



A scoping review of five selected underutilized medicinal plants of Sri Lanka: Focusing on ethnobotany, phytochemistry and bioactivities, and evaluation of their potential for novel herbal product development

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ABSTRACT

Ageratum conyzoides L., *Artocarpus gomezianus* Wall. ex Trécul, *Euphorbia hirta* L., *Plectranthus zeylanicus* Benth., and *Piper sarmentosum* Roxb. have long been utilized in traditional medical practices, particularly across South and Southeast Asia. Despite their significant ethnopharmacological potential to treat various disorders, these plants remain underutilized in Sri Lanka. This review aims to evaluate the habit, propagation, ethnomedicinal uses, phytochemistry, and pharmacological properties of these five underutilized medicinal plants to promote their sustainable utilization in the herbal products industry of Sri Lanka. The plants were selected based on data from pharmacopeias and interviews with traditional medical practitioners. Scientific information on their ethnomedicinal uses, phytochemical compositions, and pharmacological properties was gathered from key scientific databases, including PubMed, Scopus, ScienceDirect, and Google Scholar, as well as web references and books. This information was analyzed to assess the factors contributing to their underutilization and their potential for novel herbal product development in Sri Lanka. All five plants possess a wide range of ethnomedicinal uses and are rich in bioactive compounds, including alkaloids, terpenoids, stilbenoids, and polyphenolic compounds. These bioactive compounds have been scientifically validated for their pharmacological properties, making these plants strong candidates for the development of novel pharmaceuticals and cosmeceuticals. However, their full potential remains largely untapped, primarily due to the lack of detailed phytochemical characterization and bioactive studies specific to Sri Lanka. Further preclinical and clinical research is needed to evaluate their therapeutic outcomes within the local context. The findings of this scoping review will guide future research and encourage broader use of these underutilized plants. Promoting their use will provide a sustainable alternative to the overexploitation of commonly used medicinal plants and support effective biodiversity conservation and resource management.

1. Introduction

Medicinal plants can be defined as a variety of plants used in ethnomedicine, a practice of medicine based on utilizing natural remedies to treat various diseases. These plants have various bioactive compounds with numerous pharmacological properties.^{1–4} These compounds can be used in multiple methods to develop herbal products.^{5–8} Underutilized medicinal plants can be described as the specific subset of medicinal plants that have not been incorporated much into herbal medicine and herbal products industries.⁹

There are many details on underutilized medicinal plants that can be obtained from the pharmacopeias of Sri Lanka. The *Ayurveda Pharmacopeia of Sri Lanka*, published by the Department of Ayurveda, and the *Indian Ayurvedic Pharmacopeia* are primarily utilized in Sri Lanka. These pharmacopeias contain numerous herbal medicinal formulae. However, some medicinal plants have been cited multiple times in these texts and are highly utilized. *Zingiber officinale* (Ginger), *Terminalia chebula* (Aralu), and *Trachyspermum roxburghianum* (Asamodagam) are a few examples of highly utilized medicinal plants. In addition, several surveys have been conducted in Sri Lanka regarding the utility of medicinal plant materials. Based on these documents, it can be identified that there

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List of abbreviations

5-LO	5-Lipoxygenase
ABTS	2,2'-Azino-Bis(3-Ethylbenzothiazoline-6-Sulfonic Acid)
A. conyzoides	<i>Ageratum conyzoides</i> L.
A. gomezianus	<i>Artocarpus gomezianus</i> Wall. ex Trécul
CCl₄	Carbon tetrachloride
DPPH	1,1-Diphenyl-2-Picrylhydrazyl
DCM	Dichloromethane
E. coli	<i>Escherichia coli</i>
E. hirta	<i>Euphorbia hirta</i> L.
FT-IR	Fourier-Transform Infrared Spectroscopy
GC	Gas Chromatography
GC-MS	Gas Chromatography-Mass Spectrometry
IC₅₀	Half-Maximal Inhibitory Concentration
LC	Liquid Chromatography
LC-ESI-IT-MS/MS	Liquid Chromatography-Electrospray Ionization-

	Ion Trap-Mass Spectrometry/Mass Spectrometry
LC-MS	Liquid Chromatography-Mass Spectrometry
MIC	Minimum Inhibitory Concentration
MRSA	Methicillin-Resistant <i>Staphylococcus aureus</i>
NF-κB	Nuclear Factor Kappa B
NLRP3	NLR Family Pyrin Domain-Containing 3
NMR	Nuclear Magnetic Resonance
P. longum	<i>Piper longum</i> L.
P. sarmentosum	<i>Piper sarmentosum</i> Roxb
P. zeylanicus	<i>Plectranthus zeylanicus</i> Benth
ROS	Reactive Oxygen Species
UHPLC-SRM/MS	Ultra-High-Performance Liquid Chromatography-Selected Reaction Monitoring/Mass Spectrometry
UPLC-Q-TOF-MS/MS	Ultra-Performance Liquid Chromatography combined with Quadrupole-Time-of-Flight Mass/Mass Spectrometry

are more than 50 underutilized medicinal plants.¹⁰ When analyzing those plants, their phytochemistry information and pharmacological effects have been reported well in the scientific literature, and it becomes clear that most of them contain unexplored ethnomedicinal applications. Therefore, those plants have a high potential to be utilized in novel herbal remedies.^{11–14} This review aims to evaluate the ethnomedicinal uses and pharmacological potential of the selected underutilized medicinal plants in Sri Lanka. It critically analyzes the phytochemicals, extraction strategies, and screening methods of these plants. Finally, it evaluates the factors contributing to the underutilization of these plants and outlines recommendations that can help improve their utility in the Sri Lankan herbal products industry.

The study was conducted from November 2022 to September 2023. The study begins with collecting primary information from various sources, including pharmacopeias (*Ayurveda Pharmacopeia of Sri Lanka* and *Indian Ayurvedic Pharmacopeia*), books, and interviews with

traditional medical practitioners.^{15,16} Then, a list of 50 underutilized medicinal plants is compiled from this extensive data. Finally, five of these 50 plants were selected based on interviews conducted with traditional medical practitioners of Bandaranayke Memorial Ayurvedic Research Institute (BMARI), Nawinna, Sri Lanka. The selected five underutilized medicinal plants were *Ageratum conyzoides* L., *Artocarpus gomezianus* Wall. ex Trécul, *Euphorbia hirta* L., *Plectranthus zeylanicus* Benth., and *Piper sarmentosum* Roxb.¹⁷ Next, scientific information regarding ethnomedicinal uses, phytochemistry, and pharmacological properties of chosen plants was obtained from scientific databases such as PubMed, Scopus, ScienceDirect, Google Scholar, web-references, and books. The data thus collected were then critically analyzed to identify the factors that led to the underutilization of these plants and their utility in herbal products research and development in Sri Lanka with the help of the BMARI.

The morphological characteristics of the five selected medicinal

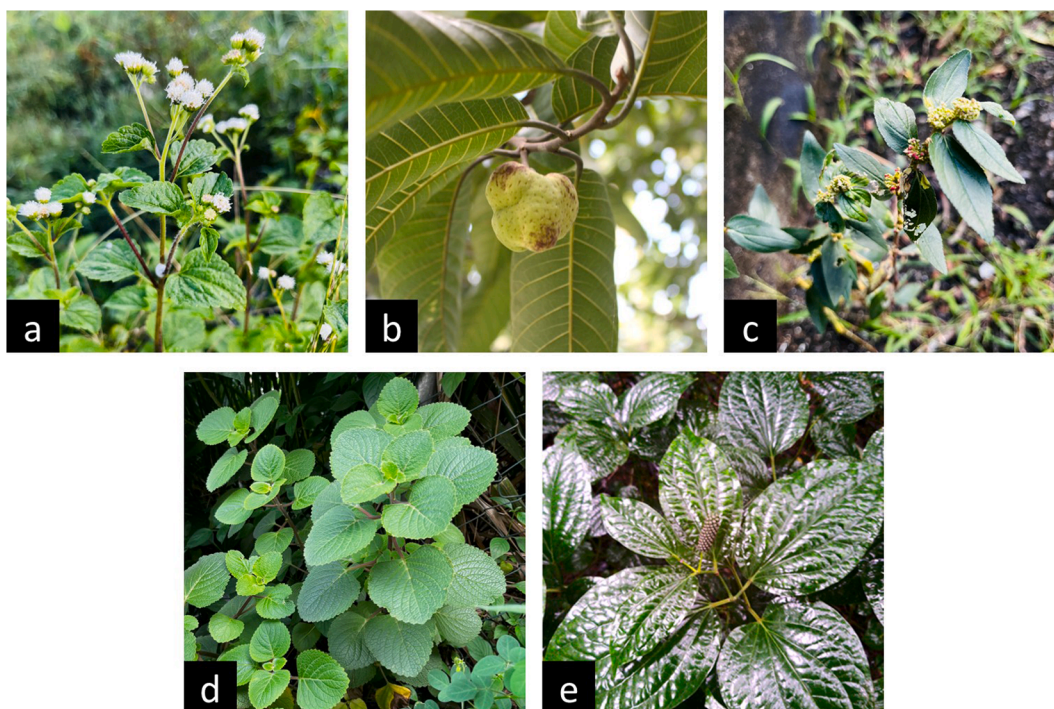


Fig. 1. The selected pharmacologically underutilized medicinal plants in Sri Lanka: a) *Ageratum conyzoides* L., b) *Artocarpus gomezianus* Wall. ex Trécul, c) *Euphorbia hirta* L., d) *Plectranthus zeylanicus* Benth., e) *Piper sarmentosum* Roxb.

plants are illustrated in Fig. 1. A comprehensive summary of the extraction, separation, and characterization techniques, along with the key bioactive compounds and pharmacological properties of these plants, is provided in Table 1.

