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Review article

Citrus hystrix: A review of phytochemistry, pharmacology and industrial applications research progress

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ABSTRACT

Citrus hystrix DC, also known as kaffir lime, is a species of lime native to Southeast Asia and the southern China. So far, 78 components have been characterized from *C. hystrix*. The main constituents of these compounds include coumarins, flavonoids, phenolic acids and terpenoids. Studies of the pharmacological research of *C. hystrix* have indicated that this edible medicinal herb shows therapeutic potential including antimicrobial, anti-mosquito, antioxidant, antitumor, anti-inflammatory and neural-protective properties. The purpose of this review is to give a summarization of *C. hystrix* studies until 2023. It is also the intention of this paper to review advances in the botanical, phytochemical, pharmacological studies and industrial applications of *C. hystrix*. This will help to provide a useful bibliography for further research of *C. hystrix* in drugs and foodstuffs.

1. Introduction

Citrus hystrix DC, also known as kaffir lime, makrut lime, Thai lime or Mauritius papeda, is a species of citrus in the family Rutaceae, native to tropical Southeast Asia and the south of China. It grows all over the world in climates suitable as a garden shrub for home fruit production, it is also well-suited for container gardens and for large garden pots on patios, terraces and in conservatories. In Southeast Asian cuisines including Indonesian, Laotian, Cambodian, and Thai cuisines, *C. hystrix* leaves are frequently utilized. The leaf, which can be utilized fresh, dried, or frozen, is the plant component that is used the most frequently. The leaves of *C. hystrix* are used in Vietnamese cookery to enhance the flavor of chicken meals and to lessen the strong odor that results from boiling snails. The leaf is used in Indonesian cooking for dishes like ayam soto and for chicken and fish along with Indonesian laurel leaves (Fig. 1). *C. hystrix* leaves are also used in Malaysian and Burmese cuisines for tea making and as a flavouring agent. In several Asian nations, *C. hystrix* juice and peel rinds are used in traditional medicine. The fruit juices are frequently found in shampoo and are said to be effective against head lice. The rough-skinned, bitter-tasting fruits of *C. hystrix* only yield a tiny amount of juice, which can be mixed with other fruit juices to improve food flavor and is also used in canned products. The pharmaceutical, agronomic, food, sanitary, cosmetic, and fragrance sectors all use *C. hystrix* oil as a feedstock. In addition, it is frequently utilized in aromatherapy and is a crucial component of many cosmetic and beauty products.

Contemporary pharmacological research has proven that *C. hystrix* ingredients show a wide range of pharmacological actions

Abbreviations: AML, acute myeloid leukemia; AChE, acetylcholinesterase; ASA, acetyl salicylic acid; CUPRAC, Cupric Reducing Antioxidant Capacity; DPPH, 2,2-diphenyl-1-picrylhydrazyl scavenging activity; DMBA, dimethylbenz[a]anthracene; FRAP, ferric reducing/antioxidant potency; FIR, far-infrared radiation; GC–MS, gas chromatography/mass spectrometry; HA, hot-air; LRH, low relative humidity; MDR, multidrug-resistant; MTT, 3- (4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-susceptible Staphylococcus aureus; ORAC, oxygen radical uptake capacity; ROS, reactive oxygen species; SK, standard streptokinase; TAC, total antioxidant capacities; TPC, total phenolic content; TFC, total flavonoid content; TPA, 12-O-tetradecanoylphorbol 13-acetate.

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including antimicrobial, antioxidant, anti-tumour and anti-inflammatory activities. These activities are largely consistent with those seen for *C. hystrix* in traditional applications. Historically, the main use of *C. hystrix* appears to be as an insecticide to wash the head and treat the feet to kill terrestrial leeches. The principal components of *C. hystrix* include coumarins, flavonoids, phenolic acids and terpenoids. Of these ingredients, bergamottin (**8**) is the most representative coumarin compound that has been shown to have multiple potential pharmacological activities. There are no authoritative comprehensive reviews of *C. hystrix* published in print as of yet. With all identified structures presented, the goal of this study is to consolidate the results of phytochemical and pharmacological investigations conducted over the previous few decades. The purpose of this essay is to understand new developments in the chemical constituents, pharmacological advantages and industrial uses of *C. hystrix*.

2. Botany

C. hystrix is a species in the genus Citrus (family Rutaceae). According to "*The Plant List*" (https://www.theplantlist.org), *C. hystrix*is is the only accepted name for the plant with relative to other synonyms including *C. aurantium* var. *saponacea* Saff., *C. auraria* Michel, *C. balincolong* (Yu.Tanaka) Yu.Tanaka, *C. boholensis* (Wester) Yu.Tanaka, *C. celebica* Koord., *C. combara* Raf., *C. hyalopulpa* Yu. Tanaka, *C. kerrii* (Swingle) Yu.Tanaka, *C. micrantha* Wester and *C. papuana* F.M.Bailey, etc.

C. hystrix is about 3–6 m high of evergreen tree. Tender blade ovate leaves of *C. hystrix* are often dark red with petiole winged. Buds globose and white petals, which is pinkish red from outside, can be found in the flowers of *C. hystrix*. Lemon yellow *C. hystrix* fruits are often slightly coarse or smooth with numerous and prominent oil dots on the thick pericarp. The shape of fruit is apex rounded and the sarcocarp is usually divided into 11–13 segments. The flowering stage ranges from March to May, and the mature fruit phase is typically from November to December (Flora of China Editorial Committee, 2001).

3. Nutritional and physiochemical composition

3.1. Nutritional composition

The nutrient composition of the *C. hystrix* fruit contains per 100 g edible portion was reported as: water 88.6 g, protein 0.8 g, fat 0.6 g, carbohydrate 8.5 g, fiber 0.8 g, carotene 16 mg, vitamin A 3 mg, vitamin B_1 0.02 mg, vitamin B_2 0.07 mg, and vitamin C 37 mg trace elements including Ca 57 mg, P 2 mg, Fe 0.1 mg, K 172 mg (Table 1). Additionally, essential oils were reported to be rich in peel and juice of *C. hystrix* (Lim and Lim 2012). The main components in the peel oil were reported as follow: β-pinene (22.7%), limonene (17.3%), sabinene (11.9%), citronellal (7.8%), terpinen-4-ol (7.2%), citronellol (3.6%), and linalool (2.6%), while in the juice were β-pinene (35.6%), sabinene (7.0%), limonene (5.9%), terpinen-4-ol (19.7%), γ-terpinene (4.4%), and linalool (2.8%). These results revealed the low-calorie and health-promoting properties of *C. hystrix*. Nowadays, lipid compositions are getting more and more attentions due to their broad implications for human disease (Al Othman et al., 2023), thus *C. hystrix* which is rich in lipids will be appreciate with great prospect.

3.2. Physiochemical and structural features

Detailed phytochemical and nutrient analyses of *C. hystrix* have been performed. The constituents isolated from *C. hystrix* include coumarins, flavonoids, phenolic acids and terpenoids, among others, which are the primary types. A summary and compilation of all compounds regarding their names, CAS numbers and formulae is given in Table 2, and the structure of these compounds has been detailed in Fig. 2.

3.2.1. Coumarins

Similar to other *Citrus* plants, coumarins are the main and representative constituents isolated from *C. hystrix*. To date, 28 kinds of coumarin constituents have been separated from *C. hystrix* (**1**–**28**). Among them, most of compounds are furocoumarins (**4**, **8**, **12**, **17**–**28**), other types including simple coumarins (**2**, **3**, **5**, **7**, **9**, **10**, **14**, **15**, **16**) and pyranocoumarins (**1**, **6**, **11** and **13**) are exiting as well. As for the substituted groups, multiple groups including methyl, ethyl, methoxy, isopentenyl and glucosides have been reported in the chemical structure of *C. hystrix* coumarins, which can be regarded as effective supplements of diversity of constituents of *C. hystrix* based on the coumarin skeletons. The contents of the coumarins are shown in Table 2 with their chemical structures listed in Fig. 2.

