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REVIEW

Advances on Ethnobotanical, Phytochemical, and Preclinical Studies of *Strobilanthes crispus* and *Strobilanthes cusia* (Acanthaceae) for Drug Development Purpose: A Narrative Review

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Abstract: Plants of the genus *Strobilanthes* are one of the most widespread vegetation in Southeast Asia. More than 100 metabolites, including alkaloids, fatty acids and derivatives, flavonoids and flavonoid glycosides, phenolic acids, sterols, and terpenoids, have been identified from these plants. The scope of this review, which covers ethnobotanical, phytochemical, and preclinical aspects of *Strobilanthes crispus* and *Strobilanthes cusia* (Acanthaceae), is limited to articles published between 2015 and 2025. It confirms that these plants are still being investigated globally, with the most reported in numerous in vitro and in vivo studies on the leaves. Considering the noteworthy findings of the in vitro and in vivo studies, which mainly point to *S. crispus*, this plant may be established as a plant-based antimicrobial, anti-inflammatory, anticancer, or hypoglycemic agent, which may be attributed to its indolo-quinazoline alkaloid and flavonoids. Despite promising pharmacological evidence, there are limited human studies during the selected publication period. However, several articles have described ethnopharmacological surveys of medicinal plants in China, Malaysia, and Thailand, which documented the folkloric use of these two plants. It should be taken to notice that the lack of human studies requires further clinical trials to validate pharmacological activity, efficacy, and safety, and confirm its potential as a therapeutic agent.

Keywords: alkaloids, drug discovery, flavonoids, *Strobilanthes* plants, phenolics

Introduction

Plant-derived drugs have attracted considerable interest, and the development of phytopharmaceuticals has prevailed through ethnopharmacological approaches. Plants of the genus *Strobilanthes* (family Acanthaceae) are among the most widespread vegetation types in tropical countries, particularly in Southeast Asia. The genus *Strobilanthes* comprises approximately 350 species, many of which were used in indigenous medicine.[1] The name *Strobilanthes* originated from *strobilos*, meaning "cone", and anthos, meaning "flower", in Latin.[2,3] The *Strobilanthes* genus shrubs are characterized by their hapaxanthic or monocarpic life cycle, meaning they complete their entire reproductive process by a massive flowering and fruiting only once at the end of life before dying.[4,5] According to Plants of the World Online, an online database published by the Royal Botanic Gardens, Kew, there are 469 plants with accepted names that belong to the genus *Strobilanthes*.[6] More than 100 metabolites have been reported to be present in *Strobilanthes crispus* (L). Blume (with homotypic synonyms of *Hemigraphis crispa* (L). T. Anderson, *Ruellia crispa* L., and *Sericocalyx crispus* (L).

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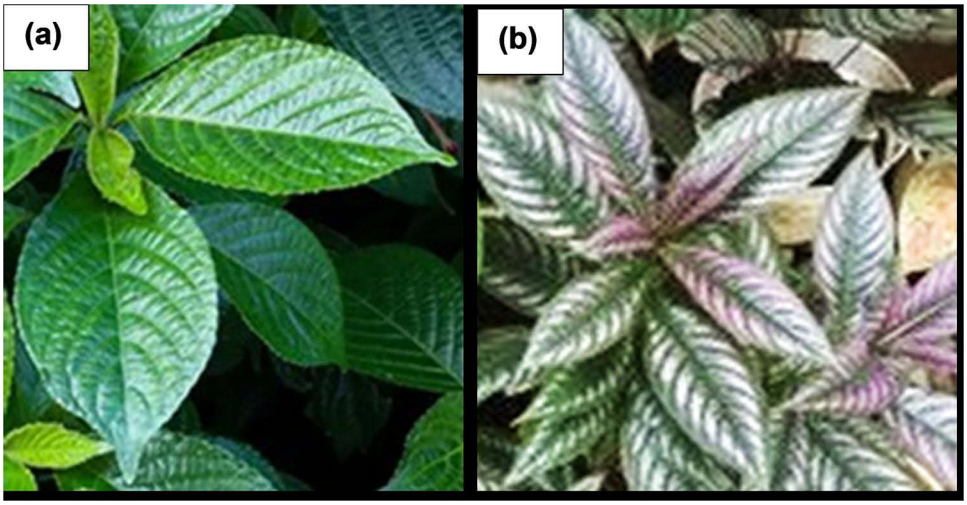

Figure 1 (**a**) *Strobilanthes crispus* (Chinese black face general or pecah beling) and (**b**) *Strobilanthes cusia* (Assam indigo or Chinese rain bell) of the family Acanthaceae.

Bremek., https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:55623-1) (Figure 1a) and *Strobilanthes cusia* (Nees) Kuntze (with homotypic synonyms of *Baphicacanthus cusia* (Nees) Bremek. and *Goldfussia cusia* Nees; https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:55627-1) (Figure 1b). As described, the native range of *S. crispus* extends from Java to the Lesser Sunda Islands. This plant grows primarily in the wet tropical biome, while the native range of *S. cusia* extends from the East Himalaya to South China, Indo-China, and Taiwan. It is an annual or subshrub and grows primarily in the temperate biome.[6]

The metabolites, including alkaloids, fatty acids and derivatives, flavonoids and flavonoid glycosides, phenolic acids, sterols, and terpenoids, are the most abundant and predominant phytochemicals found across various *Strobilanthes* species.[7–18] Considering the abundance of phytochemical metabolites in these plants, we searched for relevant scientific information to understand why *S. crispus* and *S. cusia* were indigenously used to treat various diseases, as well as the mechanisms underlying their pharmacological properties, by reviewing ethnobotanical, phytochemical, and in silico, in vitro, and in vivo studies of these plants.

Methods

This narrative review is intended to provide thorough information on the pharmacological activities of *Strobilanthes* plants, particularly *S. crispus* and *S. cusia*. *Strobilanthes* is the second largest genus within the family Acanthaceae. Articles were searched in PubMed and Scopus databases. The PubMed database contains approximately 39 million citations and abstracts in the health science field (https://pubmed.ncbi.nlm.nih.gov/about/), while the Scopus database has indexed thousands of health science titles.[19] The keywords used in the PubMed search box were "Strobilanthes" filtered to publication period from 2015 to 2025, free full-text, and article language English, resulting in 50 articles. Similarly, the keywords used in the Scopus search box within articles, abstracts, and the keywords box were "Strobilanthes", with publication period limited to between 2015 and 2025, subject area limited to "Medicine" and "Pharmacology, Toxicology, and Pharmaceutics", document type limited to "Article", keyword limited to "plant extracts", and language limited to "English", resulted in 36 papers. Articles were further screened, and only those reporting pharmacological or biological activities, phytochemical or nutritional compositions, and toxicity studies of the *Strobilanthes* genus were included to ensure scientific rigor and were thoroughly analyzed in this review. Additional articles were searched in Google Scholar to comprehend the discussion.

