REVIEW ARTICLE

A C G publications

Rec. Nat. Prod. X:X (202X) XX-XX

records of natural products

Traditional Uses, Phytochemistry and Pharmacological Properties of *Strobilanthes crispa* (L.) Blume.

Chee-Shien Chen [1], Siow-Ping Tan [1]*, Chui-Fung Loke [2] and Tze-Ven Poh [3]

[1]*Physical Science, Faculty of Applied Sciences, Tunku Abdul Rahman University of Management and Technology, 53300 Kuala Lumpur, Malaysia*

[2]*Research & Development and Commercialization, Tunku Abdul Rahman University Management and Technology, 53300 Kuala Lumpur, Malaysia*

[3]*Department of Computer Science and Embedded Systems, Faculty of Computing and Information Technology, Tunku Abdul Rahman University Management and Technology, 53300 Kuala Lumpur, Malaysia*

(Received May 14, 2023; Revised June 14, 2023; Accepted June 18, 2023)

Abstract: *Strobilanthes crispa* (L.) Blume (*S. crispa*) is a folklore medicinal plant of the genus *Strobilanthes* (Acanthaceae), traditionally used in Malaysia and Indonesia to treat various diseases such as breast and uterine cancers, diabetes mellitus, hypertension, gastrointestinal and kidney diseases, typhoid, jaundice, piles, high cholesterol, and ulcers. Several studies have shown that *S. crispa* contains a variety of phytochemicals, including terpenoids, flavonoids, phenolic compounds, sulfur-containing, steroids, chlorophylls, benzofuran, fatty acids, and other simple metabolites. Furthermore, based on its traditional uses, *S. crispa* has demonstrated a wide range of *in vitro* and *in vivo* pharmacological activities. These activities include antihyperglycemic, antioxidant, antimicrobial, wound healing, anticancer, anti-trypanosomal, anti-inflammatory, anti-obesity, anti-urolithiatic, anti-angiogenic, and vasorelaxant activity. The paper aims to provide a comprehensive review of the current understanding of traditional use, toxicity, phytochemicals, and pharmacological studies of *S. crispa*, thereby validating its ethnopharmacological applications and exploring possible research opportunities.

Keywords: *Strobilanthes crispa*; Acanthaceae; traditional uses; phytochemistry; pharmacology. © 2023 ACG Publications. All rights reserved.

1. Introduction

Strobilanthes is the second largest genus in the family Acanthaceae after Justicia, derived from the Latin words "strobilus" (cone) and "anthos" (flower or shoot) [1-6]. The genus was first described by Blume [7] based on specimens collected in West Java. It comprises approximately 350 species of

* Corresponding author: E-Mail: tansp@tarc.edu.my; Phone:+603 4145 0123 (ext 3717)

The article was published by ACG Publications
http://www.acgpubs.org/journal/records-of-natural-products Month-Month 202x EISSN:1307-6167
DOI: http://doi.org/10.25135/rnp.402.2305.2785
Available online: July 19, 2023

perennial flowering herbs and shrubs, primarily native to tropical Asia. Among them, at least 46 species are native to India, while around 32 species are found in southern China, including regions such as Xizang, Sichuan, Yunnan and Guangxi. Some species extend further north into temperate Asia [3-5, 8-10]. Notably, the genus is predominantly found in Kashmir, Bhutan, Bangladesh, and the Khasi range in northeastern India [10]. In fact, *Strobilanthes* is distinguished from other members of the Acanthaceae by a variety of floral characteristics, including filaments that are joined to form a membranous sheath and a bifid stigma with a smaller posterior lobe [6]. It is distributed throughout tropical South and Southeast Asia, with about 16 Malesian species, including *Strobilanthes bilabiata* J. R. I. Wood, *S. fragrans* J. R. I. Wood, and *S. trichantha* J. R. I. Wood from Thailand, *S. borii* J. R. I. Wood, and *S. parvifolia* J. R. I. Wood from India, *S. chrysodelta* J. R. I. Wood, *S. muratae* J. R. I. Wood, *S. ramulosa* J. R. I. Wood, *S. tanakae* J. R. I. Wood, and *S. wardiana* J. R. I. Wood from Burma, *S. disparifolia* J. R. I. Wood from Laos, *S. fusca* J. R. I. Wood from the Philippines, *S. longipedunculata* Terao ex J. R. I. Wood from Vietnam, *S. longistaminea* J. R. I. Wood and *S. pusilla* J. R. I. Wood from Indonesia and *S. orientalis* J. R. I. Wood from East Timor [2]. Traditionally, many plants within this genus have been used as traditional remedies by local populations due to their wide range of therapeutic potential and clinical value [10-11].

Strobilanthes crispa (L.) Blume (*S. crispa*), with its local name “Pecah kaca” [12-13], English name “yellow *Strobilanthus*” [14], and Chinese name “黑面将军” [15], has a long history of traditional use in Malaysia and other countries for treating various diseases, including cancer, gastrointestinal and kidney diseases, diabetes mellitus, and hypertension. According to Kew's taxonomic resource at https://science.kew.org/, *S. crispa* is the accepted scientific name of the plant referred. The name was first published in 1826 [7]. It is worth noting that some individuals refer to the plant as. However, the name *Strobilanthes crispus* is not listed on the Plant List website. Other scientific names such as *Sericocalyx crispus* (L.) Bremek, *Ruellia crispa* L., and *Hemigraphis crispa* (L.) T.Anderson, are considered synonyms. Several studies have revealed that *S. crispa* contains a variety of phytochemicals, including terpenoids, flavonoids, phenolic compounds, sulfur-containing, steroids, chlorophylls, benzofuran, fatty acids, and other simple compounds. In addition, modern pharmacological studies have shown that *S. crispa* has a wide range of pharmacological activities, consistent with its traditional uses. These activities encompass antihyperglycemic, antioxidant, antimicrobial, wound healing, anticancer, anti-trypanosomal, anti-inflammatory, anti-obesity, anti-urolithiatic, anti-angiogenic and vasorelaxant activity.

In the literature, many studies have reported the modern pharmacological effects of *S. crispa.* Three reviews focusing on *S. crispa* have already been published [16-18]. However, these reviews have certain limitations, such as incomplete data collection and a less rigorous review process that mainly involves compilation of data from pharmacological studies. Therefore, there is a critical need for a comprehensive review of *S. crispa* that thoroughly examines the existing literature and fill the gaps in the research field. This paper aims to address this need by providing a comprehensive review covering the traditional uses, phytochemical studies, pharmacological properties, and toxicity studies of *S. crispa*, as well as the study limitations are discussed. Therefore, the findings of this review will serve as a valuable reference for future research endeavors and application across various fields.

2. Method

The present review on the botanical distribution and descriptions, traditional uses, phytochemistry, pharmacological activity, and toxicity of *S. crispa* are based on several popular databases such as PubMed, Scopus, Web of Science, SciFinder, ScienceDirect, Google Scholar, journals, and books. The literature was searched and accessed using the keywords ‘*Strobilanthes crispa*’, ‘*Strobilanthes crispus*’, ‘*Sericocalyx crispus’,* ‘*Ruellia crispa*’ and ‘*Hemigraphis crispa*’ that related to the present review. Additionally, some information was collected from classic books and official websites. The Plant List (http://www.theplantlist.org), Kew Science database (https://science.kew.org/), International Plant Name Index database (http://www.ipni.org), and Flora of China database (http://www.iplant.cn/foc) were used to comprehensively understand the botanical characteristics of this plant.

3. Botanical Distribution and Description

As shown in Figure 1, *S. crispa* is a shrubby plant that can reach a height of up to 2 meters. It features segmented, round, branched, and hairy green stems. The leaves are short-stemmed and oblong-lanceolate, measuring 9 to 18 cm in length and 3 to 6 cm in width. Besides, the yellow flowers of *S. crispa* have five-funnel-shaped petals and are arranged in short, dense panicles. Each of the ribbon-shaped fruit contains 2 to 4 brown, round, flat seeds. In fact, this plant can be easily propagated through stacking. Various researchers have provided detailed descriptions of this plant [16-24]. According to Kew's taxonomic resource available at https://science.kew.org/, *S. crispa* is native to the region spanning from Jawa to the Lesser Sunda Islands (Figure 2). Presently, it is categorized as a woody shrub [14] that is distributed across different areas in Madagascar and the Malay Archipelago [17, 20, 25] (Brunei, Indonesia, East Malaysia, Papua New Guinea, and the Philippines [26]) at altitude ranging from 50 to 1,200 m [18, 23]. In fact, the plant often grows on riverbanks or in abandoned fields, and some Javanese use it as a fence hedge [17, 19, 22, 27]. Furthermore, it can also be found in shaded terrains, particularly in areas with strong monsoons in eastern Indonesia, as well as in coconut orchards, along roadsides, and within wooded areas [21, 28]. The local name and its respective regions are listed in Table 1.

Figure 1. Images of leaves (by the authors) and flowers by Kwan Han [88] of *S. crispa*.

Figure 2. Distribution of *S. crispa* [29].

Table 1. Different local names of *S. crispa*

Region/Country	Common name	Reference
Jakarta	Daun pecah beling, daun picah beling	[13, 20, 28, 30]
Java	Enyoh kilo, enyohkelo, kecibeling, kejibeling, ngokilo	[10, 13, 20, 25, 30-31]
Malaysia	Pecah kaca, jin batu, pecah beling, bayam karang	[10, 12-13, 27, 32]
China	黑面将军 Hei Mian Jiang Jun (Black face general)	[10, 15, 33]

4. Traditional Uses

S. crispa is a folklore medicinal plant traditionally used in Malaysia and Indonesia to treat a wide range of illnesses. These include breast and uterine cancers, diabetes, hypertension, gastrointestinal and kidney diseases [20, 27, 34], typhoid [23], jaundice, piles, high cholesterol and ulcers [35]. This plant can be eaten fresh, mixed with other herbs, or made into an herbal tea by boiling the fresh leaves in water for 15 to 20 minutes [12, 27]. In fact, *S. crispa* contains many calcium carbonate cystoliths [12]. The high calcium carbonate content makes the boiled water of this plant slightly alkaline, facilitating urination [27]. Moreover, due to its ability to dissolve calcium and magnesium salts in kidney stones [35], traditional treatments for kidney stones include decocting the leaves [36] or applying heated leaves on the hips [37]. In Indonesia, a leaf decoction is also effective in treating diarrhoea [38]. In addition, Roosita et al. [39] reported that the Sundanese villagers in West Java used *S. crispa* for hepatitis and postpartum remedies, while Samuel et al. [40] found that the aborigines in Kampung Bawong, Perak, West Malaysia masticated and ingested the fresh leaves of the plant to boost their immune systems. Furthermore, applying the macerated leaves of *S. crispa* topically to snakebite wounds can neutralize toxins, reduces pain, and alleviates swelling [20]. In fact, the consumption of *S. crispa* is not only used to treat various diseases, but also to prevent colds and flu, cancer and gallstones [15]. On the other hand, although *S. crispa* is well known in the local Chinese community in China, no folklore uses of this plant have been described in any databases.

5. Phytochemistry

Chemical composition analysis of leaves of *S. crispa* was carried out by Ismail et al. [22]. Their findings revealed that the leaves contained 69.30% moisture content and moderate amounts of carbohydrates (43.00%), fiber (13.90%), and protein (13.30%) [22]. In addition, the *S. crispa* leaves exhibited a high total ash content (21.60%) due to the high mineral content (10,900 mg potassium, 5,185 mg calcium, 2,953 mg sodium, 255 mg iron and 201 mg phosphorus per 100 g sample). Moreover, the leaves demonstrated a significant presence of water-soluble vitamins (C, B_1, and B_2), which may contribute to their high antioxidant activity [22]. Qualitative phytochemical screening of *S. crispa* was performed by Manaf and Daud [41], Fardiyah et al. [42] and Gul et al. [43]. The results showed the presence of alkaloids, tannins, flavonoids, saponins, terpenoids and steroids in alcoholic plant extracts. These findings are supported by Ismail et al. [22], who reported the presence of catechins (1.18%), alkaloids (3.20%), caffeine (0.01%), and tannins (1.00%).

A total of 136 compounds were identified from different types of *S. crispa* extracts using different qualitative and quantitative methods. A comprehensive summary of all the detected compounds is provided in Table 2. Only two studies [44-45] reported the isolation and elucidation of 11 compounds from *S. crispa* leaves using NMR and other spectroscopic analyses. These compounds include triterpenoids (taraxerol (**7**) and taraxerone (**8**)), a tetraterpenoid (lutein (**9**)), steroids (stigmasterol (**47**) and stigmasterol β-D-glucopyranoside (**48**))**,** chlorophylls (13^2-hydroxy-pheophytin a (**49**), pheophytin a (**50**), and 13^1-hydroxy-13^2-oxo-pheophytin a (**51**))**,** a fatty acid (tetracosanoic acid (**71**)), and some simple compounds (4-acetyl-2,7-dihydroxy-1,4,8-triphenyloctane-3,5-dione (**74**) and 1-heptacosanol (**95**)). All the reported compounds are listed in the *Dictionary of Natural Products*, except for the newly reported compounds **48** to **51.** The structures of all the isolated compounds are presented in Figure 3. However, most of the phytochemicals from *S. crispa* leaves are tentatively identified, primarily through GC techniques, including GC-MS [45-50] and GC-TOF-MS [51], as well as LC techniques, such as LC-QToF-MS/MS [52] and LC-ESI-MS [53], without further isolation and structural elucidation. Since

the resulting mass spectra obtained were only compared with those from published studies, it is highly recommended to isolate and elucidate the detected compounds for confirmation.

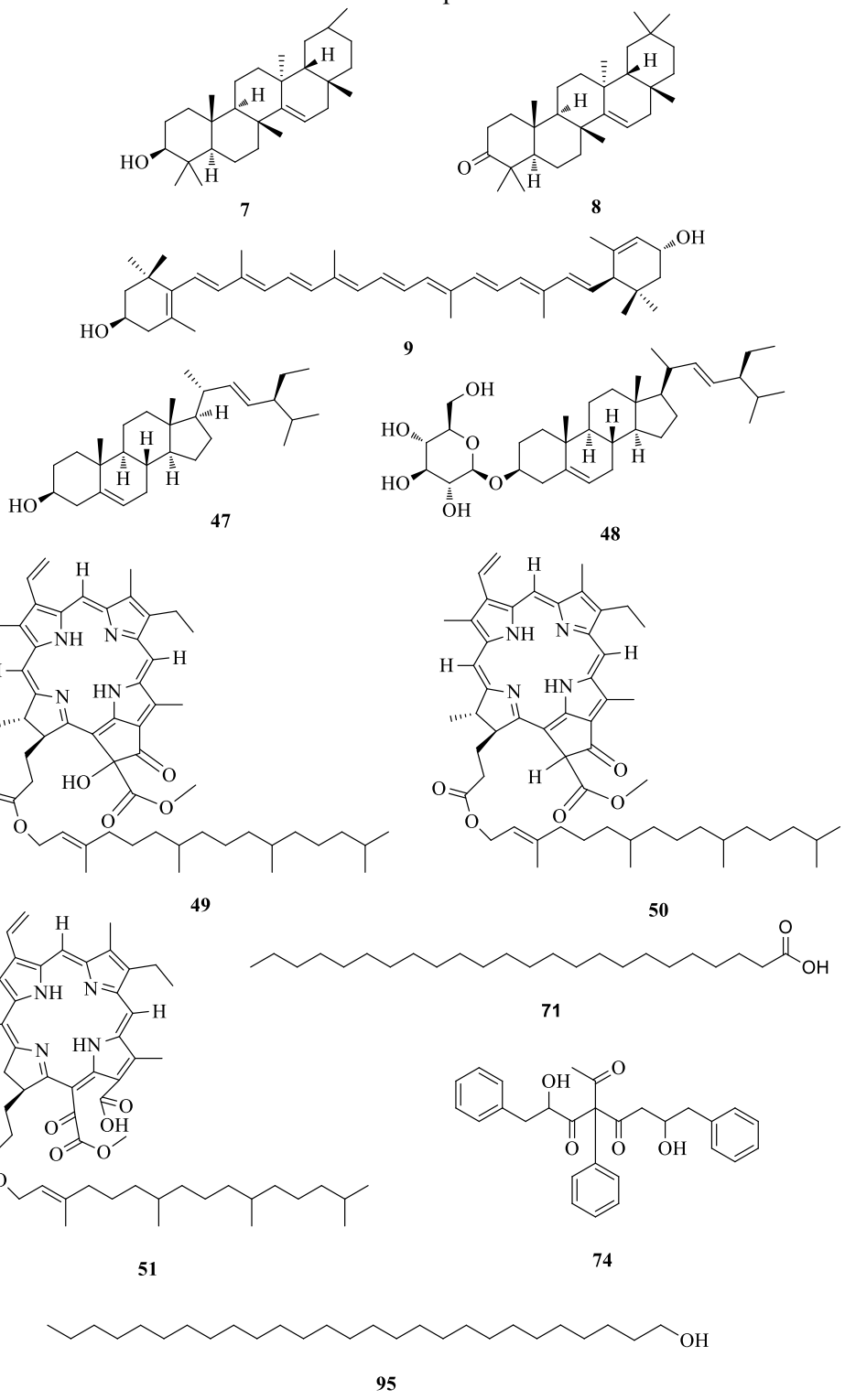

Figure 3. Structure of phytochemicals isolated from *S. crispa* leaves

Table 2. Secondary metabolites from *S. crispa*.