3.2.2. Flavonoids

Abundant flavonoids (**29**–**53**) have been separated from *C. hystrix*. The presence of flavonoids is closely linked to the antioxidant activity of *C. hystrix*, which provides important insights for the industrial applications of *C. hystrix* (Alirezalu et al., 2020; Granato et al., 2020). These structures primarily contain the flavonol backbones (**29, 30, 32, 35, 36** and **41**) and the 2-phenylchromone backbone (**31**, **34**, **38**–**40**, **46**–**49**), which can be distinguished from whether or not there is a hydroxyl group on the C-3 position as a substitution. In addition to the flavonones (**33**, **37** and **45**) that can also be found in constituents of *C. hystrix*. Anthocyanin derivatives (**50**–**53**), a type of positively charged flavonoid that is often considered to be the valuable natural pigment in plants, have been isolated and characterized from *C. hystrix* as well, most of which are epicatechin analogues (**50**–**53**) with dihydroxy groups substituted on 3‘ and 4‘ position of C ring of the anthocyanin scaffold. Table 2 shows the contents of the flavonoids mentioned with their generalized chemical structures in the form of a skeleton in Fig. 2.

3.2.3. Phenolic acids

Four kinds of phenolic acids have been isolated from *C. hystrix*. The structural identification technologies offer help to definite their name as vanillic acid (**54**), 4,6,7-trimethoxy-5-chlorogenic acid (**55**) caffeic acid (**56**) and ferulic acid (**57**), which are frequently occurring in functional ingredients of food. Phenolic acids are valuable functional ingredients of food, which have been associated with a variety of activities (Akyol et al., 2016; M'Hiri et al., 2017; Naveed et al., 2018; Romani et al., 2019). The potential bioactivity of phenolic acids from *C. hystrix* are still waiting for excavating.

3.2.4. Terpenoids

Nineteen kinds of terpenoids (**58**–**74**) have been separated from *C. hystrix*. The structure of the terpenoids have been shown in Fig. 2. Most of terpenoids can be divided into essential oils, lupeol (**72**) and agrostophillinol (**74**) are typical tetracyclic triterpenoids, and the compounds like β-sitosterol (**62**) and sitosteryl-β-D-gluco pyranoside (**63**) are steroids.

3.2.5. Other compounds

Other compounds have been isolated from *C. hystrix* as well, mainly containing glycosides and other constituents. Murakam and colleagues (Murakami et al., 1995) isolated two sorts of unique glucosides from the leaves of *C. hystrix*. Two compounds were structurally identified as 1, 2-di-*O*-linolenoyl-3-*O*-

galactopyranosyl-*sn*-glycerol (**75**) and 1-*O*-α-linolenoyl-2-*O*-palmitoyl-3-*O*-β-galactopyranosyl-*sn*-glycerol (**76**), respectively. The structure of two glucosides should be noteworthy from the point of view of phytochemistry because the coexistence of the hydrophilic glucoside group and the hydrophobic aliphatic chains gave them potential in terms of their pharmacological properties. This initial experiment proves that these compounds could be inhibitors of Epstein-Barr virus (EBV) activation induced by tumor promoters. Additionally, compounds 11-hydroxynoracronycine (**77**) and (+)-syringaresinol (**78**) have also been isolated from *C. hystrix* (Panthong et al., 2013).

4. Progress of pharmacological studies on *C. Hystrix*

Several studies to date have disclosed biological activities of *C. hystrix*. These largely effective extractions of constituents perform

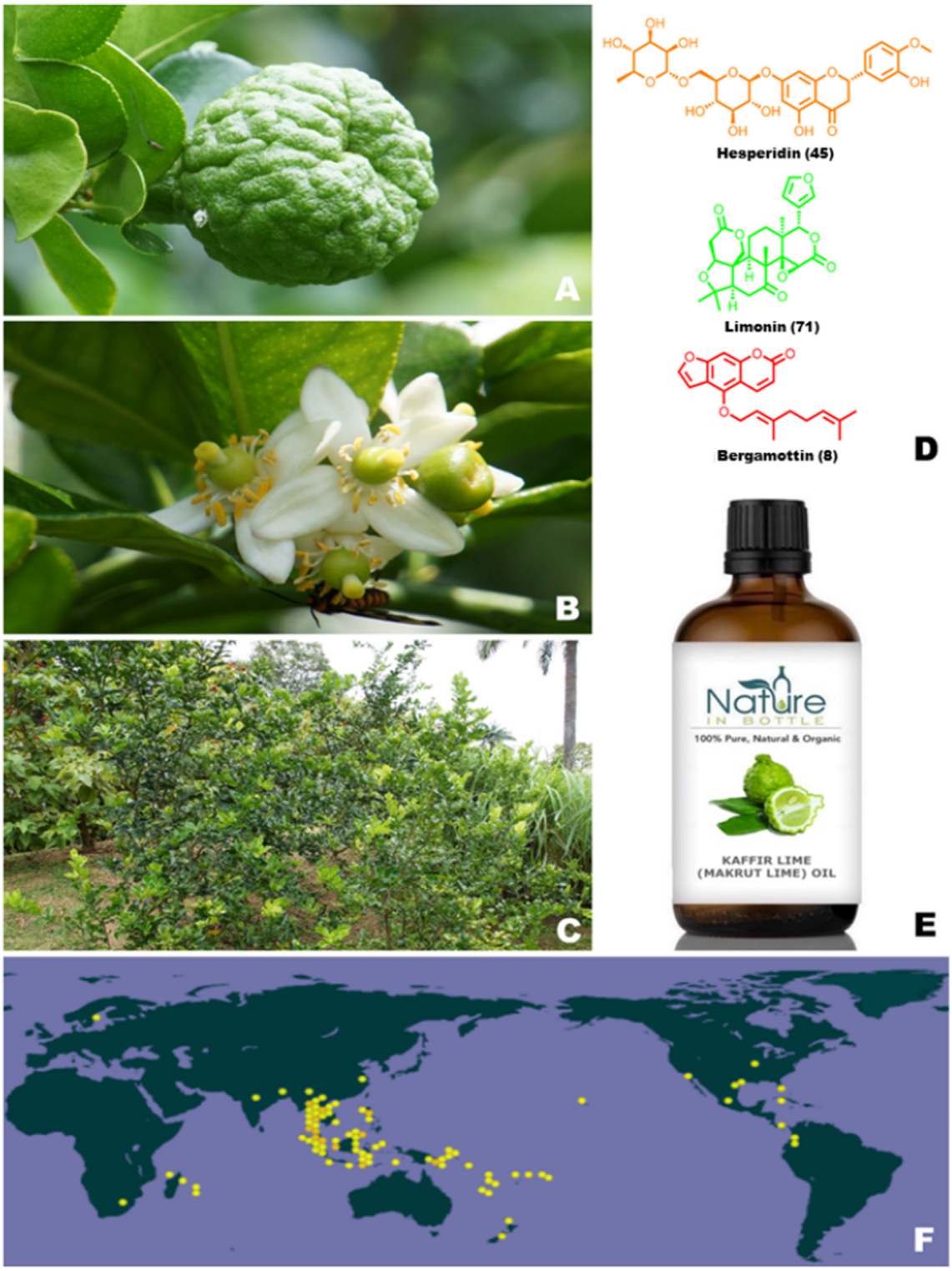

Fig. 1. *C. hystrix*: (**A**) *C. hystrix* fruits; (**B**) flower of *C. hystrix*; (**C**) bushes of *C. hystrix C. hystrix*; (**D**) chemical structure of typical constituents from *C. hystrix*; (**E**) essential oil products containing *C. hystrix*; (**F**) distribution of *P. chinensis* (https://www.gbif.org/).