Ethnobotanical Study

Ethnobotany links between people and plants, including edible plants, medicinal plants, and plants for other utilizations, such as for clothing, shelter, fuel, and furniture. Therefore, ethnobotanical studies are useful in identifying, disseminating,

and documenting indigenous knowledge of plants for human and livestock diseases, thus bridging traditional healing practices with research-based pharmacology. Identification and documentation of the plants are thought to be effective in comprehending how diverse indigenous people interact with bioresources, thus gaining benefits for medicinal purposes.[20] There were five articles in PubMed and one in Scopus, reporting on ethnobotanical or ethnoveterinary studies of *S. cusia* and *S. crispus*. Of those, three studies were conducted in East Asia (China), and two studies in Southeast Asia (Malaysia and Thailand). In these folklore ethnobotanical surveys, the plants were used as colorants, edible plants, and as natural medicines for cattle.[21–25]

In the first article, conducted from September 2015 to November 2018, 46 elderly Landian Yao informants (mostly females) from Southwest China were interviewed. The Landian Yao, which in a literal manner refers to *blue clothes Yao*, is part of the Hmong-Mien language family distributed across Southwest and Southern China, Laos, Thailand, and Vietnam. This study revealed that *S. cusia*, known as Assam indigo or Chinese rain bell, with its indigo-colored leaves, was the main source of high indigotin (an indole alkaloid natural blue pigment) for clothing dye. *S. cusia* has been planted in their home gardens by their ancestors.[21] The traditional indigo dye extraction includes collecting leaves, soaking them in water until they rot and produce coarse indigo, then refining and drying the resulting dye. In the soaking step, an important chemical reaction occurs, in which endogenous β-glucosidase hydrolyzes indole glycoside to produce indole phenol, the source of indigo and indirubin. Modern pharmacological studies have shown that indigotin exhibits anti-inflammatory, antioxidant, antibacterial, and immunomodulatory properties.[26]

The second article described an ethnoveterinary survey conducted in Baiku Yao communities in Southwest China. UNESCO has recognized the Baiku Yao people as an ethnic group with an intact culture. A total of 53 informants (27 females and 26 males) were interviewed. This study revealed that 39 ethnoveterinary plant species belonging to 27 families and 38 genera were traditionally used by the Baiku Yao people, among which were the leaves of *S. cusia* to treat external wounds in cattle.[22]

In the third article, which was conducted in Telimau, Bukit Terang, and Kampung Sat, in Malaysia, 24 informants were recruited and interviewed using a semi-structured method and ethnobotanical assessment. This study revealed that the most commonly consumed wild edible plants were *S. crispus, Sauropus androgynus* (L). Merr., *Manihot esculenta* Crantz, and *Diplazium esculentum* (Retz). Sw.[23]

An ethnobotanical study of plant colorants used by the Karen ethnic people in Chiang Mai province in Thailand, by interviewing 113 informants, revealed that 52 plant species, belonging to 49 genera and 30 families, have been used for dyeing, mostly by hot water extraction. The leaves of *S. cusia* were described as the source of blue (fidelity level of 70), green (fidelity level of 2), and grey (fidelity level of 2) dyes. The levels of indigotin in *S. cusia* range from 4 to 36%.[24] In addition, another ethnobotanical study has been conducted in 18 districts of Ganzhou, China, from 2016 to 2018. Information was collected through semi-structured interviews, personal conversations with practitioners, and direct observations using standard methods, which revealed 93 plants belonging to 84 genera in 62 families, among which *S. cusia* was listed.[25]

Phytochemical and Nutritional Composition

Of the *Strobilanthes* genus plants, *S. crispus* has been the most explored for its phytochemical (tabulated in Table 1) and nutritional profiles. Most of the studies described Malaysia as the location of plant sampling, presumably because the indigenous habitat of this plant is the wet tropical biome.[7–14,17] Only a few other *Strobilanthes* species have been investigated for their phytochemicals, such as *Strobilanthes urens*,[15] *Strobilanthes kalimantanensis*,[16] and *Strobilanthes cusia*,[18] which narrated India, Indonesia, and Thailand as the locations of sampling.[15,16,18] Leaves were the most studied part for their bioactive metabolites, contributing to their numerous pharmacological activities.[7–18]

Briefly reported in a study, the aqueous extract of *S. crispus* leaves collected from Kelantan, Malaysia, exhibited high values of total phenol content (TPC) of 12.62 mg gallic acid equivalent (GAE)/g extract, total flavonoid content (TFC) of 7.44 mg quercetin equivalent (QE)/g extract, and total saponin content (TSC) of 44.7 mg diosgenin ($C_{27}H_{42}O_3$) equivalent (DE)/g extract. The ethanol extract contained flavonoids such as, apigenin ($C_{15}H_{10}O_5$), catechin ($C_{15}H_{14}O_6$), kaempferol ($C_{15}H_{10}O_6$), naringenin ($C_{21}H_{22}O_9$), quercetin ($C_{15}H_{10}O_7$), and rutin ($C_{27}H_{30}O_{16}$), and phenolic acids such as, caffeic acid ($C_9H_8O_4$), chlorogenic acid ($C_{16}H_{18}O_9$), ferulic acid ($C_{10}H_{10}O_4$), and gallic acid ($C_7H_6O_5$).[7]

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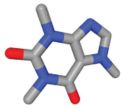
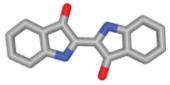
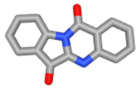
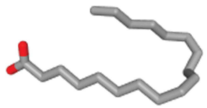
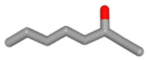
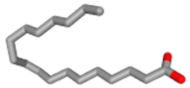
Table 1 Metabolites Isolated from the *Strobilanthes* Plants of Family Acanthaceae (in Alphabetical Order) and Total Flavonoids and Total Phenols of the Extract

Name of the Active Metabolite (IUPAC Name or Synonym)	Chemical Structure or Molecular Formula (PubChem CID)	Part of the Plant, the Botanical Name of the *Strobilanthes* Plant, Collected in, and the Extraction Method	Total Flavonoid Content (TFC)	Total Phenol Content (TPC)	Reference
Alkaloids					
Caffeine Synonym: 1,3,7-trimethylxanthine 	$C_8H_{10}N_4O_2$ (PubChem CID 2519)	The leaves of *Strobilanthes crispus* were collected from the Horticulture Unit of University Putra Malaysia. The leaves were separated from the stalks, thoroughly washed and rinsed with distilled water, dried in the oven at 60 °C, and ground to a fine powder.			[13]
Indigotin Synonym: 2-(1,3-Dihydro-3-oxo-2H-indazol-2-ylidene)-1,2-dihydro-3H-indol-3-one 	$C_{16}H_{10}N_2O_2$ (PubChem CID 10215)	The herbs of *Strobilanthes cusia* were collected from Phrae, Thailand. The bioactive phytochemicals were extracted using the MAE method.			[18]
Tryptanthrin Synonym: Indolo[2,1-b] quinazoline-6,12-dione 	$C_{15}H_8N_2O_2$ (PubChem CID 73549)	The herbs of *Strobilanthes cusia* were collected from Phrae, Thailand. The bioactive phytochemicals were extracted using the MAE method.			[18]
Fatty acids and derivatives					
1-Heptacosanol Synonym: Heptacosan-1-ol	$C_{27}H_{56}O$ (PubChem CID 74822)	The leaves of *Strobilanthes crispus* were obtained from a commercial supplier in Penang, Malaysia. The air-dried leaves were extracted sequentially with hexane, dichloromethane, and MeOH, and purified by chromatographic techniques. The structures of the compounds were elucidated with IR, GC-MS, MS, 1H-, and 13C-NMR, and compared with published data.			[9]
2-Hexenal Synonym: trans-2-Hexenal 	$C_6H_{10}O$ (PubChem CID 5281168)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.			[8]

2-Hexen-1-ol Synonym: 2-Hexenol 	$C_6H_{12}O$ (PubChem CID 5318042)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]
Linoleic acid Synonym: Telfairic acid 	$C_{18}H_{32}O_2$ (PubChem CID 5280450)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]
α-Linolenic acid Synonym: 9E,12Z,15Z-octadecatrienoic acid 	$C_{18}H_{30}O_2$ (PubChem CID 5312501)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]
1-Octen-3-ol Synonym: Vinyl amyl carbinol 	$C_8H_{16}O$ (PubChem CID 18827)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]
Oleic acid Synonym: 	$C_{18}H_{34}O_2$ (PubChem CID 445639)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]

(*Continued*)

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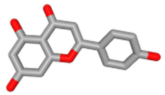
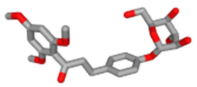
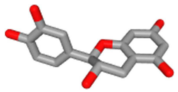
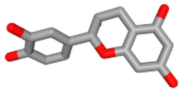
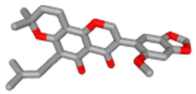
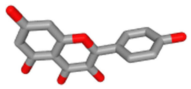
Table 1 (Continued).

