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Overview of Phytochemicals and Pharmacological Activity of Keji Beling Plant (*Strobilanthes crispus* Bl.)

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Abstract

Nowadays, traditional medicine in the form of medicinal plants or herbs is widely used by the community. Treatment with plants that exist in nature and having relatively minor side effects can also be used for an extended period. The purpose of this review article is to seek information on the phytochemical content and pharmacological activity of keji beling plants (*Strobilanthes crispus* Bl.). This information was searched through the Google Scholar search engine in the last eleven years (2010 – 2021). The results of this information show that vile beling has a chemical content in the form of potassium, sodium, silicate acid, alkaloids, carbohydrates, phenolic, tannins, saponins, flavonoids, polyphenols, terpenoids, and steroids. Pharmacologically keji beling plants have antiurolithic, antidiabetic, antioxidant, antibacterial, anti-inflammatory, antiobesity, wound healing, anticancer, cytotoxic, and peptic ulcer effects. Thus, it can be concluded that the keji beling plant is one of the plants rich in phytochemical compounds scattered on the stems and leaves. In addition, this plant has benefits for treating a wide variety of diseases. Therefore, keji beling can be developed into potential plants as an herb for various conditions, especially stone urination and antidiabetic.

Keywords: Keji beling **(***Strobilanthes crispus* Bl.), phytochemicals, pharmacological activity.

1. Introduction

Keji beling (*Strobilanthes crispus*) is locally known as "spinach coral," "broken glass," "jin stone," and "broken beling" in Malaysia. This plant has traditionally been used to improve endurance, treat kidney stones, treat diabetes mellitus, high blood treatment, and wound treatment [1].

Keji beling plant is a herbal medicinal plant that comes from Madagascar to Indonesia. The plant contains high content of minerals and vitamins C, B1, andB2. Keji beling plants have phytochemical compounds such as polyphenols, flavonoids, catechins, alkaloids, caffeine, and tannins. Pharmacological typology shows that keji beling plants have antioxidant activity, free radical exterminator, anticancer, antidiabetic, antimicrobial, wound healing, and antiulcerogenic [2].

The name of the area is keji beling is daun picah beling, enyoh kelo, keci beling (Java). Part used as a folk remedy is the leaf. The benefit is as a stone urine remedy. The standard dosage is 2 x 15 leaves/day. How to make/use is: boil the leaves with two glasses of water, filter, drink while warm [3].

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The pharmacological effect of keji beling leaves can dissolve calcium salts and magnesium kidney stones. Treatable diseases are tumors, diabetes mellitus, jaundice, piles, high cholesterol, and ulcers. Its use empirically eats three pieces of fresh leaves daily as fresh vegetables [4].

1.1 Classification of keji beling plants [5]

Synonym: *Sericocalyx crispus* L
Division: Spermatophyta
Subdivision: Angiospermae
Class: Dicotyledonae
Nation: Solanales
Family: Acanthaceae
Marga: Strobilanthes
Type: *Strobilanthes crispus* Bl.
Common Name: Keji Beling

1.2 Morphology of keji beling plants

Keji beling grows wild in forests, riversides, cliffs and is often planted as fence plants in yards or parks. This plant is found from Madagascar to Indonesia, which grows at an altitude of 50 m to 1,200 m above sea level. This shrub has a height of 0.5 - 1 m. Stems are segmented, round, branched, rough-haired, and green in color. Branches that touch the soil will disco the roots to be separated from the parent plant (Figure 1). Single leaves are short-stemmed, with a facing position. Strands of lanset leave elongated or almost ellipse, jagged or bitten edges, tapered ends, pointy base, both rough surfaces, pinnate reflection, length 9-18 cm, width 3-6 cm, and green (Figure 2). Compound inflorescences are gathered in solid threads. The flower crown is divided into five funnel-shaped petals, 1.5 - 2 cm long, haired, and yellow. Fruit is bobbin-shaped, containing 2-4 seeds. The seeds are round, flattened small, brown. Propagation of plants with roots, cuttings, stems, or branches is quite old (Figure 3) [6].

Figure 1: Leaves, stems, and flowers of keji beling plants (*Strobilanthes crispus* Bl.) [2]

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Figure 2: Leaves of keji beling plants (*Strobilanthes crispus* Bl.) [2]

Figure 3: Leaves and flowers of keji beling plants (*Strobilanthes crispus* Bl.) [4]

Keji beling leaves (*Strobilanthes crispus* Bl.) contain saponins, flavonoids, glycosides, sterols, terpene, fat, and mineral groups (high levels of potassium, silicate acid, sodium, calcium). Potassium is a strong diuretic and can dissolve stones formed from calcium oxalate and calcium carbonate salts in the bile, bladder, and kidney content. Silicate acid can stimulate the stomach so that people with gastric pain (gastritis) can not drink a decoction of this medicinal plant [6].