Table 1
Nutritional composition from *C. hystrix*.

Nutritional composition	Contents	Nutritional composition	Contents
Protein	0.8 g/100 g	Vitamin B_2	0.07 mg/100 g
Fat	0.6 g/100 g	Vitamin C	37 mg/100 g
Carbohydrate	8.5 g/100 g	Ca	57 mg/100 g
Fiber	0.8 g/100 g	P	2 mg/100 g
Carotene	16 mg/100 g	Fe	0.1 mg/100 g
Vitamin A	3 mg/100 g	K	172 mg/100 g
Vitamin B_1	0.02 mg/100 g		

multiple pharmacological properties, including antimicrobial, anti-mosquito, antioxidant, antitumor, anti-inflammatory and neural-protective properties (Fig. 3). These pharmacological properties are summarized in the following paragraphs, and the recapitulative items is generalized in Table 3.

4.1. Antimicrobial activity

C. hystrix exerted potential in antimicrobial potency including antibacterial, antifungal and anti vibrio activities. Essential oils from *C. hystrix* were reported to exhibited antimicrobial activity on multiple strains including *Staphylococcus epidermidis* (diameter of inhibition zone: 7 mm), *Candida albicans* (minimal inhibitory concentration, MIC: 75 μg/mL), *Cryptococcus neoformans* (MIC: 50 μg/mL) and *Saccharomyces cerevisiae* (MIC: 50 μg/mL) (Waikedre et al., 2010).

The antibacterial effect of the multiple compounds separated from the roots of *C. hystrix* were assessed (Panthong et al., 2013). In terms of antimicrobial activity, the compounds **14** and **78** were found to be active against multidrug resistant *Acinetobacter baumannii* JVC 1053 with the same MIC values for 100 μg/mL, whereas limonin (**71**) demonstrated improved effect with MIC 50 μg/ml.

In 2014, Wongsariya and co-workers, 2014 disclosed that the oil from the leaves of *C. hystrix* showed antibacterial potency with MICs of 1.06 mg/mL for *Porphyromonas gingivalis* and *Streptococcus mutans* and at 2.12 mg/mL for *Streptococcus sanguinis.* At a concentration of 4.25 mg/mL, leaf oil exhibited antibiofilm formation effect with 99% inhibitory effects. Lethal effects on *P. gingivalis* were determined within 2 and 4 h of treatment with 4 × MICs and 2 × MICs, respectively. The results revealed that *S. sanguinis* and *S. mutans* were completely killed following the induction of *C. hystrix* leaf oil. MIC values of the strains tested showed a 4-fold decrease indicating a synergistic interaction of the oil and chlorhexidine. The bacterial outer membrane was disrupted following leaf oil treatment. Furthermore, citronellal (**60**) was proved to be the essential active constituent of the *C. hystrix* oils.

Borusiewicz et al. (2017) declared that the essential oil isolated from *C. hystrix* displayed favorable antibacterial activities. To test the antibacterial effects of the essential oil of *C. hystrix*, disc diffusion and serial macrodilution assay were used against 50 kinds of multi-drug resistant *Acinetobacter baumannii* strains, which demonstrated its potential as expressed by MIC ranging from 0.125 to 1 μL/mL.

In 2020, Pumival et al. (2020) declared that *C. hystrix* leaf oil displayed good antifungal activities against *Trichophyton mentagrophytes*. The antifungal activity of *C. hystrix* leaf oil and its microemulsion were studied through macrodilution and agar well diffusion methods against *T. mentagrophytes* (MIC: 1.08 mg/mL). Additionally, the microemulsion of *C. hystrix* oil also exhibited promising antifungal potency with physical and chemical stability, suggesting an alternative therapeutic agent for *T. mentagrophytes*.

It was claimed that the ethanolic fraction of *C. hystrix* peel exhibited inhibitory activity towards *Salmonella* spp (Ulhaq et al., 2020). The MIC of the extract was tested to be 0.625% using an agar dilution test. To examine the antibacterial activity *in vivo*, 16 mg of *C. hystrix* extract was administered daily for 3 consecutive days in a *S. typhimurium*-infected murine model. The results showed that the bacterial loads of *S. typhimurium* in the spleen, liver, and ileum reduced after administration of the *C. hystrix* treatment with statistic differences.

Vibrio parahaemolyticus is a marine bacterium that has been shown to opportunistically cause foodborne gastroenteritis in humans and some diseases in marine animals. At an optimal concentration of 50 mg/mL and Broth's micro dilution method (MICs of 50–100 mg/mL), the ethanolic fractions from the peel of *Citrus aurantifolia* and *C. hystrix* were proved to be more active in anti-*V. parahaemolyticus* effects than the other fractions by the Agar disk diffusion method (Singhapol and Tinrat 2020), indicating potentials to be developed as a distinctive candidate for an alternative natural agent for controlling disease spread in shrimp.

In 2021, the potency of *C. hystrix* essential oil inhibiting *Colletotrichum gloeosporioides*, the causative agent of anthracnose disease in mango fruit, was studied (Chit-aree et al., 2021).Betapinene (**67**), limonene (**71**), and citronellol (**59**) were the major compounds in the essential oil according to the results of constituent analysis. *In vitro* tests revealed that *C. hystrix* essential oils (1500–50,000 ppm) exhibited the inhibitory effects against *C. gloeosporioides* mycelial growth. *In vivo* efficacy studies have shown that the essential oils of ripe *C. hystrix* (1500 ppm) inhibited the disease development of *C. gloeosporioides*, showing that essential oils of *C. hystrix* could be applied to protect against mango fungal contamination.

Recent research revealed that *C. hystrix* essential oil was effective for multidrug-resistant (MDR) methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *S. aureus* strains (MRSA) (Sreepian et al., 2023). *C. hystrix* essential oil alone showed antibacterial effect toward all MSSA isolates (MIC: 18.3 mg/mL) and MRSA isolates (MIC: 17.9 mg/mL). Time killing kinetics suggested that *C. hystrix* essential oil at 1 × MIC completely killed MSSA and MRSA within 12 h. The use of *C. hystrix* essential oil as an alternative antibacterial agent would reduce the emergence of resistant bacteria, especially MDR MRSA.

4.2. Anti-mosquito activity

At present, over 3500 genera of mosquitoes have been reported (Brisola and Melo, 2016), which play an important role in the transmission of infections to communities (Manguin et al., 2010; Sinka et al., 2010). There is evidence that *C. hystrix* has repellent activity against mosquitoes such as *Aedes aegypti*, *Anopheles minimus* Theobald, and others. In order to demonstrate the potential effectiveness of *C. hystrix* leaf essential oil as an insect repellent against *Aedes aegypti* and *Aedes minimus*, Nararak and colleagues conducted a study (Nararak et al., 2017). *C. hystrix* leaf oil demonstrated the greatest spatial repellent activity at 1% and 2%, and significant combined irritant and repellent activity responses at 1–5% concentrations. *C. hystrix* oils were confirmed to show more inhibition against *A. minimus* mosquitoes than *A. aegypti* mosquitoes.