Name of the Active Metabolite (IUPAC Name or Synonym)	Chemical Structure or Molecular Formula (PubChem CID)	Part of the Plant, the Botanical Name of the *Strobilanthes* Plant, Collected in, and the Extraction Method	Total Flavonoid Content (TFC)	Total Phenol Content (TPC)	Reference
Palmitic acid Synonym: Hexadecanoic acid 	$C_{16}H_{32}O_2$ (PubChem CID 985)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.			[8]
Stearic acid Synonym: Octadecanoic acid	$C_{18}H_{36}O_2$ (PubChem CID 5281)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.			[8]
Tetracosanoic acid Synonym: Lignoceric acid	$C_{24}H_{48}O_2$ (PubChem CID 11197)	The leaves of *Strobilanthes crispus* were obtained from a commercial supplier in Penang, Malaysia. The air-dried leaves were extracted sequentially with hexane, dichloromethane, and MeOH, and purified by chromatographic techniques. The structures of the compounds were elucidated with IR, GC-MS, MS, 1H-, and 13C-NMR, and compared with published data.			[9]
Flavonoids and flavonoids glycoside					
Apigenin Synonym: 5,7-Dihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one 	$C_{15}H_{10}O_5$ (PubChem CID 5280443)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.	12.62 mg GAE/g	7.44 mg QE/g	[7]
		The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]
Bidenoside B Synonym: 4-Hydroxy-2',4',6'-trimethoxydihydrochalcone 4-O-glucoside 	$C_{24}H_{30}O_{10}$ (PubChem CID 42607709)	The mature leaves of *Strobilanthes crispus* were collected from Bertam Ulu, Melaka, Malaysia. The leaves were air-dried at 23–26 °C for 2–3 h before being freeze-dried, ground into powder, and extracted with water, MeOH, EtOAc, and hexane. An HPLC-ESI-QToF-MS/MS system consisting of an HPLC 1260 Infinity coupled to an ESI-QToF-MS/MS was used to separate and identify polyphenols in the extracts through an existing database.	159.85 mg GAE/g	955.47 mg RE/g	[11]

Catechin Synonym: Catechuic acid 	$C_{15}H_{14}O_6$ (PubChem CID 9064)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.	12.62 mg GAE/g	7.44 mg QE/g	[7]
		The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]
Epicatechin Synonym: (2R,3R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol 	$C_{15}H_{14}O_6$ (PubChem CID 72276)	The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]
Euchrenone b3 Synonym: 5-hydroxy-3-(6-methoxy-1,3-benzodioxol-5-yl)-8,8-dimethyl-6-(3-methylbut-2-enyl) pyrano[2,3-h] chromen-4-one 	$C_{27}H_{26}O_7$ (PubChem CID 44257323)	The mature leaves of *Strobilanthes crispus* were collected from Bertam Ulu, Melaka, Malaysia. The leaves were air-dried at 23–26 °C for 2–3 h before being freeze-dried, ground into powder, and extracted with water, MeOH, EtOAc, and hexane. An HPLC-ESI-QToF-MS/MS system was used to separate and identify polyphenols in the extracts through an existing database.	159.85 mg GAE/g	955.47 mg RE/g	[11]
Kaempferol Synonym: 3,5,7-Trihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one 	$C_{15}H_{10}O_6$ (PubChem CID 5280863)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.	12.62 mg GAE/g	7.44 mg QE/g	[7]
		The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]

(*Continued*)

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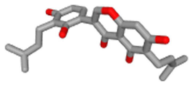
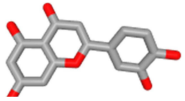
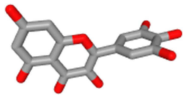
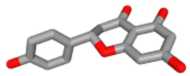
Table 1 (Continued).

Name of the Active Metabolite (IUPAC Name or Synonym)	Chemical Structure or Molecular Formula (PubChem CID)	Part of the Plant, the Botanical Name of the *Strobilanthes* Plant, Collected in, and the Extraction Method	Total Flavonoid Content (TFC)	Total Phenol Content (TPC)	Reference
Lupinisol C Synonym: 2',4',5,7-tetrahydroxy-3'-(2-hydroxy-3-methyl-3-butenyl)-6-prenylisoflavone 	$C_{25}H_{26}O_7$ (PubChem CID 14237670)	The mature leaves of *Strobilanthes crispus* were collected from Bertam Ulu, Melaka, Malaysia. The leaves were air-dried at 23–26 °C for 2–3 h before being freeze-dried, ground into powder, and extracted with water, MeOH, EtOAc, and hexane. An HPLC-ESI-QToF-MS/MS system was used to separate and identify polyphenols in the extracts through an existing database.	159.85 mg GAE/g	955.47 mg RE/g	[11]
Luteolin Synonym: 3',4',5,7-Tetrahydroxyflavone 	$C_{15}H_{10}O_6$ (PubChem CID 5280445)	The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]
Myricetin Synonym: 3,5,7-Trihydroxy-2-(3,4,5-trihydroxyphenyl)-4H-chromen-4-one 	$C_{15}H_{10}O_8$ (PubChem CID 5281672)	The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]
Naringenin Synonym: 5,7,4'-Trihydroxyflavanone 	$C_{15}H_{12}O_5$ (PubChem CID 439246)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.	12.62 mg GAE/g	7.44 mg QE/g	[7]
		The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]

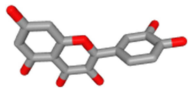
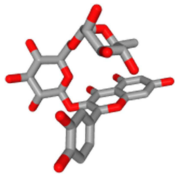
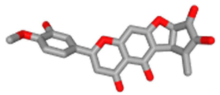
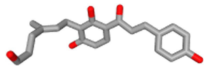
Quercetin Synonym: 2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one 	$C_{15}H_{10}O_7$ (PubChem CID 5280343)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.	12.62 mg GAE/g	7.44 mg QE/g	[7]
Rutin Synonym: Quercetin 3-rutinoside 	$C_{27}H_{30}O_{16}$ (PubChem CID 5280805)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.	12.62 mg GAE/g	7.44 mg QE/g	[7]
		The leaves of *Strobilanthes crispus* were harvested from the Herbal Garden of the Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia. The leaves were separated from the stalks, washed, rinsed with distilled water, dried at 40 °C for 24 h, and ground. The dry powdered leaves were mixed with glass beads, and placed into the SC-CO2 extractor system. The flavonoids in the extract were analyzed by HPLC.	Not described	Not described	[14]
Torosaflavone C Synonym: (11S,15R)-9,13-dihydroxy-5-(3-hydroxy-4-methoxyphenyl)-12-methyl-4,16-dioxatetracyclohexadeca-1(10),2,5,8,12-pentaene-7,14-dione 	$C_{22}H_{16}O_8$ (PubChem CID 44258233)	The mature leaves of *Strobilanthes crispus* were collected from Bertam Ulu, Melaka, Malaysia. The leaves were air-dried at 23–26 °C for 2–3 h before being freeze-dried, ground into powder, and extracted with water, MeOH, EtOAc, and hexane. An HPLC-ESI-QToF-MS/MS system was used to separate and identify polyphenols in the extracts through an existing database.	159.85 mg GAE/g	955.47 mg RE/g	[11]
Xanthoangelol C Synonym: (E)-6-[2,6-dihydroxy-3-[(E)-3-(4-hydroxyphenyl) prop-2-enoyl] phenyl]-4-methylhex-4-enal 	$C_{22}H_{22}O_5$ (PubChem CID 15731056)	The mature leaves of *Strobilanthes crispus* were collected from Bertam Ulu, Melaka, Malaysia. The leaves were air-dried at 23–26 °C for 2–3 h before being freeze-dried, ground into powder, and extracted with water, MeOH, EtOAc, and hexane. An HPLC-ESI-QToF-MS/MS system was used to separate and identify polyphenols in the extracts through an existing database.	159.85 mg GAE/g	955.47 mg RE/g	[11]