2. Data collection

In compiling this review article, the technique used is to use the method of study of libraries in the form of official books, national and international journals published in the last eleven years (2010 - 2021). In making a review of this article, we used a search of data on online media with the keyword *"Strobilanthes crispus* Bl." The primary reference searches in this review are conducted through trusted web such as Google Scholar, ResearchGate, NCBI, and other trusted journal databases.

ISSN: 2519-9889
Impact Factor: 3.426

3. Phytochemical Review

The content of phytochemistry contained in the keji beling plants is summarized in Table 1 below.

Table 1: Phytochemical content of leaves and stems of keji beling (*Strobilanthes crispus* Bl.)

No	Plant parts used	Extraction method	Solvent	Compounds contained	Ref.
1.	leaf	Maceration	N - Hexane	Alkaloids, Tannins	[7]
2.	leaf	Maceration	methanol	Steroids, Terpenoids, Tannins, Saponins	[7]
3.	leaf	Maceration	Ethyl-Acetate	Alkaloid, steroid, terpenoid	[7]
4.	trunk	Maceration	methanol	Alkaloid	[8]
5.	Leaves and Stems	Maceration	methanol	Carbohydrates	[8]
6.	Leaves and Stems	Maceration	methanol	Phytosterols	[8]
7.	Leaves and Stems	Maceration	methanol	Terpenoid	[8]
8.	Leaves and Stems	Maceration	methanol	Phenolic	[8]
9.	trunk	Maceration	methanol	Flavonoid	[8]
10.	leaf	Superkritis	Supercritical carbon dioxide + ethanol	Catechin, epicatechin, rutin, myricetin, luteolin, apigenin, naringenin, kaempferol	[9]

Phytochemical screening of the keji beling plant revealed alkaloids, steroids, terpenoids, tannins, and saponins in all extracted samples. Phytochemical compounds detected in each extract are summarized in Table 1 above [7].

Species of Strobilanthes of both leaves and stems indicate terpenoids, flavonoids, phytosterols, phenolic compounds, fatty oils, and carbohydrates. Terpenoids and phytosterols are also present in all species of Strobilanthes. On the other hand, phenolics, carbohydrates, flavonoids are found in most species of Strobilanthes. In addition, alkaloids, glycosides, saponins, proteins, fatty oils are found in some species of Strobilanthes. Among the species studied are *S. integrifolius, S. ixiocephalus, S. reticulatus* var. reticulatus, *Strobilanthes* Blume sp. and the leaves of *S. lupulinus, S. barbatus* indicate the absence of alkaloids. Glycosides are found only in *S. ciliatus* (leaves), *S. callosus* (stems), and *S. heyneanus* (branches). Saponins are found in *S. ciliatus* (leaves), *S. ixiocephalus* (leaves, stems), *S. callosus* (leaves), and the leaves and stems of *S. heyneanus.* Proteins are found only in the branches *of S. callosus* and *S. sessilis* var. Ritchie. Fat oil is also known as a yellow carrier oil found in the species *Strobilanthes.*

The bioactive flavonoid compound *Strobilanthes crispus* leaves (Broken Glass) obtained using supercritical extraction of carbon dioxide (SC-CO_2) has been investigated, and rough extract results obtained compared to each other to choose the best operating parameters. Because carbon dioxide is a non-polar solvent, ethanol is used as a co-solvent to increase liquid polarity. The parameters studied were pressure (100, 150, and 200 bar), temperature (40, 50, and 60 °C), and dynamic extraction time (40, 60, and 80 minutes). Optimum extraction conditions occur at 200 bar, 50 °C, and 60 minutes. Based on average values, pressure has a dominant effect on extraction yields. Regardless of the optimal SFE conditions, the other two conditions are the minimum level (100 bar, 40°C, 40 minutes) and the maximum (200 bar, 60°C, 80 minutes) of each parameter studied. At the same time, the control is running analyzed with HPLC to determine the main bioactive flavonoid compounds of *S. crispus.* Under optimum conditions, eight flavonoid compounds have

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been identified; they are (+)-catechin, (−)-epicatechin, rutin, myricetin, luteolin, apigenin, naringenin, and kaempferol [9].

4. Pharmacological review

The pharmacological activity of the keji beling has been investigated and summarized in Table 2 below.