2. *Ageratum conyzoides* L.

2.1. Habit, distribution, and propagation

A. conyzoides is an annual plant with an aromatic branching stem and conspicuous blue-to-white flowers.^{42–44} It is a natural species that may grow in the wild in the West and East African regions and some parts of South America and Asia. Researchers have stated that this plant is invasive in grasslands, abandoned fields, and forestlands.^{42,44–47} When considering the propagation of this plant, it is naturally propagated by seeds.⁴⁸ Based on research evidence, vegetative propagation through stem cuttings is difficult; it is only possible under rooting hormone treatment. Vegetative propagation has only been used to maintain the same varieties for research purposes.⁴⁹

2.2. Ethnobotany and ethnomedicine

In traditional medicine across Asian countries, various plant parts of *A. conyzoides* are utilized for their distinct therapeutic properties.^{48,50} The leaves possess antidiabetic, anti-tetanus, and anti-venomous (for snakes) properties.⁵¹ They address a myriad of health conditions, including pneumonia, wounds, sores, headaches, asthma, typhoid fever, uterine difficulties, malarial fever, throat infections, aching gums, and leucorrhea. Roots are utilized as an anti-tumor treatment for lithiasis and infant diarrhea.⁴⁸ Flowers have antiitch, tonic, antitussive, and vermifuge properties and are used to treat sleeping sickness and lice.¹⁹ Overall, it is clear that different parts of plants exhibit distinct properties.

2.3. Different extraction procedures, screening methods, and phytochemistry

The chemical constituents of *A. conyzoides* have been investigated in the leaf, stem, root, and flower parts.^{52–55} The ethnopharmacological literature shows that crude and aqueous extracts are more commonly used for ethnomedical treatments.^{48,51} However, ethanol and methanol

extracts are commonly utilized in ethnomedicinal validation studies and various other analyses.^{19,21,56}

Odeleye et al. performed a phytochemical screening of this plant extract using the method outlined by Harborne to identify the plant's active constituents. GC-MS analysis of the essential oil and an ethanolic extract of the plant parts has also been conducted to explore phytochemical compounds.^{18–21} Fig. 2 illustrates the major bioactive compounds identified in extracts of *A. conyzoides*. The preliminary phytochemical screening analysis established that the plant contained alkaloids, glycosides, phenols, flavonoids, saponins, tannins, steroids, and triterpenes.²⁰ A more detailed investigation of the essential oil through GC-MS analysis showed the presence of a broad array of bioactive compounds, including ageratochromene dimer, β -caryophyllene, caryophyllene epoxide, caffeic acid, fumaric acid, brassicasterol, 22,23-dihydrobrassicasterol, kaempferol-3,7-di-O-glucoside, and lycopsamine.⁴⁸ Adebayo et al. have isolated and characterized one new chromene, 2,2-dimethylchromene 7-methoxy-6-O- β -D-glucopyranoside, along with thirteen known compounds from the ethanolic extract of the whole plant of *A. conyzoides*.⁵² The aqueous extracts of *A. conyzoides* were extracted by Xu et al., and the major phytochemicals were characterized using the UPLC-Q-TOF-MS/MS technique. From that study, twenty constituents were found in the aqueous extracts. The most effective compounds, which were pointed out to be responsible for the bioactivities of the plant, include kaempferol 3,7-di-O-glucoside, kaempferol 3,7,4'-triglucoside, and 1,3,5-tricaffeoylquinic acid.²² The detailed phytochemical profiling of *A. conyzoides* highlights its potential as a rich source of bioactive compounds for the development of therapeutic agents. These findings also emphasize the importance of selecting an extraction method to isolate different target compounds. Despite the advancements in profiling techniques, there remains a gap in translating these findings into standardized formulations or clinical studies to validate their efficacy in humans.

2.4. Pharmacological properties of *A. conyzoides*

According to the cited literature, the above phytochemicals possess various characteristics, such as analgesic, anti-inflammatory, antibacterial, antifungal, and wound-healing activity.^{54,56–61} Furthermore, they exhibit inhibitory effects on helminths and nematodes, as well as insecticidal, hypoglycemic, anti-hyperglycemic, antioxidant, and anticancer activities.^{48,51,62} Studies have demonstrated the potential of plant extracts

Table 1
Summary of the extraction, separation, characterization methods, key active constituents, and pharmacological properties of five selected underutilized medicinal plants in Sri Lanka.

Plant Name	Extraction and Separation Methods	Characterization Methods	Key Active Constituents	Pharmacological Properties	References
<i>Ageratum conyzoides</i>	Ethanol, Methanol, Aqueous Extraction; Hydro-distillation (essential oils)	GC-MS, UPLC-Q-TOF-MS/MS,	Alkaloids, Glycosides, Phenolics, Saponins, Tannins, Steroids, Triterpenes, Flavonoids (kaempferol-3,7-glucoside), Chromenes (ageratochromene), Phenolic acids (caffeic acid)	Anti-inflammatory, Antidiabetic, Antimicrobial, Antioxidant, Wound healing, Anticancer	18–21,22
<i>Artocarpus gomezianus</i>	Hexane, Ethyl Acetate, Methanol extractions; Column chromatography	NMR	Dimeric stilbenes (artogomezianin), Flavones (artogomezianone, cycloartocarpin, artocarpin), 2-Arylbenzofurans, Phenolic compounds (oxyresveratrol), Flavonoids (artoinin E, cycloartobioxanthone, artobioxanthone, (+)-catechin)	Anti-tyrosinase, Antioxidant, Antiviral (HSV), α -Glucosidase inhibition	23–26
<i>Euphorbia hirta</i>	Ethanol, Methanol, Aqueous extractions; Sequential Soxhlet extraction method from hexane to ethanol	GC-MS, LC-ESI-IT-MS/MS, FT-IR, UHPLC-SRM/MS	Alkaloids, Phenolic groups (gallotannins, hydroxybenzoic acids, hydroxycinnamic acids), Flavonoids (quercetin, rutin), Tannins, Saponins, Terpenoids, Phenolic acids (gallic acid, ellagic acid), Pyrogallol	Antimicrobial, Anti-inflammatory, Antioxidant, Antidiabetic, Hepatoprotective, Antivenom	27–32
<i>Plectranthus zeylanicus</i>	Dichloromethane (DCM) extraction; Hydro-distillation (essential oils)	GC-MS	Abietane diterpenoids (7 α -acetoxy-6 β -hydroxyroyleanone), β -caryophyllene, geranyl acetate	Anti-inflammatory, Antimicrobial (MRSA), Antioxidant, 5-LO inhibition	33,34
<i>Piper sarmentosum</i>	Ethanol, Methanol, Aqueous extraction; Bioassay-guided fractionation	GC-MS, LC-MS, NMR	Phenolic compounds, Flavonoids, Amide alkaloids (piperine, sarmentine, sarmentosine, and pellitorine), Sterols, Phenylpropanoid compounds	Antimicrobial, Anti-inflammatory, Antioxidant, Hepatoprotective, Antidiabetic, Anticancer	35–41