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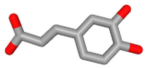
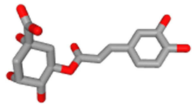
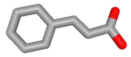
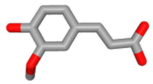
Table 1 (Continued).

Name of the Active Metabolite (IUPAC Name or Synonym)	Chemical Structure or Molecular Formula (PubChem CID)	Part of the Plant, the Botanical Name of the *Strobilanthes* Plant, Collected in, and the Extraction Method	Total Flavonoid Content (TFC)	Total Phenol Content (TPC)	Reference
Phenolic acids					
Caffeic acid Synonym: 3,4-Dihydroxycinnamic acid 	$C_9H_8O_4$ (PubChem CID 689043)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65°C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.			[7]
Chlorogenic acid Synonym: 3-(3,4-Dihydroxycinnamoyl) quinic acid 	$C_{16}H_{18}O_9$ (PubChem CID 1794427)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.			[7]
Cinnamic acid Synonym: 3-Phenylpropenoic acid 	$C_9H_8O_2$ (PubChem CID 444539)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.			[7]
Ferulic acid Synonym: 4-Hydroxy-3-methoxycinnamic acid 	$C_{10}H_{10}O_4$ (PubChem CID 445858)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.			[7]

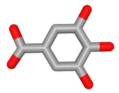
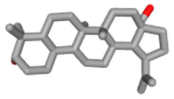
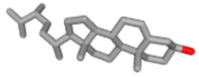
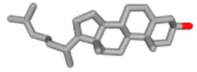
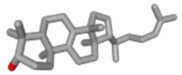
Gallic acid Synonym: 3,4,5-Trihydroxybenzoic acid 	$C_7H_6O_5$ (PubChem CID 370)	The leaves of *Strobilanthes crispus* were harvested before the flowering stage in Kelantan, Malaysia. The leaves were ground into a powder and extracted with EtOH. The solutions were refluxed for 2 h at 65 °C, cooled to room temperature, filtered, and then evaporated under reduced pressure in a rotary evaporator. The residue was freeze-dried. UHPLC was used to separate and identify the phenolics and flavonoids.	[7]
Sterols			
Betulin Synonym: Betulinol 	$C_{30}H_{50}O_2$ (PubChem CID 72326)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Sterols were analyzed using GC-MS.	[8]
		Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.	[10]
Campesterol Synonym: 24(R)-methyl cholesterol 	$C_{28}H_{48}O$ (PubChem CID 173183)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Sterols were analyzed using GC-MS.	[8]
		Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.	[10]
Desmosterol Synonym: 24-Dehydrocholesterol 	$C_{27}H_{44}O$ (PubChem CID 439577)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Sterols were analyzed using GC-MS.	[8]
Lanosterol Synonym: Lanosta-8,24-dien-3beta-ol 	$C_{30}H_{50}O$ (PubChem CID 246983)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Sterols were analyzed using GC-MS.	[8]

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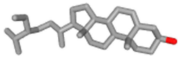
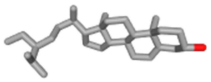
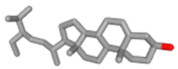
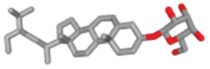
Table 1 (Continued).

Name of the Active Metabolite (IUPAC Name or Synonym)	Chemical Structure or Molecular Formula (PubChem CID)	Part of the Plant, the Botanical Name of the *Strobilanthes* Plant, Collected in, and the Extraction Method	Total Flavonoid Content (TFC)	Total Phenol Content (TPC)	Reference
β-Sitosterol Synonym: 22,23-Dihydrostigmasterol 	$C_{29}H_{50}O$ (PubChem CID 222284)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Sterols were analyzed using GC-MS.			[8]
γ-Sitosterol Synonym: Clionasterol 	$C_{29}H_{50}O$ (PubChem CID 457801)	Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.			[10]
Stigmasterol Synonym: β-Stigmasterol 	$C_{29}H_{48}O$ (PubChem CID 5280794)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Sterols were analyzed using GC-MS.			[8]
		The leaves of *Strobilanthes crispus* were obtained from a commercial supplier in Penang, Malaysia. The air-dried leaves were extracted sequentially with hexane, dichloromethane, and MeOH, and purified by chromatographic techniques. The structures of the compounds were elucidated with IR, GC-MS, MS, 1H-, and 13C-NMR, and compared with published data.			[9]
		Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.			[10]
Stigmasterol β-D-glucopyranoside Synonym: 3-O-β-d-glucopyranosyl-stigmasterol 	$C_{35}H_{58}O_6$ (PubChem CID 12895778)	The leaves of *Strobilanthes crispus* were obtained from a commercial supplier in Penang, Malaysia. The air-dried leaves were extracted sequentially with hexane, dichloromethane, and MeOH, and purified by chromatographic techniques. The structures of the compounds were elucidated with IR, GC-MS, MS, 1H-, and 13C-NMR, and compared with published data.			[9]

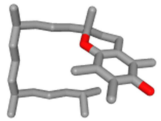
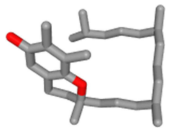
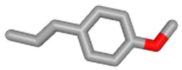
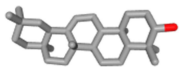
α-Tocopherol Synonym: Vitamin E 	$C_{29}H_{50}O_2$ (PubChem CID 14985)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Sterols were analyzed using GC-MS.	[8]
		Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.	[10]
γ-Tocopherol Synonym: Vitamin E-gamma 	$C_{28}H_{48}O_2$ (PubChem CID 92729)	Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.	[10]
Terpenoids			
Anethole Synonym: 4-Propenylanisole 	$C_{10}H_{12}O$ (PubChem CID 637563)	The seeds of *Strobilanthes kalimantanensis* were collected from West Kutai, Kalimantan, Indonesia, and planted in the garden of Mulawarman University, Samarinda, East Kalimantan, Indonesia. Leaf samples were dried, powdered, and macerated with 96% EtOH. Phytochemicals were analyzed using GC-MS.	[16]
β-amyrin Synonym: Olean-12-en-3beta-ol 	$C_{30}H_{50}O$ (PubChem CID 73145)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]
		The leaves of *Strobilanthes crispus* were obtained from a commercial supplier in Penang, Malaysia. The air-dried leaves were extracted sequentially with hexane, dichloromethane, and MeOH, and purified by chromatographic techniques. The structures of the compounds were elucidated with IR, GC-MS, MS, 1H-, and 13C-NMR, and compared with published data.	[9]

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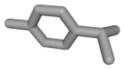
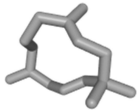
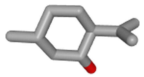
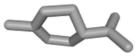
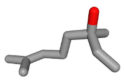
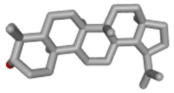
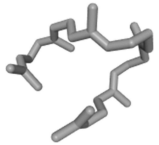
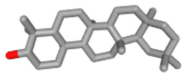
Table 1 (Continued).