In 2016, Nishan et al. (2017) disclosed that ethanolic extracts of pulps of *Citrus aurantifolia* and *C. hystrix* exerted favorable larvicidal activity against 3rd and 4th instar of *A. aegypti* larvae. When dosed at 3.75 mg/mL, the *C. hystrix* extract resulted in 66.70% mortality over a 24 h period whereas. Furthermore, the percentage mortality caused by *C. hystrix* was 56.70% at the dosage of 3.75 mg/mL for 24 h, both botanical extracts show similar results

to the synthesis products at the concentration of 3.75 mg/mL for 72 h. Through the nut shell methods, it was found that extracts of *C. aurantifolia* and *C. hystrix* also had larvicidal activity, suggesting that they should be further developed as larvicidal agents.

4.3. Antioxidant activity

As with other functional food resources, it was widely reported that *C. hystrix* also exhibited antioxidant activity. The task forces of Chaniphun Butryee made relentless efforts in this area. The leaf of *C. hystrix* was disclosed in 2008 to show total antioxidant capacities (TAC) *in vitro* as well as clastogenic and anticlastogenic potency *in vivo via* the erythrocyte micronucleus assay in mice (Butryee and Lupradinun, 2008). Two different assays, including oxygen radical uptake capacity (ORAC) and ferric reducing antioxidant potency (FRAP), were used to evaluate the antioxidant effects of the aqueous extracts and the lipid extracts of *C. hystrix*. On the basis of these findings, the TAC values assessed by ORAC and FRAP were determined to be 433 μM Trolox Equivalent/g and 95 μM Fe^{2+} Equivalent/g, respectively. In 2009, the task group investigated the potency of the treatment on content of flavonoids and antioxidant capacity of the *C. hystrix* (Butryee et al., 2009). The results revealed that boiling reduced TAC values in the trials, the order of TACs: fresh > deep-fat frying > boiling.

The antioxidant activities of the benzene, coumarin, and quinolinone derivatives with 33 kinds of known compounds separated from *C. hystrix* roots were assessed (Panthong et al., 2013). Compounds **77** and **78** showed antioxidant activity in 2,2-diphenyl-1-picrylhydrazyl scavenging activity (DPPH) test with IC_{50} values of 0.19 and 0.032 mg/mL, respectively. Compound **78** was a potential superoxide scavenger (IC_{50}: 1.52 mg/mL) as well. The activity of compounds **77** and **78** was lower than that of the crude extract, suggesting a synergistic potency in this compound.

In 2015, leaf *C. hystrix* extract was subjected to a comparative evaluation of a preliminary phytochemical screen as well as *in vitro* antioxidant effects (Ali et al., 2015). In a phytochemical research part, leaf extracts of *C. hystrix* were suggested to contain alkaloids, carbohydrates, flavonoids, glycosides, phenolic compounds, steroids and tannins. As for the evaluation of antioxidants *in vitro*, all forms of *C. hystrix* extract had a significant positive effect through the evaluation of free radical scavenging activity of DPPH, Cupric Reducing Antioxidant Capacity (CUPRAC), Nitric oxide scavenging assay. And it was observed that the total antioxidant capacity of the fractions decreased in the following order: ethanol extract > chloroform extract > methanol extract.

In 2023, *C. hystrix* extract showed antioxidant activity through mediating cell migration on human keratinocytes and fibroblasts (Ratanachamnong et al., 2023). *In vitro*, *C. hystrix* water extract displayed free radical scavenging capacity in DPPH assay (IC_{50}: 14.91 mg/mL), and nitrite radical scavenging capacity using NO assay (IC_{50}: 4.46 mg/mL). Treatment of *C. hystrix* extract as low as 50 μg/mL decreased the reactive oxygen species (ROS) from H_2O_2-induced ROS formation. *C. hystrix* extract dose-dependently promoted cell migration. The results demonstrated the positive benefit of *C. hystrix* water extract as a wound-healing accelerator.

4.4. Antitumor activity

Based on the available literature, *C. hystrix* appears to have great potential as an anticancer therapeutic agent. Compounds **75** and **76** along with their derivatives were prepared from *C. hystrix* (Murakami et al., 1995). Both compounds **75** and **76** exhibited potential to inhibit tumor promoter-induced Epstein-Barr virus (EBV) activation induced by tumor promoters with lower IC_{50} values compared to representative cancer preventive agents. In a two-step carcinogenesis experiment performed on the skin of ICR mice induced by dimethylbenz[a]anthracene (DMBA) and 12-O-tetradecanoylphorbol 13-acetate (TPA), compound **75** showed antitumor activity at a dose ten times lower than α-linolenic acid. Compounds **75** and **76** displayed stronger inhibitory effects than indomethacin in the anti-inflammation assay using edema formation induced by TPA on mouse ears. The release of arachidonic acid by phospholipase A2 triggers inflammation induced by the tumor promote. The anti-inflammatory properties of glyceroglycol lipids may be caused by the suppression of enzymes controlling such pathways.

In 2015, the antitumor potency of the *C. hystrix* leaf extracts was determined using a 3- (4,5-dimethylthiazol-2-yl)-2,5-diphenylte trazolium bromide (MTT) assay in an attempt to investigate the cytotoxic effects of *C. hystrix* extracts on cervical cancer cell lines and neuroblastoma cells (Tunjung et al., 2014). Based on the results, the ethyl acetate fraction of *C. hystrix* leaf showed antitumor potential with IC_{50} values for HeLa, UKF-NB3, IMR-5, and SK-N-AS parent cells of 40.7 μg/mL, 28.4 μg/mL, 14.1 μg/mL, and 25.2 μg/mL, respectively.

According to Borusiewicz et al. (2017), peel of *C. hystrix* essential oils showed good antitumor activity. In their study, the authors present firstly an anti-proliferative and cytotoxic potency of *C. hystrix* essential oils against human melanoma cells (WM793 and A375) as well as fibroblasts from normal human skin. Also, the acquired findings have shown that the oil has an inhibitory impact in the investigated dosages (0.05, 0.1 and 0.15 mg/mL). Of particular interest was the finding that both melanoma cell lines (WM793 and A375) were more sensitive to the effect of *C. hystrix* peel essential oil than were normal cells such as fibroblasts from human skin.

In 2018, Suresh Awale task group (Sun et al., 2018) isolated and identified ten genera of coumarins from *C. hystrix*, of which bergamottin (**8**) was found to be the most promising compound against the human pancreatic cancer cell line PANC-1. Further molecular biology studies indicated that compound **8** induced cell shrinkage, membrane blebbing and organelle disintegration, the migration of PANC-1 cells and colony formation was suppressed by compound **8** as well. In addition, compound **8** was shown to down-regulate the levels of proteins in the Akt/mTOR signaling, suggesting potential for development as pancreatic cancer candidates.

In 2020, *C. hystrix* leaves extracts and potential compounds citronellol (**59**) and citronellal (**60**) from essential oil were disclosed to suppress the growth of MDA-MB-231 cancer cell line (Ho et al., 2020). Extracts of *C. hystrix*, compounds **59** and **60** were evaluated *in vitro* against the MDA-MB-231 cells through multiple molecular biology methods. Results revealed that *C. hystrix* extracts, **59** and **60** decreased cell proliferation, colony formation and cell migration by inducing cell cycle arrest, as well as inducing apoptosis in MDA-MB-231 cells *via* inhibition of the expression of anti-apoptotic Bcl-2, activiting the caspase-3 dependent pathway.

