Trimethoxy flavone	
Chlorogenic acid	Phenolic acid[21,36,37]
Luteolin 7-glucuronide	
6-Hydroxyluteolin 7-glucuronide	
Apigenin 7-glucuronide	
α-Spinasterol	Phytosterol[36]
Verbascoside	Phenylpropanoid glycoside[36]
Ursolic acid	Pentacyclic terpenoid[9,16]
Friedelin	
Luvangetin	Coumarin[73]
Xanthyletin	



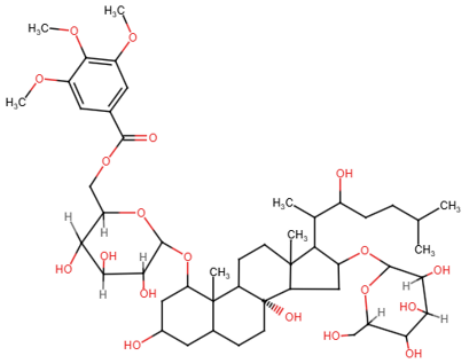
Ipolamiide (Tarphetalin)(1)



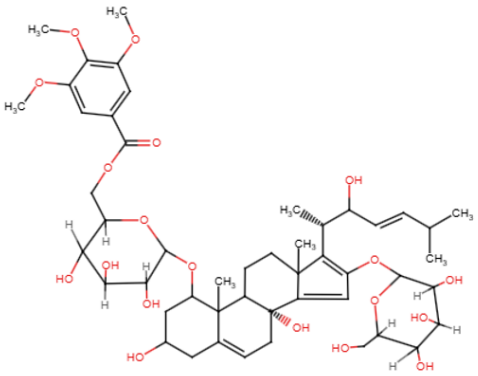
6β-Hydroxyipolamiide (2)



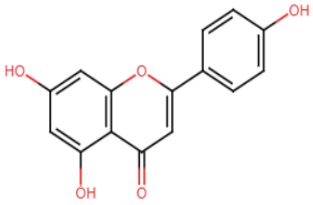
1,3,16β-yl-phenypropylacetate-lanostan-5,11,14,16,23,25- hexen-22-one (3)



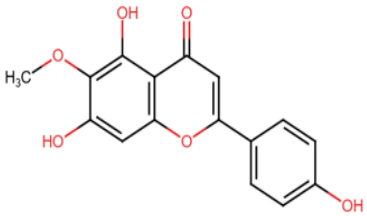
16 β- (β-D glucopyranosyl, 3, 8, 22–trihydroxy) Cholestan–1 β-yl–6–O-(3, 4, 5 –trimethoxybenzoyl) β-D, glucopyranoside (4)



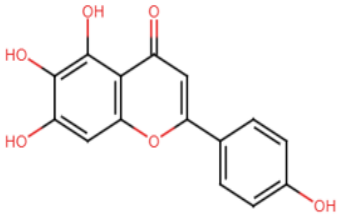
16-β (β-D–glucopyranosyl 3,8,22-trihydroxy-cholest-5,14,16,23 tetraiene 1β-yl, 6-O-(3,4,5-trimethoxybenzonyl) β-D glucopyranoside (5)



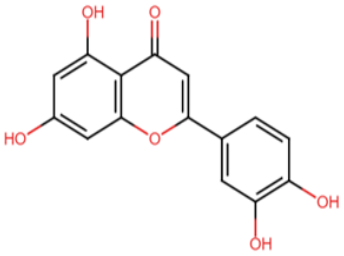
Apigenin (6)



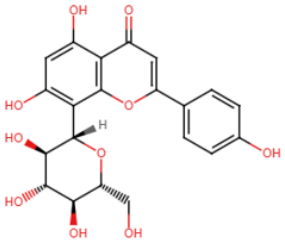
Hispidulin (7)



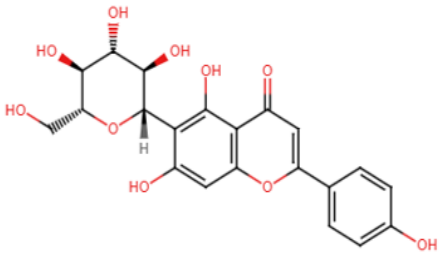
Scutellarein (8)