Name of the Active Metabolite (IUPAC Name or Synonym)	Chemical Structure or Molecular Formula (PubChem CID)	Part of the Plant, the Botanical Name of the *Strobilanthes* Plant, Collected in, and the Extraction Method	Total Flavonoid Content (TFC)	Total Phenol Content (TPC)	Reference
p-Cymene Synonym: p-Methyl cumene 	$C_{10}H_{14}$ (PubChem CID 7463)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.			[8]
Eucalyptol Synonym: 1,8-Cineole 	$C_{10}H_{18}O$ (PubChem CID 2758)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.			[8]
β-Humulene Synonym: (E,E)-1,4,4-Trimethyl-8-methylene-1,5-cycloundecadiene 	$C_{15}H_{24}$ (PubChem CID 5318102)	Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.			[10]
Isopulegol Synonym: (1R,2S,5R)-5-methyl-2-prop-1-en-2-ylcyclohexan-1-ol 	$C_{10}H_{18}O$ (PubChem CID 170833)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.			[8]

Limonene Synonym: 4-Isopropenyl-1-methylcyclohexene 	$C_{10}H_{16}$ (PubChem CID 22311)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]
Linalool Synonym: 3,7-Dimethyl-1,6-octadien-3-ol 	$C_{10}H_{18}O$ (PubChem CID 6549)	The leaves of *Strobilanthes crispus* were collected in Seremban, Malaysia. The leaves were vacuum-oven dried at 60 °C for 24 h, ground, and extracted with 80% MeOH. Volatiles were analyzed using HS-SPME. After the extraction was completed, the SPME fiber was placed in the GC–MS injection port at 220 °C for 15 min, and the volatiles were identified by comparing with the NIST14 database.	[8]
Lupeol Synonym: Fagarasterol 	$C_{30}H_{50}O$ (PubChem CID 259846)	Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.	[10]
Squalene Synonym: Spinacene 	$C_{30}H_{50}$ (PubChem CID 638072)	Fresh leaves of *Strobilanthes crispus* were purchased from the herbal supplier in Kinabalu, Sabah, Malaysia. The leaves were placed on Murashige Skoog (MS) agar media containing 1 mg/L NAA and 1 mg/L BAP. The leaf callus was harvested by washing away the attached agar, weighed, and dissolved in absolute MeOH. The extract was directly subjected to GC-MS analysis.	[10]
Taraxerol Synonym: D-Friedoolean-14-en-3β-ol 	$C_{30}H_{50}O$ (PubChem CID 92097)	The leaves of *Strobilanthes crispus* were obtained from a commercial supplier in Penang, Malaysia. The air-dried leaves were extracted sequentially with hexane, dichloromethane, and MeOH, and purified by chromatographic techniques. The structures of the compounds were elucidated with IR, GC-MS, MS, 1H-, and 13C-NMR, and compared with published data.	[9]

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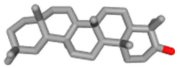
Name of the Active Metabolite (IUPAC Name or Synonym)	Chemical Structure or Molecular Formula (PubChem CID)	Part of the Plant, the Botanical Name of the *Strobilanthes* Plant, Collected in, and the Extraction Method	Total Flavonoid Content (TFC)	Total Phenol Content (TPC)	Reference
Taraxerone Synonym: D-Friedoolean-14-en-3-one 	$C_{30}H_{48}O$ (PubChem CID 130962)	The leaves of *Strobilanthes crispus* were obtained from a commercial supplier in Penang, Malaysia. The air-dried leaves were extracted sequentially with hexane, dichloromethane, and MeOH, and purified by chromatographic techniques. The structures of the compounds were elucidated with IR, GC-MS, MS, 1H-, and 13C-NMR, and compared with published data.			[9]

Notes: Molecules are visualized in a 3D stick model, without showing the hydrogen atoms. Grey sticks represent carbon atoms; red sticks represent oxygen atoms; blue sticks represent nitrogen atoms.

Abbreviations: BAP, 6-enzylaminopurine; BuOH, butanol; CC, column chromatography; $CHCl_3$, chloroform; DMSO, dimethyl sulfoxide; 1H–1H COSY, homonuclear correlation spectroscopy; EtOAc, ethyl acetate; EtOH, ethanol; GAE, gallic acid equivalent; GC, gas chromatography; GC-MS, gas chromatography-mass spectroscopy; HPLC, high-performance liquid chromatography; HPLC-ESI-QToF-MS/MS, high-performance liquid chromatography-electrospray ionization-quadrupole time-of-flight-mass spectrometry/mass spectrometry; HS-SPME, headspace solid-phase microextraction; IR, infrared; MAE, microwave-assisted extraction; MeOH, methanol; MS, mass spectrometry; NAA, 1-naphthaleneacetic acid); 1H-NMR, proton-nuclear magnetic resonance; 13C-NMR, carbon-nuclear magnetic resonance; QE, quercetin equivalent; RE, rutin equivalent; SC-CO2, super critical carbon dioxide; TLC, thin layer chromatography; UHPLC, ultra-high performance liquid chromatography; UV, ultra-violet.

The phytochemical profile analysis of the leaves from Seremban, Malaysia, revealed a TPC ranging between 10.87 and 12.22 mg GAE/g extract, phytosterols such as α-tocopherol ($C_{29}H_{50}O_2$), campesterol ($C_{28}H_{48}O$), desmosterol ($C_{27}H_{44}O$), lanosterol ($C_{30}H_{50}O$), β-sitosterol ($C_{29}H_{50}O$), and stigmasterol ($C_{29}H_{48}O$), volatile compounds such as 2-hexen-1-ol ($C_6H_{12}O$), 2-hexenal ($C_6H_{10}O$), 1-octen-3-ol ($C_8H_{16}O$), and benzaldehyde (C_7H_6O), and terpenoids such as linalool ($C_{10}H_{18}O$), p-cymene ($C_{10}H_{14}$), limonene ($C_{10}H_{16}$), eucalyptol ($C_{10}H_{18}O$), and isopulegol ($C_{10}H_{18}O$).[8] Three compounds, namely 1-heptacosanol ($C_{27}H_{56}O$), tetracosanoic acid ($C_{24}H_{48}O_2$), and stigmasterol ($C_{29}H_{48}O$), were isolated from the hexane extract of air-dried leaves of *S. crispus* collected in Malaysia. Four fatty acid esters, namely β-amyrin ($C_{30}H_{50}O$), and terpenoids, namely taraxerone ($C_{30}H_{48}O$) and taraxerol ($C_{30}H_{50}O$), were found in the dichloromethane extract, and 4-acetyl-2,7-dihydroxy-1,4,8-triphenyloctane-3,5-dione and stigmasterol β-D-glucopyranoside were present in the methanol extract.[9] Fresh leaves and stems of *S. crispus* collected in Sabah, Malaysia, contained squalene, vitamin E ($C_{29}H_{50}O_2$), γ-sitosterol ($C_{29}H_{50}O$), and campesterol ($C_{28}H_{48}O$),[10] while the leaves collected from Bertam Ulu, Melaka, Malaysia, contained a TPC of 159.85 mg GAE/g extract and TFC of 955.47 mg rutin equivalent (RE)/g extract. HPLC-ESI-QToF-MS/MS identified 20 polyphenolic compounds, among which were bidenoside B ($C_{24}H_{30}O_{10}$), torosaflavone C ($C_{21}H_{20}O_8$), euchrenone b3 ($C_{27}H_{26}O_7$), lupinisol C ($C_{25}H_{26}O_7$), and xanthoangelol C ($C_{22}H_{22}O_5$).[11] The leaves harvested at the Horticulture Unit of University Putra Malaysia contained potassium, calcium, sodium, iron, and phosphorus minerals and vitamins such as vitamin C ($C_6H_8O_6$), B1 ($C_{12}H_{17}N_4OS$), and B2 ($C_{17}H_{20}N_4O_6$).[12] Another study on the proximate and mineral composition of *S. crispus* collected in Malaysia revealed 4.2% total ash, 4.6% fiber, less than 0.1% fat, 2.9% protein, 25.6 kcal/100 g energy, and 81.6% moisture. Potassium and calcium minerals were found to be abundant, at 295 mg/100 g and 176 mg/100 g, respectively.[13] *S. crispus* leaves harvested from the same horticulture unit contained apigenin ($C_{15}H_{10}O_5$), catechin ($C_{15}H_{14}O_6$), kaempferol ($C_{15}H_{10}O_6$), naringenin ($C_{21}H_{22}O_9$), epicatechin ($C_{15}H_{14}O_6$), rutin ($C_{27}H_{30}O_{16}$), myricetin ($C_{15}H_{10}O_8$), and luteolin ($C_{15}H_{10}O_6$).[14] The leaves of *S. crispus* collected at Kuching, Sarawak, Malaysia, extracted using ethanol, revealed a TPC of 1.88 mg GAE/g and TFC of 0.25 mg RE/g defatted extract.[17]