Constituents from extracts of *C. hystrix* leaves have been shown to display antileukemic cell proliferation (Anuchapreeda et al., 2020a, 2020b). This proved that hexane fraction exhibited the best inhibition on levels of WT1 of several leukemia cell lines and reduced expression of WT1 protein levels from K562 cells. It was confirmed that phytol (**73**) and lupeol (**72**) isolated from the extracts were the anti-proliferative agents for decreasing the proliferation of leukemic cells tested by the bioassay. And a further study was the first report showing anticancer activity of agrostophillinol (**74**) that had been isolated from the leaves of *C. hystrix* in the blood (Anuchapreeda et al., 2020a, 2020b). It is important to note that **74** was nontoxic to normal cells (e.g., PBMCs). Compound **74** was tested to show inhibition against acute myeloblastic leukaemia cell lines like EoL-1 (IC_{50}: 36.3 μg/mL) and HL-60 cells (IC_{50}: 36.3 μg/mL). The anti-leukemic and anti-inflammatory activities of **74** were confirmed by biological assays against leukemic cells.

Table 2
Constituents isolated from *C. hystrix*.

NO.	Name	Formula	CAS	Ref.
Coumarins				
1	Xanthoxyletin	$C_{15}H_{14}O_4$	84-99-1	(Murakami et al., 1999)
2	Umbelliferone	$C_9H_6O_3$	93-35-6	(Murakami et al., 1999)
3	Osthol	$C_{15}H_{16}O_3$	484-12-8	(Murakami et al., 1999)
4	Bergaptol	$C_{11}H_6O_4$	486-60-2	(Murakami et al., 1999)
5	Seselin	$C_{14}H_{12}O_3$	523-59-1	(Murakami et al., 1999)
6	Xanthyletin	$C_{14}H_{12}O_3$	553-19-5	(Murakami et al., 1999)
7	Suberosin	$C_{15}H_{16}O_3$	581-31-7	(Murakami et al., 1999)
8	Bergamottin	$C_{21}H_{22}O_4$	7380-40-7	(Murakami et al., 1999)
9	Suberenol	$C_{15}H_{16}O_4$	18529-47-0	(Murakami et al., 1999)
10	7-Demethylsuberosin	$C_{14}H_{14}O_3$	21422-04-8	(Murakami et al., 1999)
11	Dentatin	$C_{20}H_{22}O_4$	22980-57-0	(Murakami et al., 1999)
12	Oxypeucedanin	$C_{16}H_{14}O_5$	26091-73-6	(Murakami et al., 1999)
13	5-Methoxyseselin	$C_{15}H_{14}O_4$	31525-76-5	(Murakami et al., 1999)
14	Tamarin	$C_{15}H_{16}O_4$	65451-76-5	(Murakami et al., 1999)
15	Murraol	$C_{15}H_{16}O_4$	109741-38-0	(Murakami et al., 1999)
16	*trans*-Dehydroosthol	$C_{15}H_{14}O_3$	112667-50-2	(Murakami et al., 1999)
17	4- [(6, 7-Dihydroxy-3, 7-dimethyl-2-octen-1-yl) oxy] −7H-furo[3, 2-g] [1] benzopyran-7-one; 5- [(6′, 7′-Dihydroxy-3′, 7′-dimethyl-2-octenyl) oxy] psoralen	$C_{21}H_{24}O_6$	71339-34-9	(Murakami et al., 1999)
18	Citrusoside B	$C_{36}H_{48}O_{15}$	1255789-52-6	(Youkwan et al., 2010)
19	Citrusoside C	$C_{31}H_{40}O_{15}$	1255789-53-7	(Youkwan et al., 2010)
20	Citrusoside D	$C_{31}H_{40}O_{15}$	1255789-54-8	(Youkwan et al., 2010)
21	Isoimperatorin	$C_{16}H_{14}O_4$	482-45-1	(Youkwan et al., 2010)
22	(+)-Oxypeucedanin hydrate	$C_{16}H_{16}O_6$	2643-85-8	(Youkwan et al., 2010)
23	(+)-Oxypeucedanin	$C_{16}H_{14}O_5$	3173-02-2	(Youkwan et al., 2010)
24	(R) - (+)-6′-Hydroxy-7′-methoxybergamottin	$C_{22}H_{26}O_6$	1255117-90-8	(Youkwan et al., 2010)
25	(R) - (+)-Oxypeucedaninmethanolate	$C_{17}H_{18}O_6$	52939-12-5	(Sun et al., 2018)
26	Pangelin	$C_{16}H_{14}O_5$	33783-80-1	(Sun et al., 2018)
27	2′-Methoxyoxypeucedanin hydrate	$C_{17}H_{18}O_6$	2376519-64-9	(Sun et al., 2018)
28	Xanthotoxol	$C_{11}H_6O_4$	2009-24-7	(Umran et al., 2020)
Flavonoids				
29	Quercetin	$C_{15}H_{10}O_7$	117-39-5	(Butryee et al., 2009)
30	Isorhamnetin	$C_{16}H_{12}O_7$	480-19-3	(Butryee et al., 2009)
31	Luteolin	$C_{15}H_{10}O_6$	491-70-3	(Butryee et al., 2009)
32	Kaempferol	$C_{15}H_{10}O_6$	520-18-3	(Butryee et al., 2009)
33	Hesperetin	$C_{16}H_{14}O_6$	520-33-2	(Butryee et al., 2009)
34	Apigenin	$C_{15}H_{10}O_5$	520-36-5	(Butryee et al., 2009)
35	Myricetin	$C_{15}H_{10}O_8$	529-44-2	(Butryee et al., 2009)
36	Tamarixetin	$C_{16}H_{12}O_7$	603-61-2	(Butryee et al., 2009)
37	Naringin	$C_{27}H_{32}O_{14}$	10236-47-2	(Butryee et al., 2009)
38	Nobiletin	$C_{21}H_{22}O_8$	478-01-3	(Sadasivam et al., 2018)
39	Tangeretin	$C_{20}H_{20}O_7$	481-53-8	(Sadasivam et al., 2018)
40	5, 7, 8, 4′-Tetramethoxyflavone	$C_{19}H_{18}O_6$	6601-66-7	(Sadasivam et al., 2018)
41	Natsudaidain	$C_{21}H_{22}O_9$	35154-55-3	(Sadasivam et al., 2018)
42	5, 6, 4′-Trihydroxypyranoflavone	$C_{20}H_{16}O_6$	2166018-83-1	(Sadasivam et al., 2018)
43	5, 4′-Dimethyl-6-prenylpyranoflavone	$C_{27}H_{30}O_3$	2169947-22-0	(Sadasivam et al., 2018)
44	Eldrin	$C_{27}H_{30}O_{16}$	153-18-4	(Umran et al., 2020)
45	Hesperidine	$C_{28}H_{34}O_{15}$	520-26-3	(Umran et al., 2020)
46	Diosmin	$C_{28}H_{32}O_{15}$	520-27-4	(Umran et al., 2020)
47	Cosmosiin	$C_{21}H_{20}O_{10}$	578-74-5	(Umran et al., 2020)
48	Saponarin	$C_{27}H_{30}O_{15}$	20310-89-8	(Umran et al., 2020)
49	Apiin	$C_{26}H_{28}O_{14}$	26544-34-3	(Umran et al., 2020)
50	Peonidin	$C_{16}H_{13}O_6$	18736-36-2	(Butryee et al., 2009)
51	(-)-Epicatechin	$C_{15}H_{14}O_6$	490-46-0	(Butryee et al., 2009)
52	(-)-Epigallocatechin	$C_{15}H_{14}O_7$	970-74-1	(Butryee et al., 2009)
53	(-)-Epigallocatechin 3-gallate	$C_{22}H_{18}O_{11}$	989-51-5	(Butryee et al., 2009)
Phenolic acids				
54	Vanillic acid	$C_8H_8O_4$	121-34-6	(Butryee et al., 2009)
55	Chlorogenic acid	$C_{16}H_{18}O_9$	327-97-9	(Butryee et al., 2009)
56	Caffeic acid	$C_9H_8O_4$	331-39-5	(Butryee et al., 2009)
57	Ferulic acid	$C_{10}H_{10}O_4$	1135-24-6	(Butryee et al., 2009)
Terpenoids				
58	Isopulegol	$C_{10}H_{18}O$	89-79-2	(Youkwan et al., 2010)
59	Citronellol	$C_{10}H_{20}O$	106-22-9	(Youkwan et al., 2010)
60	Citronellal	$C_{10}H_{18}O$	106-23-0	(Youkwan et al., 2010)
61	Citronellol acetate	$C_{12}H_{22}O_2$	150-84-5	(Youkwan et al., 2010)
62	β-Sitosterol	$C_{29}H_{50}O$	83-46-5	(Youkwan et al., 2010)
63	Sitosteryl-β-D-glucopyranoside	$C_{35}H_{60}O_6$	474-58-8	(Youkwan et al., 2010)
64	Linalool	$C_{10}H_{18}O$	78-70-6	(Wongsariya et al., 2014)
65	2, 6-Dimethyl-5-heptenal	$C_9H_{16}O$	106-72-9	(Wongsariya et al., 2014)
66	Peruviol	$C_{15}H_{26}O$	142-50-7	(Wongsariya et al., 2014)