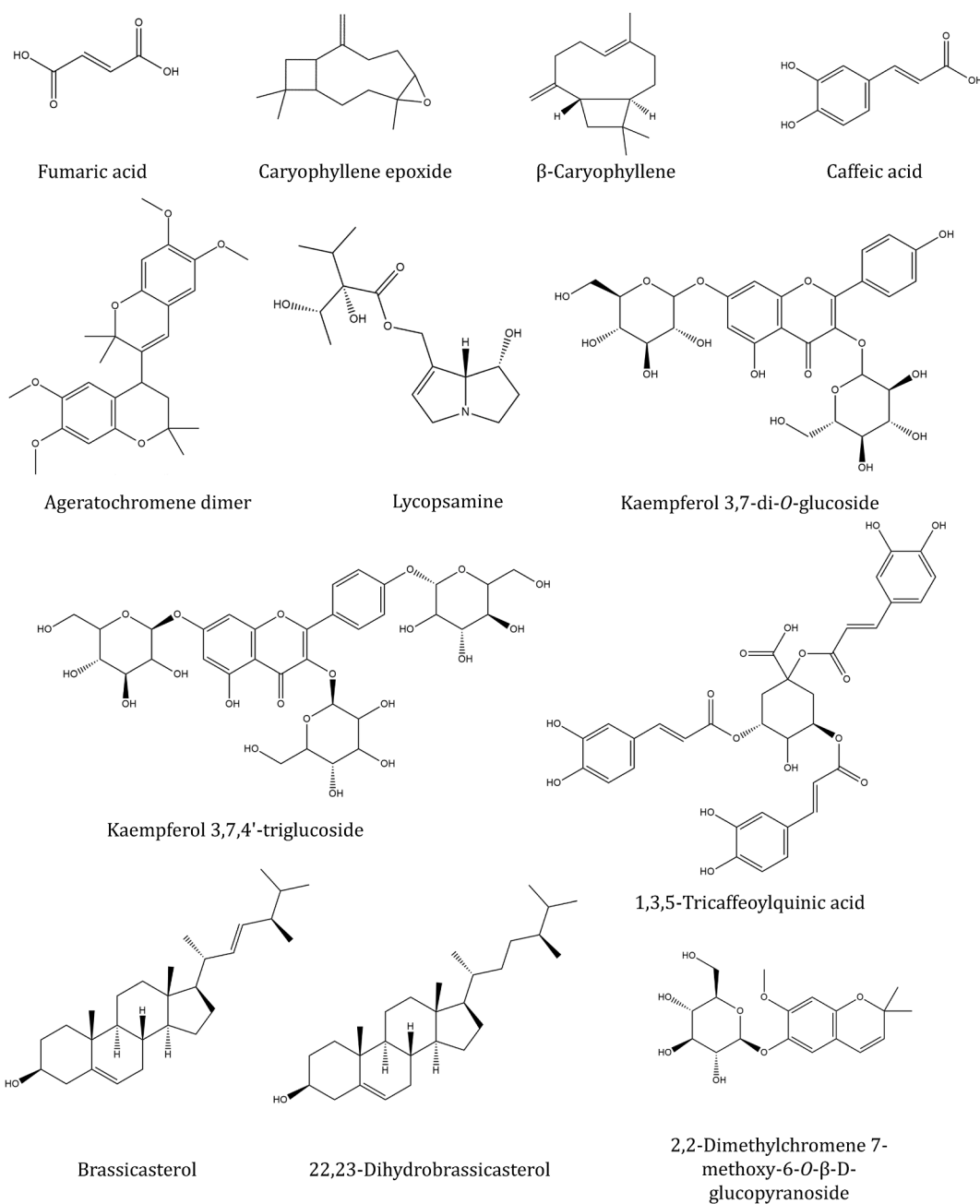


Fig. 2. Major bioactive compounds identified in the extracts of *A. conyzoides*.

in various therapeutic areas. Its methanol extracts have demonstrated mitochondrial-mediated apoptosis-inducing properties, showing promise for protecting against monosodium glutamate-induced hepatic and uterine disorders.⁶³ In addition, bioactive components in aqueous extracts of *A. conyzoides* have improved ovarian and uterine histoarchitecture in polycystic ovary syndrome models, indicating effects on the ovarian-uterine and hypophysis-gonadal axis.⁵⁷ Moreover, the essential oil of *A. conyzoides* has been found to exhibit anti-*Ehrlichia* properties, and its interaction with doxycycline enhances this effect, providing potential for anti-*Ehrlichia* treatment.⁶⁴ Thus, the anti-inflammatory effect of *A. conyzoides* is very conspicuous in various ways. Xu et al. investigated aqueous leaf extract of *A. conyzoides*, which has been reported to suppress the NLRP3 inflammasome activation in macrophages by blocking the NF- κ B and decreasing the ROS production, all of which contributed to reducing the release of pro-inflammatory cytokines.^{22,65} Regarding anti-diabetic properties, a study demonstrated that the aqueous plant extract of

A. conyzoides significantly reduced fasting blood glucose levels in animal models when administered orally at a dose of 500 mg/kg body weight. Nyunai et al. further confirmed the antidiabetic efficacy of *A. conyzoides* extracts, observing a reduction in hyperglycemia in both standard and streptozotocin-induced rats with high blood glucose levels.^{56,66,67} These findings collectively highlight the therapeutic versatility of *A. conyzoides*. However, while preclinical evidence is compelling, clinical studies validating its efficacy and safety in humans are needed.

2.5. Reasons behind the underutilization of this plant and ways to improve utilization in Sri Lanka

As evidenced by a substantial body of literature, this plant is recognized for its diverse ethnomedicinal properties, including wound healing, antidiabetic, anti-inflammatory, and antimicrobial properties. These details are documented in international literature, particularly in Asian and

African contexts. Much of these ethnomedicinal potentials are confirmed pharmacologically *in vitro* and *in vivo*. However, there are no adequate details on the utility of this plant in Sri Lanka. This may be primarily due to limited awareness and the concentration of ethnobotanical knowledge, mainly in rural areas. Additionally, the plant's minimal mention in Ayurvedic and traditional pharmacopeia is also associated with underutilization. As a result, there is an opportunity to raise awareness of this plant's medicinal potential and develop user-friendly applications. For instance, by harnessing its antimicrobial, anti-inflammatory, and wound-healing properties, it is possible to validate appropriate concentrations for formulary use, facilitating the development of wound-healing products such as creams or gels.^{68–70} Additionally, its antidiabetic properties could be utilized by incorporating the plant extracts into herbal teas or tablets or by identifying active components through spectroscopic analysis for antidiabetic drug development.^{71–75} By bridging the gap between ethnomedicinal knowledge and pharmacological validation, *A. conyzoides* holds promise for contributing to innovative and sustainable herbal product development in Sri Lanka.

3. *Artocarpus gomezianus* Wall. ex Trécul.

3.1. Habit, distribution, and propagation

The evergreen *A. gomezianus* trees may reach heights of up to 40 m. The stem is straight and cylindrical, and can remain unbranched for at least 10 m. Leaves are arranged in two rows on opposite sides of the stem. Small, white, and hairy stipules are present and fall off early. The stamens are approximately 0.6 mm long, with anthers measuring around 0.2 mm. The fruits are ellipsoid in shape and measure about 1.2 cm in length. The wild plant is collected and brought into cultivation, so that people can consume the edible fruit. In southern India and Sri Lanka, the plant is also occasionally planted specifically for the fruit it bears.^{76,77}

3.2. Ethnobotany and ethnomedicine

Although genus *Artocarpus* has mentioned many ethnomedicinal potentials, this plant is not explicitly cited for ethnomedicinal utilities in Sri Lanka. However, the fruit of this plant is commonly consumed as a wild fruit in Sri Lanka, and ethnic groups have traditionally utilized its bark for diverse medicinal purposes. However, *A. gomezianus* is native to Sri Lanka; the closest relative species, *Artocarpus lakoocha* sensu Fischer non Roxb. of India, has similar morphological characteristics to *A. gomezianus* and is widely utilized ethnobotanically. For example, the decoction of bark and bark powder is used to cure wounds, heartwood is used as a skin-whitening agent, and fresh fruit is used to cure liver diseases.^{78–82} Interviews with medical practitioners and rural communities in Sri Lanka confirm that the fruit of *A. gomezianus* is consumed as a wild fruit, suggesting its nutritional potential. Furthermore, traditional uses of its bark and heartwood indicate the presence of bioactive compounds with potential medicinal properties.

3.3. Different extraction procedures, screening methods, and phytochemistry

Phytochemical extractions of this plant are primarily prepared from its roots, stem bark, and heartwood.²⁵ Fig. 3 illustrates the major bioactive compounds identified in the extracts of *A. gomezianus*. Likhitwitayawuid et al. utilized petroleum ether, ethyl acetate, and methanol to extract compounds from the roots of *A. gomezianus*. The extraction procedure utilized column chromatography to fractionate and isolate novel dimeric stilbenes. The fractions obtained were then analyzed using NMR spectroscopy to characterize compounds. The compounds *N*-phenyl- β -naphthylamine, isocyclomorusin, artocarpin, cycloartocarpin A, norartocarpin, albanin A, cudraflavone C, and resveratrol were detected in this process.²³ Another research group isolated specific flavones, including artogomezianone and

oxyresveratrol, along with cycloartocarpin and artocarpin, from the heartwood of *A. gomezianus*.²⁴

Hakim et al. also found two more compounds in the *A. gomezianus*, which is a prenylated stilbene known as artoindonesianin N and a prenylated arylbenzofuran known as artoindonesianin O. The chemical structure of these compounds was elucidated using NMR spectroscopy. They also identified a phenolic compound known as oxyresveratrol.⁸³ Sritularak et al. used a methanolic extract from the stem bark of this plant, and four flavonoids, namely artonin E, cycloartobioxanthone, artobioxanthone, and (+)-catechin, were isolated through bio-assay guided fractionation.⁸⁴ More recently, Nuntawong et al. have isolated novel 2-arylbenzofurans from the root bark of *A. gomezianus*; those compounds are named 13-O-methylakoochin B and artogomezianin. Six previously identified compounds were also detected in that study. The structures of the newly identified compounds were determined through NMR spectroscopic methods.²⁶ However, detailed phytochemical studies on the local *A. gomezianus* species remain limited, highlighting the need for further research to explore its potential applications.