Intriguingly, another species, *S. urens*, collected from Kalgi village, Kalaburagi District, Karnataka, India, also showed promising nutritional composition, including 28.62% protein, 17.85% carbohydrates, 12.0% lipids, 14.26% total ash, and 2.35% moisture content. The TPC in the extracts ranged from 199.25 to 270.50 mg GAE/g extract, and TFC from 135.57 to 260.57 mg QE/g extract. Alkaloids and tannins were also present in the extracts.[15] The dry leaves of *S. kalimantanensis* from West Kutai, Kalimantan, Indonesia, were reported to contain a total ash content of 7.83%. Trans-anethole ($C_{10}H_{12}O$) was successfully isolated from the leaf extract at a concentration of 23.0% using a GC-MS analysis.[16] It should be taken into consideration that obtaining the phytochemical profiles is necessary, as many studies have reported a good correlation between the levels of phytochemicals of plant extracts and their biological activities.[27–29]

In vitro Biological Activity Studies

Radical-Scavenging Activity

S. crispus leaf extracts, regardless of the geographical location of plant harvesting, extraction methods, and solvents (ethanol, methanol, acetone, and chloroform), have been reported to exhibit strong radical-scavenging activity. Different reagents have been used to assay the radical-scavenging activity, such as 2,2′-azinobis-3-ethylbenzthiazoline-6-sulfonic acid (ABTS), ferric-reducing antioxidant power (FRAP), Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), and 2,2-diphenyl-1-picrylhydrazyl (DPPH).[7,8,11,13,17] Free radicals have dual effects: (1) in physiological cell signaling pathways that regulate vascular tone, immune response, and apoptosis; and (2) cause numerous degenerative diseases such as cancer, acute inflammation, hypertension, diabetes mellitus, acute kidney injury, atherosclerosis, Alzheimer's disease and Parkinson's disorders, aging, and cardiovascular disorders. The radical-scavenging properties of plant antioxidants contribute to the inhibition of excessive lipid oxidation and the prevention of cell damage in the body.[30,31]

Anticancer Activity

The anticancer activity of *S. crispus* leaf extract, collected from different geographical locations, was confirmed in innumerable human cancer cells, such as the human cervical cancer cells (HeLa),[7] human breast cancer cells MD

Anderson-Metastatic Breast-231 (MDA-MB-231),[32–36] human breast cancer cells (MCF-7),[36] human breast cancer cells (T47D),[36] human colorectal adenocarcinoma cells (HT29),[34] human cervical cancer cells (C33A),[36] human colorectal carcinoma cells (HCT116),[36] human monocytic leukemia (U937),[36] human liver cancer cells (HepG2),[33] human liver cancer cells (SNU-182, SNU-449),[36] human ovarian epithelial cancer cells (OVCAR-5, PA-1, SK-OV-3)[36] human uterine cancer cells (MES-SA/DX5),[36] and mouse breast cancer cells (4T1).[37] Additionally, the plant extract was also studied for its anti-carcinogenesis activity via inhibition of CYP3A4 and CYP2E1, the subfamilies of cytochrome P450 that play a vital role in metabolizing drugs, toxins, and endogenous compounds.[38] The key factor in the development of cancer is cellular oxidative stress. The accumulation of intracellular reactive oxygen species (ROS) may lead to deoxyribonucleic acid (DNA) damage, instigate inflammatory responses, impede cellular homeostasis, and eventually cause carcinogenesis.[39]

Anti-Inflammatory, Immunomodulatory, and Wound-Healing Activities

The anti-inflammatory, immunomodulatory, and wound-healing activities of *Strobilanthes* species extract have been reported in two articles. In the first article, *S. crispus* leaves collected at Kuching, Sarawak, Malaysia, which were extracted using ethanol, were co-incubated with the pseudo-wound in OUMS-36T-4F human fibroblast cells, revealing a full recovery of the wound after 24 h of incubation.[17] Another species, *Strobilanthes cusia*, which was collected in Putian City, Fujian Province, China, and extracted with MeOH, contained indole alkaloids, indigodoles A, C, and D, and has shown inhibition towards interleukin 17A (IL-17A) production during the polarization of T helper cells 17 (Th17) at an EC_{50} of 2.16 μg/mL, or after the polarization at an EC_{50} of 5.99 μg/mL, without cytotoxicity towards Th17 cells.[40] Recent investigations have associated Th17/IL-17 with systemic autoimmune diseases, including their role in metabolic dysfunctions, where an excessive pathogenic Th17 cell population and a suppression in CD69+ T regulatory cells intensify low-grade inflammatory conditions.[41] Dysregulation of Th17 cell responses serves as a basis of multiple inflammatory and autoimmune diseases. More specifically, Th17 cells are regulated by IL-17A, which attaches to its binding site on Th17 cells, activating the intracellular nuclear factor-kappaB (NF-κB) signaling pathway and subsequently stimulating the production of IL-24.[42]

Antidiabetic Activity

The antidiabetic activity of *Strobilanthes* species extract has been reported in two studies, although not in *Strobilanthes crispus* or *Strobilanthes cusia*. In the first article, the whole plant of *S. glutinosus* was collected in Abbottabad, Pakistan, extracted using methanol, and fractionated with *n*-hexane, exhibiting a strong inhibitory potential against α-amylase and α-glucosidase.[43] Another species of *Strobilanthes*, as described in the second article, such as the fresh leaves of *S. cordifolia*, which were collected in the Salem district of Tamil Nadu, India, synthesized in iron and copper nanoparticles, also exhibited inhibitory effects on α-amylase and α-glucosidase enzymes,[44] thus confirming the antidiabetic effects of the genus *Strobilanthes* plants. These two enzymes, α-amylase and α-glucosidase, are involved in the degradation of carbohydrates into monosaccharides and disaccharides, leading to an elevation in blood glucose level.[45]