No.	Compounds	Molecular formula	Molecular weight (g/mol)	CAS	Identification method	References
Terpenoids						
Diterpenoid						
1	Phytol (3,7,11,15-Tetramethyl-2-hexadecen-1-ol)	$C_{20}H_{40}O$	296.53	7541-49-3	GC-MS, GC-TOF-MS	[46, 51]
Triterpenoids						
2	β-Amyrin	$C_{30}H_{50}O$	426.72	559-70-6	GC-MS	[48]
3	Betulin	$C_{30}H_{50}O_2$	442.72	473-98-3	GC-MS	[48]
4	Cycloartenol	$C_{30}H_{50}O$	426.72	469-38-5	GC-MS	[50]
5	Lupeol	$C_{30}H_{50}O$	426.72	545-47-1	GC-TOF-MS	[51]
6	Squalene	$C_{30}H_{50}$	410.72	111-02-4	GC-MS	[48-49]
7	Taraxerol	$C_{30}H_{50}O$	426.72	127-22-0	IR, GC-MS, NMR	[44]
8	Taraxerone	$C_{30}H_{48}O$	424.71	514-07-8	IR, GC-MS, NMR	[44]
Tetraterpenoid						
9	Lutein	$C_{40}H_{56}O_2$	568.87	127-40-2	Flash column chromatography, NMR	[45]
Sesquiterpenoids/Sesquiterpenes						
10	α-Cadinol	$C_{15}H_{26}O$	222.37	481-34-5	GC-MS	[46]
11	β-Humulene	$C_{15}H_{24}$	204.35	116-04-1	GC-MS	[48]
12	Ledol	$C_{15}H_{26}O$	222.37	577-27-5	GC-MS	[46]
13	Tau-muurolol	$C_{15}H_{26}O$	222.37	19912-62-0	GC-MS	[46]
14	2,6,10-Trimethyl pentadecane	$C_{18}H_{38}$	254.50	3892-00-0	GC-MS	[46]
Flavonoids						
15	Bidenoside B	$C_{24}H_{30}O_{10}$	478.18	-	LC-QToF-MS/MS	[52]
16	3,6-Dimethoxy-6”,6”-dimethyl-3’,4’-methylenedioxypyranol [2,3:7,8] flavone	$C_{23}H_{20}O_7$	408.12	-	LC-QToF-MS/MS	[52]
17	Euchrenone b3	$C_{27}H_{26}O_7$	462.17	-	LC-QToF-MS/MS	[52]
18	8-p-Hydroxybenzylquercetin	$C_{22}H_{16}O_8$	408.08	-	LC-QToF-MS/MS	[52]
19	5-Hydroxy-7,8-dimethoxyflavanone 5-rhamnoside	$C_{23}H_{26}O_9$	446.16	-	LC-QToF-MS/MS	[52]
20	Lupinisol C	$C_{25}H_{26}O_7$	438.17	-	LC-QToF-MS/MS	[52]
21	Patuletin 3-(6"-(E)-feruloylglucoside)	$C_{32}H_{30}O_{16}$	670.15	-	LC-QToF-MS/MS	[52]
22	Quercetin 3-(2'''-galloylglucosyl)-(1->2)-alpha-L-arabinofuranoside	$C_{33}H_{32}O_{20}$	748.15	-	LC-QToF-MS/MS	[52]
23	Quercetin 3-methyl ether 7-glucuronide	$C_{22}H_{20}O_{13}$	492.09	98751-52-1	LC-QToF-MS/MS	[52]

24	Quercetin 3-(6”-methylglucuronide)	$C_{22}H_{20}O_{13}$	492.09	-	LC-QToF-MS/MS	[52]
25	Quercetin 3-sophoroside-7-glucuronide	$C_{33}H_{38}O_{23}$	802.18	-	LC-QToF-MS/MS	[52]
26	Scutellarein 7-glucuronide-6-ferulate	$C_{31}H_{26}O_{15}$	638.13	-	LC-QToF-MS/MS	[52]
27	Torosaflavone C	$C_{22}H_{16}O_8$	408.08	-	LC-QToF-MS/MS	[52]
28	Veronicafolin 3-glucosyl- (1- >3)-galactoside	$C_{30}H_{36}O_{18}$	684.19	-	LC-QToF-MS/MS	[52]
29	Vitexin 2"-O-rhamnoside 6"-acetate	$C_{29}H_{32}O_{15}$	620.17	-	LC-QToF-MS/MS	[52]
Phenolic compounds						
30	2,4-Bis(dimethylbenzyl)-6-t-butylphenol	$C_{28}H_{34}O$	86.57	244080-16-8	GC-TOF-MS	[51]
31	2,4-Bis(1,1-dimethylethyl)-phenol	$C_{14}H_{22}O$	206.32	96-76-4	GC-TOF-MS	[51]
32	Eugenol	$C_{10}H_{12}O_2$	164.20	97-53-0	GC-MS	[46]
33	Phenol	C_6H_6O	94.11	108-95-2	GC-MS	[46]
34	α-Tocopherol (Vitamin E)	$C_{29}H_{50}O_2$	430.70	59-02-9	GC-TOF-MS, GC-MS	[48, 51]
35	γ-Tocopherol	$C_{28}H_{48}O_2$	416.68	7616-22-0	GC-MS	[48]
Sulphur-containing						
36	Dimethyl sulfoxide	C_2H_6OS	78.13	67-68-5	GC-TOF-MS	[51]
Steroids						
37	Campesterol	$C_{28}H_{48}O$	400.68	474-62-4	GC-TOF-MS, GC-MS	[45, 48, 50-51]
38	Cholesterol	$C_{27}H_{46}O$	386.65	57-88-5	GC-MS	[48]
39	Desmosterol	$C_{27}H_{44}O$	384.64	313-04-2	GC-MS	[50]
40	Lanosterol	$C_{30}H_{50}O$	426.72	79-63-0	GC-MS	[50]
41	1-Naphthalenol	$C_{10}H_8O$	144.17	90-15-3	GC-MS	[46]
42	α-Sitosterol	$C_{30}H_{50}O$	426.72	474-40-8	GC-TOF-MS	[51]
43	β-Sitosterol	$C_{29}H_{50}O$	414.71	83-46-5	GC-MS	[45, 48, 50]
44	γ-Sitosterol	$C_{29}H_{50}O$	414.71	83-47-6	GC-MS	[48]
45	4,22-Stigmastadiene-3-one	$C_{29}H_{46}O$	410.67	20817-72-5	GC-MS	[48]
46	Stigmast-4-en-3-one	$C_{29}H_{48}O$	412.69	1058-61-3	GC-MS	[48]
47	Stigmasterol	$C_{29}H_{48}O$	412.69	83-48-7	GC-TOF-MS, IR, GC-MS, NMR	[44-45, 48, 50-51]
48	Stigmasterol β-D-glucopyranoside	$C_{35}H_{58}O_6$	574.83	-	IR, GC-MS, NMR	[44]
Chlorophylls						
49	13^2-Hydroxy-pheophytin a	$C_{55}H_{74}N_4O_6$	887.20	-	Flash column chromatography, NMR	[45]
50	Pheophytin a	$C_{55}H_{74}N_4O_5$	871.20	603-17-8	Flash column chromatography, NMR	[45]

51	13^1-Hydroxy-13^2-oxo-pheophytin a (Purpurin 7-monomethyl phytyl ester)	$C_{55}H_{74}N_4O_7$	903.20	-	Flash column chromatography, NMR	[45]
Benzofuran						
52	2,3-Dihydrobenzofuran	C_8H_8O	120.15	496-16-2	GC-MS	[46]
Fatty acids						
53	Arachidic acid	$C_{20}H_{40}O_2$	312.53	506-30-9	GC-MS	[50]
54	Behenic acid	$C_{22}H_{44}O_2$	340.58	112-85-6	GC-MS	[50]
55	Capric acid	$C_{10}H_{20}O_2$	172.26	334-48-5	GC-MS	[50]
56	cis-4,7,10,13,16,19-Docosahexaenoic acid	$C_{22}H_{32}O_2$	328.49	6217-54-5	GC-MS	[50]
57	Elaidic acid	$C_{18}H_{34}O_2$	282.46	2027-47-6	GC-MS	[50]
58	Erucic acid	$C_{22}H_{42}O_2$	338.57	112-86-7	GC-MS	[50]
59	Heptadecanoic acid	$C_{17}H_{34}O_2$	270.45	506-12-7	GC-MS	[50]
60	cis-10-Heptadecenoic acid	$C_{17}H_{32}O_2$	268.43	29743-97-3	GC-MS	[50]
61	n-Hexadecanoic acid (Palmitic acid)	$C_{16}H_{32}O_2$	256.42	57-10-3	GC-MS	[49-50]
62	Lauric acid	$C_{12}H_{24}O_2$	200.32	143-07-7	GC-MS	[50]
63	Linoleic acid	$C_{18}H_{32}O_2$	280.45	60-33-3	GC-MS	[50]
64	Myristic acid	$C_{14}H_{28}O_2$	228.37	544-63-8	GC-MS	[50]
65	Nonadecanoic acid	$C_{19}H_{38}O_2$	298.50	646-30-0	GC-MS	[46]
66	Octadecanoic acid (Stearic acid)	$C_{18}H_{36}O_2$	284.48	57-11-4	GC-MS	[49-50]
67	(*Z,Z,Z*)-9,12,15-Octadecatrienoic acid	$C_{18}H_{30}O_2$	278.43	463-40-1	GC-MS	[48]
68	Oleic acid	$C_{18}H_{34}O_2$	282.46	112-80-1	GC-MS	[50]
69	Palmitoleic acid	$C_{16}H_{30}O_2$	254.41	373-49-9	GC-MS	[50]
70	Pentadecanoic acid	$C_{15}H_{30}O_2$	242.40	1002-84-2	GC-MS	[50]
71	Tetracosanoic acid	$C_{24}H_{48}O_2$	368.63	557-59-5	IR, GC-MS, NMR	[44]
72	Tridecanoic acid	$C_{13}H_{26}O_2$	214.34	638-53-9	GC-MS	[50]
Others						
73	Acetic acid	$C_2H_4O_2$	60.05	64-19-7	GC-MS	[47]
74	4-Acetyl-2,7-dihydroxy-1,4,8-triphenyloctane-3,5-dione	$C_{28}H_{28}O_5$	444.52	-	IR, GC-MS, NMR	[44]
75	L-Alanine, ethyl ester	$C_5H_{11}NO_2$	117.15	3082-75-5	GC-TOF-MS	[51]
76	Ammonium acetate	$C_2H_7NO_2$	77.08	631-61-8	GC-TOF-MS	[51]
77	Aromadendrene oxide-(2)	$C_{15}H_{24}O$	220.35	85710-39-0	GC-TOF-MS	[51]
78	Benzoic acid	$C_7H_6O_2$	122.12	65-85-0	GC-MS	[47]

79	Bis(2-ethylhexyl) phthalate	$C_{24}H_{38}O_4$	390.56	117-81-7	GC-MS	[48]
80	Butyrolactone	$C_4H_6O_2$	86.09	96-48-0	GC-TOF-MS, GC-MS	[47, 51]
81	Cyclobutanol	C_4H_8O	72.11	2919-23-5	GC-TOF-MS	[51]
82	Cyclododecyne	$C_{12}H_{20}$	164.29	1129-90-4	GC-MS	[48]
83	3-Cyclohexene-1-carboxylic acid	$C_7H_{10}O_2$	126.15	4771-80-6	GC-MS	[47]
84	Cyclopentaneundecanoic acid, methyl ester	$C_{17}H_{32}O_2$	268.40	25779-85-5	GC-TOF-MS	[51]
85	2,5-Dimethoxy-4-(methylsulfonyl)amphetamine	$C_{12}H_{19}NO_4S$	273.35	-	GC-TOF-MS	[51]
86	1,1-Dimethylamino-1-butene	$C_6H_{13}N$	99.17	14548-12-0	GC-TOF-MS	[51]
87	Di-n-octyl phthalate	$C_{24}H_{38}O_4$	390.56	117-84-0	GC-MS	[46]
88	3,5-Dithiahexanol 5,5-dioxide	$C_4H_{10}O_3S_2$	170.25	68483-74-9	GC-TOF-MS	[51]
89	Eicosane	$C_{20}H_{42}$	282.55	112-95-8	GC-MS	[46, 48]
90	Formic acid	CH_2O_2	46.03	64-18-6	GC-MS	[47]
91	Glycolaldehyde	$C_2H_4O_2$	60.05	141-46-8	GC-MS	[47]
92	Heneicosane	$C_{21}H_{44}$	296.57	629-94-7	GC-MS	[48]
93	10-Heneicosene (c,t)	$C_{21}H_{42}$	294.56	95008-11-0	GC-MS	[48]
94	Heptacosane	$C_{27}H_{56}$	380.73	593-49-7	GC-MS	[46]
95	1-Heptacosanol	$C_{27}H_{56}O$	396.73	2004-39-9	IR, GC-MS, NMR	[44]
96	Heptadecane	$C_{17}H_{36}$	240.47	629-78-7	GC-MS	[46]
97	1-Heptatriacotanol	$C_{37}H_{76}O$	537.00	105794-58-9	GC-TOF-MS	[51]
98	Hexadecane	$C_{16}H_{34}$	226.44	544-76-3	GC-MS	[48]
99	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	$C_{19}H_{38}O4$	330.50	23470-00-0	GC-MS	[48]
100	Hexadecanoic acid, methyl ester	$C_{17}H_{34}O_2$	270.45	112-39-0	GC-TOF-MS	[51]
101	7-Hexadecenoic acid, methyl ester	$C_{17}H_{32}O_2$	268.43	56875-67-3	GC-TOF-MS	[51]
102	Hexamethyl-cyclotrisiloxane	$C_6H_{18}O_3Si_3$	222.46	541-05-9	GC-MS	[47]
103	2-Hexyl,1-decanol	$C_{16}H_{34}O$	242.44	2425-77-6	GC-MS	[46]
104	Hexyl octyl ether	$C_{14}H_{30}O$	214.39	17071-54-4	GC-MS	[46]
105	Histamine dichloride	$C_5H_9Cl_2N_3^{-2}$	182.05	-	GC-MS	[47]
106	Hydrazine carboxamide	CH_5N_3O	75.07	57-56-7	GC-TOF-MS	[51]
107	4-Hydroxy-4-methyl-2-pentanone	$C_6H_{12}O_2$	116.16	123-42-2	GC-MS	[47]
108	Isophytol	$C_{20}H_{40}O$	296.53	505-32-8	GC-MS	[46]
109	Megastigmatrienone	$C_{13}H_{18}O$	190.28	38818-55-2	GC-MS	[46]