Table 2: Pharmacological activity of keji beling plants

No	Plant Parts	Extraction Methods	Solvent	Active Compounds	Test Method	Activity	Ref.
1.	leaf	Maceration	Hexane, Ethyl Acetate, Methanol	Terpenoid, steroid	*In vitro*	Antiurolytic	[7]
2.	leaf	Maceration	Ethanol 96 %	-	*In vivo* on mice	Antiurolytic	[10]
3.	leaf	Maceration	Ethyl Acetate	Monoterpene D - limonene	Brine Shrimp Lethality Test (BSLT)	Cytotoxic	[11]
4.	leaf	Maceration	Water, ethanol	Flavonoid	1,1-diphenyl-1-picrylhydrazil (DPPH) dan ferric reducing antioxidant	Antioxidant	[12]
5.	leaf	Maceration	ethanol	phenol	DPPH, FRAP	Antioxidant	[12]
6.	leaf	Maceration	Methanol, acetone, water	Polyphenols, folic acid, flavonoids	DPPH, FRAP	Antioxidant	[13]
7.	leaf	Maceration	ethanol	Flavonoids, alkaloids	DPPH	Antioxidant	[14]
8.	leaf	Maceration	ethanol	Flavonoids, alkaloids	Disc method	Antibacterial	[14]
9.	leaf	Maceration	ethanol	acetic acid, butyrolactone, and hexanedioic acid	Disc method	Antibacterial	[15]
10.	leaf	Maceration	ethanol 70 %	Flavonoid, Steroid	In vitro	Inhibition of α enzymes - Glucosidase	[16]

ISSN: 2519-9889
Impact Factor: 3.426

11.	Leaf Stem	Maceration	methanol	Flavonoid	MTT assay	Anti-inflammatory	[17]
12.	leaf	Maceration	Chloroform, methanol	Catechins	*In vivo*	Antiobesity	[18]
13.	leaf	Maceration	ethanol	Catechins, Alkaloids, caffeine, tannin	In vivo	Wound healing	[19]
14.	Leaves, stems	Soxhlet extraction, liquid-liquid partition	Methanol, ethyl acetate	Alkaloid	MTT assay	CANCER MCF - 7's Activity	[20]
15.	leaf	Maceration	Diklometana	Lutein	LDH	Cancer cells MDA-MB-231, MCF-7	[21]
16.	Leaves and Stems	Maceration	Hexane, chloroform, ethyl acetate, methanol, water	tannin	MTT assay	Cancer Cells heal	[22]
17.	Leaves and Stems	Maceration	Ethyl acetate, hexane, chloroform	Alkaloids, Tannins	MTT assay	Nasopharyngeal Cancer CNE-PC	[23]
18.	leaf	Maceration	ethanol	Phenolics, Flavonoids	DPPH	Colorectal cancer	[24]
19.	leaf	Maceration	Distilled water (juice)	Polyphenols	MTT assay	Liver cancer Salt HepG2	[25]
20.	leaf	Maceration	ethanol	Flavonoid	MTT assay	Breast adenocarcinoma MCF-7	[26]
21.	Leaves and stems	Maceration	Ethyl acetate, methanol	Phenolic	MTT assay	HT-29, MCF-27. DU-145, H460	[27]

ISSN: 2519-9889
Impact Factor: 3.426

22.	Leaves and Stems	Maceration	Hexane, Ethyl Acetate, Chloroform, Methanol, and Water	Alkaloid	MTT assay	Sel HepG-2 dan MDA-MB-231 Liver and breast cancer	[28]
23.	leaf	Maceration	Distilled water (juice)	Alkaloid	*In vivo*	Toxicity	[29]
24.	leaf	filtration	Ethanol, distilled water	Flavonoid	*In vitro*	Ulcer Pepticum	[30]

4.1 Antiurolithic

Traditionally, *Strobilanthes crispus was* famous for the treatment of kidney disease. The purpose of this study was to validate the traditional use of *S. crispus* by evaluating its antiurolithic activity in vitro. The titrimetry method was assessed the inhibitory activity of calcium oxalate (CaOx) through aggregation and dissolution tests. The influence of *S. crispus* and sistone on nucleation and aggregation slope and calcium oxalate crystal growth is evaluated spectrophotometrically. *S. crispus* is extracted using n-hexane, ethyl acetate, methanol, and water. Methanol (5.92 %) produced the highest percentage of extracts and showed the most increased inhibitory activity against CaOx crystal aggregation (50.54 ± 2.11 %). Ethyl acetate extract has the most effective dissolution effect against CaOx crystals (52.50 ± 2.50 %). *S. crispus* significantly ($p<0.05$) inhibits the nucleation and aggregation of CaOx crystals and lowers crystal density. This study validated the traditional use of *S. crispus*, which was found to exhibit significant antiurolithic activity. However, further research is recommended to isolate and identify active constituents and their in-vivo analysis [7].

Research has been conducted on the influence of ethanol extract of keji beling leaf (*Strobilanthes crispus* (L) Blume) on the solubility of calcium and oxalate as a component of kidney stones in the urine of white male rats. Kidney stones in experimental animals were induced by using 0.75 % ethylene glycol and 2% ammonium chloride to form calcium oxalate crystals. The animals in the study were divided into five groups. Group I; negative control, given regular food and water, group II; The positive control group, groups III, IV, and V were induced. The last three groups were given extracts at doses of 100, 200, and 400 mg. Treatment is provided for 14 days, and urine is accommodated on the 15th day. Calcium levels in urine are measured using atomic absorption spectrophotometers, while oxalate levels are measured using UV-Vis Spectrophotometers. The results showed that *Strobilanthes crisp*us L Blume leaf extract affects the solubility of calcium and oxalate as a component of kidney stones in the urine. The larger the dose given, the more calcium and oxalate levels dissolved in the urine [10].