Antimicrobial Activity

S. crispus and *S. cusia* extracts have been reported to have inhibitory activity against various bacteria, such as *Pseudomonas aeruginosa, Streptococcus pneumoniae, Staphylococcus aureus, Streptococcus mutans*, and *Escherichia coli*, against the human coronavirus NL63 (HCoV-NL63), and against the influenza virus. A study reported that *S. crispus* leaves collected at Kuching, Sarawak, Malaysia, exhibited antibacterial properties against *P. aeruginosa* on Mueller–Hinton agar.[17] In another study, the leaves of *S. cusia* were harvested from Guangdong, China, and demonstrated antibacterial effects against clinical penicillin-resistant *S. pneumoniae* (PRSP) by disrupting cell wall integrity and capsule thickness of the PRSP. Tryptanthrin, an indole alkaloid isolated from the leaf extract, showed the potential to effectively inhibit PRSP F3983 with an MIC of 25 μg/mL. The MIC value of the ethanol extract of the leaves against *S. aureus* ATCC 29213 and *S. pneumoniae* ATCC 49619 was 100 μg/mL and 200 μg/mL.[46] Tryptanthrin isolated from *S. cusia* leaf was also reported in another study to prevent human coronavirus NL63 (HCoV-NL63) replication by blocking viral ribonucleic acid (RNA) genome synthesis and papain-like protease 2 activity.[47] The antibacterial activities of

synthesized *S. crispus*-mediated silver nanoparticles (SC-AgNPs) against *Streptococcus mutans, Escherichia coli*, and *P. aeruginosa* were also reported.[48] Furthermore, strobilanthes A, an isocoumarin metabolite which has been isolated from *S. cusia* cultivated in Guizhou, China, exhibited anti-influenza virus activity in vitro.[49]

Other in vitro Pharmacological Activity Studies

Antiplatelet aggregation using collagen-induced aggregation in human whole blood and the blood coagulation effects of *S. crispus* collected from the National University of Singapore (NUS) medicinal plant garden were recently reported by Zareisedehizadeh et al (2025). These findings are beneficial for preventing heart attacks and ischemic stroke.[50] Intriguingly, a low probability of inhibition by *S. crispus* on CYP2B6, CYP2C19, CYP2D6, and CYP3A4, the cytochrome P450 subfamilies involved in tamoxifen metabolism, was reported. These findings confirm the potential of *S. crispus* as an adjuvant for breast cancer treatment.[51]

In vivo Biological Activity Studies

Anticancer and Chemopreventive Activity

In accordance with the in vitro anticancer results of *S. crispus* leaf extract, the in vivo anticancer properties of *S. crispus* were reported in four articles as follows:

S. crispus leaf extract showed protection against colorectal cancer by inhibiting oxidative damage and the following apoptotic cascade, decreasing total colonic aberrant crypt foci formation, malondialdehyde (MDA), and lactate dehydrogenase (LDH), increasing superoxide dismutase (SOD), upregulating adenomatous polyposis coli (*APC*), BCL2 associated X (*Bax*), and solute carrier family 24 member 3 (*Slc24a3*), and downregulating defensin alpha 24 (*Defa24*) and *Bcl*-2 in azoxymethane-induced rats.[32] *S. crispus* exhibited antitumorigenic immunogenicity by inducing a significant increase in major histocompatibility complex (MHC) class I and class II molecules, $CD4^+$, $CD8^+$, and IL-2^+ cells infiltration, and decreasing the number of $CD68^+$ macrophages in the 4T1 cell-induced mammary carcinoma mouse model.[37] The active fraction of *S. crispus* containing lutein and β-sitosterol was described to significantly suppress the total tumor burden and secondary tumor development in metastatic breast cancer without significant toxicities in the 4T1-induced mouse mammary carcinoma model. Histomorphological examination confirmed the safety of the *S. crispus* fraction.[52] The in vivo anticancer activity of *S. crispus* leaves harvested in Malaysia was further confirmed in a study by activating the immune system in rats bearing N-methyl-N-nitrosourea (NMU)-induced mammary tumors, and additionally supports the traditional use of *S. crispus* leaves to boost the immune system.[53] Signaling pathways that are responsible for proliferation, cell cycle arrest, apoptosis, and angiogenesis are thought to be connected with the actions of phytochemicals, such as phenolics, flavonoids, alkaloids, and terpenoids contained in the leaves.[54]

Antidiabetic Activity

The antidiabetic properties of *Strobilanthes* leaf extract were reported in four studies, two of which were those of *S. crispus*, and the other two were those of *S. sarcorrhiza* and *S. cuspidata*. One study described that *S. crispus* leaves collected in Pulau Penang, Malaysia, increased lipolysis and fat oxidation in obese mice fed high-fat and low-fat diets, without altering food intake, body weight, and abdominal adipose tissue weight.[55] Additionally, *S. crispus* leaves collected in Yogyakarta, Indonesia, at a dose of 16.8% extract/day for 14 days of administration significantly reduced blood glucose levels and improved the lipid profiles in streptozotocin (STZ)-induced diabetes in rats.[56]

Intriguingly, the root of another *Strobilanthes* species procured in Panan, China, namely *S. sarcorrhiza*, demonstrated a prevention of diabetic nephropathy in STZ-induced mice by regulating NF-kappaB/IL-1β signaling pathway and glycerophospholipid metabolism. *S. sarcorrhiza* root extract normalized blood glucose and lipid levels, reduced ALT, creatinine, urea, IL-1β, and IL-17 in the serum, improved pathological damage and fibrosis in the kidneys, and suppressed vascular endothelial growth factor (VEGF), laminin, TNF-α, and NF-kappaB expression in kidney tissue.[57] *S. cuspidata* leaves collected at Niligiris, India, at doses of 150 and 300 mg/kg body weight significantly reduced the blood glucose level within 60 min after a glucose load in normoglycemic rats. After 14 days of daily treatment with the

extract at a dose of 150 and 300 mg/kg body weight, a significant dose-dependent decrease in blood sugar levels was observed by 38 and 41%, respectively.[58]

Other in vivo Pharmacological Activity Studies

Only one article has described the in vivo anti-inflammatory activities of the *Strobilanthes* plants, but none in *S. crispus* or *S. cusia*. The anti-inflammatory and anti-arthritic activities of lupeol and 19α-H lupeol isolated from *S. callosus* and *S. ixiocephala* roots have been reported in India;[59] however, this publication has not been indexed in the PubMed and Scopus databases. The hepatoprotective activity of *S. kunthianus* obtained from Nilgiris, India, has also been reported.[60] In this study, the methanol extract of *S. kunthianus* normalized the levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, triglyceride, total cholesterol, total bilirubin, and thiobarbiturate-reacting substances, and increased the levels of creatinine, total protein, albumin, catalase, and superoxide dismutase in serum in carbon tetrachloride-induced hepatotoxicity in Wistar albino rats.[60]

In silico Biological Activity Studies

Few studies have described the in silico biological activity of phytochemicals in *Strobilanthes* plants. In one study, six phytochemicals obtained from GC-MS analysis, namely lupeol, beta-amyrin, stigmasterol, gamma sitosterol, 9,12-octadecadienoic acid, and *n*-hexadecanoic acid, were molecularly docked towards α-glucosidase and α-amylase enzymes, and their binding affinities were compared to the standard acarbose. This study revealed that β-amyrin, stigmasterol, and sitosterol bind strongly to α-glucosidase and α-amylase, leading to their potential in altering carbohydrate degradation.[43] In another article, tryptanthrin isolated from the leaf extract was reverse-docked to 623 target proteins obtained from the database of *S. pneumoniae*, resulting in 63 top proteins, among which β-galactosidase, acetylglucosaminidase, β-hexosaminidase, and α-fucosidase were selected. To provide sufficient space for ligand-free movement, the grid boxes of the molecular docking simulation were constructed to completely cover the binding pockets of *S. pneumonia* proteins. Tryptanthrin occupies the binding pockets of these four proteins by building hydrogen bonds or aromatic stacking interactions, thus confirming its antibacterial properties by disrupting the growth of *S. pneumoniae*.[46]

Metabolites and Their Mechanism of Action

Strobilanthes crispus and *S. cusia* are known for their metabolites, including alkaloids, fatty acids and derivatives, flavonoids and flavonoid glycosides, phenolic acids, sterols, and terpenoids.[7–18] These bioactive metabolites contribute to the plants' wide range of biological and pharmacological effects.