110	2-Methoxy-1-propanol	$C_4H_{10}O_2$	90.12	1589-47-5	GC-MS	[47]
111	2-Methyl-3-(3-methyl-but-2-enyl)-2-(4-methyl-pent-3-enyl)-oxetane	$C_{15}H_{26}O$	222.37	108287-20-3	GC-MS	[48]
112	2-Methyl-*Z,Z*-3,13-octadecadienol	$C_{19}H_{36}O$	280.50	519002-96-1	GC-MS	[48]
113	Methyl tetradecanoate	$C_{15}H_{30}O_2$	242.40	124-10-7	GC-TOF-MS	[51]
114	Monoethanolamine	C_2H_7NO	61.08	141-43-5	GC-TOF-MS	[51]
115	Nitrous oxide	N_2O	44.01	10024-97-2	GC-TOF-MS	[51]
116	Nonadecane	$C_{19}H_{40}$	268.52	629-92-5	GC-MS	[48]
117	1,3,12-Nonadecatriene	$C_{19}H_{34}$	262.50	-	GC-MS	[48]
118	Octacosane	$C_{28}H_{58}$	394.76	630-02-4	GC-MS	[46]
119	9,17-Octadecadienal	$C_{18}H_{32}O$	264.45	85263-73-6	GC-MS	[46]
120	9,12-Octadecadienoic acid, methyl ester	$C_{19}H_{34}O_2$	294.47	2462-85-3	GC-TOF-MS	[51]
121	Octadecanoic acid, methyl ester	$C_{19}H_{38}O_2$	298.50	112-61-8	GC-TOF-MS	[51]
122	(*Z,Z,Z*)-9,12,15-Octadecatrienoic acid, methyl ester	$C_{19}H_{32}O_2$	292.46	301-00-8	GC-TOF-MS, GC-MS	[50-51]
123	(*Z*)-9-Octadecenamide	$C_{18}H_{35}NO$	281.48	301-02-0	GC-MS	[48]
124	Octamethyl-cyclotetrasiloxane	$C_8H_{24}O_4Si_4$	296.62	556-67-2	GC-MS	[47]
125	Pentadecane	$C_{15}H_{32}$	212.41	629-62-9	GC-MS	[46]
126	2-Pentadecyn-1-ol	$C_{15}H_{28}O$	224.38	2834-00-6	GC-TOF-MS	[51]
127	n-Propyl acetate	$C_5H_{10}O_2$	102.13	109-60-4	GC-TOF-MS	[51]
128	Tetracosane	$C_{24}H_{50}$	338.65	646-31-1	GC-MS	[48]
129	Tetradecanal	$C_{14}H_{28}O$	212.37	124-25-4	GC-MS	[46]
130	6-Tetradecanesulfonic acid, butyl ester	$C_{18}H_{38}O_3S$	334.60	-	GC-MS	[48]
131	13-Tetradecen-11-yn-1-ol	$C_{14}H_{24}O$	208.34	-	GC-MS	[46, 48]
132	Tetratetracontane	$C_{44}H_{90}$	619.19	7098-22-8	GC-MS, GC-TOF-MS	[46, 51]
133	Tridecyl iodide	$C_{13}H_{27}I$	310.256	35599-77-0	GC-MS	[46]
134	Undecane	$C_{11}H_{24}$	156.31	1120-21-4	GC-TOF-MS	[51]
135	2-Undecanone	$C_{11}H_{22}O$	170.29	112-12-9	GC-MS	[46]
136	Verbascoside	$C_{29}H_{36}O_{15}$	624.59	61276-17-3	LC-ESI-MS	[53]

6. Pharmacological Activities

This section provides a comprehensive overview of the pharmacological activities of *S. crispa*. The information presented is based on an extensive review of journals published between 2000 and 2022, ensuring that the data included is up to date. The pharmacological studies on *S. crispa* are summarized in Table 3. The study limitations are discussed.

6.1. Antihyperglycemic Activity

In two separate reports, it was observed that hot water extracts of fermented and unfermented tea made from *S. crispa* leaves [13] and *S. crispa* juice [54] exhibited significantly superior antihyperglycemic activities in streptozotocin-induced hyperglycemic rats compared to the standard drug glibenclamide. Both studies claim that epicatechin may be the main phytochemical responsible for the insulin-like activity of *S. crispa*. However, further isolation and characterization of the effective components are required to verify its activities. Moreover, more studies are needed to confirm the pharmacokinetic and pharmacodynamic activities of the plant.

6.2. Antioxidant Activity

The antioxidant properties of *S. crispa* leaves have been evaluated by various *in vitro* studies (Table 3). These extracts were found to have higher antioxidant activity than vitamin E [22, 46]. In addition, studies have shown that *S. crispa* extract has a strong inhibitory effect on xanthine oxidase activity [51] and can effectively scavenge DPPH free radicals [14, 51-52, 55-59] and reduce ferric ions [14, 55-56, 58] at non-toxic concentrations. The ability of different extracts to scavenge free radicals and reduce ferric ions may be affected by factors such as solvent polarity [60], plant age [61], and plant growth location [62]. In addition, a cell-based experiment using the 2′,7′-dichlorodihydrofluorescein diacetate assay conducted by Tan et al. [57] demonstrated that the methanolic extract of *S. crispa* is a powerful ROS scavenger. Furthermore, an *in vivo* study revealed that *S. crispa* juice increased the levels of endogenous antioxidant enzymes in diabetic-treated rats, thereby protecting cells from diabetes-induced oxidative stress [54]. However, current studies mainly focused on the antioxidant activity of *S. crispa* extracts rather than individual isolated compounds. Further studies are required to isolate and identify the potent antioxidants responsible for the antioxidant properties of *S. crispa.*

6.3. Antimicrobial Activity

The hydromethanolic crude leaf extract of *S. crispa* displayed potent antifungal activity against *Aspergillus niger* (*A. niger*) and *Penicillium oxalium* (*P. oxalicum*). However, the isolated compound did not exhibit any antifungal activity [63]. This suggests the presence of synergetic effects among the compounds. In addition, different extracts of *S. crispa* exhibited varying degrees of inhibitory activity against several bacterial strains, including *Pseudomonas aeruginosa* (*P. aeruginosa*) [59], *Escherichia coli* (*E. coli*)*, Klebsiella pneumoniae* (*K. pneumoniae*), *Bacillus subtilis* (*B. subtilis*), *Salmonella typhimurium* (*S. typhimurium*) [44], *Staphylococcus aureus* (*S. aureus*) [44, 47], *Aeromonas hydrophila* (*A. hydrophila*), *Streptococcus agalactiae* (*S. agalactiae*) and *Enterobacter cloacae* (*E. cloacae*) [41], and *Bacillus cereus* (*B. cereus*) [64]. These studies support its traditional use in the treatment of ulcers, jaundice, and piles [35]. However, further investigation is required to elucidate their antibacterial mechanisms. In addition, it is recommended to consider further studies involving the isolation and identification of active ingredients, as well as *in vitro* and *in vivo* studies.

6.4. Wound Healing Activity

A total of three reports have shown the wound-healing potential of aqueous and ethanolic leaf extracts of *S. crispa* in normal and streptozotocin-induced diabetes Sprague Dawley rats [30, 65-66]. In the reports by Norfarizan-Hanoon et al. [30] and Al-Henhena et al. [65], the extracts demonstrated positive effects on wound healing in both normal and diabetic rats, with reductions in wound length observed on different days of treatment. However, these studies lack the use of positive control to validate the findings [67]. Furthermore, in the study by Al-Henhena et al. [65], only two independent sets of *in vivo* experiments (n = 2) were performed, and the authors incorrectly reported the name "*B. rotunda*" instead of *S. crispa* in Table 2. Another study evaluated the anti-ulcerogenic activity of *S. crispa* leaf extract on ethanol-induced mucosal injury in rats, showing a dose-dependent reduction in gastric lesion formation [66]. However, the rationale for selecting very high doses (250, 500 and 1000 mg/kg) was not provided. For *in vivo* studies involving extracts, a dose range of not more than 200 mg/kg should be considered to ensure meaningful pharmacological studies [68]. Further research, such as isolation of effective components, investigation of the mode of mechanism, and clinical studies, is needed to prove any pharmacological effects in humans.

6.5. Anticancer Activity

To date, nine *in vitro* and two *in vivo* studies have investigated the anticancer effect of *S. crispa* on human breast cancer [24, 55, 69-77]. Additionally, seven *in vitro* studies explored its effects on liver cancer [51, 57, 69, 71, 73, 78-79], four *in vitro* studies focused on colon cancer [9, 51, 69, 71], two *in vitro* studies investigated its effects on cervical cancer [14, 80], and individual *in vitro* studies focused on lung [51], prostate [24] and nasopharyngeal cancers [31].

Baraya's group reported the *in vivo* anticancer activity of the dichloromethane bioactive subfraction F3 of the leave extract, lutein (**9**), and β-sitosterol (**43**) [74-75]. They observed a significant reduction in tumour growth in the treated groups compared to the untreated group [74]. They also evaluated the *in vitro* and *in vivo* anti-tumour immunogenicity of metastatic breast carcinoma [75]. Fraction F3 resulted in an increase in immune molecules and cell infiltration in the breast tumour microenvironment. However, these studies only provide single-dose experiments without positive controls, which hindered the analysis of reported dose-effect relationships of plant extracts [67]. Further research is needed to determine the effective dose. Clinical studies are also required to establish a complete pharmacological profile and to demonstrate any pharmacological effects in humans. In addition, Yankuzo et al. [77] also reported that fraction F3 led to increased expression of immune molecules and T cells, as well as decreased levels of certain proteins and macrophages. The study showed that F3 can activate the immune system in rats with mammary tumours.

In the reports by Gordani et al. [76] and Koh et al. [73], the hexane stem extract was shown to be cytotoxic and induced apoptosis in MDA-MB-231 cells. In fact, the methanol, chloroform, and aqueous leaf extracts, as well as the chloroform and ethyl acetate stem extracts, also showed cytotoxic effects on MCF-7 cells. However, due to the unknown origin of the cell line used in the study, the reproducibility of the data was an issue. In another study by Bakar et al. [55], *S. crispa* tea inhibited the proliferation of MCF-7 cells but not MDA-MB-231 cells. However, the dichloromethane bioactive subfractions showed greater cytotoxicity against MDA-MB-231 cells compared to MCF-7 cells [24]. Additionally, γ-sitosterol (**44**) [71], β-sitosterol (**43**), and stigmasterol (**47**) [69], isolated from *S. crispa* leaves also showed cytotoxic effects on breast cancer cells. However, both studies lacked positive controls. More detailed studies on mechanistic modelling and the isolation of bioactive compounds are strongly recommended.

Furthermore, several studies have reported on the anticancer and cytotoxic effects of *S. crispa* on various cancer cell lines, including HepG-2 [51, 57, 69, 73, 78-79], HT-29 [9], Caco-2 [69, 71], HCT 116 [51], HeLa [14, 80], NCI-H23 [51], PC-3 [24], DU-145 [24] and CNE-1 [31]. However, most of these studies only focused on the crude extracts of *S. crispa* rather than individual isolated bioactive compounds. Therefore, further studies, such as the verification of effective components and modes of

mechanism, are still needed. Furthermore, since most studies were conducted *in vitro,* it is crucial to consider animal and clinical studies, as well as toxicology studies. In addition, most authors performed only one or two sets of triplicate *in vitro* experiments, which limits the validity of the experimental results. In fact, the analysis of three or more independent replicates is required to ensure the reliability of the observations [67].

6.6. Other Activities

Other activities such as anti-trypanosomal [81], anti-inflammatory [82], anti-obesity [83-84], anti-urolithiatic [43], anti-angiogenic [51] and vasorelaxant activities [85], have also been reported on the extracts of *S. crispa*. The antitrypanosomal effects of aqueous and ethanolic leaf extracts of *S. crispa* were evaluated *in vitro* [81]. The study suggested that the ethanolic extract of *S. crispa* has potential anti-trypanosomal activity, making it a promising candidate for the discovery of novel anti-trypanosomal compounds. However, animal models and clinical studies, as well as toxicity studies, must be considered. A study by Wong et al. [82] investigated the anti-inflammatory properties of the methanolic leaf extract of *S. crispa*. The extract demonstrated significant inhibition of LPS-stimulated nitric oxide (NO) production and dose-dependent promotion of interleukin-10 (IL-10) production (anti-inflammatory mediator) in RAW264.7 macrophages. However, there was only a slight reduction in IL-6 (a pro-inflammatory mediator). Further studies are required to identify the compounds responsible for the inhibition. The chloroform-methanol leaf extract showed anti-obesity activity in diet-induced rats by improving various obesity-related parameters [83]. In a follow-up study by the same group of researchers, the extract was found to significantly reduce the respiratory exchange rates, but had no effect on food intake, body weight, and abdominal adipose tissue weight [84]. However, important aspects such as positive controls, identification of chemical composition, toxicity evaluation, and clinical studies were lacking in these reports. Gul et al. [43] found that the methanolic extract of *S. crispa* leaves showed significant inhibitory activity on the aggregation of CaOx crystals, while the ethyl acetate extract demonstrated effective dissolution effects. The study suggested that *S. crispa* leaf extract has potential anti-urolithiatic activity. However, further studies of the mechanism of action, isolation of active constituents, and animal studies are still needed to validate the traditional use of *S. crispa* in treating kidney stones. Muslim et al. [51] conducted a study on the *ex-vivo* anti-angiogenic properties of methanolic and aqueous extracts of *S. crispa* using the rat aortic ring assay. The extracts showed moderate activity compared to the positive control, suramin. This study provides scientific support for the traditional use of *S. crispa* in cancer treatments. However, the study had limitations, such as data reported in a single set of triplicates and the lack of information on the toxicity of the extracts. A study by Ch'ng et al. [85] investigated the vasodilation effect of different *S. crispa* leaf extracts on pre-contracting aortic rings of SD rats. This study again supported the claim about the traditional use of *S. crispa* in the treatment of hypertension [20, 27, 34]. However, the analysis was based on a single experiment and a single dose, making it difficult to determine the effective dose. Furthermore, the study lacked a positive control. Additional studies, including the identification of active components and determination of optimum dosage, are necessary to establish a complete pharmacological profile and verify its traditional claim.

6.7. Toxicity

To date, information on the toxicity of *S. crispa* is limited. The ancient prescriptions and clinical reports on the toxicity of *S. crispa* are also very rare. However, several studies on *S. crispa* leaf extracts were found to be safe and had no adverse effects *in vitro* or *in vivo*. First, the MTT assay showed that methanolic leaf and stem extracts had maximal non-toxic doses of 160 and 2 µg/mL on RAW 264.7 macrophages, respectively [82]. In addition, according to the report by Dyary et al. [81], the ethanolic and aqueous leaf extracts of *S. crispa* had CC_{50} of 355 ± 9 µg/mL and 6452 ± 364 µg/mL, respectively, and were considered non-cytotoxic to the Vero normal cell line. Another study by Rahmat et al. [69] showed that no cytotoxic effects were observed on normal Chang liver cells treated with hexane, chloroform, and ethyl acetate extracts (100 µg/mL) and isolated steroids (247.5 µM). Norfarizan-Hanoon et al. [86] also showed that no adverse effects or mortality were observed in Sprague Dawley

mice after oral administration of the leaf extract at doses of 0.7, 2.1, 3.5 and 4.9 g/kg body weight for 14 days during preliminary toxicity tests. Likewise, the acute oral toxicity of the aqueous leaf extract observed at doses of 1, 2 and 5 g/kg was found to be safe within 2 weeks, and no adverse effects or mortality were observed in Sprague Dawley rats [66]. Acute oral toxicity studies were also studied by Lim et al. [87] at doses up to 600 mg/kg. From the results, no adverse effects or lethality were observed in the liver and kidney of the Sprague Dawley rats. However, these are insufficient to provide a conclusion on the toxicity and safety of this plant. Therefore, the toxicity studies of the plant still need to be further explored.