Table 2 (*continued*)

NO.	Name	Formula	CAS	Ref.
67	β-Pinene	$C_{10}H_{16}$	127-91-3	(Wongsariya et al., 2014)
68	(-)-Caryophyllene oxide	$C_{15}H_{24}O$	1139-30-6	(Wongsariya et al., 2014)
69	Sabinene	$C_{10}H_{16}$	3387-41-5	(Wongsariya et al., 2014)
70	β-Caryophyllene	$C_{15}H_{24}$	87-44-5	(Sammi et al., 2016)
71	Limonin	$C_{26}H_{30}O_8$	1180-71-8	(Sadasivam et al., 2018)
72	Lupeol	$C_{30}H_{50}O$	545-47-1	(Anuchapreeda et al., 2020a, 2020b)
73	Phytol	$C_{20}H_{40}O$	150-86-7	(Anuchapreeda et al., 2020a, 2020b)
74	Agrostophillinol	$C_{31}H_{53}O$	–	(Anuchapreeda et al., 2020a, 2020b)
Other compounds				
75	1, 2-Di-*O*-linolenoyl-3-*O*-galactopyranosyl-*sn*-glycerol	$C_{45}H_{74}O_{10}$	63180-02-9	(Murakami et al., 1995)
76	1-*O*-α-Linolenoyl-2-*O*-palmitoyl-3-*O*-β-galactopyranosyl-*sn*-glycerol	$C_{43}H_{76}O_{10}$	121249-84-1	(Murakami et al., 1995)
77	11-Hydroxynoracronycine	$C_{19}H_{17}NO_4$	11361-79-0	(Panthong et al., 2013)
78	(+)-Syringaresinol	$C_{22}H_{26}O_8$	487-35-4	(Panthong et al., 2013)

4.5. Anti-inflammatory activity

Th The development of anti-inflammatory agents is closely linked to public health due to the extensive links between the inflammatory response and multiple morbidities (Zhao et al., 2020). Several constituents isolated from *C. hystrix* were reported to show anti-inflammatory potency in different models (Murakami et al., 1999). A cluster of coumarins were separated and characterized from *C. hystrix* with significant anti-inflammatory activities. The inhibitory effect of bergamottin (**8**, IC_{50}: 14 μM) was close to the reference standard *N*-(iminoethyl)-ornithine (IC_{50}: 7.9 μM), whereas other monomers structurally different from compound **8** only in their side-chain moieties, were notably less active.

The isolation of agrostophillinol (**74**) from *C. hystrix* leaves and its anti-inflammatory activity was firstly reported (Anuchapreeda et al., 2020a, 2020b).The IC_{20} values of compound **74** and *C. hystrix* leaf extracts (2.7 and 90 μg/mL, respectively) were used as test dosages to evaluate the inhibitory effects on IL-6 and TNF-α. At the same dosage, compound **74** (2.7 μg/mL) showed more significant IL-6 inhibitory effects than the reference standard dexamethasone, indicating that promising anti-inflammatory potential against IL-6-induced inflammation.

4.6. Neural-protective activity

Several neurodegenerative diseases, including Alzheimer's, Huntington's, and Parkinson's disease, as well as several mental conditions, such as schizophrenia, affect cholinergic neurotransmission. The majority of these disorders are now treated with drugs that aim to increase neurotransmission by either decreasing acetylcholinesterase (AChE) activity or by positively modulating cholinergic receptors (Sammi et al., 2016). *C. hystrix* has been reported to show AChE inhibitory activity in previous researches.

Derivatives of furanocoumarin were isolated from *C. hystrix* in 2010 and assessed for cholinesterase inhibitory activity (Youkwan et al., 2010), among which compound **24** showed the strongest AChE inhibition with an IC_{50} value of 11.2 μM, indicating promising potency curing Alzheimer's disease. Initial Structure-Activity Relationship can be generalized as the presence of a deoxygenated geranyl chain in the isolated constituents was found to be important for the inhibitory effect.

In 2016, Sammi and his colleagues (2016) determined the synaptic Ach levels evident using aldicarb assay, following treatment with *C. hystrix* extract being orchestrated by the attenuation of AChE activity, recorded at levels of genomic and biochemical, as well as high genomic expression of the choline transporter. Based on this result, it was found that the active components citronellal (**60**) extracted from *C. hystrix* was able to inhibit the activity of AChE at both biochemical and transcriptomic levels, moreover, it can also possess its function through regulating the genomic levels of choline transporter and choline acetyltransferase.

In terms of enzyme-inhibiting effects, in 2014 (Abirami et al., 2014), fresh juice from *C. hystrix* fruit was shown to inhibit multiple enzymes including α-amylase, α-glucosidase, tyrosinase, AChE, β-glucuronidase with an inhibitory ratio ranging from 60% to 80%, respectively, indicating a good potential in the development of healthcare production.

In 2020, the anti-senescent mechanisms of *C. hystrix* extracts were investigated through human neuroblastoma cells SH-SY5Y (Pattarachotanant and Tencomnao 2020). The effects of *C. hystrix* extracts on high glucose-induced cytotoxicity, generation of ROS, cell cycle arrest, and cell cycle associated proteins were evaluated. This result showed that the neuroprotective effects of *C. hystrix* peel and leaf extracts were mediated through cell cycle progression in cell cycle checkpoint proteins and the up regulation of SIRT1 following activation of the SIRT1/GAPDH pathway. Extracts of *C. hystrix* can be developed as agents to protect neuronal senescence induced by high glucose. And diseases associated with neuronal senescence will hopefully be clarified in future research.

4.7. Other activities

Apart from the activities introduced above, other activities of *C. hystrix* have also been explored. In 2015, Ali et al. (2015) evaluated the thrombolytic and membrane-stabilizing activities of *C. hystrix* leaf extracts using human erythrocytes, and the results were compared with those of standard streptokinase (SK) and acetyl salicylic acid (ASA), respectively. The results of this study are presented in Table 3. In terms of thrombolytic activity and membrane stabilizing effects, ethanolic leaf fraction had a clot lysing value of 13.69% against standard SK (37.43 %) and a highest percentage hemolytic value of 74.40% against standard ASA (93.24%), respectively.

C. hystrix was reported to show skin-stimulating effects. In 1999 (Koh and Ong, 1999), a case report disclosed that the phytophotodermatitis on a hiker caused by the application of the juice of *C. hystrix* because of the abundant content of psoralens, suggesting the more attention should be paid in the application of *C. hystrix* productions. In 2007 (Hongratanaworakit and Buchbauer, 2007), *C. hystrix* oil was demonstrated to promote the blood pressure and reduce the skin temperature.