4.2 Cytotoxic

It has been done isolation and identification of one of the mono-terpenes chemical compounds of the plant Keji beling (local name) (*Strobilanthes crispus*). Extraction is carried out by maceration of keji beling leaf powder with ethanol 96%, then partitioned with water-ethyl acetate. Ethyl acetate extract is isolated and purified by cytotoxic guidance fractionation system with Brine Shrimp Lethality Test (BSLT) on column chromatography (SiO_2; n-hexane - ethyl acetate = 20:1). Preparative Thin Layer Chromatography (TLC) (SiO_2; n-hexane - ethyl acetate = 10: 1) produces one compound in oily form. Based on identification with the infrared spectrum and gas chromatography-mass spectrometry (GC-MS), the compound is a D-Limon monoterpene that has cytotoxic power of 73.11 ppm [11].

ISSN: 2519-9889
Impact Factor: 3.426

4.3 Antioxidant

Aqueous extracts and ethanol from various traditional Malaysian plants (*Polygonum minus*, *Andrographis paniculata*, *Curcuma xanthorrhiza*, *Momordica charantia*, and *Strobilanthes crispus)* are evaluated for their antioxidant properties, total phenolic content, and cytotoxic activity. Antioxidant activity was assessed using a 1,1-diphenyl-1-picrylhidrazil (DPPH) and ferric reduction antioxidant power test (FRAP). The results showed that ethanol extract contains high antioxidant activity compared to water extract. The findings showed a strong correlation between antioxidant activity and total phenol content. In addition, all plant extracts show a non-toxic effect on regular human lung fibroblast cell lines (Hs888Lu). Although water extracts are traditionally used, we determined that ethanol extracts usually achieve a better activity in testing.

Other studies tested using water, methanol, and acetone extract of keji beling leaves (*Strobilanthes crispus* Bl.) with concentrations (25, 50, 75, and 100 %) to know the content of phenolics and antioxidants, using the methods of DPPH and FRAP. The results stated that the highest polyphenols and phenolic acids were in 50 % acetone extract, namely 10.80 and 33.86 mg GAW/g DW. In comparison, flavonoids had the highest total of 4.98 mg QE/g DW in 100 % acetone extract. DPPH from acetone extract 75 % value of 24.88 mg TE/g DW at the highest antioxidant results, while the highest value FRAP obtained from 25 % acetone extract, namely 47.21 mg TE/g DW. Inferred acetone extract leaves *Strobilanthes crispus* as the most suitable solvent for phenolic content and antioxidant properties [13].

Keji beling (*Strobilanthes crispus* Bl.) has pharmacological activity as an antioxidant. The antioxidant test was conducted using the DPPH method with vitamin C as a standard medicine, ethanol extract of keji beling leaves able to ward off free radicals DPPH with IC_{50}, 102.85 ppm, and IC_{50} value of vitamin C as a comparison solution of 19.268 ppm [14].

4.4 Antibacterial

Antibacterial activity of ethanol extract of keji beling leaf (*Strobilanthes crispus* Bl.) was evaluated against bacteria *Staphylococcus aureus* and *Escherichia coli*, with the method of disc paper using Ampicillin as a positive control and distilled water as a negative control. Test results of antibacterial activity of ethanol extract keji beling *leave in Staphylococcus aureus* bacteria with extract concentration of 100% (5.75 mm) can inhibit the growth of Staphylococcus *aureus* bacteria and *Escherichia coli* bacteria [14].

Research conducted by Lim *et al.* [15] aims to examine the potential antimicrobial activity of *Strobilanthes crispus* leaf ethanol extract by determining the vulnerability of various microbial strains to extracts and profiles of bioactive compounds in extracts using GC-MS. The antimicrobial activity was assessed using disc diffusion in *Aspergillus brasiliensis, Candida albicans, Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Streptococcus pneumoniae*. GC-MS analysis is used to determine the profile of bioactive components of plant parts. The extract showed inhibitory activity against *Staphylococcus aureus* and *Streptococcus pneumoniae* at a concentration of 200 mg/mL. At the same time, no inhibition was seen against *Aspergillus brasiliensis, Candida albicans, Klebsiella pneumonia,* and *Pseudomonas aeruginosa.* GC-MS analysis of ethanol extract reveals several constituents, including acetic acid, butyrolactone, and hexanedioic acid, described in the literature as proven antimicrobial agents. These results suggest that *Strobilanthes crispus* leaf ethanol extract can be used as a nutraceutical against *S. aureus* and *S. pneumoniae.*