7. Conclusions and Future Perspective

Since *S. crispa* is a folklore medicinal plant traditionally used to treat a variety of diseases, its phytochemical and pharmacological properties have been extensively studied and reported. However, there are several research gaps in the literature that need to be addressed, and more in-depth research is needed. A total of 136 metabolites belonging to different chemical classes have been identified in *S. crispa*. However, reports on the isolation and characterization of pure compounds are limited. Therefore, it is critical to establish qualitative methods to verify and validate the presence of the reported phytochemicals. Furthermore, most of the current studies only focus on the pharmacological properties of *S. crispa* extracts. In fact, the pharmacological activity of the *S. crispa* extracts may be due to the synergetic effect of several bioactive components in the extract, and the concentrations used are often too high for clinical use. Therefore, contemporary bioassay-guided or molecular network-guided phytochemical analyzes are needed to correlate the pharmacology activity with specific bioactive compounds. Additionally, current studies are limited to *in vitro* experiments, and the correlation of bioactive components with pharmacokinetics and *in vivo* metabolism remains unclear. Therefore, it is important to perform *in vivo* animal studies to investigate the underlying mechanistic patterns. Efforts such as toxicity studies to explore potential adverse effects of plant extracts and isolated bioactive compounds, as well as clinical studies to estimate first doses in humans, are also strongly recommended. Although *S. crispa* exhibits a wide variety of pharmacological activities, the modern pharmacological activities of traditionally applied *S. crispa* have not been well studied. Therefore, more experimental studies are needed to reveal other pharmacological activities of *S. crispa* based on its traditional use. To sum up, this paper aims to provide an in-depth review of the traditional uses, phytochemical, pharmacological, and toxicological studies of *S. crispa*, and offer valuable information for future research and application of *S. crispa.*

Table 3. Pharmacological activities of *S. crispa* extracts

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Antihyperglycemic	Leaves	Selangor, Malaysia	(i) Aqueous extract of fermented tea (ii) Aqueous extract of unfermented tea	*In vivo* - on streptozotocin-induced hyperglycemic rats and normal rats	2% of fermented and unfermented tea	Male albino *Sprague Dawley* rats (200 - 250 g)	Glibenclamide (10 mg/kg body weight)	Hyperglycemic and normal untreated rats	In experimental animal models, both tea extracts exhibited significant antihyperglycemic effects by lowering blood glucose levels and improving blood lipid profiles (lowering total cholesterol, triglycerides, and LDL-cholesterol while increasing HDL-cholesterol).	[13]
	Leaves	Selangor, Malaysia	Juice (4% of *S. crispa*)	*In vivo* - on streptozotocin-induced diabetic rats and normal rats	1.0, 1.5 & 2.0 mg/kg body weight for 30 days	Male and female albino *Sprague Dawley* rats (150 - 200 g)	Glibenclamide (10 mg/kg body weight)	Diabetic and normal untreated rats	Juice exhibited a significant antihyperglycemic effect by reducing serum glucose levels and improving liquid profile (reducing total cholesterol, triglyceride and LDL-cholesterol levels and increasing HDL-cholesterol levels) compared with the control group.	[54]

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td rowspan="3">Antioxidant</td><td>Leaves</td><td>Selangor, Malaysia</td><td>Ethyl acetate extract</td><td>In vitro:
(i) FTC assay
(ii) TBA assay</td><td>0.02%</td><td>-</td><td>Vitamin E</td><td>Solvent</td><td>The absorbance values of the FTC and TBA methods showed that S. crispa had higher antioxidant activity than vitamin E, with the least increase in absorbance values.</td><td>[22]</td></tr>
<tr><td>Leaves</td><td>Selangor, Malaysia</td><td>(i) Aqueous extract of fermented tea (young & old)
(ii) Aqueous extract of unfermented tea (young & old)</td><td>In vitro:
(i) DPPH free radical scavenging assay
(ii) FRAP assay</td><td>0.04 g/mL</td><td>-</td><td>C. sinensis (Sencha, Green tea) & C. sinensis (Boh, Black tea)</td><td>Distilled water</td><td><table><tr><th>Sample</th><th>DPPH free radical scavenging activity (%)</th><th>FRAP value</th></tr><tr><td>S. crispa unfermented tea (young)</td><td>61.22 ± 0.47</td><td>1305.45 ± 36.67 µmol/L</td></tr><tr><td>S. crispa unfermented tea (old)</td><td>63.21 ± 0.72</td><td>2091.00 ± 188.68 µmol/L</td></tr><tr><td>S. crispa fermented tea (young)</td><td>12.59 ± 1.06</td><td>452.94 ± 28.82 µmol/L</td></tr><tr><td>S. crispa fermented tea (old)</td><td>27.58 ± 1.83</td><td>601.83 ± 8.12 µmol/L</td></tr><tr><td>Green tea (C. sinensis, Sencha)</td><td>79.56 ± 0.28</td><td>56.79 ± 0.57 mmol/L</td></tr><tr><td>Black tea (C. sinensis, Boh)</td><td>74.27 ± 0.07</td><td>34.30 ± 0.22 mmol/L</td></tr></table></td><td>[55]</td></tr>
<tr><td>Leaves</td><td>Selangor, Malaysia</td><td>Essential oil extract</td><td>In vitro:
(i) FTC assay
(ii) TBA assay</td><td>(i) 4 mg
(ii) 1 mL</td><td>-</td><td>(i) & (ii) Vitamin E</td><td>(i) Ethanol solvent</td><td>The results of the FTC and TBA methods revealed that the essential oil obtained from S.crispa had higher antioxidant activity than α-tocopherol.</td><td>[46]</td></tr>
</table>

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td rowspan="2">Antioxidant</td><td>Leaves</td><td>Selangor, Malaysia</td><td>Juice (4% of S. crispa)</td><td>In vivo - on strepto-zotocin-induced diabetic rats and normal rats</td><td>1.0, 1.5 & 2.0 mg/kg body weight for 30 days</td><td>Male and female albino Sprague Dawley rats (150 - 200 g)</td><td>Gliben-clamide (10 mg/kg body weight)</td><td>Diabetic and normal untreated rats</td><td>Juice had a significant antioxidant effect with increased antioxidant enzymes activities (glutathione peroxidase and superoxide diastase) compared with control group.</td><td>[54]</td></tr>
<tr><td>Leaves</td><td>Padang, Indonesia</td><td>(i) Meth-anolic extract (ii) Aque-ous extract</td><td>In vitro: (i) Xan-thine oxidase inhibi-tion assay (ii) DPP H free radical scaveng-ing assay</td><td>(i) 100 µg/mL (ii) 100, 200, 400, 600 & 800 µg/mL</td><td>-</td><td>Gallic acid, ascorbic acid, quer-cetin & BHA (500 µg/mL)</td><td>(i) - (ii) Methanol 1.0 & 0.1 mM DPPH (iii) Ethanol & blank emulsion</td><td>(i)
Extract | Inhibition (%)
Methanol | 90.25 ± 0.20
Aqueous | 89.06 ± 0.28

(ii)
Concentration (µg/mL) | Free radical scavenging activity (%): Methanolic extract | Aqueous extract
100 | 1.67 ± 0.11 | 1.88 ± 0.67
200 | 3.40 ± 0.52 | 3.93 ± 0.78
400 | 6.31 ± 0.51 | 8.34 ± 0.96
600 | 9.58 ± 0.43 | 13.44 ± 0.91
800 | 12.38 ± 0.35 | 17.46 ± 0.26

Reference standard | EC_{50} (µg/mL)
Gallic acid | 13
Ascorbic acid | 26
BHA | 22
Quercetin | 15</td><td>[51]</td></tr>
</table>

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td rowspan="2">Antioxidant</td><td>Leaves</td><td>Selangor, Malaysia</td><td>(i) Aqueous extract (ii) Ethanolic extract</td><td>In vitro: (i) DPPH free radical scavenging assay (ii) FRAP assay</td><td>(i) 5 different concentrations from stock 1 mg/mL (ii) 1 mg/mL</td><td>-</td><td>Gallic acid</td><td>-</td><td>
<table>
<tr><th>Plant/Drug</th><th>Extract</th><th>DPPH (%)</th><th>FRAP (mmol/g)</th></tr>
<tr><td>S. crispa</td><td>Aqueous</td><td>28.50 ± 14.53</td><td>150.30 ± 0.01</td></tr>
<tr><td></td><td>Ethanol</td><td>14.50 ± 0.64</td><td>108.00 ± 0.01</td></tr>
<tr><td>Gallic acid</td><td>-</td><td>88.80 ± 0.85</td><td>1216.67 ± 0.03</td></tr>
</table>
</td><td>[56]</td></tr>
<tr><td>Leaves</td><td>(i) Penang, Malaysia (ii) Kelantan, Malaysia (iii) Selangor, Malaysia</td><td>(i) Aqueous extract (ii) Ethanolic extract</td><td>In vitro: (i) DPPH free radical scavenging assay (ii) FRAP assay</td><td>(i) 10, 20, 40, 80 and 160 µg/mL (ii) 100 µL</td><td>-</td><td>BHT (≥ 99.0%) & α-tocopherol (≥ 95.5%)</td><td>-</td><td>
<table>
<tr><th>Sampling Location</th><th>Solvent</th><th>DPPH free radical scavenging activity (%)</th><th>IC_{50} (µg/mL)</th><th>FRAP value (µM of Fe(II)/g)</th><th>IC_{50} (µg/mL)</th></tr>
<tr><td>Penang</td><td>Aqueous</td><td>54.60 ± 2.78</td><td>78 ± 3</td><td>117.60 ± 4.31</td><td>81 ± 3</td></tr>
<tr><td></td><td>Ethanol</td><td>41.70 ± 3.26</td><td>147 ± 4</td><td>59.80 ± 4.03</td><td>148 ± 3</td></tr>
<tr><td>Selangor</td><td>Aqueous</td><td>62.40 ± 2.23</td><td>58 ± 2</td><td>180.60 ± 6.21</td><td>63 ± 2</td></tr>
<tr><td></td><td>Ethanol</td><td>49.20 ± 1.89</td><td>118 ± 3</td><td>126.70 ± 4.55</td><td>123 ± 3</td></tr>
<tr><td>Kelantan</td><td>Aqueous</td><td>73.80 ± 3.39</td><td>44 ± 3</td><td>267.50 ± 9.57</td><td>53 ± 2</td></tr>
<tr><td></td><td>Ethanol</td><td>55.40 ± 2.63</td><td>81 ± 3</td><td>201.80 ± 7.45</td><td>81 ± 3</td></tr>
<tr><td>BHT</td><td></td><td>51.60 ± 3.44</td><td>38 ± 2</td><td>250.60 ± 7.26</td><td>41 ± 1</td></tr>
<tr><td>α-Tocopherol</td><td></td><td>60.20 ± 4.27</td><td>26 ± 1</td><td>322.10 ± 10.15</td><td>29 ± 2</td></tr>
</table>
</td><td>[14]</td></tr>
</table>

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td rowspan="2">Antioxidant</td><td>Leaves</td><td>Negeri Sembilan, Malaysia</td><td>Methanolic extract</td><td>In vitro: (i) 2′,7′-Dichlorodihydrofluorescein diacetate assay (ii) DPPH free radical scavenging assay</td><td>(i) 0 - 500 µg/mL (ii) 0 - 1000 µg/mL</td><td>(i) HepG-2 cell line (ii) -</td><td>(i) tert-Butyl hydroperoxide (ii) Vitamin C</td><td>(i) Untreated cells (ii) -</td><td>(i) The extracts were found to be potent ROS scavengers in liver cells. 63 µg/mL extract reduced ROS levels two-fold (68.27%) compared to untreated control cells, and no further significant differences were observed above 125 µg/mL.
(ii) At 1000 µg/mL, the extract scavenged DPPH radicals up to 95%.</td><td>[57]</td></tr>
<tr><td>Leaves</td><td>Negeri Sembilan, Malaysia</td><td>Methanolic-acetone extract</td><td>In vitro: (i) DPPH free radical scavenging assay (ii) FRAP assay</td><td>25, 50, 75 & 100% methanol; 25, 50, 75 & 100% chloroform</td><td>-</td><td>Trolox</td><td>-</td><td><table><tr><th>Treatment</th><th>DPPH (mg TE g^{-1} DW)</th><th>FRAP (mg TE g^{-1} DW)</th></tr><tr><td>100% Methanol</td><td>10</td><td>35</td></tr><tr><td>75% Methanol</td><td>19</td><td>37</td></tr><tr><td>50% Methanol</td><td>11</td><td>33</td></tr><tr><td>25% Methanol</td><td>9</td><td>29</td></tr><tr><td>100% Acetone</td><td>13</td><td>30</td></tr><tr><td>75% Acetone</td><td>25</td><td>39</td></tr><tr><td>50% Acetone</td><td>18</td><td>36</td></tr><tr><td>25% Acetone</td><td>13</td><td>47</td></tr></table></td><td>[58]</td></tr>
</table>

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td>Antioxidant</td><td>Leaves</td><td>Melaka, Malaysia</td><td>(i) Aqueous extract (ii) Methanolic extract (iii) Ethyl acetate extract (iv) Hexane extract</td><td>In vitro: (i) DPPH free radical scavenging assay (ii) FRAP assay (iii) TEAC</td><td>0 - 1000 µg/mL</td><td>-</td><td>Gallic acid & rutin</td><td>-</td><td><table><tr><th>Sample</th><th>Extraction Solvent</th><th>DPPH (µg extract/ mL)</th><th>FRAP (mmol Fe2+/g extract)</th><th>TEAC (mmol TE/g extract)</th></tr><tr><td>S. crispa</td><td>Water</td><td>> 1000</td><td>1.22 ± 0.06</td><td>0.02 ± 0.03</td></tr><tr><td></td><td>Methanol</td><td>204 ± 7</td><td>6.84 ± 1.12</td><td>1.01 ± 0.25</td></tr><tr><td></td><td>Ethyl acetate</td><td>> 1000</td><td>1.38 ± 0.08</td><td>0.04 ± 0.01</td></tr><tr><td></td><td>Hexane</td><td>> 1000</td><td>1.28 ± 0.07</td><td>0.09 ± 0.05</td></tr><tr><td>Positive control</td><td>Gallic acid</td><td>7</td><td>29.17 ± 0.25</td><td>4.29 ± 0.01</td></tr><tr><td></td><td>Rutin</td><td>61</td><td>19.92 ± 0.38</td><td>1.67 ± 0.09</td></tr></table></td><td>[52]</td></tr>
<tr><td></td><td>Leaves</td><td>Kuching, Sarawak</td><td>(i) Ethanolic extract (ii) Acetone extract (iii) Chloroform extract</td><td>In vitro: DPPH free radical scavenging assay</td><td>10-100 µg/mL</td><td>-</td><td>Ascorbic acid (IC_{50} = 6 µg/mL)</td><td>-</td><td><table><tr><th>Extract</th><th>Ascorbic acid equivalent antioxidant content (%)</th></tr><tr><td>Ethanol</td><td>> 55</td></tr><tr><td>Acetone</td><td>> 55</td></tr><tr><td>Chloroform</td><td>> 55</td></tr></table></td><td>[59]</td></tr>
<tr><td>Antimicrobial</td><td>Leaves</td><td>Selangor, Malaysia</td><td>Methanolic extract</td><td>(i) Well diffusion method (ii) MIC assay</td><td>1, 2, 4, 6, 8, 10, 15 & 20 mg/mL</td><td>B. Cereus</td><td>-</td><td>(i) 80% (v/v) methanol & 5% (v/v) of DMSO (ii) -</td><td>When the concentration was 2 mg/mL, the methanolic crude extract of S. crispa began to show inhibitory effect on the growth of B. cereus, with an average inhibitory rate of 6.18 µm/h. The MIC and MBC values of S. crispa crude extract were 2 mg/mL and 6 mg/mL, respectively.</td><td>[64]</td></tr>
</table>

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Antimicrobial	Leaves	-	(i) Hexane extract (ii) Dichloromethane extract (iii) Methanol extract	Microdilution antibacterial assay	-	(i) *B. subtilis* (ii) *E. coli* (iii) *K. pneumoniae* (iv) *S. typhimurium* (v) *S. aureus*	Gentamicin	-	See table below	[44]