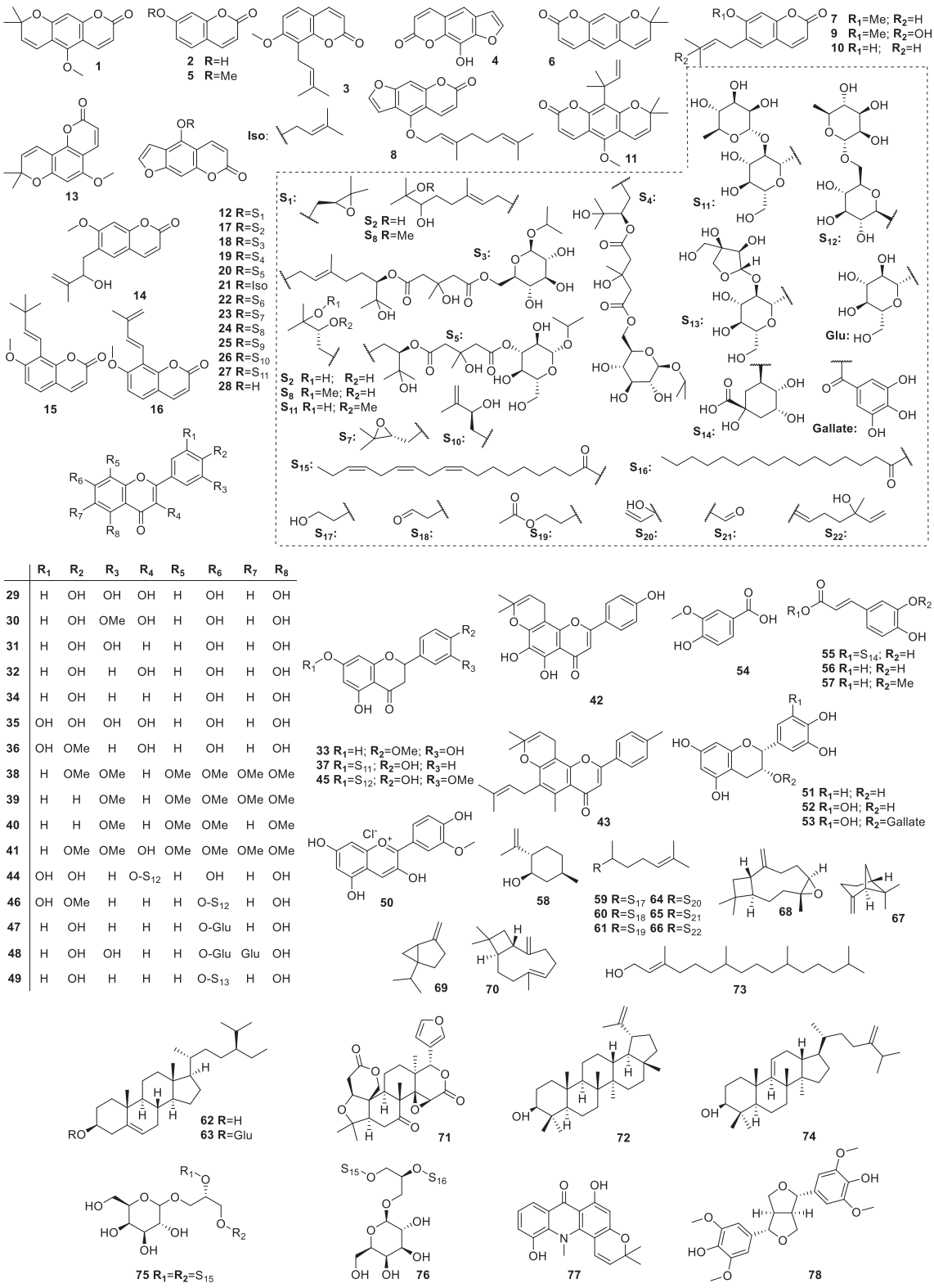

Fig. 2. Chemical structure of coumarins isolated from *C. hystrix*.

5. Industrial applications

Industrial applications of *C. hystrix* in the food service industry offer a novel choice for people to choose health care foods such as beverages that contain certain *C. hystrix* derivatives (Table 4). In addition, *C. hystrix* is used in the cosmetics industry, several patents have disclosed the potential of *C. hystrix* to be developed as skin or hair care agent (CN104379219, JP2001031528A, TW201740922A, JP2004083416A, JP2011016756A, US6426080B1, JPH11199427A). Industrial applications more extensive, correspondent advanced extraction conditions are urgently needed (Lubinska-Szczygel et al., 2023). Extraction methods reported in published studies mainly contain water and ethanol extracts, acid extraction conditions and suitable temperature (60–90 °C) are

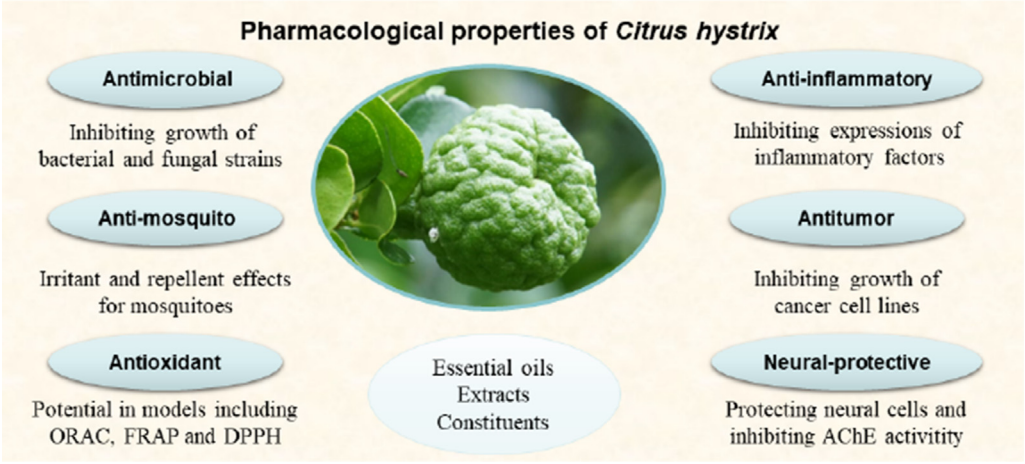

Fig. 3. Pharmacological properties of *C. hystrix*.

Table 3
Pharmacological studies of *C. hystrix*.