4.5 Antidiabetic

The keji beling leaf (*Sericocalyx crispus* (L.) Bremek) [Synonym *Strobilanthes crispus* (L.)] is one of the plants empirically used by the community to help with treatment. According to research, vile leaves are known to have properties as antidiabetic. This study aims to identify the group of compounds contained in the extract, the quality of the extract, and the inhibitory activity of enzymes α-Glucosidase *in vitro*. The powder is extracted with ethanol solvent 70% kinetic maceration, then performed phytochemical screening, determination of extract quality, and test of inhibition activity of enzymes α-Glucosidase. Screening results showed the extract contained flavonoid compounds, saponins, steroids, and triterpenoids. The results of the

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determination quality of the extract showed a form of viscous extract in a blackish green color, bitter taste. Water-soluble cider content of 60.46%; soluble ethanol juice content of 73.45%; total ash content of 15.06%; insoluble acid ash content of 3.10%; water-soluble ash content of 11.29%; the moisture content of 7.68%; shrink drying 9,25%; remaining solvent 0.38%; Pb rate of 0.4941 ppm; Cd rate 0.0222 ppm; Total Plate Number (TPC) 4.52x102 colonies/g; The yeast number is too small to be calculated (TSUD); and total flavonoid content of 2.39%. The inhibitory activity of α-Glucosidase enzymes in the root base and thick extracts of keji beling showed IC50 of 50 ppm and 86.2 ppm, respectively. It can be concluded that the thick extract of keji beling meets the quality requirements of the extract and has acted as an inhibitor of the enzyme α-Glucosidase. Keji beling has the potential to be further developed as an antidiabetic herbal remedy.

4.6 Anti-inflammatory

Inflammation is the body's rapid response to dealing with injuries, foreign particles, and damaged cells. Untreated inflammation can lead to complications in the cerebrovascular, cardiovascular system, joints, and intestines. However, conventional drugs available today show adverse effects on many organ systems in addition to treating inflammation. *Strobilanthes crispus*, a native plant believed to have anti-inflammatory properties, has been used in traditional medicine to treat various diseases. Nevertheless, no scientific research has been conducted to prove this conventional claim. Therefore, this study focused on investigating the anti-inflammatory properties of *S. crispus* in an experimental model of lipopolysaccharide-stimulated RAW macrophages (LPS). The maximum non-toxic dose (MNTD) of Methanol extract S. crispus and optimum LPS concentration are determined before determining the anti-inflammatory effect of S. crispus. MNTD S. crispus is determined using the MTT test, and optimum LPS is determined based on nitric oxide production (NO) using Griess reaction. Finally, the anti-inflammatory effect of S. crispus is determined by examining levels of NO and cytokines, namely interleukin-6 (IL-6) and interleukin-10 (IL-10), using the Procarta immunoassay kit. MNTD for S. crispus leaf and stem extract is 160 g/mL and 1.5 g/mL, respectively. The optimum LPS required to induce maximum inflammation is 1 g/mL. After initial treatment with half MNTD leaf extract (1/2MNTD), no production was significantly reduced, while MNTD stem extract resulted in increased levels of IL-10. On the other hand, no significant decrease in IL-6 production was seen in treatment except indomethacin, which acts as a positive control drug. This study showed that S. crispus could have anti-inflammatory properties in RAW macrophages 264.7 stimulated lipopolysaccharide through suppression of NO production and increased levels of IL-10 [17].

4.7 Antiobesity

Strobilanthes crispus leaves are consumed traditionally because of their weight loss effect. In this study, we investigated the antiobesity effects of *S. crispus* leaf extract (SCE). Mice (n =48) were fed a high-fat diet (HFD) for 25 weeks to induce obesity, after which half were maintained on HFD, and half switched to a low-fat diet (LFD) while they were given ordinary water (H_2O) or 0.1% (b/v) of SCE in water at weeks 0–4 which was increased to 1% (b/v) in weeks 5–9. The treatment with SCE was compared between the HFDH_2O, HFDSCE, LFDH_2O, and LFDSCE groups. The respiratory exchange ratio (RER) is measured in weeks 0, 5, and 10. Food, water intake, and weight are measured weekly. Plasma lipid profile and organ weight are determined in week 10. SCE significantly reduced the RER in week 9 (P =0.011). Food intake, weight, and weight of abdominal adipose tissue were not altered by SCE at weeks 5 and 10. However, a significant increase in plasma and liver cholesterol (P <0,050) was also observed. Our findings suggest that SCE induces lipolysis and oxidation of body fat and increases energy expenditure. Further studies on other animal models should be conducted to confirm the consistency of these results [18].