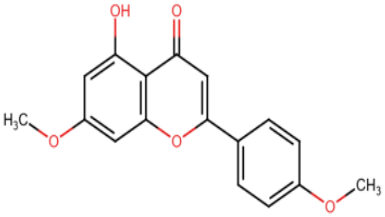
Luteolin (9)



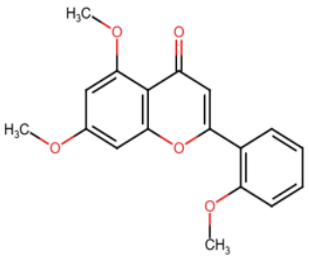
Vixetin (10)



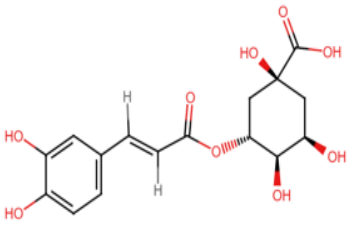
Isovixetin (11)



Apigenin 7,4'-dimethyl ether (12)



5,7,2'-Trimethoxy flavone (13)



Chlorogenic acid (14)

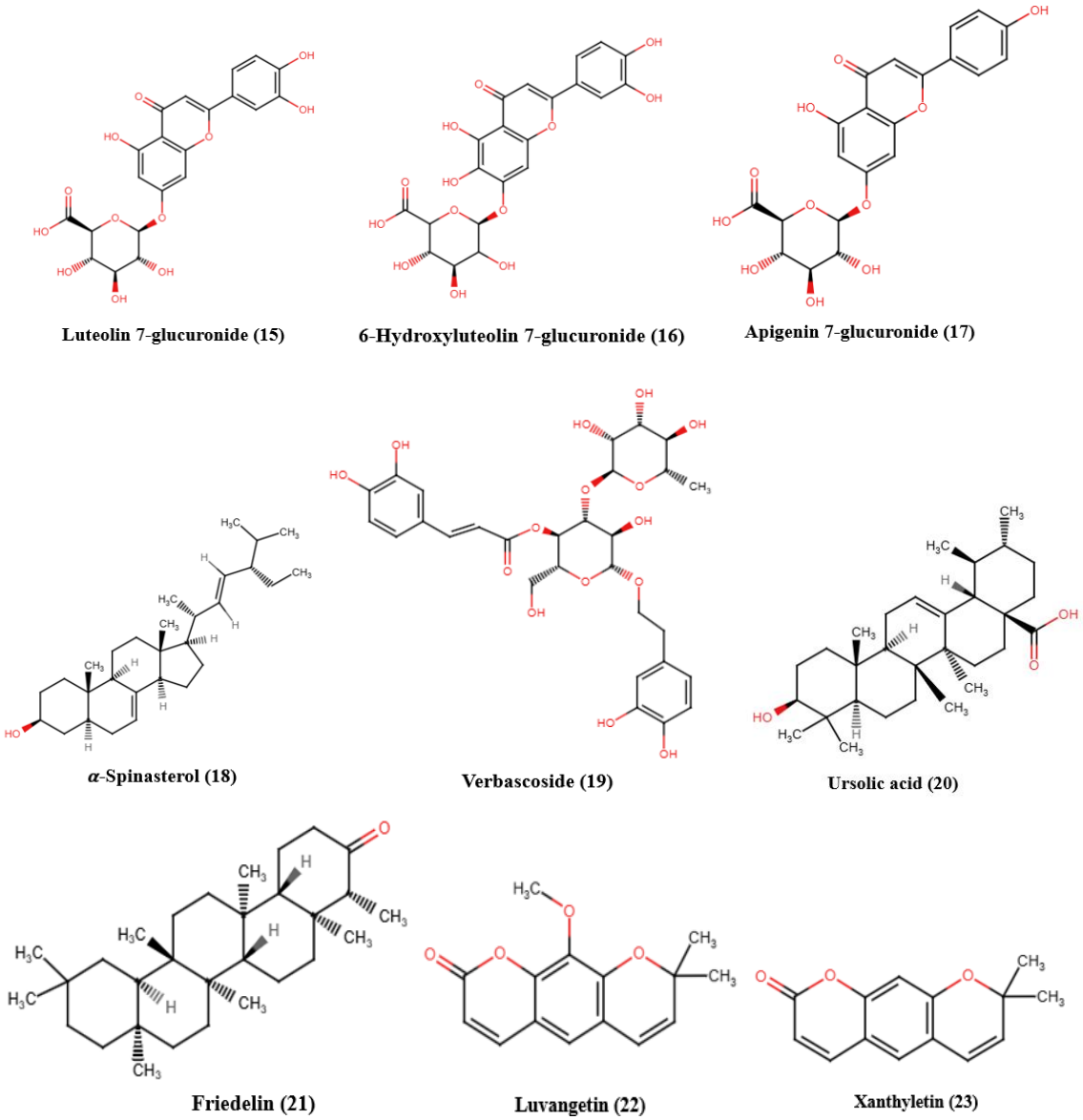


Figure 2: Structures of compounds reported from *Stachytarpheta jamaicensis*

Compounds such as alkaloids, carbohydrates, flavonoids, glycosides, phytosterols, phenolic compounds, saponins, steroids, tannins and terpenoids were reported[5,22,24,31,33,50,58,60,67]. *S. jamaicensis* possesses numerous bioactive compounds. Some of the listed compounds have been isolated and their structures are listed in table 2 and figure 2.

Therapeutical properties

Anti-oxidant activity: Reactive oxygen species (ROS) are produced often while utilizing oxygen in essential cell metabolism. ROS were generated during normal body functions including respiration and cell enabled immune functions. Free radicals including superoxide anion radicals ($O_2^{\bullet-}$), hydroxyl radicals ($OH^{\bullet}$) and non-free radical species such as hydrogen peroxide (H_2O_2) and singlet oxygen ($^1O_2$) were classified as ROS. Vitamins A, C and E, carotenoids, polyphenolic compounds and flavonoids are grouped together as anti-oxidants. Vegetables and fruits remain as primary resource of these compounds and they avert the alterations caused by ROS lowering the chance of chronic disorders[1,4,36,46].

Antioxidant activity of essential oils derived from *S. jamaicensis* leaves was studied by Onyedikachi et al[46] suggesting that at 400 µg/mL, the essential oil displayed highest 2,2-diphenyl-1-picrylhydrazyl (DPPH) inhibition and FRAP (Ferric Reducing Antioxidant Power) activities. Kalaâ et al[29] indicated that 96% of the *S. jamaicensis* leaves