3.4. Pharmacological properties of *A. gomezianus*

However, a lack of ethnobotanical details about this subspecies has been cited; many pharmacological activities have been identified from its phytochemicals. The root extract's stilbenoids have intense anti-tyrosinase activity.²⁵ Moreover, flavonoids isolated from the stem bark have been reported to show powerful antioxidant ability through DPPH-free radical scavenging activity and inhibitory effects on nitric oxide production in experimental cell lines.⁸⁴ Inhibitory activities against types I and II of the herpes simplex virus (HSV) have been shown in flavones extracted from this species' heartwood.²⁴ Nuntawong et al. assessed root-bark extracts of *A. gomezianus* for their ability to inhibit α -glucosidase. Compounds artogomezianin and lakoochin A demonstrated potent α -glucosidase inhibitory activity, with IC₅₀ values of 18.25 and 26.19 μ M, respectively, surpassing the positive control acarbose.²⁶ Although ethnobotanical evidence was limited, the strong pharmacological findings position *A. gomezianus* as a species with considerable medicinal potential, warranting further investigation for future therapeutic applications.

3.5. Reasons behind the underutilization of this plant and ways to improve utilization in Sri Lanka

The main reason this plant is underutilized is the lack of ethnobotanical knowledge. Experiments regarding extracts of this plant have only been done in a few countries, and no possible data has been reported in Sri Lanka. Furthermore, this plant is not explicitly mentioned in the Sri Lankan Ayurvedic and traditional pharmacopeia.¹⁵ However, utilization methods for this plant may be developed. Tyrosinase inhibitors, such as kojic acid, hydroquinone, and related compounds, are essential to curing hyperpigmentation in humans. They are also utilized as whitening agents in cosmetic products because they suppress dermal melanin production.^{85–87} Due to the potent tyrosinase inhibitory activity of this plant's root extract, novel cosmeceuticals for skin whitening can be developed.^{88,89} Flavonoids from the stem bark and heartwood can be further studied and developed for anticancer and antiviral medications due to their potent antioxidant and antiviral activities.^{90–93} However, no herbal product or remedy has been developed from *A. gomezianus* to date, highlighting a significant gap in product innovation and underscoring its substantial potential for future research and commercial development.

4. *Euphorbia hirta* L.

4.1. Habit, distribution, and propagation

E. hirta is commonly found in tropical regions.²⁷ It has a slender,

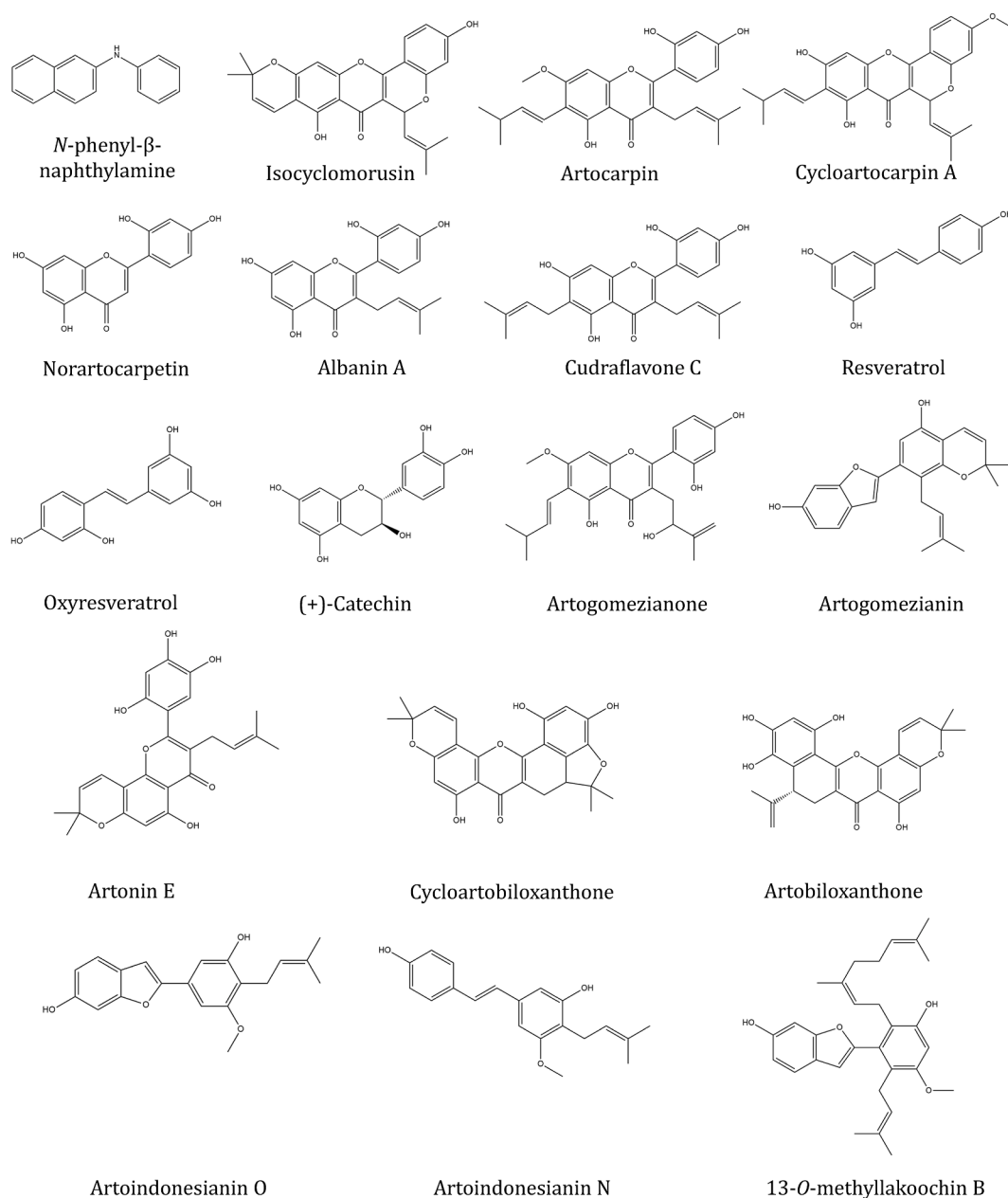


Fig. 3. Bioactive compounds identified in the extracts of *A. gomezianus*.

hairy stem with numerous branches from the base to the apex. The plant can grow up to 40 cm tall and is reddish or purplish. The oppositely arranged leaves are elliptic in shape (oblong to oblong-lanceolate) with acute or subacute apices. The leaf's upper surface is dark green, while the underside is lighter in color. The length of the leaves ranges from 1 to 2.5 cm. The leaves have toothed margins and purple blotches in the center. The fruits are three-celled yellow capsules with a hairy, keeled surface. They have a 1–2 mm diameter and three wrinkled, brown seeds with a four-sided, angular shape. Propagation typically occurs through seeds.^{12,28,94}

4.2. Ethnobotany and ethnomedicine

There is a descending history of using this plant, particularly for treating and preventing gastrointestinal illnesses, diseases of the mucous membranes, and respiratory disorders.⁹⁵ According to a review by Gosh et al. in Nigeria, a cold aqueous extract of the leaves is given to infants with skin illnesses.¹² It is also employed in folk medicine as a treatment for

gynecological diseases. Traditional medicine in India prescribes the extractions of this plant for a wide range of conditions, including worm infestations in newborns, diarrhea, gonorrhea, jaundice, acne, pimples, digestive problems, cancer, diabetes, and other tumors. The root extracts treat gastrointestinal issues such as nausea, diarrhea, and snake bites due to their antivenom properties. Leaf extracts are used to treat hypertension and inflammation in Africa and Australia, respectively.^{12,27,94,96,97}

4.3. Different extraction procedures, screening methods, and phytochemistry

Aqueous and methanolic extracts are mainly utilized to investigate phytochemicals. Ahmad et al. used the sequential Soxhlet extraction method from hexane to ethanol to isolate phytochemicals.²⁷ FT-IR and GC-MS assays have been carried out to further characterize the phytochemicals of *E. hirta*.⁹⁸ The major bioactive compounds identified in the extracts of *E. hirta* are shown in Fig. 4. When considering the literature, preliminary screening validates the presence of alkaloids, phenols,

flavonoids, tannins, saponins, terpenoids, and carbohydrates in *E. hirta* extracts.^{27–29,32} Further characterization of plant extracts isolated afzelin, myricitrin, rutin, quercetin, kaempferol, gallic acid, protocatechuic acid, and euphorbins (euphorbin E).^{94,95,98} Gopi et al. utilized advanced analytical methods of UHPLC-SRM/MS. They identified ellagic acid, gallic acid, and quinic acid as the predominant phenolic compounds in methanolic leaf extracts of *E. hirta*. GC-MS analysis showed that pyrogallol, constituting 60.07%, was the primary volatile component of the leaf extract.³⁰ Mekam et al. identified an estimated 123 individual phenolic compounds and 18 non-phenolic phytochemicals from water and ethanol extracts of *E. hirta* leaves using an untargeted approach via LC-ESI-IT-MS/MS, a hyphenated chromatographic and spectrometric method. Many identified compounds were reported in *E. hirta* leaves for the first time. According to that study, three phenolic classes as gallotannins, hydroxybenzoic acids, and hydroxycinnamic acids were the major groups of phenolics in the leaves, contributing to 71% of the total phenolics. Among the identified phenolic compounds, those occurring in the highest concentrations included coumaric acid, ferulic acid, caffeoyl-quinic acid, feruloyl-quinic acid, feruloyl-coniferin, quercetin-7-O-pentoside, apigenin-6-C-hexoside, kaempferol-3-O-hexoside, di-galloyl-quinic acid, tri-galloyl-quinic acid, brevifolin-carboxylic acid, and protocatechuic acid-O-pentoside-O-hexoside. These compounds contribute significantly to the bioactivity of *E. hirta* leaves. Notably, the ethanol extract contained approximately six times more feruloyl-coniferin than the water extract.³¹ *E. hirta* includes a wide range of bioactive compounds, including alkaloids, flavonoids, and phenolic acids, highlighting its potential for therapeutic applications. However, these compounds can vary within the geographical region; therefore, more studies needed to be conducted in Sri Lanka.