4.8 Wound healing

This study was conducted to evaluate the influence of the topical application of *Strobilanthes crispus* leaf ethanol extract on the speed of wound healing closure and histology of healed wounds. Four groups of

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Sprague Dawley male rats were all experimentally injured in the posterior neck area. The wound area is uniform with a diameter of 2 cm using a circular stamp, cut nape of the neck of the back of all mice with the help of a round seal. The animal groups were given topical treatment with 0.2 mL each vehicle (acacia gum), intrasite gel, 100 and 200 mg/mL of ethanol extract. Macroscopically, wounds wrapped in leaf extract and groups that were given intrasite gel recovered significantly earlier than those treated by vehicle. Histological analysis of wounds healed with leaf extract showed relatively less wound width at wound closure. It cured wounds containing fewer inflammatory cells and more collagen with angiogenesis compared to vehicle-wrapped damages. In conclusion, injuries wrapped in leaf extract significantly improved the acceleration of wound healing in rats, which was confirmed by histological studies.

4.9 Anticancer activity

Despite advances in chemical biology and combinatorial chemistry, natural products remain a potential source of development of anticancer drugs today. *Strobilanthes crispus* (*S. crispus*) derived from the family Acanthaceae has been used traditionally as a medicine in several countries and is reported to have an anticancer, antioxidant, free radical antidote, antidiabetic, antimicrobial, wound healing, and antiulcerogenic activity. Therefore, the purpose of this study is to find out the antiproliferative properties of *S. crispus* against breast cancer cells. Chemical compounds are extracted from various parts of the plant using methanol then continued with liquid-liquid partitions. The antiproliferative effects of this extract were tested on MCF-7. Among the extracts, only five showed inhibition of cell proliferation in MCF-7. The best antiproliferative activity was observed in ethyl acetate stem extract and leaf water with IC50 values of 38 g/mL and 23 g/mL, respectively. However, IC50 values for stem chloroform extract, leaf methanol, and leaf chloroform are in the range of 70-90 g/mL. Treatment with S. crispus extract also causes morphological changes in MCF-7 cells. Chromatin condensation and peripheral aggregation of nuclear chromatin are observed in treated cells. However, further investigation is needed to understand the underlying mechanisms [20].

Cancer patients seek alternative treatments such as traditional medicinal plants for safe and effective treatment and help overcome the side effects of conventional therapies. Current knowledge suggests that *Strobilanthes crispus extracts* from the Acanthaceae family exhibit solid anticancer properties in vitro and are non-toxic in vivo. *S. crispus is* also reported to be protective against chemical hepatocarcinogenesis. We have previously shown that the bioactive fraction of *S. crispus* leaves also synergizes with tamoxifen to cause apoptosis of human breast cancer cells without damaging non-malignant epithelial cells. This study aimed to evaluate the antitumor effect of *S. crispus* (F3) dichloromethane fraction using a mouse mammae tumor model induced N-methyl-N-Nitrosourea (NMU). Tumor regression was observed in 75% of rats after eight weeks of oral administration of F3 without the formation of secondary tumors and no signs of anemia or infection. However, no improvement in liver and kidney function profiles was observed. The main constituents of F3 are lutein, 131-hydroxy-132-oxo-pheophytin campesterol, stigmasterol, β-sitosterol, pheophytin a, and 132-hydroxy-pheophytin a. However, this compound may not significantly contribute to the antitumor effect of F3 [21].

Strobilanthes crispus extract was found to provide cytotoxicity in some cancer cell lines and reduce chemically induced hepatocarcinogenesis in mice. In this study, the cytotoxicity of S. crispus extract isolated from leaves and stems with hexane, chloroform, ethyl acetate, methanol, and water solvents was determined, and the possible underlying mechanisms of apoptosis were investigated further in HeLa cell lines. MTT analysis showed that only hexane stem extract showed cytotoxic effects on HeLa cells with IC50 160 g/mL. Chloroform extract shows a tendency to inhibit cells, while other extracts show little or no cytotoxic effect. Hexane stem extract was further analyzed in this study. It was found to induce apoptosis, which was confirmed by apparent morphological changes in HeLa cells accompanied by the detection of sub-G1 peaks in cell cycle analysis with flow cytometry. Hexane stem extract does not induce cell cycle termination at any phase based on the data shown. Detected caspase-3/7 activity indicates involvement of caspase-3/7 activation in apoptogenic effects induced by hexane stem extract. The activity of caspase-8 and caspase-9 was found to be insignificant in this study. More research can be done to explain the mechanism of apoptosis better clearly. The

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overall findings suggest that *S. crispus* acts as an apoptosis induction that can be used as a potential anticancer agent in the future [22].