contain secondary metabolite chemicals including alkaloids, flavonoids, triterpenoids, tannins and saponins, when extracted using ethanol. There are tannins and steroid secondary metabolite chemicals in the ethyl acetate extract. The n-hexane extract contains tannins, saponins and steroid metabolite chemicals. The n-hexane extract, ethyl acetate extract and ethanol extracts possess antioxidant activity and the best of the three is ethyl acetate extract. From the calculations, the extracts' IC_{50} values for n-hexane, ethyl acetate and ethanol extracts were 19.76 µg/mL, 12.91 µg/mL and 16.66 µg/mL.

DPPH free radical absorption test was carried out using the n-hexane, ethyl acetate and methanol extracts of *S. jamaicensis* leaves prepared at different concentrations and vitamin C was used as positive control by Kumala et al[34]. Findings of the antioxidant activity test revealed that in comparison to other extracts, methanol extract exhibited the highest active IC_{50} value. The IC_{50} concentrations of the n-hexane, ethyl acetate and methanol extracts were found to be 667.46 µg/mL, 182.97 µg/mL and 14.28 µg/mL correspondingly.

Inhibitory effect of ethyl acetate extract of *S. jamaicensis* against ROS was documented by Álvarez et al[2]. At a concentration of 40 µg/mL, the extract was found to suppress ROS production in rat peritoneal-exudate macrophages by two mechanisms: inhibition of xanthine oxidase (XO), which is essential for ROS generation in most cells and scavenging of already formed reactive oxygen species (ROS). Ololade et al[44] reported that at different doses between 10-750 µg/mL, the methanolic extract's percentage inhibitions ranged from 51.30 to 78.99. Compared to the reference and similar species, the leaf extract of *S. jamaicensis* studied in this study demonstrated greater antioxidant levels.