4.4. Pharmacological properties of *E. hirta*

E. hirta exhibits diverse bioactivities, as evidenced by recent studies. Rat models have confirmed the diuretic properties, antidiarrheal activity, and anti-inflammatory activity of this plant.⁹⁴ Das et al. comparatively investigated the ethanolic extracts of leaves and roots of *E. hirta*, and leaves demonstrated significantly greater anti-inflammatory activity compared to the root, as evidenced by its ability to inhibit albumin denaturation, proteinase activity, and lipoxigenase activity.⁹⁹ Murakami et al. validated the antimalarial efficacy by employing bioassay-guided fractionation on the methanolic extract derived from the aerial components of *E. hirta*. As per their findings, the primary active chromatographic fraction exhibited a substantial 90% growth inhibition of *Plasmodium falciparum* at a 5 µg/mL concentration.¹⁰⁰ Furthermore, this plant is reported to have anti-asthmatic activity due to its relaxation effect on the bronchial tubes and depressant action on respiration, and it also has antiamebic activity.^{94,95,99}

The ethanolic and aqueous extracts of *E. hirta* show significant antioxidant properties and hepatoprotective effects against carbon tetrachloride-induced hepatotoxicity in rats, demonstrating its potential for liver protection.¹⁰¹ The plant also displays anxiolytic and sedative effects, validating its traditional use for managing stress-related conditions.⁹⁶ In wound healing, *E. hirta* proves effective, particularly in diabetic models, enhancing recovery through both oral and topical applications.¹⁰² Additionally, *E. hirta* exhibits anti-mutagenic properties, inhibiting mutagenic effects in various test systems. Its phenolic compound profile supports notable antidiabetic and antioxidant activities, which are especially relevant in managing diabetes.^{31,103} The flavonoids enriched from *E. hirta* contribute to its antioxidant capacity, while studies on its immunomodulatory properties suggest benefits for immune health.^{104,105} Furthermore, it possesses antifilarial activity against *Onchocerca volvulus*, indicating potential for tropical disease treatment.¹⁰⁶ These studies highlight *E. hirta* as a multifunctional plant with applications across different therapeutic areas. Specific pharmacological properties are further elaborated below.

4.4.1. Anti-venom activity

Gopi et al. demonstrated that the methanolic extract of *E. hirta* fully inhibited venom enzymes *in vitro* and significantly reduced edema through mice models. Additionally, the extract prolonged the survival time of mice to over 24 h, a finding further supported by histopathological examination of vital organs. That study also demonstrated that pyrogallol can selectively inhibit venom protease without affecting phospholipase A2. It is established that the methanolic extract of *E. hirta* could completely neutralize the toxicity caused by *Naja naja* venom in both *in vitro* and *ex vivo* settings. These scientific findings validate the plant's traditional use with scientific support.³⁰

4.4.2. Antimicrobial activity

Different extractions of this plant inhibited the growth of *E. coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtili*. Aqueous, ethanolic, and chloroform extracts are mainly studied, considering the plant's antibacterial properties.^{27,107} Perumal et al. showed that the ethanolic extract displayed the most potent antimicrobial activity against *Salmonella typhi*, with an MIC of 0.031 mg/mL. In contrast, the DCM and ethyl acetate extracts exhibited moderate antimicrobial effects, with MIC values ranging from 0.5 to 1 mg/mL.¹⁰⁸ Aqueous and ethanolic extracts of *E. hirta* have shown antifungal activity against *Aspergillus niger* and *Candida albicans*.^{31,95}

4.4.3. Antioxidant activity

An aqueous and ethyl acetate extract of *E. hirta* showed an antioxidant effect and free radical scavenging activity in various *in vitro* models using ABTS, DPPH, and hydroxyl radical scavenging assays.^{28,29,94}

Based on all literature, *E. hirta* demonstrates a broad range of pharmacological activities, including anti-inflammatory, antimalarial, antimicrobial, antioxidant, and hepatoprotective effects. Its diverse bioactive compounds, such as flavonoids and phenolic acids, position the plant as a promising candidate for therapeutic applications across multiple areas, including diabetes management, wound healing, and tropical disease treatment.

4.5. Reasons behind the underutilization of this plant and ways to improve utilization in Sri Lanka

From the literature, it is evident that the ethnomedicinal values and the pharmacological values of this plant are complementary, and the plant has pharmacological importance. Nonetheless, the plant is poorly employed in traditional medicine and herbal products industries in Sri Lanka. It is referred to as a weed plant even though it has ethno-pharmacological significance. This underutilization can be mainly associated with this herb not being well publicized in Sri Lankan ayurvedic and ethnomedicinal literature. Based on the pharmacological information, the plant has potent anti-inflammatory, antimicrobial, respiratory illness therapy, and wound-healing properties, which are nicely integrated with the plant's ethnomedicinal utilities. Until now, no herbal medicine or product has been developed utilizing extracts or bioactive compounds from *E. hirta*. Hence, the plant can be used to develop new herbal products in Sri Lanka. For instance, its demonstrated antimicrobial activity indicates it could be a candidate for antimicrobial medications.^{109,110} Additionally, its potent antioxidant properties and ethnobotanical evidence of anticancer effects suggest it could be further characterized, fractionated for bioactive compounds, and explored for anticancer drug discovery.^{111–115} The proven antivenom properties of this plant also present opportunities for treating snake bites effectively.^{116–120} Despite its complementary ethnomedicinal and pharmacological values, *E. hirta* remains underutilized in Sri Lanka. Yet, its potent antimicrobial, antioxidant, anticancer, and antivenom properties present significant opportunities for developing novel herbal products and therapies.