Chemotherapy agents used to treat nasopharyngeal cancer (NPCs) show low efficacy. *Strobilanthes crisp*us Blume is widely used for its anticancer, diuretic, and antidiabetic properties. This study aims to determine the cytotoxic and apoptogenic effects of *S. crisp*us on CNE-1 NPC cells. Test 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide was used to evaluate the cytotoxic effect of S. crispa on CNE-1 cells. The level of apoptosis is determined using propidium iodide staining and caspase test. Extracts of ethyl acetate, hexane, and chloroform *of S. crisp*us leaves all show cytotoxic effects on CNE-1 cells, at half-maximum inhibitory concentrations (IC50) of 119, 123.5, and 161.7 g/mL, respectively. In addition, hexane, chloroform, and ethyl acetate extracts from the stem of *S. crisp*us inhibit the proliferation of CNE-1 cells, an IC50 of 49.4, 148.3, and 163.5 g/mL, respectively. Cytometric flow analysis revealed an increase in the proportion of cells in the sub-G1 phase and decreased the proportion of cells in the G2/M phase after treatment with extracts. However, the extract does not change the activity of caspase -3/7, 8, and 9. No cytotoxic effect is observed when cells are treated with methanol and water extract from the stems and leaves of *S. crispus*. In conclusion, *S. crisp*us extract is cytotoxic to CNE-1 cells, and this extract can induce apoptosis, regardless of caspase activation [23].

In this study, microscopic and histological studies showed that *Strobilanthes crispus* ethanol extract reduced azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) in rats. *S. crispus* is considered a folk remedy and is used as an antioxidant. Its leaves contain many phenolic compounds that act as radical catchers and enhance their ability to eradicate oxidative stress reactions. This study was designed to determine the chemopreventive effects of S. crispus in vivo and in vitro ethanol extract by explaining the impact of the extract on intermediate biomarkers that can be used as effective predictors of colon cancer. S. crispus was analyzed for free radical DPPH, nitric oxide (NO), and iron acid reduction. The results showed that oral administration of *S. crispus* significantly inhibited colorectal carcinogenesis induced by AOM, as indicated by a decrease in the amount of ACF. *S. crispus* lowers the regulation of expression of PCNA, Bcl2, and β-catenin. In addition, it provides a noticeable inhibitory effect on MDA and NO levels and a stimulatory effect on the activity of CAT and GPx. These results suggest that *S. crispus* is a chemopreventive agent for colorectal cancer through suppression of early and intermediate carcinogenic phases that may be associated with its flavonoid content [24].

Hepatocellular carcinoma is one of the most common cancers in the world. Its prevalence is increasing in many countries. Plant products can be used to protect against cancer due to their natural anticancer and chemopreventive constituents. *Strobilanthes crispus* is one of the plants that have the potential to have chemopreventive abilities. This study aims to evaluate the anticancer effect *of Strobilanthes crispus* juice on hepatocellular carcinoma cells. MTT tests, flow cytometry, comet tests, and reverse transcription-polymerase chain reaction (RT-PCR) are used to determine the effect of juice on DNA damage and the number of cancer cells. This juice induces apoptosis after exposure to HepG2 cell lines for 72 hours. The percentage of apoptosis cell death and significant DNA damage was seen in juice concentrations above 0.1%. It was found that the juice was not toxic to normal cells. In addition, exposure to fluid increases the level of expression of the c-myc gene and reduces the level of expression of the c-fos and c-erbB2 genes in HepG2 cells. The cytotoxic effect of juice on abnormal cells depends on the dosage. It was concluded that *Strobilanthes crispus* juice might have a chemopreventive effect on hepatocellular carcinoma cells [25].

Strobilanthes crispus is traditionally used as an antidiabetic, anticancer, diuretic, antilithic, and laxative agent. However, the cytotoxicity and antiproliferative effects of *S. crispus* are still unclear. *Strobilanthes cripus* was able to reduce cell viability and proliferation in MTT and BrdU tests. Cell cycle progression and Tunel tests show that IC50 *S. crispus* ethanol extract induces sub-G1 cell cycle phases and DNA fragmentation. On the other hand, translocation of mitochondrial cytochrome c release, induction of caspase 3/7 and p53 while suppressing XIAP in treated MCF-7 cells was also observed in this study. Our findings suggest that *S. crispus* ethanol extract induces apoptosis and DNA fragmentation in breast cancer cell pathways that depend on the hormone MCF-7 through the mitochondrial-dependent p53 apoptosis pathway [26].

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Different parts of the four edible medicinal plants (*Casearia capitellata, Baccaurea motleyana, Phyllanthus pulcher*, and *Strobilanthes crispus*), native to Malaysia, are extracted in different solvents, sequentially. Twenty-eight extracts obtained were evaluated for their in vitro anticancer properties, using MTS tests, on four lines of human cancer cells: colon (HT-29), breast (MCF-7), prostate (DU-145), and lung (H460) cancer. The best anticancer activity observed for ethyl acetate extract (EA) leaves *Casearia capitellata* on MCF-7 cell strains with IC50 2.0 g/mL and methanol extract (MeOH) shows remarkable activity against lung cancer cells. The dichloromethane extract (DCM) air part of the *Phyllanthus pulcher* showed the highest anticancer activity against the DU-145 cell line. In contrast, significant activity was demonstrated by the *Phyllanthus pulcher* root DCM extract in colon cancer cells with an IC50 value of 8.1 g/mL. The total phenolic content (TPC) ranges from more than 1-40 mg to the equivalent of error acid (GAE)/g. For all samples, the highest phenolic results were obtained for MeOH extract. Among all the extracts analyzed, the MeOH extract of *Strobilanthes crispus* leaf showed the highest TPC compared to other samples ($p < 0.05$). This study indicates that phenol properties determine their anticancer activity and not the number of phenols present [27].