Fatmawati et al[18] isolated the compound 6β-hydroxyipolamiide from the methanol extract of *S. jamaicensis* leaves. In addition, DPPH, 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and α-glucosidase enzyme activity studies were carried out to find that inhibition was better by the methanolic extract of *S. jamaicensis* leaves in comparison with other solvent extracts and the chemical 6β-hydroxyipolamiide.

Monton et al[39] testified that 95% ethanolic extract of twigs and 50% ethanol extract of leaves of *S. jamaicensis* have shown the highest antioxidant activity for DPPH radical scavenging assay and FRAP assay correspondingly[38]. Kavitha et al[31] demonstrated that several phytochemical substances that function as the body's free radical scavengers, may be responsible for the antioxidant capacity of the aqueous extract of *S. jamaicensis* aerial portion and it aids in shielding the body from the destructive effects of free radicals. With an IC_{50} value of 172.87 µg/mL, they discovered that the free radical scavenging activity rose with increasing dosages of DPPH radical scavenging activity using an aqueous extract of the aerial portion of *S. jamaicensis*.

Similarly, IC_{50} value of 178.58 µg/mL and 232.79 µg/mL was observed for hydroxyl radical scavenging activity and superoxide radical scavenging activity. Based on all findings, it was concluded that *S. jamaicensis* is a reliable source of naturally occurring antioxidants[28]. Khummueng et al[33] observed antioxidant activity and large levels of antioxidant compounds in the *S. jamaicensis* methanol extract than hexane, dichloromethane and water extracts of aerial parts.

Hypoglycemic Activity: According to the WHO[75], "Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves". The most prevalent kind, type 2 diabetes, usually affects adults and is brought on by insufficient or resistant insulin production in the body. Type 2 diabetes has been more common over the last three decades in all nations, regardless of wealth. Diabetes type 1 is a chronic illness in which the pancreas generates little or no insulin on its own. It was formerly referred to as juvenile diabetes or insulin-dependent diabetes. The disease is directly responsible for 1.5 million fatalities annually. Over the past few decades, there has been a steady rise in both the number of cases and the incidence of diabetes.

Fatmawati et al[18] reported that, rather than the dichloromethane, ethyl acetate and methanolic extract of *S. jamaicensis* leaves, the chemical 6β-hydroxyipolamiide obtained from it suppressed the activity of the α-glucosidase enzyme. Egharevba et al[13] investigation on leaf extract of *S. jamaicensis* showed potential as an antioxidant and hypoglycemic agent with streptozotocin-induced diabetic rats. The study found that ethyl acetate leaf extracts at 200 mg/kg decreased the blood glucose levels at the 1st hour, increased at the 4th hour and then decreased up to the 7th day. At 400 mg/kg, it showed significant hypoglycemic activity from the 1st hour to the 7th day. Methanol leaf extracts at 200 mg/kg considerably reduced the blood glucose levels in diabetic rats at the 1st hour, with an increase at the 4th hour, followed by a gradual decrease up to the 7th day. At 400 mg/kg, the extract showed significant hypoglycemic activity from the 1st hour to the 7th day.

According to this study by Rozianoor et al[55], the ethanol extract of *S. jamaicensis* leaves exhibited promising antioxidant and hypoglycemic activities on alloxan-induced diabetic Sprague-Dawley rats. Male diabetic rats' blood glucose levels were lowered to 6.7 mmol/L and their catalase activity was raised to 0.027 µmol/min/mg protein. Based on GC-MS analysis, these properties can be attributed to bioactive substances such as genipin and linolenic acid.

Ursolic acid, a triterpenoid from Leaves of *S. jamaicensis* isolated by Odoh et al[40,41] was examined for anti-diabetic activity on alloxan-induced diabetic rats and it lowered the blood glucose levels in rats that had diabetes. The blood glucose levels dropped significantly when compared to diabetic control mice (p 0.05) after just 14 days of ursolic acid treatment, which is comparable to the effects of glibenclamide, the positive control. Also, a significant anti-inflammatory effect was observed. In another study, they isolated apigenin from leaves of *S. jamaicensis* showing positive hypoglycemic activity on alloxan-induced diabetic rats. As per the findings, there was a variance in the effect of the 25 mg/kg and 50 mg/kg dosages of apigenin at 1 and 3 hours after administration and a noteworthy ($p > 0.05$) decrease in blood glucose levels at both administered doses.