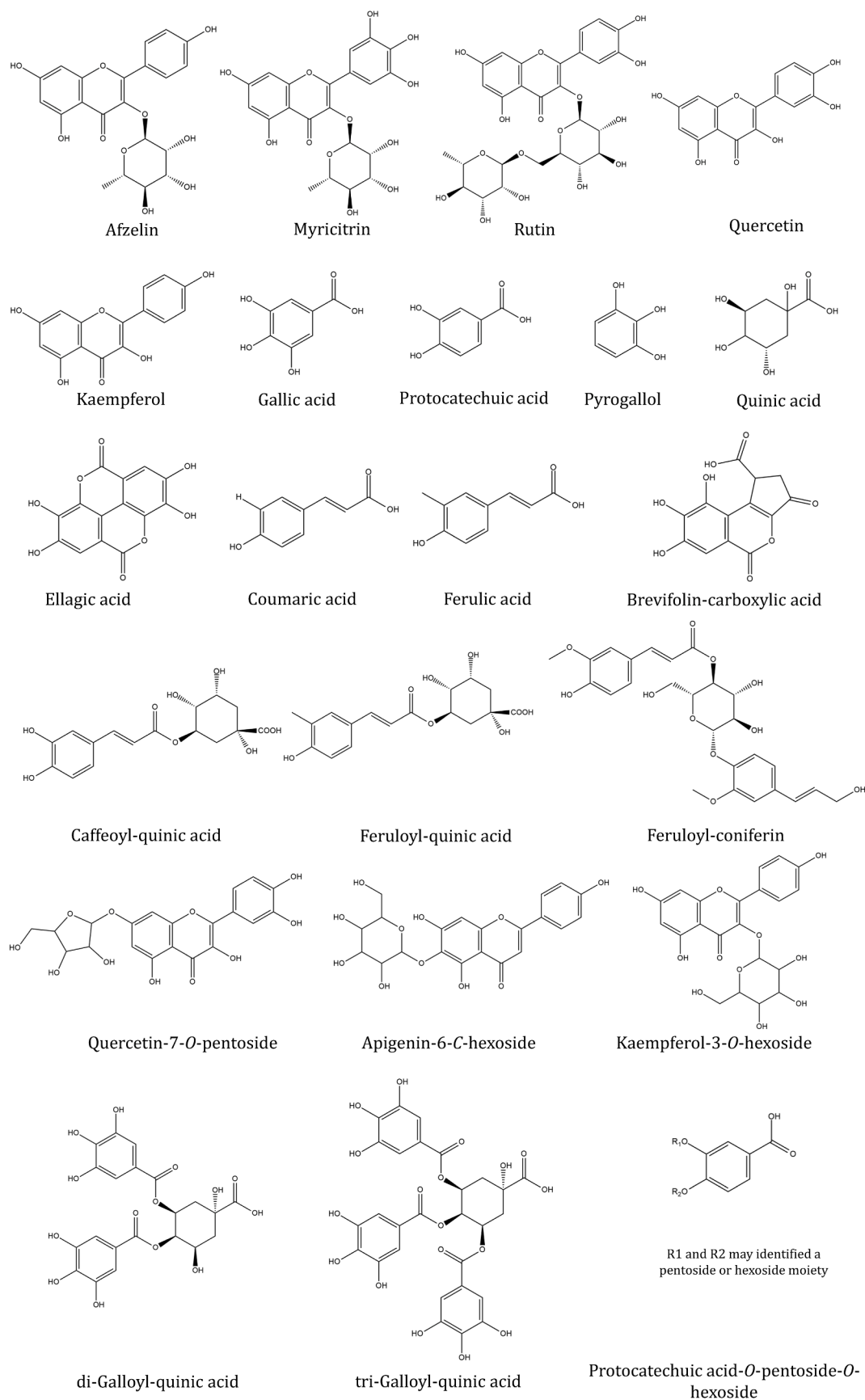


Fig. 4. Major bioactive compounds identified in the extracts of *E. hirta*.

5. *Plectranthus zeylanicus* Benth.

5.1. Habit, distribution, and propagation

P. zeylanicus is an herb endemic to Sri Lanka. It is grown in mid- and low-country elevations and is commonly cultivated in most gardens for medicinal purposes and as an ornamental plant. There is not much research that has been done regarding this plant. It is a succulent plant with a quadrangular stem and reddish-purple coloration, like many other species in the genus *Plectranthus*. The leaves are highly succulent, thick, and hairy, with a greyish-green color. Under the surface of the leaves, there are visible veins. The blooms are pale and bluish and group in a long and thin raceme. Flowers blossom throughout May and June. This herb is usually vegetatively reproduced as a bush. It flowers occasionally, and the plant can be propagated quite easily by stem-cutting.^{34,121}

5.2. Ethnobotany and ethnomedicine

In Sri Lankan indigenous medicine, *P. zeylanicus* has been used to cure inflammatory and infectious diseases. Because of its aromatic, astringent, and stomachic properties, it can be used in many treatment

forms. Tinctures prepared from areal parts are often used to cure gastrointestinal diseases. *P. zeylanicus* is recognized by the Ayurveda pharmacopeia of Sri Lanka as an ingredient in several traditional Ayurveda formulations, including Punarnawadyaristaya, Danyapanchakakwathaya, Chandrahkanthi oil, and Iramusuadee Kashaya. These formulations have been used for the treatment of edema, fever, burning sensation, eye diseases, and epilepsy.³⁴

5.3. Different extraction procedures, screening methods, and phytochemistry

Phytochemical analysis of *P. zeylanicus* has not received much attention. DCM extract is the main solvent used in general and systematic phytochemical screening.¹²² Essential oils have been extracted from plant material using hydro-distillation, while volatile constituents of essential oils have been analyzed using GC characterization.¹²¹ Fig. 5 illustrates the major bioactive compounds identified in the extracts of *P. zeylanicus*. According to Napagoda et al., GC-MS analysis of the DCM extract of *P. zeylanicus* revealed the presence of β -caryophyllene, α -caryophyllene, γ -selinene, valencene, 7-*epi*- α -selinene, viridiflorol, globulol, α -bisabolol, neophytadiene, phytol, phytol acetate, heptacosane, squalene, palmitic acid, stearic acid, linoleic acid, α -linolenic acid, α -tocopherol, stigmasta-5,

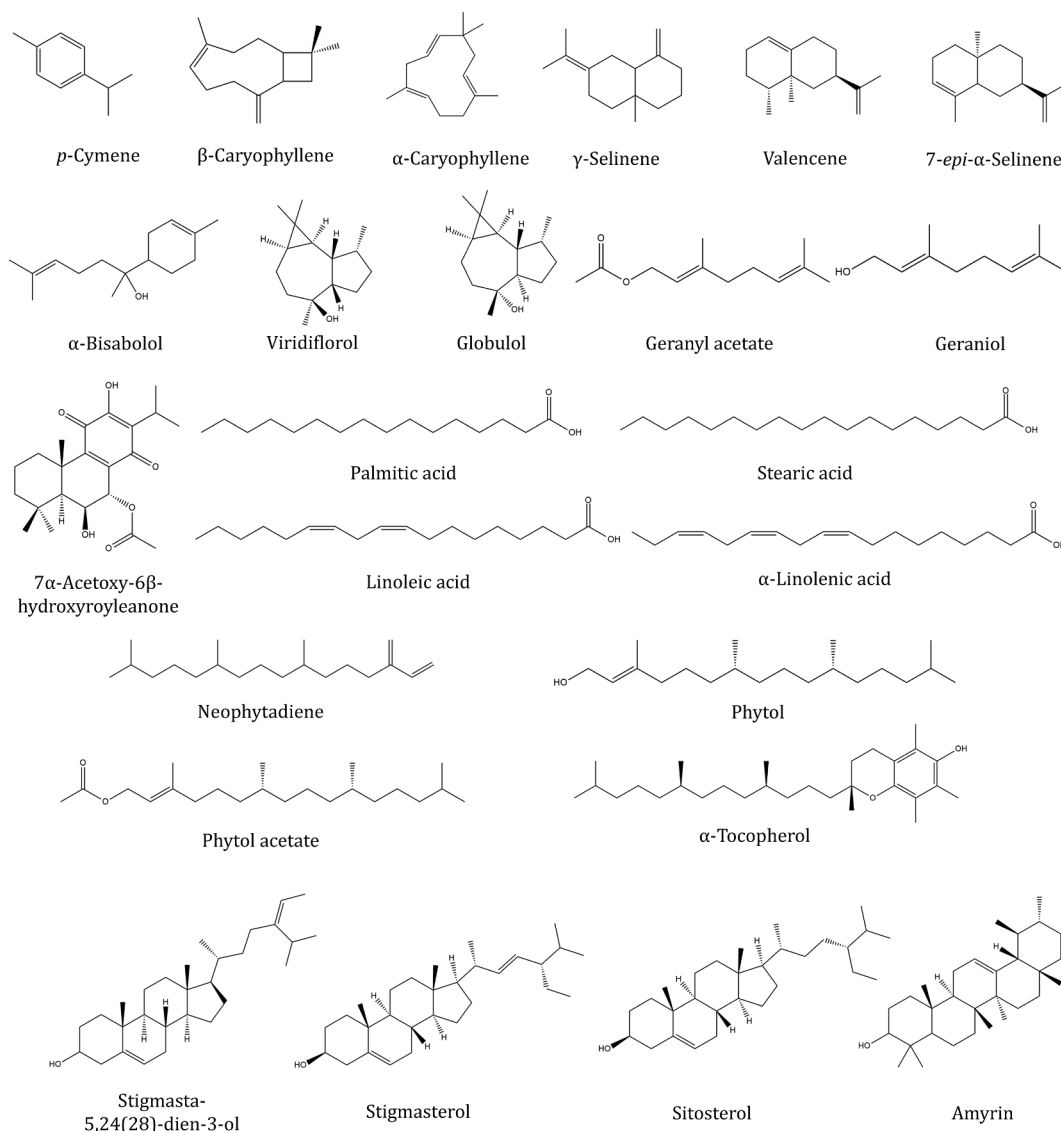


Fig. 5. Major bioactive compounds identified in the extracts of *P. zeylanicus*.

24 (28)-dien-3-ol, stigmasterol, sitosterol, and amyirin.³³ Fonseka et al. found higher percentages of the chemical composition of essential oils, such as geranyl acetate, geraniol, and *p*-cymene in the shoot of *P. zeylanicus*.³⁴ Abietane-type diterpenoids are the significant bioactive compounds in Lamiaceae family plants.^{123,124} *P. zeylanicus* was also found in India, and Mehrotra et al. reported the ethanolic extract of this plant contained two new abietane-type diterpenoids, which were named 7 β -acetoxy-6 β -hydroxyroyleanone and 7 β ,6 β -dihydroxyroyleanone. Furthermore, the known stereoisomer 7 α -acetoxy-6 β -hydroxyroyleanone was also identified from the extract by them.¹²⁵ Napagoda et al. executed the bioassay-guided fractionation process of the most active DCM extract of *P. zeylanicus* in Sri Lanka, and isolated the abietane diterpenoid compound 7 α -acetoxy-6 β -hydroxyroyleanone which was previously reported by Mehrotra et al.^{33,126} However, extraction and characterization methods of this plant have some limitations. Previous studies mainly focus on identifying volatile compounds through GC-MS analysis, further extracting using polar solvents, and characterization through LC-MS and NMR methods that need to be carried out.