Tested sample	MIC value (µg/mL)				
	B. subtilis	*E. coli*	*K. pneumoniae*	*S. typhimurium*	*S. aureus*
DCM extract	31 ± 2	63 ± 3	63 ± 2	63 ± 2	16 ± 4
Mixture of four fatty acid esters of β-amyrin	125 ± 3	250 ± 1	250 ± 1	125 ± 1	125 ± 221
Taraxerone	125 ± 3	125 ± 2	63 ± 1	125 ± 2	63 ± 16
Taraxerol	16 ± 2	63 ± 2	63 ± 1	63 ± 2	16 ± 2
Mixture of two fatty acid esters of taraxerol	31 ± 1	63 ± 3	125 ± 2	63 ± 2	16 ± 5
MeOH extract	16 ± 5	63 ± 3	63 ± 4	31 ± 4	8 ± 4
4-Acetyl-2,7-dihydroxy-1,4,8-triphenyloctane-3,5-dione	16 ± 3	63 ± 1	63 ± 2	31 ± 1	8 ± 1
Stigmasterol β-D-glucopyrano-side	63 ± 1	250 ± 2	125 ± 2	125 ± 1	125 ± 3
Gentamicin	4	16 ± 2	7 ± 2	8 ± 2	8 ± 1

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td></td><td>Leaves</td><td>Negeri Sembilan, Malaysia</td><td>Ethanolic extract</td><td>Disc diffu-sion method</td><td>50-250 mg/mL</td><td>(i) Bacteria : K. pneumonia e, P. aeruginosa , S. aureus & S. pneumonia (ii) Fungi: A. brasiliensis (iii) Yeast: C. albicans</td><td>Oxacil-lin (1 µg)</td><td>DMSO (10% v/v)</td><td>Concentration | Zone of inhibition (%) | S. aureus | S. pneumoniae
50 mg/mL | 31.91 | 0.00
100 mg/mL | 42.87 | 24.08
150 mg/mL | 49.40 | 25.20
200 mg/mL | 57.85 | 25.79
250 mg/mL | 64.40 | 24.67
Oxacillin | 100.00 | 100.00
In this study, the S. crispa ethanolic extract exhibited inhibitory activity against S. aureus and S. pneumoniae at a concentration of 200 mg/mL, while no significant inhibitory effect was observed against K. pneumoniae, P. aeruginosa, A. brasiliensis and C. albicans.</td><td>[47]</td></tr>
<tr><td>Antimicrobial</td><td>Leaves, stems & flowers</td><td>Selangor, Malaysia</td><td>(i) Aque-ous extract & metha-nolic extract (ii) Meth -anolic extract</td><td>(i) Disc diffu-ion method (ii) MI C assay</td><td>(i) 0.5 g/mL (ii) 0.625 - 50 mg/mL.</td><td>(i) Fresh-water pathogens: A. hydrophila, S. agalactiae & E. cloacae (ii) Fresh-water pathogens: A. hydrophila & S. agalactiae</td><td>(i) Oxy-tetracy-cline, chloram-phenicol , thrimeth -oprim & strepto-mycin (ii) -</td><td>(i) Solvents (deionized distilled water and methanol) (ii) -</td><td>(i) For A. hydrophila, S. agalactiae and E. cloacae, the zones of inhibition of the methanolic extract were 11, 13 and 11 mm, respectively. In contrast, for A. hydrophila and E. cloacae, the zones of inhibition of the aqueous extract were 8 and 7 mm, respectively.
(ii) The MIC values for the methanolic extract of S. crispa were 6 mg/mL for A. hydrophila and 13 mg/mL for S. agalactiae.</td><td>[41]</td></tr>
</table>

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Antimicrobial	Leaves	Kelantan, Malaysia	Methanolic extract	(i) Disc diffusion method (ii) MIC assay	(i) 50 µL (ii) 0, 1.25, 2.5, 5 & 10 mg/mL	*A. niger* & *P. oxalicum*	-	-	(i) Average diameter of inhibition zone (in mm): *A. niger*: 11 ± 0 *P. oxalicum*: 19 ± 1 (ii) The MIC values for *A. niger* and *P. oxalicum* were 10 mg/mL and 5 mg/mL, respectively.	[63]
	Leaves	Kuching, Sarawak	(i) Ethanolic extract (ii) Acetone extract (iii) Chloroform extract	Disc diffusion method	1 mg/mL	(i) Gram positive bacteria: *S. pyogenes, S. aureus* & Methicillin-resistant *S. aureus* (ii) Gram negative bacteria: *P. aeruginosa*, *E. coli, Shigella* sp., *S. typhimuriu* & *K. pneumonia*	Levofloxacin	Mueller–Hinton broth	Zone of inhibition (mm):	[59]

	Strobilanthes crispa									Control		
Extract	Ethanol			Acetone			Chloroform			Levofloxacin		
Duration of exposure (h)	2	4	7	2	4	7	2	4	7	2	4	7
	4	8	2	4	8	2	4	8	2	4	8	2
Gram positive bacteria												
S. pyogenes	x	x	x	x	x	x	x	x	x	4	4	4
										3	2	3
S. aureus	x	x	x	x	x	x	x	x	x	1	1	1
										0	1	1
MRSA	x	x	x	x	x	x	x	x	x	7	x	x
Gram-negative bacteria												
E. coli	x	x	x	x	x	x	x	x	x	4	4	3
										2	1	9
P. aeruginosa	1	1	1	1	1	1	1	1	1	2	2	2
	5	4	3	2	2	2	1	1	1	7	5	4
S. typhimurium	x	x	x	x	x	x	x	x	x	3	3	3
										0	1	1
Shigella sp.	x	x	x	x	x	x	x	x	x	3	3	3
										0	3	4
K. pneumoniae	x	x	x	x	x	x	x	x	x	2	2	2
										4	8	7

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Wound Healing	Leaves	Selangor, Malaysia	Juice (Plant mix with filtered water containing 0.1% (w/w) sodium meta-bisulphite, honey and 0.2% (w/w) xantham gum)	*In vivo:* Streptozotocin-induced diabetic rats and normal rats	70, 105 & 140 mg/kg body weight	Male albino *Sprague Dawley* rats (150 - 200 g)	-	Diabetic and normal untreated rats	*S. crispa* juice significantly increased the percentage of wound healing on days 3 and 7 in the treated groups compared to diabetic and normal controls, especially those treated with 140 mg/kg body weight of *S. crispa* juice in diabetic and normal rats. Besides, there was a significant correlation between wound healing, glutathione peroxidase (GPx) and superoxide dismutase (SOD) enzymes as it increased GPx and SOD activity in the treated group of diabetic rats.	[30]
	Leaves	Selangor, Malaysia	Ethanolic extract	*In vivo*	100 & 200 mg/mL (twice daily); all groups received a placebo (gum acacia in normal saline)	Male *Sprague Dawley* rats (8 weeks old, 220 - 250 g)	Intrasite gel (0.2 mL)	Placebo, gum acacia in normal saline (0.2 mL)	The extract significantly accelerated the rate of wound healing, as wounds coated with the extract healed earlier than those treated with a placebo. Besides, histological analysis of healed wounds coated with the leaf extract showed comparatively smaller scar width, fewer inflammatory cells, and more angiogenic collagen compared to wounds given placebo.	[65]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Wound Healing	Leaves	Selangor, Malaysia	Aqueous extract	*In vivo* anti-ulcero-genic activity on ethanol-induced mucosal injury rats	250, 500 & 1000 mg/kg body weight	Anti-ulcero-genic activity: Male Sprague Dawley rats (180 - 200 g)	Omepra-zole (20 mg/kg body weight)	Distilled water	The extract exhibited significant anti-ulcerogenic activity by increasing gastric mucin production and pH of gastric contents to reduce gastric lesion formation. The gastroprotective effect of the 1000 mg/kg *S. crispa*-treated group was more prominent.	[66]
Cytotoxic/ Anticancer	Leaves	Selangor, Malaysia	Aqueous extract of fermen-ted tea (young & old)	*In vitro* cyto-toxic activity by MTT assay	5, 10, 20, 40, 60, 80 & 100 µg/mL	(i) MCF-7 (ii) MDA-MB-231	-	-	IC_{50} (in µg/mL): Sample / MCF-7 / MDA-MB-231: *S. crispa* unfermented tea (young) > 100 / > 100; *S. crispa* unfermented tea (old) 81 / > 100; *S. crispa* fermented tea (young) > 100 / > 100; *S. crispa* fermented tea (old) 73 / > 100	[55]

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td>Cytotoxic/ Anticancer</td><td>Leaves</td><td>-</td><td>(i) Catechin extract (ii) Ethanolic extract, methanolic extract & chloroform extract. (iii) Hexane extract, chloroform extract, ethyl acetate extract & methanolic extract. (iv) β-sitosterol extract & stigmasterol extract</td><td>In vitro cytotoxic activity by MTT assay</td><td>-</td><td>(i) Hep-G2 (ii) MCF-7 (iii) MDA-MB-231 (iv) Caco-2 (v) Chang liver cells</td><td>-</td><td>-</td><td>IC_{50} (in µg/mL):
(i)<table><tr><th>Extract</th><th>HepG-2</th><th>MCF-7</th><th>MDA-MB-231</th><th>Caco-2</th><th>Chang liver</th></tr><tr><td>Catechin</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td></tr></table>(ii)<table><tr><th>Extract</th><th>Hep G-2</th><th>MCF-7</th><th>MDA-MB-231</th><th>Caco-2</th><th>Chang liver</th></tr><tr><td>Ethanol</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td></tr><tr><td>Methanol</td><td>29</td><td>22</td><td>> 100</td><td>27</td><td>> 100</td></tr><tr><td>Chloroform</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td></tr></table>(iii)<table><tr><th>Extract</th><th>Hep G-2</th><th>MCF-7</th><th>MDA-MB-231</th><th>Caco-2</th><th>Chang liver</th></tr><tr><td>Hexane</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td></tr><tr><td>Chloroform</td><td>28</td><td>25</td><td>> 100</td><td>> 100</td><td>> 100</td></tr><tr><td>Ethyl Acetate</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td></tr><tr><td>Methanol</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td><td>> 100</td></tr></table></td><td>[69]</td></tr>
</table>

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td rowspan="2">Cytotoxic/ Anticancer</td><td>Leaves</td><td>Selangor, Malaysia</td><td>Chloro-form extract</td><td>In vitro apopto-genic effect by TUNEL assay</td><td>20 & 30 µg/mL</td><td>HepG-2 cell line</td><td>-</td><td>Untreated cell line</td><td>Nuclei condensation, cell shrinkage, and apoptotic bodies were successfully observed in the cells, indicating that apoptosis had been induced.</td><td>[78]</td></tr>
<tr><td>Leaves</td><td>Padang, Indonesia</td><td>(i) Meth-anolic extract (ii) Aque-ous extract</td><td>In vitro cyto-toxic activity by MTT assay</td><td>5, 10, 20, 40, 60, 80, 100 & 150 µg/mL</td><td>Cyto-toxicity: (i) MCF-7 (ii) T-47D (iii) HCT 116 (iv) HepG-2 (v) NCI-H23 (vi) CCD-18Co</td><td>Vincris-tine (60 ng/mL)</td><td>Medium in 0.01% DMSO</td><td></td><td>[51]</td></tr>
</table>

IC_{50} (in µM): (iv)

Extract	HepG-2	Caco-2	MCF-7	MDA-MB-231	Chang liver
β-sitosterol	53	20	71	> 248	> 248
Stigmasterol	182	133	156	186	> 248

Cell line	IC_{50} (µg/mL)	
	Methanolic extract	Aqueous extract
HepG-2	> 200	> 200
HCT 116	> 200	> 200
T-47D	122	> 200
NCI-H23	> 200	> 200
CCD-18Co	> 200	> 200
MCF-7	160	121

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leaves	Pulau Pinang, Malaysia	Dichloro-methane bioactive sub-fraction	Cyto-toxicity: *In vitro* cyto-toxic activity by LDH assay Apopto-genic effect: *In vitro* apopto-genic effect by: (i) An-nexin V-FLUOS assay (ii) Cas-pase 3/7 activity	Cyto-toxicity: 100 µg/mL; 8.5 & 10.0 µg/mL for compara-tive study on breast cancer; 7.2 & 7.4 µg/mL for compara-tive study on prostate cancer Apopto-genic effect: Human breast cancer cell line: 8.5 or 10.0 µg/mL (24 hours); Prostate cancer cell lines:	Cyto-toxicity: (i) MCF-7 (ii) MDA-MB-231 (iii) PC-3 (iv) DU-145 (v) MCF-10A Apopto-genic effect: (i) Human breast cancer cell lines: MCF-7 & MDA-MB-231 (ii) Pros-tate cancer cell lines: PC-3 & DU-145	Cyto-toxicity: (i) Ta-moxifen (ii) Dox-orubicin (iii) Pacli-taxel (iv) Doce-taxel Apopto-genic effect: (i) Hu-man breast cancer cell lines: Ta-moxifen (15 µM for 24 h); Prostate cancer cell lines: Pacli-taxel (50	Cyto-toxicity: DMSO (≤ 0.1%) Apoptogenic effect: DMSO (0.1%)	Cytotoxicity: Cell line / EC_{50} (µg/mL) MCF-7: 9 MDA-MB-231: 10 DU-145: 7 PC-3: 7 Compared with tamoxifen, paclitaxel, docetaxel, and doxorubicin, the dichloromethane bioactive subfraction of *S. crispa* displayed relatively high cytotoxicity against cancer cells. Apoptogenic effect: The strong response of cancer cells to Annexin V antibodies and activation of effector caspase 3 or 7 suggested that cell death induced by the dichloromethane bioactive subfraction of *S. crispa* was caused by apoptosis.	[24]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leaves	Selangor, Malaysia	Ethanolic extract	*In vitro* cyto-toxic activity by: (i) MT T assay (ii) BrdU assay (iii) Cell cycle progres-sion (iv) TUNEL DNA frag-menta-tion analysis (v) ELI SA cyto-chrome c release and activa-	7.4 & 7.2 µg/mL (48 hours) (i) 0 - 100 µg/mL (ii) 30 µg/mL (iii) 30 µg/mL (iv) 30 µg/mL (v) 30 µg/mL (vi) 30 µg/mL	Cyto-toxicity: (i) HeLa, HT-29, MDA-MB-231 & MCF-7 (ii)-(vi) MCF-7	nM for 48 h) (ii) - (i) Dox-orubicin (ii) - (iii) - (iv) - (v) - (vi) -	(i) - (ii) - (iii) Un-treated cells (iv) Un-treated cells (v) Un-treated cells (vi) Un-treated cells	(i) Cell line: HeLa — IC_{50} (µg/mL): *S. crispa* 78 ± 2, Doxorubicin N/A; HT-29 — 52 ± 6, 52 ± 3; MDA-MB-231 — > 100, 5; MCF-7 — 30 ± 3, 3 (ii) *S. crispa* extract showed anti-proliferative effects in MCF-7 cells, as evidenced by a decrease in the percentage of cells bound to BrdU. (iii) A sub-G_1 population with hypo-diploid DNA was detected in cell cycle analysis of MCF-7 cells treated with *S. crispa* extract. (iv) TUNEL positivity in *MCF-7* cells treated with *S. crispa* extract indicated the presence of apoptosis. (v) Exposure to *S. crispa* extracts increased the relative concentration of cytochrome c in the cytosol of MCF-7 cells as well as the concentrations of initiator caspase 9 and active caspase 3/7. (vi) In MCF-7 cells, *S. crispa* extract increased the expression of the tumor suppressor proteins p53, cyclin-dependent kinase 4 and cyclin-dependent kinase 2, while decreasing the expression of the inhibitor of apoptosis protein XIAP.	[70]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
				tion of cas-pases 3/7, 8 and 9 detec-tions (vi) Cell cycle regula-tors protein quanti-fication						
Cytotoxic/ Anticancer	Leaves & Flowers	-	(i) Hex-ane extract (ii) Di-chloro-methane extract (iii) Ethyl acetate extract (iv) Meth-anolic extract	*In vitro* anti-cancer activity by MTS assay	0.1 – 100 µg/mL	HT-29 cell line	-	Blank medium	Plant material / Extract / IC_{50} (µg/mL) Leaves / Hexane / N/A Dichloromethane / N/A Ethyl acetate / 70 ± 1 Methanol / 59 ± 1 Flowers / Hexane / N/A Dichloromethane / 90 ± 1 Ethyl acetate / 42 ± 2 Methanol / N/A	[9]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leaves & stems	Terengganu, Malaysia	Cyto-toxicity: (i) Hex-ane extract (ii) Ethyl acetate extract (iii) Chlo-roform extract (iv) Meth-anolic extract (v) Aque-ous extract Apopto-genic effect: Hexane extract	Cyto-toxicity: *In vitro* cyto-toxic activity by: (i) MTT assay (ii) Cell cycle analysis Apopto-genic effect: *In vitro* apopto-genic effect by caspase activity assay	Cyto-toxicity: (i) 12.5, 25, 50, 100 & 200 µg/mL (ii) 160 µg/mL Apopto-genic effect: 160 µg/mL for 72 h	Cyto-toxicity: HeLa cell line Apopto-genic effect: HeLa cell line	Cyto-toxicity: - Apopto-genic effect: -	Cytotoxicity: Cells treated with cell culture medium. Apoptogenic effect: Untreated cell line	Cytotoxicity: (i) Most stem and leaf extracts had little or no cytotoxic effect on HeLa, except hexane stem extract (IC_{50} = 160 ± 10 µg/mL) and chloroform stem extract which showed a possible cell inhibition trend. (ii) The sub-G_1 peak detected by flow cytometry in the cell cycle analysis indicated that the hexane stem extract could induce apoptosis. Apoptogenic effect: Caspase-3/7 activity was significantly increased in treated HeLa cells compared to controls. Besides, caspase-8 activity was slightly decreased, and caspase-9 activity was slightly increased.	[80]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leaves	Selangor, Malaysia	γ-sitosterol obtained from chloro-form extract	*In vitro* cyto-toxic activity by: (i) MTT assay (ii) RT-PCR (iii) TU NEL assay	(i) 0.468, 0.937, 1.875, 3.750, 7.5, 15 and 30 µg/mL (ii) - (iii) -	Cyto-toxicity: (i) HepG-2, Caco-2, MCF-7 & Chang Liver (ii) HepG-2 & Caco-2 (iii) HepG-2 & Caco-2	-	-	(i) IC_{50} (in mg/mL): HepG2: 22 Caco-2: 8 MCF-7: 29 (ii) & (iii) γ-sitosterol induced apoptosis and suppressed c-Myc genes expression in Caco-2 and HepG-2 cell lines.	[71]
	Leaves	(i) Penang, Malaysia (ii) Kelantan, Malaysia (iii) Selangor, Malaysia	Aqueous extract	*In vitro* anti-cancer activity by MTT assay	20, 40, 80, 160, 320 & 640 µg/mL	(i) HeLa cell line (ii) Normal human mammary epithelial cell line	Ta-moxifen	DMSO (0.1% v/v) in medium	Compared with the extracts from Selangor (IC_{50} = 266 µg/mL) and Penang (IC_{50} = 332 µg/mL) as well as tamoxifen (IC_{50} = 63 µg/mL), the leaf extract from Kelantan showed potent anticancer activity with IC_{50} of 183 µg/mL	[14]