Anti-microbial activity: Aromatic compounds are primarily synthesized by plants. Majority of these compounds are phenols as well as their oxygen-substituted derivatives. These compounds frequently act as barriers for plants protecting them from herbivores, insects and microbes. The scent and pigment of the plants are the result of compounds like terpenoids, quinones and tannins in them[8]. The development of antibiotic resistance in microorganisms arises from genetic modifications within them and other organisms. Such challenges have led to the search for options emerging out of ethnobotanical origins[36].

Anti-bacterial activity: According to the investigation by Sasidharan et al[57] by the disk diffusion method, three pathogenic bacterial strains that cause dysentery and diarrhea were susceptible to the antibacterial activity of the methanol extract of *S. jamaicensis* leaves. It was stated that the extract had an effect even at very low concentration with an MIC value of 5.00 mg/ml on the strains of *E. Coli, P. aeruginosa* and *S. epidermidis*. Phytochemical examination findings by Idu et al[23] indicate the existence of certain secondary metabolites, indicating the *S. jamaicensis* therapeutic significance. Their studies using both aqueous extract and alcoholic extract have shown anti-bacterial results against *B. subtillis, E. coli, C. albicans, S. aureus, P. aureginosa, P. vulgaris, K. arogenes* and *P. mirabilis.*

The alcoholic extract exhibited antimicrobial activity against *B. subtilis, E. coli, C. albicans, P. aeruginosa and P. mirabilis*, with a minimum inhibitory concentration (MIC) of 0.25 g/mL for *E. coli* and 0.5 g/mL for *P. aeruginosa*[12]. Thangiah et al[67] reported that *B. cereus, S. typhi, P. vulgaris* and *S. pyogenes* were all able to sustain harm from the ethanolic aqua leaf extract of *S. jamaicensis*.

Ruma et al[56] investigated the antibacterial effect of *S. jamaicensis* leaf ethanolic extract on *S. aureus* using the disc diffusion method, observing dose-dependent inhibition zones ranging from 5 to 26 mm. When compared to the standard, the discs impregnated with a concentration of 10 mg/mL produced the largest zone of inhibition deemed to be active. One significant factor influencing the prevalence of oral disorders is microorganisms. The tissues in the mouth will become inflamed and aggressive when pathogenic bacteria are present.

Ethanolic extract of leaves of *S. jamaicensis* was tested for the antibacterial activity against three bacterial colonies causing oral infections such as *Actinomyces sp, E. faecalis* and *A. actinomycetemcomitans* by Utami et al[72]. At concentrations of 2000, 8000 and 8000 µg/mL, the extract inhibited the growth of *A. actinomycetemcomitans, E. faecalis and Actinomyces spp*. respectively, showing statistically significant differences ($p = 0.0001$; $p < 0.05$).

M. smegmatis rarely causes infections, but when it does, it can easily be harmful to immunocompromised individuals. Ramadhani et al[49] concluded that with an MIC of 5000 µg/mL (extremely weak activity), *S. jamaicensis* ethanolic leaf extract might suppress the development of *M. smegmatis*. However, even at the maximum concentration of 10000 µg/mL, the M. smegmatis could not be killed.

Studies by Ololade et al[44] stated that the *S. jamaicensis* methanolic leaf extract's antibacterial screening produced a broad range of zones of inhibition. When compared to a synthetic antibiotic (gentamicin), the *S. jamaicensis* leaf extract's zones of inhibition showed strong bactericidal activity ranging from sensitive to ultra-sensitive. The anti-bacterial activity was effectively reported against *E. faecalis, M. varians, S. agalactiae, S. aureus*, *E. coli, K. pneumoniae, P. mirabilis, P. aeruginosa, S. marcescens* and *S. typhimurium*[44]. Okwu et al[42,43] isolated a lanostane triterpenoid from the leaves of *S. jamaicensis* and reported the antibacterial activity against *S. fecalis, S. aureus, E. coli* and *P. aeruginosa* which was performed by a filter paper disc diffusion method.