Pharmaceutical effects	Part	Comp./ Extract	Model and effective concentrations	Ref.
Antimicrobial		Oils	Active against strains including *Staphylococcus epidermidis*, *Candida albicans*, *Cryptococcus neoformans* and *Saccharomyces cerevisiae*	(Waikedre et al., 2010)
Antimicrobial	Roots	**14**	Active against multidrug resistant *Acinetobacter baumannii* JVC 1053 (MIC: 100 μg/mL)	(Panthong et al., 2013)
Antimicrobial	Roots	**71**	Active against multidrug resistant *Acinetobacter baumannii* JVC 1053 (MIC: 100 μg/mL)	(Panthong et al., 2013)
Antimicrobial	Roots	**78**	Active against multidrug resistant *Acinetobacter baumannii* JVC 1053 (MIC: 50 μg/mL)	(Panthong et al., 2013)
Antimicrobial	Leaves	Oils	Active against *Trichophyton mentagrophytes* (MIC: 1.08 mg/mL)	(Pumival et al., 2020)
Antimicrobial	Peels	Ethanolic fraction	Inhibitory activity towards *Salmonella* spp	(Ulhaq et al., 2020)
Antimicrobial		Oils	Active against *Colletotrichum gloeosporioides* (1500–50,000 ppm)	(Chit-aree et al., 2021)
Anti-mosquito	Leaves	Oils	Active against *Aedes aegypti* and *Aedes minimus* in the concentrations of 1–5%	(Nararak et al., 2017)
Antioxidant	Leaves	Lipid extracts	Showing antioxidant potential in ORAC and FRAP assay	(Butryee and Lupradinun 2008)
Antioxidant	Roots	**77**	Showing antioxidant potential in DPPH assay (IC_{50}: 0.19 mg/mL)	(Panthong et al., 2013)
Antioxidant	Roots	**78**	Showing antioxidant potential in DPPH assay (IC_{50}: 0.032 mg/mL)	(Panthong et al., 2013)
Antitumor		**75**	Inhibited tumor promoter-induced EBV activation induced by tumor promoters	(Murakami et al., 1995)
Antitumor		**76**	Inhibited tumor promoter-induced EBV activation induced by tumor promoters	(Murakami et al., 1995)
Antitumor	Peels	Oils	Inhibiting growth of melanoma cells	(Borusiewicz et al., 2017)
Antitumor		**8**	Inhibited growth of cancer cell line PANC-1 inducing cell shrinkage, membrane blebbing and organelle disintegration	(Sun et al., 2018)
Antitumor		**61**	Inducing apoptosis in MDA-MB-231 cells *via* inhibiting Bcl-2 and activating caspase-3 dependent pathway	(Ho et al., 2020)
Antitumor		**62**	Inducing apoptosis in MDA-MB-231 cells *via* inhibiting Bcl-2 and activating caspase-3 dependent pathway	(Ho et al., 2020)
Antitumor	Leaves	**72**	Decreasing the proliferation of leukemic cells	(Anuchapreeda et al., 2020a, 2020b)
Antitumor	Leaves	**73**	Reducing the proliferation of leukemic cells	(Anuchapreeda et al., 2020a, 2020b)
Antitumor	Leaves	**74**	Inhibiting growth of lines of acute myeloblastic leukaemia against EoL-1 (36.3 μg/mL) and HL-60 (53.4 μg/mL) cells	(Anuchapreeda et al., 2020a, 2020b)
Anti-inflammatory	Leaves	**74**	Inhibiting the release of IL-6 and TNF-α	(Anuchapreeda et al., 2020a, 2020b)
Neural-protective		**24**	Active in AChE inhibition (IC_{50}: 11.2 μM)	(Youkwan et al., 2010)
Neural-protective		**60**	Active in AChE inhibition	(Sammi et al., 2016)
Neural-protective	Peels and leaves	Extracts	Protecting neuroblastoma cells SH-SY5Y through mediating activation of the SIRT1/ GAPDH pathway	(Pattarachotanant and Tencomnao 2020)

favorable for the retention of effective substances. With the development of pharmacological related technologies, more and more *C. hystrix* based functional products will be developed in the future.

6. Conclusion

The purpose of this review was to summarize the phytochemistry, pharmacological activities, and industrial applications of *C. hystrix* based on published literatures. Current studies on *C. hystrix* mostly focus on the components found in leaves or fruits, but more research into other elements and other plant parts is urgently needed because the current findings are ambiguous and inadequate. Studies of biological activity must be combined with clinical application research that focuses on the structural underpinnings of its efficacy. As for the pharmacological studies, *C. hystrix* has been proved to show potential to be developed as drug candidates

Table 4
Patents list of products containing constituents from *C. hystrix* and their claimed pharmacological properties.

Application	Main composition	Properties	Publish number
Hair products	Boiled *C. hystrix* without seeds	Stimulating the hair growth and colored	CN104379219
Hair products	*C. hystrix* extracts	Providing a safe hair restorer effect without allergic reaction to the scalp	JP2001031528A
Skin care agent	*C. hystrix* honey, glycerinum	Preserving skin moisture and reducing the side effects	TW201740922A
Skin care agent	*C. hystrix* extracts	Accelerating the action of collagen and hyaluronic productions	JP2004083416A
Skin care agent	*C. hystrix* extracts	Melanin inhibitory effect with formulation stability	JP2011016756A
Skin care agent	*C. hystrix* extracts	Natural products as cosmetic substances with high protection factor against free radicals	US6426080B1
Skin care agent	*C. hystrix* leaves extracts	Active in antioxidant effects	JPH11199427A
Skin care agent	*C. hystrix* leaves extracts	Reducing moisture content of horny layer from getting rough	JP2022087646A
Treating skin and hair damages agents	Peel or leaf extracts of *C. hystrix*	Natural products as radical scavengers for protecting and treating skin and hair damages	KR101159392B1
Detergent	Fermented *C. hystrix* with rock salt and surfactant	Cleaning with less environmental impact and less rough skin	JP2007270134A
Herbal smoking blend	Essential oil of *C. hystrix* as additive agent	Providing herbal terpenoid solution to improve taste	US9532593B2
Tea beverage	Extracts of *C. hystrix* as additive agent	Quickly preparing a cup of tea with good taste and aroma	RU2690651C2
Flavor modifying composition	*C. hystrix* extracts	Natural products as flavor modifying composition	CN106998761A
Promoting small intestinal motility agent	Constituents isolated from *C. hystrix*	Promoting small intestinal motility for further drug development	CN105168200A
Medicated toothpaste inhibiting plaque	*Polygonatum cyrtonema* extracts and *C. hystrix* extracts	Natural products as ingredients of toothpaste inhibiting plaque	CN108354875A
Weight loss products	Extracts of *C. hystrix* as additive agent	Natural products as lipase inhibitor	WO2010010949A1
Adipocyte differentiation inhibitor	*C. hystrix* extracts	Natural products as adipocyte differentiation inhibitor	JP4363825B2
Carcinogenic promotion-inhibiting agent	*C. hystrix* extracts	Inhibiting the activation of Epstein-Barr virus *via* the promoter teleocidin B-4	JPH06336437A
Antiviral agents	*C. hystrix* essential oil	Natural products as antiviral agents for multiple virus	EP3964221A1
Antiplasmin agent	*C. hystrix* extracts	Natural products as antiplasmin agent	CN114007632A
Detergent	Fermented *C. hystrix* with rock salt and surfactant	Cleaning with less environmental impact and less rough skin	JP2007270134A
Cleansing skin dried pad	*C. hystrix* extracts	Cleaning skin with minimizes irritation	KR20210017704A
Mosquito repellent	*C. hystrix* extracts	Natural products as ingredients of mosquito repellent	WO2017168449A1

for multiple disorders. However, most of the studies conducted thus far are still at the initial stages of using crude extracts *in vitro*. *In vivo* investigations should be conducted to confirm the observed *in vitro* effects (Siti et al., 2022). Bioactive compounds should although though *C. hystrix* has been utilized widely as a food and medicine source, there is still a lack of safety data, and there have only been a few toxicity studies conducted. Thus, more toxicological research is also necessary.

In summary, *C. hystrix* has a wide range of bioactivities, making it a kind of important edible medicinal plant resource deserving of further study. Unfortunately, there is not enough information available on clinical value about *C. hystrix*. Multiple constituents have been identified from *C. hystrix*, although research on these components may just be at the beginning of the story. Future study will likely concentrate on comprehensive phytochemical analyses of *C. hystrix* and its pharmacological characteristics, particularly its bioactivity mechanism, to show its ethnomedicinal applicability and to help the creation of new pharmaceuticals. Development and application of *C. hystrix* should be facilitated by this paper.

Author agreement

All the authors agree to publish the article on the Arabian Journal of Chemistry.

Declaration of Competing Interest

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

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