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td>Cytotoxic/ Anticancer</td><td>Leaves</td><td>Selangor, Malaysia</td><td>Juice (Plant mix with filtered water containing 0.1% (w/w) sodium meta-bisulphite, honey and 0.2% (w/w) xantham gum)</td><td>In vitro cytotoxic activity by: (i) MTT assay (ii) Flow cytometry (iii) Comet assay (iv) Gene expression and RT-PCR</td><td>(i) 0.001, 0.01, 0.1, 1.0 & 10% in volume of 100 µL (ii) 0.1, 0.4 & 1% (iii) 0.1, 0.4 & 1% (iv) 0.1, 0.4 & 1%</td><td>(i) Chang liver cell line & HepG-2 cell line (ii) HepG-2 cell line (iii) HepG-2 cell line (iv) HepG-2 cell line</td><td>(i) - (ii) - (iii) - (iv) House-keeping genes including ß-actin and 15s</td><td>(i) - (ii) Un-treated cell line (iii) - (iv) Sample without DNA template</td><td>
<table>
<tr><th rowspan="2">Concentration (%)</th><th colspan="3">Expression of oncogenes Strobilanthes in HepG2 (INT/mm^2)</th></tr>
<tr><th>c-Myc</th><th>c-Fos</th><th>c-erbB2</th></tr>
<tr><td>0.0</td><td>0.76</td><td>0.55</td><td>0.76</td></tr>
<tr><td>0.1</td><td>1.28</td><td>0.91</td><td>0.55</td></tr>
<tr><td>0.4</td><td>1.15</td><td>0.42</td><td>0.53</td></tr>
<tr><td>1.0</td><td>1.25</td><td>0.42</td><td>0.48</td></tr>
</table>
(i) S. crispa juice was cytotoxic to cancer cells starting at a concentration of 0.1% and incubation time over 72 hours.
(ii) In juice-treated cell lines, the number of sub-G_1 phases increased from 3% to 25%, and the number of G_2/M phases decreased from 33% to 7%, indicating apoptosis.
(iii) DNA damage was significantly increased in HepG2 cells after treatment with different concentrations of S. crispa juice at 0.1, 0.4, and 1.0% for 72 hours.
(iv) In juice-treated HepG2 cells, the expression level of c-Myc gene increased, while the expression level of c-Fos and c-erbB2 genes decreased in a dose-dependent manner.</td><td>[79]</td></tr>
</table>

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td>Cytotoxic/ Anticancer</td><td>Leaves & stems</td><td>Terengganu, Malaysia</td><td>(i) Hexane extract (ii) Chloroform extract (iii) Ethyl acetate extract (iv) Methanolic extract (v) Aqueous extract</td><td>Cytotoxicity: In vitro cytotoxic activity by: (i) MTT assay (ii) Flow cytometric analysis

Apoptogenic effect: In vitro apoptogenic effect by caspase activity assay</td><td>Cytotoxicity: (i) 12.5, 25, 50, 100 & 200 µg/mL (ii) Respective IC_{50} concentration for each of the extract

Apoptogenic effect: Respective IC_{50} concentration for each of the extract</td><td>Cytotoxicity: (i) CNE-1 & NRK-52E cell lines (ii) CNE-1 cell line

Apoptogenic effect: CNE-1 cell line</td><td>Cytotoxicity: 5-fluorouracil (12.5, 25, 50, 100 & 200 µg/mL)
(i) 5-fluorouracil (IC_{50} = 3 µg/mL)

Apoptogenic effect: Doxorubicin (3 ± 1 µg/mL)</td><td>Cytotoxicity: -

Apoptogenic effect: -</td><td>Cytotoxicity:
(i)<table><tr><th>Plant material</th><th>Extract/ treatment</th><th>IC_{50} (µg/mL) CNE-1</th><th>IC_{50} (µg/mL) NRK-52E</th><th>Selectivity index</th></tr><tr><td>Leaves</td><td>Hexane</td><td>124 ± 38</td><td>84 ± 1</td><td>0.68</td></tr><tr><td></td><td>Chloroform</td><td>1612 ± 20</td><td>185 ± 12</td><td>1.14</td></tr><tr><td></td><td>Ethyl acetate</td><td>119 ± 48</td><td>167 ± 2</td><td>1.40</td></tr><tr><td></td><td>Methanol</td><td>N/A</td><td>N/A</td><td>-</td></tr><tr><td></td><td>Water</td><td>N/A</td><td>N/A</td><td>-</td></tr><tr><td>Stems</td><td>Hexane</td><td>49 ± 8</td><td>11 ± 3</td><td>0.22</td></tr><tr><td></td><td>Chloroform</td><td>148 ± 23</td><td>N/A</td><td>> 1.35</td></tr><tr><td></td><td>Ethyl acetate</td><td>164 ± 16</td><td>174 ± 6</td><td>1.06</td></tr><tr><td></td><td>Methanol</td><td>N/A</td><td>N/A</td><td>-</td></tr><tr><td></td><td>Water</td><td>N/A</td><td>N/A</td><td>-</td></tr><tr><td>-</td><td>5-fluorouracil</td><td>3 ± 1</td><td>10 ± 5</td><td>3.15</td></tr></table>(ii) After extract treatment, the proportion of cells in sub G_1 phase increased and the proportion of cells in G_2/M phase decreased.

Apoptogenic effect:
The extracts did not change the activity of caspase -3/7, -8 and -9.</td><td>[31]</td></tr>
</table>

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leaves & stems	Sabah, Malaysia	(i) Methanolic extract (ii) Hexane extract (iii) Chloroform extract (iv) Ethyl acetate extract (v) Aqueous extract	*In vitro* cytotoxic activity by MTT assay	0 - 90 µg/mL	Anti-proliferative activity: MCF-7 cell line	-	-	Extract: Methanol — IC_{50} value (µg/mL): Leaves 74, Stems - Hexane — Leaves -, Stems - Chloroform — Leaves 80, Stems 86 Ethyl acetate — Leaves -, Stems 38 Water — Leaves 23, Stems -	[72]

<table>
<tr><th>Assay tested</th><th>Plant part</th><th>Origin/ Country/ Region</th><th>Extract type</th><th>Model/ Assay</th><th>Dose range/ Duration</th><th>Organism/ Cell line</th><th>Positive Control</th><th>Negative Control</th><th>Results</th><th>Ref</th></tr>
<tr><td>Cytotoxic/ Anticancer</td><td>Leaves & stems</td><td>-</td><td>Cyto-toxicity:
(i) Hex-ane extract
(ii) Ethyl acetate extract
(iii) Chlo-roform extract
(iv) Meth-anolic extract
(v) Aque-ous extract

Apopto-genic effect: Hexane extract</td><td>Cyto-toxicity: In vitro cyto-toxic activity by:
(i) MTT assay
(ii) Cell doubling time.
(iii) Cell cycle analysis

Apopto-genic effect: In vitro apopto-genic effect by detec-tion of caspase-8</td><td>Cyto-toxicity:
(i) 12.5, 25, 50, 100 & 200 µg/mL
(ii) IC_{50} and 2x IC_{50} of stem hexane extract
(iii) IC_{50} of stem hexane extract

Apopto-genic effect:
(i) 39 ± 9 µg/mL
(ii) 43 ± 40 µg/mL</td><td>Cyto-toxicity:
(i) HepG-2, MDA-MB-231 & NRK-52E cell lines
(ii) HepG-2 & MDA-MB-231 cell lines
(iii) HepG-2 & MDA-MB-231 cell lines

Apopto-genic effect:
(i) HepG-2 cell line MDA-MB-231 cell line</td><td>Cyto-toxicity:
(i) 5-fluro-uracil (12.5, 25, 50, 100 & 200 µg/mL)
(ii) -
(iii) 5-fluoro-uracil (IC_{50} = 37 µg/mL & 60 µg/mL)

Apopto-genic effect: -</td><td>Cytotoxicity:
(i) -
(ii) Untreated cells
(iii) -

Apoptogenic effect: Untreated cell line</td><td>Cytotoxicity:
(i)<table><tr><th>Plant material</th><th>Extract/ treatment</th><th colspan="2">IC_{50}, µg/mL (SI)</th></tr><tr><th></th><th></th><th>HepG-2</th><th>MDA-MB-231</th></tr><tr><td>Leaves</td><td>Hexane</td><td>N/A</td><td>193 ± 4 (0.44)</td></tr><tr><td></td><td>Chloroform</td><td>176 ± 35 (1.05)</td><td>N/A</td></tr><tr><td></td><td>Ethyl acetate</td><td>177 ± 15 (0.94)</td><td>N/A</td></tr><tr><td></td><td>Methanol</td><td>N/A</td><td>N/A</td></tr><tr><td></td><td>Water</td><td>N/A</td><td>N/A</td></tr><tr><td>Stems</td><td>Hexane</td><td>39 ± 9 (0.28)</td><td>43 ± 40 (0.26)</td></tr><tr><td></td><td>Chloroform</td><td>1739 ± 6 (>1.15)</td><td>N/A</td></tr><tr><td></td><td>Ethyl acetate</td><td>N/A</td><td>N/A</td></tr><tr><td></td><td>Methanol</td><td>N/A</td><td>N/A</td></tr><tr><td></td><td>Water</td><td>N/A</td><td>N/A</td></tr><tr><td>-</td><td>5-fluorouracil</td><td>37 ± 7 (0.26)</td><td>60 ± 14 (0.16)</td></tr></table>(ii) There was no significant difference in cell population doubling time when HepG-2 cells were exposed to extracts at IC_{50}. However, cells treated with doubled IC_{50} extracts showed a significant increase in cell doubling time compared to the untreated controls. On the other hand, the response of MDA-MB-231 cells to SH was dose-dependent. IC_{50} treatment resulted in a 2.5-fold delay in cell proliferation, while twice the IC_{50} resulted in a 3.4-fold delay in cell doubling.</td><td>[73]</td></tr>
</table>

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref

(iii)

Cell	Cell cycle phase	Percentage of cells		P-value
		Control	Stem hexane	
HepG-2	Sub-G	0.79 ± 0.01	0.41 ± 0.01	0.017
	G_0/G_1	60.68 ± 1.22	71.16 ± 0.68	0.009
	S	2.22 ± 0.05	1.80 ± 0.01	0.008
	G_2/M	35.37 ± 0.71	26.13 ± 0.25	0.003
MDA-MB-231	Sub-G	0.56 ± 0.59	5.04 ± 3.44	0.181
	G_0/G_1	70.25 ± 9.68	57.86 ± 10.23	0.270
	S	0.94 ± 0.86	8.57 ± 8.02	0.293
	G_2/M	28.31 ± 8.29	28.98 ± 13.75	0.956

Apoptogenic effect:
Extract treatment significantly induced caspase-8 activation in HepG-2 and MDA-MB-231 cell lines.