Anti-fungal activity: Thomas et al[69] investigation of the Verbenaceae family confirmed *S. jamaicensis* leaves possessing anti-fungal activity. The petroleum ether extract of *S. jamaicensis* showed efficacy against mainly *Penicillium sp.* (12.11+0.88) and *Curvularia sp.* (13.71+0.71). However, methanolic extract exhibited prone to *Penicillium sp.* (13.09+1.04), *Fusarium sp.* (13.01+0.08) and *Curvularia sp.* (18.70+1.08)[69]. Studies by Kusuma et al[35] suggest that *S. jamaicensis* extract of whole plant possessed anticandidal activity against *C. albicans*. The n-hexane, ethyl acetate and ethanol were tested against *C. albicans* using agar well disc diffusion method. Among them, the ethyl acetate and n-hexane extracts have shown highest activity in concentrations 400 µg/well with inhibition zone of 14 mm and 15 mm accordingly[35]. Phenolic extract of *S. jamaicensis* leaves hinders the activity of certain fungal species such as *Aspergillus niger, Aspergillus flavus* and *Mucor Sp,* as testified by Suneetha et al[65]. The phenolic extract showed greater susceptibility to *Mucor* compared to the other two fungal strains.

Anti-inflammatory activity and Antinociception: Inflammation refers to a biological response triggered by injury or infection, resulting in symptoms such as redness, increased temperature, swelling, pain and reduced function. An essential bodily defensive mechanism, inflammation drives out germs and foreign objects while shielding the host from additional harm. On the other hand, if the damaging inflammation is not addressed, it will eventually become the cause of several illnesses like sepsis, atherosclerosis and cancer formation[36]. The inhibition of nociceptive (pain) neurons' ability to perceive a painful input is known as antinociception[13].

In every nociceptive modelling studied by Sulaiman et al[64], the 80% ethanolic extract of *S. jamaicensis* demonstrated noteworthy ($p< 0.05$) antinociceptive action, with concentration-dependent effect utilizing the formalin and

belly writhing tests. The antinociceptive activity of the extract, assessed by abdominal writhing and formalin-induced paw-licking tests, was partially but significantly ($p < 0.05$) reversed by naloxone pretreatment and when the hot-plate test was employed, its activity was entirely inhibited. The extract demonstrated significant ($p < 0.05$) anti-inflammatory activity in both chronic and acute inflammation models, as shown by the cotton-pellet granuloma and carrageenan-induced paw edema tests.

Wound healing agent: An important physiological process, cutaneous wound healing involves the cooperation of numerous cell types and their byproducts. The body begins repairing lesions caused by localized injury early in the inflammatory stage. This process ultimately results in regeneration, cell proliferation and subsequent differentiation involving stem cells and existing tissue cells and repair, which involves replacing specialized structures through collagen deposition[20].

Based on the research findings by Ratulangi et al[52], it can be presumed that the ethanol extract of *S. jamaicensis* is useful for mending wounds in the *Mus musculus*. Based on the average percentage of healing from the first to the seventh day, it was observed that in many treatments, the concentration of *S. jamaicensis* extract with a concentration of 75% had a faster ability to cure wounds than *S. jamaicensis* extract with a concentration of 50% and 25%. This is due to the fact that 75% concentration of *S. jamaicensis* has more active ingredients than 25% and 50% concentrations[52].

In a study by Chitra et al[7], the aqua-alcoholic extract of *S. jamaicensis* leaves was tested for wound healing potential in streptozotocin-induced diabetic rats. When compared to untreated animals, animals treated with extract demonstrated a dose-dependent significant decrease in blood glucose levels and a simultaneous significant increase in hydroxyproline, hexosamine, DNA, total protein content and percentage wound closure. In diabetic rats, the extract significantly aided in wound healing; this may have been because it included phytochemical elements such as sterols, triterpenes and flavonoids[7]. Caluya[6] studies specified that the *S. jamaicensis* leaves' hydroethanolic extract has positive effects and is important for wound healing. When *S. jamaicensis* extract is applied externally, albino rats' wounds heal more quickly. Phytoconstituents with antibacterial, antioxidant and antimicrobial properties, like tannins, flavonoids, saponin, terpenoids, glycosides and phenols, may have contributed to the healing of wounds. The outcome demonstrated that the *S. jamaicensis* leaf crude extract could be useful for treating wounds, as demonstrated by the development of scabs, improved wound shrinkage and faster wound closure as indicators of wound healing.