One of the bioactive metabolites, namely tryptanthrin, which is a natural, indolo-quinazoline alkaloid primarily isolated from *S. cusia*, has been reported for its strong cytotoxicity against tumor and microbial cells. This alkaloid and its derivatives inhibit the cell cycle of tumor cells from the G_1 phase to the S phase.[61] Tryptanthrin also exhibits antimicrobial, anti-inflammatory, anticancer, antiviral, antiparasitic, antiallergic, and antioxidant.[62–64] Flavonoids have been known for their capability to interact with bacterial proteins and nucleic acids, causing denaturation and inhibition of metabolic processes, and disruption of cell membrane synthesis.[65] Flavonoids inhibit the growth of numerous pathogenic microorganisms, including multidrug-resistant bacteria. The hydroxylation of C5, C7, C3′, and C4′, and geranylation or prenylation at C6 are attributed to the antibacterial activity.[66] Most flavonoids exhibit antioxidant activity because of their stable backbone structure. However, the hydroxyl substituents in positions 2' and 6' in ring B, and in positions 3 and 5 with the carbonyl substituent in C4, and the double bond between C2 and C3 with the carbonyl in C4, further strengthen the antioxidant properties.[67–69] Moreover, the most abundant phytosterol (β-sitosterol) and fatty acid (α-linolenic acid) in *S. crispus* have shown a strong antioxidant activity.[8]

Pharmacokinetics

The pharmacokinetics profile of *Strobilanthes* plants has been described for one of their bioactive phytochemicals, namely tryptanthrin. Tryptanthrin has been studied in male Sprague-Dawley rats administered intravenously at a dose of 2 mg/kg body weight. Tryptanthrin showed a half-life (T1/2) of 40.63 ± 6.66 min and a clearance of 1.00 ± 0.36 L/h/kg, suggesting a fast distribution and clearance.[70] Additionally, oral administration of tryptanthrin at a dose of 100 mg/kg

body weight in rodents revealed that its accumulation is at a higher concentration in the liver than in other tissues. Tryptanthrin was also found to be deposited in the kidneys, lungs, heart, and spleen, but not in the brain, under the experimental conditions.[71] In rats, tryptanthrin underwent a Phase 1 metabolism, as proven by its metabolite, showing mono-hydroxylated on the aromatic ring of the indole moiety of protonated tryptanthrin, structurally confirmed as 8-hydroxytryptanthrin.[72]

Toxicity Assays

Only one article published between 2015 and 2025 reported that a sub-acute oral toxicity assay of the ethanol extract of *S. crispus* leaves was performed in young female Sprague Dawley rats. The rats were orally administered a single dose of 150, 300, or 600 mg/kg body weight of the extract for 14 consecutive days. This investigation confirmed the safety of the extract up to the highest dose of 600 mg/kg body weight, as indicated by the absence of adverse effects or death, no significant changes in serum biochemical parameters, and no damage to the liver and kidneys.[73]

Human Studies and Case Reports

Unfortunately, there are very limited human studies and case reports on *Strobilanthes* extracts indexed in the PubMed and Scopus databases. In fact, only one systematic review and meta-analysis study reported the evidence and potential mechanism of action of *S. cusia* and its active components in the treatment of psoriasis. In their study, Wang et al (2024) included 26 clinical trials comprised six interventions in the form of *S. cusia* decoctions and Chinese herbal medicine. The Psoriasis Area and Severity Index (PASI) score was considered an indicator of the effectiveness of psoriasis treatment; however, the original articles sourced in this systematic review and meta-analysis study were found to be written in Chinese.[74] Meanwhile, the other plant, *S. crispus*, is widely used in Indonesia and Malaysia by directly consuming fresh leaves or boiling them in water to cure numerous ailments, such as diabetes mellitus, kidney stones, high blood pressure, and constipation.[75,76]

Limitations of the Study and Future Perspectives

Although this review provides a profound understanding of the potential therapeutic effects of two *Strobilanthes* plants, namely *S. crispus* and *S. cusi*a, some limitations were identified during the analysis, such as (1) the fact that there was variability in extraction methods, solvents, and experimental conditions across studies, shows a lack of standardized protocol, and (2) that all data described in the articles were primarily derived from in vitro and in vivo studies, thus may not fully translate to human physiology. Furthermore, animal studies only covered a limited or minimum sample size, different rodent species or strains, such as rats or mice, Wistar or Sprague-Dawley rats, and the heterogeneity of sex used, thus resulting in varying observed effects between sexes caused by hormonal factors such as estrogen. As a serendipitous outcome, only one article reported a sub-acute oral toxicity study, thus unlocking further toxicity studies, such as acute oral single-dose toxicity, sub-chronic oral multiple-dose toxicity, and chronic oral toxicity. In addition, the variety of geographical locations for plant harvesting, extraction methods, solvents used, and mechanisms by which phytochemicals exert their biological properties requires more in-depth exploration to provide data supporting clinical settings and to confirm therapeutic benefits in humans. From a future perspective, clinical trials to bridge the gap between preclinical findings and human applications will validate the pharmacological activity, efficacy, and safety, particularly in vulnerable populations such as pediatric and geriatric patients with comorbidities. Investigations should focus on various demographic populations, considering factors such as age, ethnicity, and sex, in relation to hormonal status, pharmacodynamics, and pharmacokinetics, to clearly understand how these variables influence treatment outcomes.

Conclusion

This study clarifies the multifaceted roles of *Strobilanthes crispus* and *Strobilanthes cusia* in alleviating various disorders. Our review of articles published between 2015 and 2025 confirms that these two *Strobilanthes* plants are still being investigated globally, with the most studied being their leaves, as the active parts. Ethanol and methanol are the commonly used solvents for extraction, and room temperature is a popular choice. More than 100 metabolites have been reported to be present in *Strobilanthes crispus* and *Strobilanthes cusia*, including alkaloids, fatty acids and derivatives,

flavonoids and flavonoid glycosides, phenolic acids, sterols, and terpenoids. One of the bioactive metabolites, namely tryptanthrin, has shown a strong cytotoxicity against tumor and microbial cells, and the flavonoids and phytosterols exhibited antibacterial and antioxidant properties. Considering the noteworthy findings from preclinical studies, which point to *S. crispus*, this plant may be established as a plant-based antimicrobial, anti-inflammatory, anticancer, or hypoglycemic agent. As only one article reported a sub-acute oral toxicity study, further toxicity studies are necessary to confirm its safety. Despite promising pharmacological evidence, we cannot locate human studies during the selected publication period; however, several articles describing ethnopharmacological surveys of medicinal plants in China, Malaysia, and Thailand were found, among which *Strobilanthes* plants were used as colorants, edible plants, and natural medicines for cattle, which is not related to the results of preclinical pharmacological activity assays. The lack of human studies presents challenges in determining its safety, dosage, and long-term effects. Further clinical trials will validate pharmacological activity, efficacy, and safety, and confirm its potential as a therapeutic agent.

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Disclosure

The authors declare no potential conflicts of interest regarding the study, authorship, or publication of this article.

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