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
	Leaves	Selangor, Malaysia	Dichloro-methane bioactive sub-fraction	*In vivo* immune stimula-tory effect on NMU-induced breast cancer rats	40 mg/kg body weight daily for eight weeks. Tumour control groups received an equiva-lent volume of corn oil once daily for eight weeks.	Immuno-modulatory effect: Female Sprague Dawley rats (35 days)	-	Tumour-bearing untreated rats	F3 fraction exhibited significant immune stimulatory effects compared to tumour controls, partly by increasing MHC-II, $CD4^+$ and $CD8^+$ T cells and CIITA expression in F3-treated rats. F3-treated rats also showed significantly reduced serum levels of CCL2 and $CD68^+$ infiltrating macrophages. Besides, serum IFN-γ levels were increased by 1.7-fold in this group, suggesting that increased T cell infiltration and upregulation of CIITA and MHC-II expression in tumour cells may be triggered by F3-induced IFN-γ-production.	[77]
Cytotoxic/ Anticancer										
	Leaves	Negeri Sembilan, Malaysia	Metha-nolic extract	*In vitro* cytotoxic activity by MTT assay and photo-dynamic therapy	3.125, 6.25, 12.5, 25, 50, & 100 µg/mL	Anti-proliferative activity: HepG-2 cell line	-	Treated cells without photo-dynamic therapy	In the absence of photoactivation, extract-treated HepG-2 showed no significant cell death. However, after 10 minutes of light activation, the antiproliferative effect of the extract was clearly seen with an IC_{50} of 9 ± 1 µg/mL.	[57]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leaves	Penang, Malaysia	Dichloro-methane bioactive sub-fraction	*In vivo* anti-meta-static activity on 4T1-induced mouse mam-mary carci-noma model	100 mg/kg/ day over 30 days	Anti-metastatic activity: Female Balb/c mice (4 to 6 weeks)	-	(i) Untreated tumour-bearing mice (ii) Untreated normal mice (iii) Treated normal mice (100 mg/kg/day for 30 days)	According to the study, physical tumour growth (weight and volume) was significantly lower in all tumour-bearing mice treated with the *S. crispa* dichloromethane bioactive subfraction, lutein, and β-sitosterol compared with the untreated tumour-bearing group. Besides, the *S. crispa* dichloromethane bioactive subfraction was able to inhibit tumour growth at secondary metastatic sites such as the lungs, liver, kidneys, and spleen due to the normal features of the organ observed in the histomorphological examination of tissue sections. Moreover, administration of the *S. crispa* dichloromethane bioactive subfraction did not result in significant changes in full blood count values. Lastly, body weight gain was observed in tumour-bearing mice treated with the *S. crispa* dichloromethane bioactive subfraction, lutein, and β-sitosterol.	[74]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leaves	Pulau Pinang, Malaysia	Dichloro -methane bioactive sub-fraction	(i) *In vitro* flow cyto-metric analysis (ii) *In vivo* anti-tumor immuno - genicity activity on 4T1-induced mouse mam-mary tumor model	(i) 50 µg/mL (ii) 100 mg/kg/ day for 30 days	Anti-tumor immuno-genic activity: (i) 4T1 cell line (ii) Female Balb/c mice (4 to 6 weeks)	-	(i) Untreated cells and isotype controls (rabbit IgG & mouse IgG1) (ii) Untreated tumor-bearing mice & normal mice	(i) Treatment of 4T1 cells with the dichloromethane bioactive subfraction of *S. crispa* for 24 hours significantly increased the expression of MHC class I and MHC class II surface proteins compared to untreated controls. (ii) Higher increases in MHC class I and MHC class II expression were detected in treated breast tissues from the treated tumour-bearing group compared to tumours from the untreated tumour-bearing group. Besides, the infiltration of CD4, CD8 and IL-2 cells in the microenvironment of breast tumours in treated mice was much higher compared to tumours in untreated mice. However, the number of $CD68^{+}$ macrophages was significantly reduced in treated mice.	[75]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Cytotoxic/ Anticancer	Leave & Stems	Sabah, Malaysia	Anti-proliferative activity: (i) Metha-nolic extract (ii) Hex-ane extract (iii) Chlo-roform extract (iv) Ethyl acetate extract (v) Aque-ous extract Apopto-genic effect: (i) Stem hexane extract (ii) Leaf aqueous extract	Anti-prolife-rative activity: *In vitro* cyto-toxic activity by MTT assay Apopto-genic effect: *In vitro* apopto-sis activity by: (i) Apopto-sis assay (ii) RT-PCR (iii) Western blotting	Anti-proliferative activity: 10 - 90 mg/mL for 3 days Apopto-genic effect: (i) Leaf aqueous extract (45 µg/mL) & stem hexane extract (60 µg/mL) (ii) - (iii) -	Anti-proliferative activity: (i) MDA-MB-231 cell line (ii) 293T cell line Apopto-genic effect: MDA-MB-231 cell line	Anti-proliferative activity: Campto-thecin (0.17 ng/mL for 3 days) Apopto-genic effect: (i) Camp-tothecin (0.17 ng/mL) (ii) - (iii) -	Anti-proliferative activity: Untreated cell line Apoptogenic effect: -	Anti-proliferative activity: In this study, only leaf aqueous extract (IC_{50} = 45 µg/mL) and stem hexane extract (IC_{50} = 60 µg/mL) were found to prevent MDA-MB-231 cell growth. Apoptogenic effect: Stem hexane extract could induce apoptosis by inhibiting BCL-2 protein expression without affecting pro-apoptotic proteins such as BAX and caspase 9. The reduction of cyclin A2 in stem hexane-treated cells suggested that this effect was related to cell cycle dysregulation. On the other hand, leaf aqueous extract had no effect on apoptosis and cell cycle arrest of treated cells.	[76]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Anti-trypanosomal	Leaves	Selangor, Malaysia	(i) Ethanolic extract (ii) Aqueous extract	*In vitro* anti-trypanosomal screening	1 - 250 µg/mL	*Trypanosoma evansi* strain Te7	Diminazene aceturate	Untreated trypanosome culture	Plant/Drug: *S. crispa*; Extract: Ethanol, Aqueous; IC_{50} (ng/mL): 52540 ± 1050, 800970 ± 278330 Plant/Drug: Diminazene aceturate; Extract: -; IC_{50} (ng/mL): 15 ± 3	[81]
Anti-inflammatory	Leaves & stems	-	Methanolic extract	*In vitro* lipopolysaccharide-stimulated RAW 264.7 macrophage cells viability test via MTT assay	Leaf extracts: 160 µg/mL & 80 µg/mL; Stem extracts: 2 µg/mL & 1 µg/mL	RAW 264.7 macrophage cells	Indomethacin (25 µM)	Untreated cells	Leaf extracts exerted anti-inflammatory activity *in vitro* by suppressing nitric oxide production, while stem extracts exerted anti-inflammatory activity *in vitro* by promoting Interleukin-10 production.	[82]
Anti-obesity	Leaves	Selangor, Malaysia	Chloroform-methanolic extract	*In vivo:* on diet-induced obese rats	1% w/w	Male Sprague Dawley rats (3 months, 350 - 450 g)	Diet-induced obese rats treated with tap water	Normal rats treated with tap water	Extract treatment improved obesity status by significantly lowering body weight gain, leptin levels, adipose tissue, and liver weight, increasing lipolysis rate, improving liver color and improving hepatic steatosis.	[83]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Anti-obesity	Leaves	Pulau Pinang, Malaysia	Chloro-form-metha-nolic extract	*In vivo*: on high-fat diet induced obese LDLr knock-out mice	Mice fed with high-fat diet and mice fed with low-fat diet received 0.1% for weeks 0 - 5 & 1% for weeks 5 - 10	Male LDL-receptor knockout mice (35 weeks, 45 - 60 g)	-	Untreated high-fat diet mice and low-fat diet mice	The extract significantly reduced the respiratory exchange ratio in week 9. At weeks 5 and 10, the extract did not alter food intake, body weight, and abdominal adipose tissue weight, but significant increases in plasma and liver cholesterol were observed.	[84]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Anti-urolithiatic	Leaves	Negeri Sembilan, Malaysia	(i) Hexane extract (ii) Ethyl acetate extract (iii) Methanolic extract (iv) Aqueous extract	*In vitro* anti-urolithiatic activity by: (i) Inhibition activity against CaOx crystals by aggregation assay (ii) Dissolution of CaOx crystals by titrimetric method	(i) 1 mg/mL in the volume of 1 mL (ii) 100 mg	-	(i) Cystone (1 mg/mL) (ii) Cystone (100 mg)	(i) Distilled water (ii) -	(i) Plant/Drug – Extract – Inhibition percentage (%) *S. crispa* – Hexane – 14.39 ± 1.61 Ethyl acetate – 23.16 ± 2.11 Methanol – 50.54 ± 2.11 Aqueous – 44.83 ± 2.89 Cystone – - – 92.28 ± 0.61 (ii) Plant/Drug – Extract – Dissolution percentage (%) *S. crispa* – Hexane – 45.05 ± 2.20 Ethyl acetate – 52.50 ± 2.50 Methanol – 36.67 ± 3.82 Aqueous – 44.50 ± 1.73 Cystone – - – 73.33 ± 3.82	[43]
Anti-angiogenic	Leaves	Padang, Indonesia	(i) Methanolic extract (ii) Aqueous extract	*Ex vivo* rats aortic ring assay	6.25 - 100 µg/mL	Male Sprague Dawley rats	Suramin	-	Both extracts were found to have anti-angiogenic activity. At 100 µg/mL, the aqueous extract exhibited moderate activity (16.67 ± 8.11%), while the methanolic extract exhibited the lowest activity (6.25 ± 3.60%).	[51]

Assay tested	Plant part	Origin/ Country/ Region	Extract type	Model/ Assay	Dose range/ Duration	Organism/ Cell line	Positive Control	Negative Control	Results	Ref
Vasorelaxant activity	Whole plant	Penang, Malaysia	(i) Aqueous extract (ii) Ethanolic extract	*In vivo* vasorelaxant activity	0.125 - 128 mg/mL	Male Sprague Dawley rats (250-300 g)	-	-	Extract: Water; 50% Ethanol; 95% Ethanol EC_{50} (mg/mL): 39 ± 13; 56 ± 6; 21 ± 14	[85]

Funding

This work was financially supported by MOSTI – Technology Development Fund 2 (Ted2) Malaysia, under the grant TEF09211087 with a vote head number 76031.

Declaration of competing interest

The authors declare that they have no known competing interests that could have appeared to influence the work reported in this review paper.

ORCID
Chee-Shien Chen: 0009-0007-6957-030X
Siow-Ping Tan: 0000-0002-5861-6962
Chui-Fung Loke: 0000-0003-2268-9139
Tze-Ven Poh: 0000-0001-8583-4845

References

[1] J. R. Bennett and R. W. Scotland (2003). A revision of *Strobilanthes* (Acanthaceae) in Java, *Kew Bull* **58**, 1-82.
[2] J. R. I. Wood and R. W. Scotland (2009). New and little-known species of *Strobilanthes* (Acanthaceae) from India and South East Asia, *Kew Bull* **64**, 3-47.
[3] S. L. Deore, S. S. Khadabadi and B. A. Baviskar (2013). Pharmacognosy and phytochemistry: A comprehensive approach. BSP Books, India.
[4] F. Preethi and S. R. Suseem (2014). A comprehensive study on an endemic Indian genus-*Strobilanthes, Int. J. Pharmacogn.* **6**, 459-66.
[5] H. L. Raghavendra, T. R. Prashith Kekuda, S. Akarsh, M. C. Ranjitha and H. S. Ashwini (2017). Phytochemical analysis, antimicrobial and antioxidant activities of different parts of *Pleocaulus sessilis* (Nees) Bremek (Acanthaceae), *Int. J. Green Pharm.* **11**, 98-107.
[6] R. M. R. Nilanthi (2019). Diversity, distribution pattern of genus *Strobilanthes* Blume in Sri Lanka and their implications for conservation planning, *Wildlanka* **7**, 145-180.
[7] C. L. Blume (1826). Bijdragen tot de flora van Nederlandsch Indië. ter lands Drukkerij, Batavia.
[8] H. Terao (1983). Taxonomic study of the genus *Strobilanthes Blume* (Acanthaceae): Generic delimitation and infrageneric classification. Unpublished thesis submitted for the degree of PhD at Kyoto University, Kyoto, Japan.
[9] M. Ismail, G. Bagalkotkar, S. Iqbal and H. A. Adamu (2012). Anticancer properties and phenolic contents of sequentially prepared extracts from different parts of selected medicinal plants indigenous to Malaysia, *Molecules* **17**, 5745-5756.
[10] X. -L. Zhu, Y. Xu, D. -J. Sun, H. Li and L. -X. Chen (2022). The genus *Strobilanthes*: Phytochemistry and pharmacology, *TMR Modern Herb Med*. **5**, 15.
[11] I. Khan, S. A. Jan, Z. K. Shinwari, M. Ali, Y. Khan and T. Kumar (2017). Ethnobotany and medicinal uses of folklore medicinal plants belonging to family Acanthaceae: An updated review, *MOJ Biol. Med.* **1**, 34-38.
[12] L. M. Perry and J. Metzger (1980). Medicinal plants of east and southeast Asia: Attributed properties and uses. MIT Press, Cambridge.
[13] A. B. Mohd Fadzelly, R. Asmah and O. Fauziah (2006). Effects of *Strobilanthes crispus* tea aqueous extracts on glucose and lipid profile in normal and streptozotocin-induced hyperglycemic rats, *Plant Foods Hum. Nutr.* **61**, 7-12.
[14] A. Ghasemzadeh, H. Z. Jaafar and A. Rahmat (2015). Phytochemical constituents and biological activities of different extracts of *Strobilanthes crispus* (L.) Bremek leaves grown in different locations of Malaysia, *BMC Complement Altern. Med.* **15**, 422.
[15] Y. -Y. Siew, S. Zareisedehizadeh, W. -G. Seetoh, S. -Y. Neo, C. -H. Tan and H. -L. Koh (2014). Ethnobotanical survey of usage of fresh medicinal plants in Singapore, *J. Ethnopharmacol.* **155**, 1450-1466.
[16] H. Nurraihana and N. A. Norfarizan-Hanoon (2013). Phytochemistry, pharmacology and toxicology properties of *Strobilanthes crispus, Int. Food Res. J.* **20**, 2045-2056.
[17] M. G. Ng, C. H. Ng, K. Y. Ng, S. M. Chye, A. P. K. Ling and R. Y. Koh (2021). Anticancer properties of *Strobilanthes crispus*: A review, *Process.* **9**, 1370.

[18] V. Ramadhani, Rusdi, Z. Azizah and H. Rivai (2021). Overview of phytochemicals and pharmacological activity of Keji Beling Plant (*Strobilanthes crispus* Bl.), *Int. J. Pharm. Pharm. Sci.* **6**, 25-39.

[19] C. A. D. Backer and R. C. V. Bakhuizen (1963). Flora of Java (spermatophytes only). Noordhoff Press, Groningen.

[20] P. A. Sunarto (1977). Materia medika Indonesia (1st ed.). Penerbit Direktorat Jenderal Pengawasan Obat dan Makanan, Jakarta.

[21] K. Heyne (1987). Acanthaceae: Strobilanthes crispus BL. Tumbuhan Berguna Indonesia III (Badan Litbang Kehutanan Jakarta ed.). Yayasan Sarana Wana Jaya, Jakarta.

[22] M. Ismail, E. Manickam, A. M. Danial, A. Rahmat and A. Yahaya (2000). Chemical composition and antioxidant activity of *Strobilanthes crispus* leaf extract, *J. Nutr. Biochem.* **11**, 536-542.

[23] S. Dalimartha (2006). Atlas tumbuhan obat Indonesia jilid 4. Puspa Swara, Jakarta.

[24] N. S. Yaacob, N. Hamzah, N. N. Nik Mohamed Kamal, S. A. Zainal Abidin, C. S. Lai, V. Navaratnam and M. N. Norazmi (2010). Anticancer activity of a sub-fraction of dichloromethane extract of *Strobilanthes crispus* on human breast and prostate cancer cells *in vitro, BMC Complement Altern. Med.* **10**, 42.

[25] I. H. Burkill, W. Birtwistle, F. W. Foxworthy, J. B. Scrivenor and J. G. Watson (1935). A dictionary of the economic products of the Malay Peninsula. Crown Agents for the Colonies, London.

[26] Britannica (The Editors of Encyclopaedia) (2014). Malay Archipelago, available at https://www.britannica.com/place/Malay-Archipelago. Accessed 16 January 2023.

[27] A. Noraida (2005). Penyembuhan semula jadi dengan herba. PTS Millennia Sdn. Bhd., Kuala Lumpur.

[28] S. Yogespiriya, P. Hanachi, I. Patimah, R. Asmah and O. Fauziah (2005). Histological study during hepatocarciniogenesis in rats treated with *Strobilanthes crispus* extract, *J. Biol. Sci.* **5**, 153-157.

[29] POWO (2022). Plants of the World Online, available at http://www.plantsoftheworldonline.org/. Accessed 10 December 2022.

[30] N. A. Norfarizan-Hanoon, R. Asmah, M. Y. Rokiah, O. Fauziah and H. Faridah (2009). Effects of *Strobilanthes crispus* juice on wound healing and antioxidant enzymes in normal and streptozotocin-induced diabetic rats, *J. Biol. Sci.* **9**, 662-668.

[31] R. Y. Koh, Y. C. Sim, H. J. Toh, L. K. Liam, R. S. L. Ong, M. Y. Yew, Y. L. Tiong, A. P. K. Ling, S. M. Chye and K. Y. Ng (2015). Cytotoxic and apoptogenic effects of *Strobilanthes crispa* Blume extracts on nasopharyngeal cancer cells, *Mol. Med. Rep.* **12**, 6293-6299.

[32] Y. S. Baraya, K. K. Wong and N. S. Yaacob (2018). *Strobilanthes crispus* inhibits migration, invasion and metastasis in breast cancer, *J. Ethnopharmacol.* **233**, 13-21.