Anti-hypertensive activity: As stated by WHO, blood vessel pressure that is too high, is known as hypertension, or high blood pressure. Though common, untreated high blood pressure can pose serious risks. Many individuals with hypertension remain asymptomatic, making regular blood pressure checks essential for diagnosis. It may be the result of old age or inheritance. People having high-salt diet, physically inactive, using tobacco, consuming alcohol and obese are highly prone to hypertension[77].

Kamyab et al[30] have reported many traditional medicinal plants which potentially act against hypertensive activity. Aqueous extract of *S. jamaicensis* possessing hypotensive effects was documented by Idu et al[23-25]. The response of heart rate and blood pressure seems to be correlated with the dosage in anaesthetized normotensive male rabbits. As there was a dose-dependent reduced cardiac rhythm, it is concluded that the extract's hypotensive action must have resulted from either an effect on the heart or from a direct effect on vascular smooth muscle that has not yet been identified, or from a combination of both[25].

According to the study by Ikewuchi et al[26,27] aqueous infusion (tea) made from *S. jamaicensis* has hypotensive properties. It has the ability to control hypertension by functioning as a potassium-sparing diuretic since it lowers plasma sodium and raises plasma potassium levels. This is due to its suppression of aldosterone or Na^+/K^+ exchange processes in the distal tubules. The aqueous infusion (tea) may be useful in treating abnormal sodium and potassium metabolism in hypertension, as suggested by its hyponatremic and potassium-sparing properties.

Parasiticidal activity: Ayurvedic medicine uses thousands of therapeutic herbs, many of which are recognized to have antiparasitic potential. Based on cultural utilization, it has led to captivating research in isolating anti-parasitic drugs from these plants[51]. *Paramphistomum sp* belongs to the Paramphistomidae trematodes, also referred to as rumen flukes. It is one of the primary parasitic worms that cause illness in cattle and other ruminants and cause significant financial losses to the global livestock sector. In its early stages, paragonimiasis may not show any symptoms. Serious symptoms such as fever, dyspnea, chest pain and a prolonged cough with blood-stained sputum can arise when worms enter the lungs as stated by World Health Organization.

Paragonimiasis is the most common kind and ectopic paragonimiasis is less common. Recent investigation by Umami et al[71] evidenced the anti-trematode activity of aqueous extract *S. jamaicensis*. Kruskal-Wallis and Mann-Whitney tests were carried out by them to determine if the concentration affects the time of death of the worm. The concentration of extract has an effect on dose-dependent manner in the fluke's death time and was faster at 10% concentration.

They concluded that this activity may be the result of secondary metabolites in *S. jamaicensis* which include alkaloids, flavonoids, triterpenoids, steroids and tannins[71,76]. According to *in vitro* study by Robinson et al[54], 90% of the

nematode worm *Strongyloides stercoralis* can be made inactive after 42 hours by a 10% hydroalcoholic extract of *S. jamaicensis* leaves.

Research by Udo et al[70] has demonstrated methanolic leaf extract of *S. jamaicensis* showing a suppressing effect in mice infected by *T. brucei*. All extract-treated groups of infected mice had a constant decline in their packed cell volume values. However, this value exceeded that of the infected group significantly ($p < 0.05$) that received no treatment evidencing anti-trypanosomal activity.

Aqueous infusion (tea) made from the leaves of *S. jamaicensis* has shown anthelmintic activity against *Fasciola sp.* as reported by Fahlevi et al[17]. The occurrence of saponins, tannins, alkaloids, flavonoids and triterpenoids contributes to the plants anti-parasitic activity against worms of the Trematoda class. Mann-Whitney test reveals that in comparison to the negative control, all tea concentrations (2.5%, 5%, 10%) significantly increased the number of Fasciola fluke deaths ($p<0.05$).