Cancer is a significant public health problem not only in developed countries but also in developing countries. It is one of the leading causes of death worldwide. However, current treatments can cause severe and dangerous side effects. Therefore, recent research has focused on identifying alternative therapeutic agents extracted from plant-based sources to develop new treatment options for cancer. *Strobilanthes crispa* Blume is a plant native to countries including Madagascar and Indonesia. It has been used as an antidiabetic, diuretic, and laxative in traditional medicine.

Furthermore, *S. crisp*us has potential in treating cancer, as evidenced in previous research. In this study, cytotoxic activity and apoptosis of crude extracts of *S. crisp*us were investigated on liver and breast cancer cell lines. Extracts of hexane, ethyl acetate, chloroform, methanol, and water made from leaves and stems of *S. crisp*us were evaluated for cytotoxicity in HepG-2 and MDA-MB-231 cells the MTT test. The antiproliferative properties of hexane stem extract (SH) in both cell lines were analyzed using cell doubling timing and cell cycle analysis, while apoptogenic properties were determined through caspase-8 detection. Among the extracts tested, SH extracts showed the lowest half-maximum inhibitory concentration in both cell lines. SH extract induces morphological changes in HepG-2 and MDA-MB-231 cells and significantly delays the doubling time of cell populations. Additionally, it changes the cell cycle profile and significantly increases the activity of caspase-8 in HepG-2 cells but not in MDA-MB-231 cells. In conclusion, SH extract from *S. crisp*us has potent anticancer properties and can be the target of appropriate chemotherapy [28].

4.10 Anti-ulcerogenic

The anti-ulcerogenic activity of *Strobianthes crispus* leaf extract was evaluated against ethanol-induced mucosal injury in rats. Five groups of Sprague Dawley mice were given initial treatment each with: vehicle, distilled water (ulcer control), omeprazole (20mg/kg, reference control), 250 mg/kg, 500 mg/kg, and 1000 mg/kg of *S. crispus* leaf extract (experimental group), 60 minutes before oral administration of absolute ethanol to produce gastric mucosal injury. Sixty minutes later, the rats were sacrificed, and gastric contents, mucus, and walls were collected. In general, ulcer control mice showed severe injury to the gastric mucosa. They decreased the pH of gastric mucus content. At the same time, mice treated with *S. crispus* leaf extract resulted in a significant reduction in the formation of dose-dependent gastric lesions accompanied by a substantial increase in the stomach. Mucous production and pH of gastric fluid. Gastric protection is more prominent in the 1000 mg/kg treatment group *S. crispus.* Histology ulcer control mice showed the most severe and most bottomless necrotic damage to the gastric mucosa, with edema and leukocyte infiltration in the submucosal layer compared to experimental and reference control groups. Thus, our data suggest that the protective activity of *S. crispus* ulcer may be due to defensive mucin secretion and increased pH of gastric contents, and fewer mucosal injuries, no edema, and infiltration of leukocytes in the submucosal. Furthermore, acute toxicity studies have shown no death at a dose of 5 g/kg *of S. crispus* in Sprague Dawley and produced no significant clinical signs of toxicity [30].

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5. Toxicity

The study evaluated four different doses *of Strobilanthes crisp*us juice (700, 2100, 3500, and 4900mg/kg body weight) administered orally in female and male Sprague Dawley mice to possible changes in various physical, behavioral, morphological, and biochemical parameters. The mice were given a single dose of squeezing and observed for 14 days. No significant toxicity was observed in connection with the clinical parameters and morphology of the organ. In addition, no significant changes were observed at levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, creatinine, and albumin. *S. crispus* juice was found safe at the maximum dose used in this study (4900 mg/kg body weight) [29].

6. Conclusion

Keji beling plant (*Strobilanthes crispus* Bl.) is one of the plants that can be used for folk remedies rich in chemical compounds scattered on each part of the stem and its leaves. The chemical compound is flavonoids, saponins, steroids, triterpenoids, alkaloids, terpenoids, tannins, carbohydrates, phytosterols, and phenolic. Keji beling plant has various pharmacological effects that have antiurolithic effects, antidiabetic, antioxidant, antibacterial, anti-inflammatory, antiobesity, wound healing, anticancer, cytotoxic, and peptic ulcer. Keji beling can be categorized as plants that are safe to eat.

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