[33] Q. Wang, S. Huang, X. Chen and Y. Deng (2021). The complete chloroplast genome of *Strobilanthes biocullata* (Acanthaceae), *Mitochondrial DNA B: Resour.* **6**, 1668-1669.

[34] K. L. Goh (2001). Malaysian herbs: Volume 1. Benar Padu Sdn Bhd, Selangor.

[35] Badan Pengawas Obat dan Makanan Republik Indonesia (BPOM RI) (2006). Acuan Sediaan Herbal. Jakarta.

[36] W. Sujarwo, A. P. Keim, V. Savo, P. M. Guarrera and G. Caneva (2015). Ethnobotanical study of Loloh: Traditional herbal drinks from Bali (Indonesia), *J. Ethnopharmacol.* **169**, 34-48.

[37] H. C. Ong and J. Norzalina (1999). Malay herbal medicine in Gemencheh, Negri Sembilan, Malaysia, *Fitoterapia* **70**, 10-14.

[38] A. Romulo, E. A. M. Zuhud, J. Rondevaldova and L. Kokoska (2018). Screening of *in vitro* antimicrobial activity of plants used in traditional Indonesian medicine, *Pharm. Biol.* **56**, 287-293.

[39] K. Roosita, C. M. Kusharto, M. Sekiyama, Y. Fachrurozi and R. Ohtsuka (2008). Medicinal plants used by the villagers of a Sundanese community in West Java, Indonesia, *J. Ethnopharmacol.* **115**, 72-81.

[40] A. J. S. J. Samuel, A. Kalusalingam, D. K. Chellappan, R. Gopinath, S. Radhamani, H. A. Husain, V. Muruganandham and P. Promwichit (2010). Ethnomedical survey of plants used by the Orang Asli in Kampung Bawong, Perak, West Malaysia, *J. Ethnobiol. Ethnomed*. **6**.

[41] S. R. Promwichit and H. M. Daud (2016). Screening of phytochemical properties and antimicrobial activity of malaysian medicinal plants against aquatic bacteria, *Malays. J. Microbiol.* **12**, 284-290.

[42] Q. Fardiyah, Suprapto, F. Kurniawan, T. Ersam, A. Slamet and Suyanta (2020). Preliminary phytochemical screening and fluorescence characterization of several medicinal plants extract from East Java Indonesia, *IOP Conf. Ser.: Mater. Sci. Eng.* **833**, 012008.

[43] M. T. Gul, A. S. Dheyab, E. K. Shaker, N. Muhammad and A. N. Pauzi (2020). *In vitro* evaluation of anti-urolithiatic properties of *Strobilanthes crispus* extracted using different solvents, *Res. J. Chem. Environ.* **24**.

[44] Y. C. Koay, K. C. Wong, H. Osman, I. M. S. Eldeen and M. Z. Asmawi (2013). Chemical constituents and biological activities of *Strobilanthes crispus* L., *Rec. Nat. Prod.* **7**, 59-64.

[45] N. S. Yaacob, H. M. Yankuzo, S. Devaraj, J. K. M. Wong and C. S. Lai (2015). Anti-tumor action, clinical biochemistry profile and phytochemical constituents of a pharmacologically active fraction of *S. crispus* in NMU-induced rat mammary tumour model, *PLoS One* **10**, e0126426.

[46] A. Rahmat, S. Edrini, P. Ismail, T. Y. H. Yap and M. F. A. Bakar (2006). Chemical constituents, antioxidant activity and cytotoxic ffects of essential oil from *Strobilanthes crispus* and *Lawsonia inermis, J. Biol. Sci.* **6**, 1005-1010.

[47] V. Lim, C. S. Yap, H. W. Chong, M. S. A. Shukkoor and M. Priya (2015). Antimicrobial evaluation and GC-MS analysis of *Strobilanthes crispus* ethanolic leaf extract, *European J. Med. Plants* **10**, 1-8.

[48] B. E. Cheong, N. A. Zakaria, A. Y. F. Cheng and P. L. Teoh (2016). GC-MS analysis of *Strobilanthes crispus* plants and callus, *Transactions on Science and Technology* **3**, 155-161.

[49] Angelina, M. Yumna, Abdullah, R. Arbianti, T. S. Utami and H. Hermansyah (2018). The usage of enzyme in ultrasound-assisted enzymatic extraction method and its effect on yield extract from Keji Beling (*Strobilanthes crispus.*) leaves, *E3S Web Conf.* **67**, 03002.

[50] L. Y. W. Chua, B. L. Chua, A. Figiel, C. H. Chong, A. Wojdyło, A. Szumny and T. S. Y. Choong (2019). Antioxidant activity, and volatile and phytosterol contents of *Strobilanthes crispus* dehydrated using conventional and vacuum microwave drying methods, *Molecules* **24**, 1397.

[51] N. S. Muslim, K. W. Ng, A. Itam, Z. D. Nassar, Z. Ismail and A. M. S. Abdul Majid (2010). Evaluation of cytotoxic, anti-angiogenic and antioxidant properties of standardized extracts of *Strobilanthes crispus* leaves, *Int. J. Pharmacol.* **6**, 591-599.

[52] H. M. Tan, K. H. Leong, J. Song, N. S. F. Mohd Sufian, U. H. A. Mohd Hazli, L. Y. Chew and K. W. Kong (2020). Antioxidant and LC-QToF-MS/MS analysis of polyphenols in polar and non-polar extracts from *Strobilanthes crispus* and *Clinacanthus nutans, Int. Food Res. J.* **27**, 903-914.

[53] H. Hanisa, M. L. Mohd Azmi, M. Suhaila and M. N. Somchit (2012). Liquid chromatography-mass spectrometry-electrospray ionisation analysis of *Centella asiatica* I., *Curcuma longa* L. and *Strobilanthes crispus* L. methanol extracts, *J. Med. Plant Res.* **6**, 3908-3918.

[54] N. A. Norfarizan-Hanoon, R. Asmah, M. Y. Rokiah, O. Fauziah and H. Faridah (2009). Antihyperglycemic, hypolipidemic and antioxidant enzymes effect o*f Strobilanthes crispus* juice in normal and streptozotocin-induced diabetic male and female rats, *Int. J. Pharmacol.* **5**, 200-207.

[55] M. F. A. Bakar, A. H. Teh, A. Rahmat, F. Othman, N. Hashim and S. Fakurazi (2006). Antiproliferative properties and antioxidant activity of various types of *Strobilanthes crispus* tea, *Int. J. Cancer Res.* **2**, 152-158.

[56] S. W. Qader, M. A. Abdulla, L. S. Chua, N. Najim, M. M. Zain and S. Hamdan (2011). Antioxidant, total phenolic content and cytotoxicity evaluation of selected malaysian plants, *Molecules* **16**, 3433-3443.

[57] S. -A. Tan, S. Y. Lim, C. S. Law, C. S. Yue, T. V. Poh, W. Z. Saad, S. Ismail, K. M. Yusoff, C. F. Loke (2019). Antioxidative and photocytotoxic effects of standardized *Clinacanthus nutans* and *Strobilanthes crispus* extracts toward HepG2 liver cells, *Pharmacogn. Mag.* **15**, 613.

[58] Z. Haida, J. J. Nakasha and M. Hakiman (2020). Phenolics content and antioxidant properties of *Strobilanthes crispus* as affected by different extraction solvents, *Fundam. Appl. Agric.* **5**, 584-589.

[59] W. K. Ban, I. L. Fong, H. Y. Khong and J. H. Y. Phung (2022). Wound healing, antimicrobial and antioxidant properties of *Clinacanthus nutans* (Burm. f.) Lindau and *Strobilanthes crispus* (L.) Blume extracts, *Molecules* **27**, 1722.

[60] M. Rahman, S. Hossain, A. Rahaman, N. Fatima, T. Nahar, B. Uddin and M. A. Basunia (2013). Antioxidant activity of *Centella asiatica* (Linn.) Urban: Impact of extraction solvent polarity. *J. Pharmacogn, Phytochem.* **1**, 27-32.

[61] N. M. A. Abd Samat, S. Ahmad, Y. Awang, R. A. H. Bakar and M. Hakiman (2020). Alterations in herbage yield, antioxidant activities, phytochemical contents, and bioactive compounds of Sabah snake grass (*Clinacanthus nutans* L.) with regards to harvesting age and harvesting frequency, *Molecules* **25**, 2833.

[62] Z. Zargoosh, M. Ghavam, G. Bacchetta and A. Tavili (2019). Efects of ecological factors on the antioxidant potential and total phenol content of *Scrophularia striata* Boiss, *Sci. Rep.* **9**, 16021.

[63] M. A. Abas, K. A. Hambali, N. H. Hassin, M. F. B. Karim, L. Ismail and H. Rosli (2020). Antifungal activity of selected Malaysia's local medicinal plants against sick building syndrome (SBS) fungi, *Asian J. Plant Sci.* **19**, 240-245.

[64] M. Muskhazli, M. Dirnahayu, A. A. Nor Azwady, Y. Nurhafiza, E. Nor Dalilah, C. K. N. Che Ku Nurshaira (2009). Antibacterial activity of methanolic crude extracts from selected plant against *Bacillus cereus, Pertanika J. Trop. Agric. Sci.* **32**, 175-185.

[65] N. Al-Henhena, A. A. Mahmood, A. Al-magrami, A. B. Nor Syuhada, A. A. Zahra, M. D. Summaya, M. S. Suzi and I. Salmah (2011). Histological study of wound healing potential by ethanol leaf extract of *Strobilanthes crispus* in rats, *J. Med. Plant Res.* **5**, 3660-3666.

[66] A. A. Mahmood, A. A. Fard, H. Harita, Z. A. Amin and I. Salmah (2011). Evaluation of gastroprotective effects of *Strobianthes crispus* leaf extract on ethanol-induced gastric mucosal injury in rats, *Sci. Res. Essays* **6**, 2306-2314.

[67] K. Mullane and M. Williams (2015). Unknown unknowns in biomedical research: Does an inability to deal with ambiguity contribute to issues irreproducibility?, *Biochem. Pharmacol.* **97**, 133-136.

[68] M. Heinrich, G. Appendino, T. Efferth, R. Fürst, A. A. Izzo, O. Kayser, J. M. Pezzuto and A. Viljoen (2020). Best practice in research – overcoming common challenges in phytopharmacological research, *J. Enthopharmacol.* **246**, 112230.

[69] A. Rahmat, S. Edrini, A. Md Akim, P. Ismail, T. Y. H. Yap and A. B. Mohd Fadzelly (2006). Anticarcinogenic properties of *Strobilanthes crispus* extracts and its compounds *in vitro, Int. J. Cancer Res.* **2**, 47-49.

[70] H. Z. Chong, A. Rahmat, S. K. Yeap, A. Md Akim, N. B. Alitheen, F. Othman and C. L. Gwendoline-Ee (2012). *In vitro* cytotoxicity of *Strobilanthes crispus* ethanol extract on hormone dependent human breast adenocarcinoma MCF-7 cell, *BMC Complement Altern. Med.* **12**, 35.

[71] S. Endrini, A. Rahmat, P. Ismail and Y. H. Taufiq-Yap (2014). Cytotoxic effect of γ-sitosterol from Kejibeling (*Strobilanthes crispus*) and its mechanism of action towards c-Myc gene expression and apoptotic pathway, *Med. J. Indones.* **23**, 203-208.

[72] N. Gordani, B. E. Cheong and P. L. Teoh (2017). Antiproliferative effect of *Strobilanthes crispus* on MCF-7 cell line, *Transactions on Science and Technology* **4**, 414-419.

[73] R. Y. Koh, F. P. Lim, L. S. Y. Ling, C. P. L. Ng, S. F. Liew, M. Y. Yew, Y. L. Tiong, A. P. K. Ling, S. M. Chye and K. Y. Ng (2017). Anticancer mechanisms of *Strobilanthes crispa* Blume hexane extract on liver and breast cancer cell lines, *Oncol. Lett.* **14**, 4957-4964.

[74] Y. S. Baraya, H. M. Yankuzo, K. K. Wong and N. S. Yaacob (2020). *Strobilanthes crispus* bioactive subfraction inhibits tumor progression and improves hematological and morphological parameters in mouse mammary carcinoma model, *J. Ethnopharmaco.* **267**, 113522.

[75] Y. S. Baraya, C. L. Wee, Z. Mustapha, K. K. Wong and N. S. Yaacob (2022). *Strobilanthes crispus* elicits anti-tumor immunogenicity in *in vitro* and *in vivo* metastatic reast carcinoma, *PLoS One* **17**, e0271203.

[76] N. Gordani, B. E. Cheong and P. L. Teoh (2022). Stem hexane extract of *Strobilanthes crispus* induces apoptosis in triple-negative breast cancer cell line, *Nutr. Cancer* **74**, 299-305.

[77] H. M. Yankuzo, Y. S. Barayaa, A. Mustaphaa, K. K. Wong and N. S. Yaacoba (2018). Immunomodulatory effects of a bioactive fraction of Strobilanthes crispus in NMU-induced rat mammary tumor model, *J. Ethnopharmacol.* **213**, 31-37.

[78] S. Endrini, Suherman, A. Rahmat, P. Ismail, Y. H. Taufiq-Yap and F. Othman (2007). Effects of *Strobilanthes crispus* extract on the apoptotic pathway of human liver carcinoma cell lines, *Jurnal Kedokteran YARSI* **15**.

[79] F. Hussin, S. A. Eshkoor, A. Rahmat, F. Othman, A. Akim and Z. Eshak (2015). *Strobilanthes crispus* juice concentrations and anticancer effects on DNA damage, apoptosis and gene expression in hepatocellular carcinoma cells, *Asian Pac. J. Cancer Prev.* **16**, 6047-6053.

[80] Y. H. Chong, R. Y. Koh, A. P. K. Ling, S. M. Chye and M. Y. Yew (2014). *Strobilanthes crispus* extract induces apoptosis through enhanced caspases activities in cervical cancer cells, *BEFE-2014*, 4-5.

[81] H. O. Dyary, A. K. Arifah, R. S. Sharma, A. Rasedee, M. S. Mohd-Aspollah, Z. A. Zakaria, A. Zuraini and M. N. Somchit (2014). Antitrypanosomal screening and cytotoxic effects of selected medicinal plants, *Trop. Biomed.* **31**, 1-8.

[82] Y. P. Wong, Y. S. A. A. Rao, A. P. K. Ling and R. Y. Koh (2016). Anti-inflammatory effect of *Strobilanthes crispus* methanolic extract on lipopolysaccharide-stimulated RAW 264.7 macrophages, *J. Biomed. Sci.*.

[83] N. Zawawi, A. H. Azizah and I. Maznah (2016). *Strobilanthes crispus* leaves extracts (SCE) induced lipolysis and increased leptin level in diet-induced obese rats fed high-fat diet, *Int. Food Res. J.* **23**, 1115-1122.

[84] N. Zawawi and M. Ismail (2018). *Strobilanthes crispus* extract reduces respiratory exchange ratio in obese mice fed high fat and low fat diets, *Malays J Med Sci.* **25**, 46-58.

[85] Y. S. Ch'ng, C. S. Tan, Y. C. Loh, M. Ahmad, M. Z. Asmawi and M. F. Yam (2016). Vasorelaxation study and tri-step infrared spectroscopy analysis of Malaysian local herbs, *J. Pharmacopuncture* **19**, 145-154.

[86] N. A. Norfarizan-Hanoon, R. Asmah, M. Y. Rokiah, O. Fauziah and H. Faridah (2012). Absence of toxicity of *Strobilanthes crispa* juice in acute oral toxicity study in Sprague Dawley rats, *Sains Malays.* **41**, 403-409.

[87] K.T. Lim, V. Lim and J.H. Chin (2012). Subacute oral toxicity study of ethanolic leaves extracts of *Strobilanthes crispus* in rats, *Asian Pac. J. Trop. Biomed.* **2**, 948-952.

[88] H. Kwan (2022). *Strobilanthes crispa* [Black Face General, Bayam Karang], available at http://www.natureloveyou.sg/Strobilanthes%20crispa/Main.html. Accessed 14 May 2023.

A C G
publications
© 2023 ACG Publications