Anti-dyslipidemic activity: Cardiovascular complications rank among the leading causes of death. Dyslipidemia is a key risk factor in the development of cardiovascular disease and is closely associated with obesity, diabetes mellitus and hypertension[26,73,79]. Ikewuchi's studies demonstrated that an aqueous infusion (herbal tea) prepared from *S. jamaicensis* influenced the plasma lipid profile and atherogenic indices in rabbits. The results showed reduced levels of total cholesterol, low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL) and triglycerides, along with an increase in high-density lipoprotein (HDL) cholesterol, suggesting potential anti-dyslipidemic effects[26].

Miscellaneous: Thiagarajan et al[68] reported that the kidney's net generation of reactive oxygen species (ROS) contracted when ethyl acetate extract of *S. jamaicensis* leaves is used. It also reduced relapse in Bowman's space, tubular epithelial cells and vascular congestion and also in reducing the lesion in the LPS-induced liver and kidney injury in ICR mice.

Studies by Sasidharan et al[57] show that castor oil and magnesium sulphate-induced diarrhea models in swiss albino mice had shown significant antidiarrheal activity when methanol extract of *S. jamaicensis* leaves was administrated at doses 250 and 500 mg/kg[45]. ZnO and Cu-doped ZnO nanoparticles of aqueous leaf extract of *S. jamaicensis* have shown antibacterial properties *against B. subtilis* and *S. aureus* as reported by Khan et al[32].

Eskander et al[14] noted in rats that the methanol extract of *S. jamaicensis* aerial portions exhibited both preventative and therapeutic benefits on stomach ulcers; in fact, its therapeutic effects outweighed its preventive ones The extract's flavonoid component content had anti-inflammatory and antioxidant benefits[27]. Studies by Vikasari et al[73,74] evidenced the immunomodulatory effect of water extract of *S. jamaicensis*. The extract acts as an immunosuppressant and significantly raised the lymphocyte count which shows its potential as an immunomodulator.

Toxicological studies: The Indian subcontinent is widely recognized for its abundance of medicinal plants, forest products and ancient healthcare customs. Traditional (herbal) medicine has been increasingly investigated over the past few years. It is believed that Ayurvedic medicines, which are widely used in India, have fewer negative effects than allopathic medications. Therefore, an enormous amount of effort is being put into identifying plants that are safe for consumption by humans[19,38].

According to the data by Idu et al[23-25], there was no apparent distinction between the experimental and control rats' normal serum biochemistry or echogenic pattern, indicating a broad therapeutic safety margin when using *S. jamaicensis* on wistar rats[23]. On the other hand, conclusions from Ataman et al[3] contradicted the results of Idu et al[23-25].

Although the physical characteristics of the animals showed slight variation, histopathological lesions such as congestion, fatty changes and necrosis were observed in various tissues including the liver, blood vessels, kidneys, lungs and testis. However, the brain, eyes, small and large intestines and heart tissues were all essentially normal. In certain particular tissues, *S. jamaicensis* appears to cause modest, non-dose-dependent systemic toxicity[36].

Investigation by Estella et al[16] concludes long-term usage of methanolic leaf extract *S. jamaicensis* causing no damage to body tissues[78]. The results of the histological study by Omorodion et al[45] indicate that even when given at a dosage of 2000 mg/kg body weight, the ethanol and aqueous extracts made from the leaves and roots of *S. jamaicensis* did not exhibit any toxicity and were considered safe[45].

The findings by Sutjiatmo et al[66] indicated that none of the experimental animals displayed any signs of toxicity following a single oral dosage of *S. jamaicensis* water extract up to 10,000 mg/kg body weight throughout a 14-day observation period. The findings suggest that the aqueous extract of *S. jamaicensis* has an LD_{50} of more than 5,000 mg/kg bw[66].

Conclusion

We have summarized various bioactive compounds, therapeutic properties and toxicological studies of *Stachytarpheta jamaicenisis*. Studies report that *S. jamaicensis* possesses anti-oxidant, hypoglycemic, anti-microbial, anti-inflammatory, anti-nociceptive, wound healing, hypotensive, parasiticidal, anti-dyslipidemic and anti-diarrheal properties. Given these facts, it is notable that compounds obtained from *S. jamaicensis* showed biological activity in afflicted organisms without altering its biological profile evidencing lack of toxicity.

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