5.4. Pharmacological properties *P. zeylanicus*

Essential oils are complex combinations of volatile secondary compounds extracted from different parts of various plants. They determine the smell, taste, and medicinal value of the plant and are a major contributor to its healing properties. Due to these qualities, essential oils of this plant are considered valuable in the fragrance, food and beverages industries, and medicinal applications.^{34,127}

Abietane diterpenoid compound, 7 α -acetoxy-6 β -hydroxyroyleanone isolated by Napagoda et al., showed moderate antibacterial efficacy against MRSA with an MIC value of 62.5 μ g/mL. An interesting fact is that the value was equally effective as commercial disinfectants. They also found that the lipophilic preparations of this plant have a highly effective 5-LO inhibition. These findings validated the ethnomedicinal shreds of evidence of the plant's utility in treating inflammatory diseases.^{33,126} Despite this, the chemistry of the Sri Lankan species of this genus, *P. zeylanicus*, requires further research utilizing advanced chromatographic and spectroscopic strategies.³⁴ However, research findings reported by Napagoda et al. are adequate to support and correlate the ethnobotanical uses and therapeutic benefits of *P. zeylanicus*.

5.5. Reasons behind the underutilization of this plant and ways to improve utilization in Sri Lanka

The main reason behind the underutilization of this plant is the lack of knowledge. Although *P. zeylanicus* shows promising health benefits, which are mentioned in traditional Sri Lankan medicine recipes, they are not used much. Another reason is that this plant is endemic to Sri Lanka, and Sri Lankan herbal medicine is mainly developed based on *Indian Ayurvedic Pharmacopeia*.^{15,16} Therefore, this is not much cited in the standard ayurvedic formulary. However, there is enormous potential to develop a method to utilize this plant, because, like other species of this genus, this plant has easy propagation abilities and a high growth rate. Moreover, there is another advantage because of the endemic status of this plant. Based on the literature, the main bioactivities of this herb are anti-inflammatory and antimicrobial properties. Those properties aid in developing utilization methods. Due to its anti-inflammatory and antimicrobial properties, plants can efficiently utilize it to develop either cosmeceuticals or pharmaceuticals for external applicability or internal use. For example, it is possible to develop herbal shampoo with antimicrobial and anti-inflammatory potential to treat scalp disorders.¹²⁸ Due to the presence of aromatic components, the essential oil of this plant can be further evaluated and utilized for aromatherapeutic purposes.^{129,130} It is also possible to develop herbal nutraceuticals because of their bioactive potential. Utilization methods are easy regarding those plants since they have long ethnobotanical and ethnopharmacological utility.

6. *Piper sarmentosum* Roxb.

6.1. Habit, distribution, and propagation

P. sarmentosum is an herbaceous shrub that can grow as a creeper or an upright plant. It can reach up to 50–60 cm in height. The leaves have a petiole of 1.0–2.5 cm in length and a thin to thick papery leaf blade that is light to dark green, broadly ovate to elliptic, 4.5–6.0 cm wide, 7.5–9.5 cm long, and has an acute apex. The leaves on the epiphytic base are deeply and equally cordate with rounded lobes. There are seven veins. The plant bears straight and cylindrical spikes containing male and female flowers, which are 1.5 cm long and 0.3–0.5 cm in diameter.¹³¹ It is common in Asia, including Cambodia, Laos, the Philippines, Burma, Thailand, Malaysia, and Indonesia.^{132,133} The fruit of *P. sarmentosum* has a berry that is spherical and, at the same time, quadrilateral. Its diameter ranges from 2.5 to 3 mm; it is connected to the inflorescence axis and is located inside it entirely. Propagation can be done through seeds¹²⁸; vegetative propagation is possible with the help of the rooting hormone.³⁸

6.2. Ethnobotany and ethnomedicine

This plant's leaves, roots, and fruits are primarily utilized in ethnomedicinal practices.¹³⁴ Chinese tribal people use the leaves of this plant to cure fever and indigestion. The roots of this plant are used for treating dermatomycoses, coughing, and lung inflammation ethnobotanically by South Asian countries.^{135,136} Furthermore, the plant's fruit is used to cure coughs, and the leaves are used externally to treat headaches in southern Thailand and Malaysia. In Malaysia, crushed leaves of *P. sarmentosum* are used as an ethnomedicinal treatment for kidney stones. The Indonesian people use the plant's roots to treat coughs, asthma, and toothaches, while the leaves treat chest pain.^{37,131} In summary, *P. sarmentosum* demonstrates wide ethnomedicinal use across various regions, with its leaves, roots, and fruits being employed to treat a range of ailments such as fever, indigestion, cough, lung inflammation, and dermatomycoses. The diverse applications of this plant in traditional medicine highlight its potential for further pharmacological exploration and development into novel therapeutic products across different medical fields. Based on the literature, it is clear that *P. sarmentosum* demonstrates wide ethnomedicinal use across various regions, with its leaves, roots, and fruits employed to treat various ailments. The diverse applications of this plant in traditional medicine highlight its potential for further pharmacological exploration.

6.3. Different extraction procedures, screening methods, and phytochemistry

Crude, ethanolic, methanolic, and aqueous extracts are widely used in phytochemical and bioactivity screening investigations.³⁸ Fig. 6 illustrates the major bioactive compounds identified in the extracts of *P. sarmentosum*. Yusof et al. have also affirmed the existence of glycosides, flavonoids, terpenoids, alkaloids, and phenolics, in the methanolic leaf extract.¹³⁷ Crude extract from this plant's fruit, leaves, and root contains phenolic compounds, flavonoids, amide alkaloids, sterols, and phenylpropanoid compounds.^{38,138} Feng et al. obtained piperine, sarmentine, sarmentosine, and pellitorine from the ethanolic extract through bioassay-guided fractionation. These phytochemicals were purified using column chromatographic techniques and characterized using NMR spectroscopic methods.¹³⁹ Sun et al. stated that from the various parts of *P. sarmentosum*, about 142 phytochemicals have been isolated. Essential oils are characteristic components of this genus, and various parts of this plant contain many essential oils. *P. sarmentosum* has yielded 89 volatile components from different parts, most of which are sesquiterpenes and phenylpropanoids, although monoterpenes, alkanes, and diterpenoids have also been identified. Among these compounds, *P. sarmentosum* essential oils predominantly contain *trans*-caryophyllene, spatulenol,

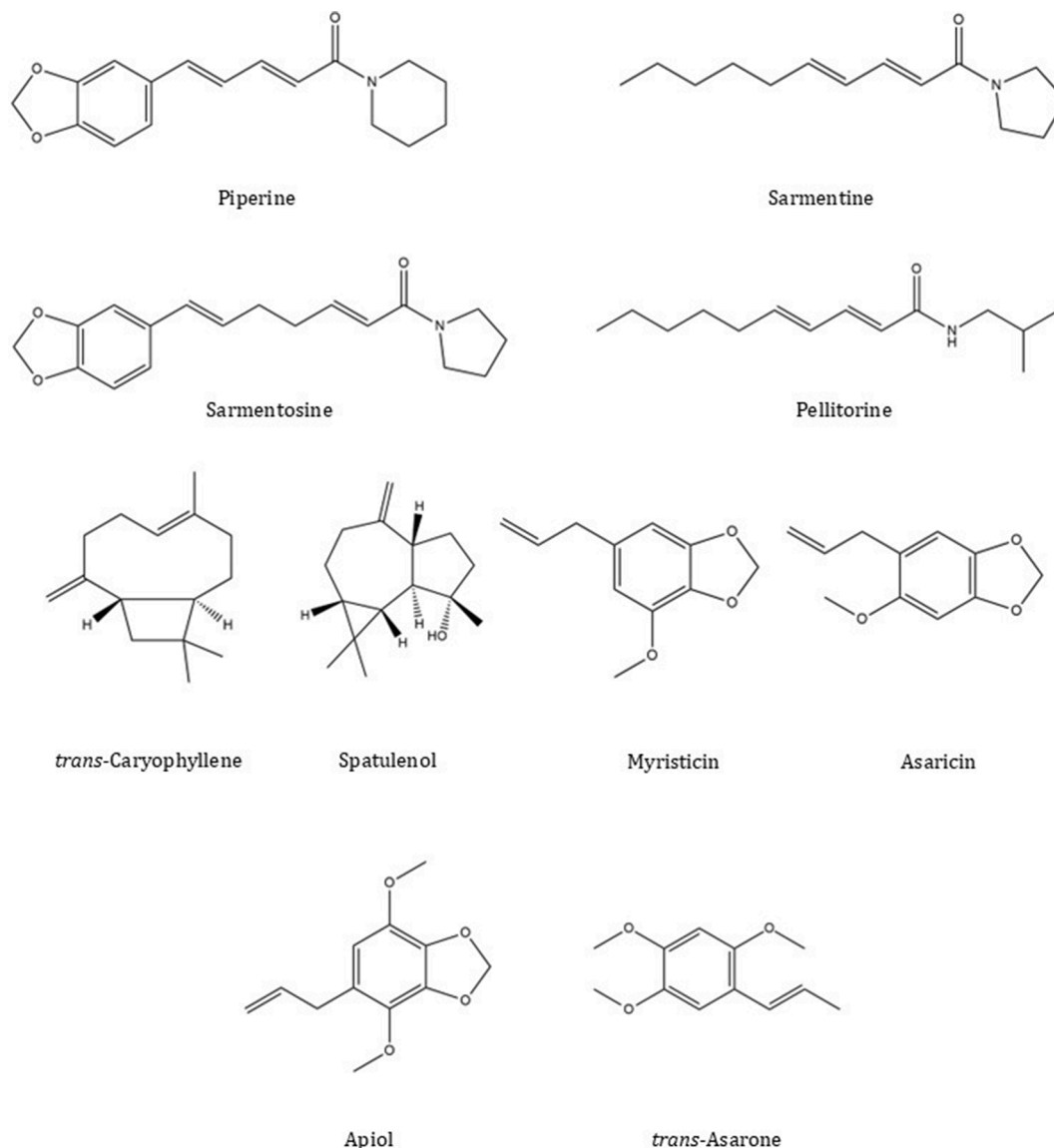


Fig. 6. Major bioactive compounds identified in the extracts of *P. sarmentosum*.

myristicin, asaricin, apiol, and trans-asarone as its major constituents.³⁸ However, limited phytochemical studies have been conducted on *P. sarmentosum* in Sri Lanka. Therefore, an in-depth study is crucial to fully explore and harness the plant's potential in the herbal product industry.

6.4. Pharmacological properties of *P. sarmentosum*

P. sarmentosum extracts show potential pharmacological effects in various areas, such as antimicrobial, antifungal, antimalarial, antituberculosis, anti-mycobacterial, anti-carcinogenic, antioxidant, antinociceptive, anti-inflammatory, antiamebic, neuromuscular blocking activity, anti-obesity, anti-angiogenesis, wound healing, cardiovascular activity, anti-hypertensive, anti-ulcer, and anticoccidial activity.^{35–41}

6.4.1. Hepatoprotective activity

Hussain et al. reported that in a rat model induced with CCl₄, the ethanol extracts from both the leaves and the fruit exhibited notable hepatoprotective activity. To validate this activity, various liver enzymes, including aspartate aminotransferase, alanine aminotransferase, and total plasma proteins, were assessed and analyzed across several model animals. The effectiveness of the action was duly observed.¹³¹

6.4.2. Anti-inflammatory activity

According to Aslam et al., it was observed that the leaves of *P. sarmentosum* demonstrate anti-inflammatory and anti-nociceptive characteristics in extracts obtained through methanol and water. The carrageenan-induced paw edema test was used to determine the anti-inflammatory properties of the plant, while the plant's anti-nociceptive activity was determined using the abdominal constriction and hot plate tests.¹³²

6.4.3. Antioxidant activity

The action of antioxidants in plants is responsible for most of the drugs' effects, such as anticancer, anti-hypertensive, and antidiabetic. *P. sarmentosum* has antioxidant activity, and the bioactive compounds, polyphenols, and flavonoids are involved in the antioxidant activities of the plant extracts.¹³⁴

6.4.4. Antimicrobial activity

Based on previous research, the antimicrobial activity of the *P. sarmentosum* extracts, which were prepared using different solvents, including methanol, *n*-hexane, chloroform, ethyl acetate, butanol, and water, was examined. The total flavonoid content in the methanol

extract of *P. sarmentosum* was moderate, while the antibacterial activity was moderate against *E. coli*, *Burkholderia* sp., and *Haemophilus parasuis*. As mentioned, antimicrobial activities require more assessment.³⁸ In addition, the crude extract was found to possess antibacterial properties against *E. coli*, *Vibrio cholera*, MRSA, and *Streptococcus pneumonia*. Aslam et al. have also stated that bioactive amide alkaloids are very important in the antifungal effect of *P. sarmentosum*. Several bioactive phytochemicals have been reported from *P. sarmentosum*, which exhibits antifungal activity.¹³² These compounds include sarmentosine and brachyamide B.¹⁴⁰ However, considering much literature, antimicrobial activities must be further validated with standards.

In addition to the above-elaborated properties, *P. sarmentosum* has also been reported to possess anti-carcinogenic, antimalarial, anti-tuberculosis, anti-moebic, neuromuscular blocking, anti-obesity, anti-angiogenesis, wound healing, cardiovascular, anti-hypertensive, anti-ulcer, and anticoccidial activities. However, these pharmacological activities needed to be further studied through clinical studies.^{38,131,132}

6.5. Reasons behind the underutilization of *P. sarmentosum* and ways to improve utilization in Sri Lanka

This plant's ethnomedicinal and latest pharmacological activity studies tally well, especially with anti-inflammatory, antioxidant, and antimicrobial properties. However, in Sri Lanka, *P. sarmentosum* is not utilized much. Another plant, "Wel thithpili" (*Piper longum* L.), is highly utilized in Sri Lanka.¹⁴¹ That species is abundantly cited in herbal formularies in ayurvedic systems. At times the *P. sarmentosum* is consumed as *P. longum*. However, there is a limited record of its utility as a substitute for *P. longum*.¹⁴² However, based on the diverse ethnomedicinal and pharmacological data, it is possible to suggest the development of the utilization method for this plant because of its significant impact on human health. The main reason that can be attributed to the underutilization of this plant is knowledge deficit. Therefore, it is recommended to formulate herbal products or medicines by considering this plant, which has anti-inflammatory, antioxidant, and antimicrobial activities.^{143,144} Investigating this plant's volatile essential oil fraction and creating aromatherapeutic medications is possible.^{130,145–147} Continued studies on this plant in Sri Lanka could lead to its increased use in herbal remedies.

7. Perspective on the development and uses of selected underutilized medicinal plants

However, the potential for the development and application of underutilized medicinal plants like *A. conyzoides*, *A. gomezianus*, *E. hirta*, *P. zeylanicus*, and *P. sarmentosum* necessitates an integrated approach combining traditional wisdom, scientific validation, sustainable cultivation, and commercial innovation. Despite their significant pharmacological activities, much of these plants' potential remains untapped due to a lack of research, standardization, and cultivation practices. To avoid overexploitation and ensure long-term availability, we need sustainable harvesting and cultivation strategies, such as community-led agroforestry programs and propagation initiatives. However, further scientific research needs clinical validation, toxicity evaluations, and standardized extracts to aid their inclusion in modern therapeutics. Their abundant and diverse phytochemicals also provide novel applications targeting healthcare, cosmeceuticals, and nutraceuticals, especially when advanced extraction and processing technologies can improve product functionalities and commercial value. Regulatory norms, supportive policy frameworks, and strategic market integration are essential to guide these plants toward the international herbal industry while safeguarding ecosystem sustainability. By promoting multi-stakeholder collaboration between traditional practitioners, academia, and industry, synergies between ethnomedicine and evidence-based clinical care adaptation can be made, and innovation can be ensured while preserving Sri Lanka's rich botanical heritage.

Dealing with these issues via interdisciplinary research, public-private partnerships, and conservation efforts would allow these undiscovered medicinal plants to play a crucial role in national healthcare, biodiversity conservation, and economic growth goals, unleashing their full potential for sustainable herbal product development.

8. Conclusion

In conclusion, this review highlights that the selected medicinal plants possess significant ethnobotanical and ethnomedicinal value. Bioactive phytochemicals have been successfully isolated from these plants, and their bioactivities have been validated. However, a major limitation is the lack of studies conducted in Sri Lanka, emphasizing the need for further research. The primary reason for the underutilization of these plants in Sri Lanka is their absence from the *Ayurveda Pharmacopeia* and a general lack of ethnobotanical knowledge among the population. Nevertheless, their known uses and proven properties offer great potential for recognition and value addition. They hold promise as valuable sources for novel pharmaceuticals, herbal products, and alternatives to commonly used medicinal plants. No validated drugs have been developed from these plants, and their herbal products remain limited. It is essential to establish research protocols and conduct further investigations to unlock their potential, particularly to assess the dosages and toxicity of their phytochemicals. By enhancing the utilization of these underutilized plants, we can reduce the overexploitation of commonly used species and contribute to the sustainable management and conservation of biodiversity and natural resources in Sri Lanka.

CRediT authorship contribution statement

Isuru Sakbo Uyangoda: Writing – review & editing, Writing – original draft, Conceptualization. **Mayuri Munasinghe:** Supervision.

Data availability

Data will be made available on request.

Declaration of interest statement

The authors declare that there are no conflicts of interest regarding the publication of this manuscript. We have no financial, personal, or professional affiliations that could be perceived to influence the research outcomes or the interpretation of the data presented in this study.

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