

## REVIEW ARTICLE

Essential Oils of *Garcinia* spp. and Their Biological Activities\*Wen-Nee Tan<sup>1</sup>, Juzaili Azizi<sup>2</sup>, Nurul Awanis Che Omar<sup>3</sup>, Chean-Ring Leong<sup>4</sup>, \*Woei-Yenn Tong<sup>5</sup><sup>1</sup> Chemistry Section, School of Distance Education, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia<sup>2</sup> Centre for Drug Research, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia<sup>3</sup> School of Chemical Sciences, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia<sup>4</sup> Universiti Kuala Lumpur, Malaysian Institute of Chemical and Bioengineering Technology, Bioengineering Section, Lot 1988 Kawasan Perindustrian Bandar Vendor, Taboh Naning, 78000 Alor Gajah, Melaka, Malaysia<sup>5</sup> Universiti Kuala Lumpur, Institute of Medical Science Technology, A1-1, Jalan TKS 1, Taman Kajang Sentral, 43000 Kajang, Selangor, Malaysia

## ABSTRACT

*Garcinia* is the largest genus in the Clusiaceae family. Plants of *Garcinia* are widely distributed in Africa, Asia, Australia, Central America, Madagascar, and Polynesia. There are over 400 species of *Garcinia* found in the lowland tropical forests. *Garcinia* are known for their medicinal values due to the presence of biologically active constituents. Plants with medicinal values play a key role in human health and disease prevention. Plant-based natural products such as essential oils (EOs) have been employed for centuries owing to their beneficial effects. Generally, EOs are a mixture of volatile chemical constituents comprising mainly terpenoids and phenylpropanoids. They play diverse roles as biologically active agents. To date, EOs have found wide applications in pharmaceutical, food, flavour and fragrance. This review discusses the volatile chemical constituents of EOs extracted from different plant parts of *Garcinia*. The biological activities of *Garcinia* EOs are highlighted to explore their therapeutic potential.

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## INTRODUCTION

Essential oils (EOs) are concentrated aromatic liquids with volatile chemical constituents. They comprise a complex mixture of polar, semi-polar, and non-polar constituents at various concentrations. EOs are characterised by a strong odour due to the presence of specific aromatic constituents (1). Plants evolve volatile aromas to attract specific insects for pollination. Sometimes, the aromas are used to deter certain predators. EOs act as a buffer towards herbivores by minimising their appetite for plants (2). EOs can be derived from various plant parts. They are accumulated in the secretory and epidermal cells, ducts or cavities (3). EOs exhibit various biological activities, notably insecticidal, antimicrobial, antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, anti-allergic, and anticancer (4). Globally, the production of EOs is constantly increased over the last few decades. EOs possess wide applications in pharmaceutical, medical, cosmetic, food, flavour and

fragrance (5). For instance, the antioxidant property of EOs protects and slows down the food from oxidation (6). Owing to its biological activity against food-borne pathogens, a low dosage of EOs could slow the growth of microorganisms in foodstuff and meat products. Thus, the usage of EOs in the food industry is increasing (7).

The genus *Garcinia* is an important genus with essential pharmaceutical entities. Plants from *Garcinia* are famous for their bioactive EOs. This review summarises the volatile chemical constituents of EOs from *G. atroviridis*, *G. celebica*, *G. gummi-gutta*, *G. huillensis*, *G. kola*, *G. imberti*, *G. indica*, *G. mangostana*, *G. morella*, *G. nigrolineata*, *G. pushpangadaniana*, *G. rubro-echinata*, *G. talbotii*, *G. travancorica*, *G. wightii* published between 2005 and 2021. The extracted EOs exhibited potent bioactivities, particularly cytotoxic, anti-inflammatory, and antimicrobial (8-13).

**The genus *Garcinia***

The genus *Garcinia* belongs to the family of Clusiaceae, previously known as Guttiferae. *Garcinia* is widely distributed in Africa, Asia, Australia, Central America, Madagascar, and Polynesia, with over 400 species of trees and small bushes (14,15). To date, 49 species

of *Garcinia* have been found in Malaysia. The locally known species are *G. atroviridis* ('asam gelugor'), *G. bancana* ('cempurah'), *G. cowa* ('kandis'), *G. dulcis* ('mundu'), *G. forbesii* ('rose-kandis'), *G. hombroniana* ('beruas'), *G. mangostana* (mangosteen) and *G. prainiana* ('cerapu') (16,17). In Malaysia, Sabah was reported to have the largest number of *Garcinia* species, followed by Kelantan, Terengganu, Pahang, Perak, Kedah, and Johor. Trees of mangosteen and 'asam gelugor' are commonly found in Malaysia, while 'mundu' and 'beruas' are rare. "Rose-kandis" was discovered to be grown only in Sabah (16). Plants of *Garcinia* are primarily found in lowland tropical forests (18). They are evergreen plants, varying in size from small to medium. Occasionally, some trees may reach up to 30 m in height (19). The leaves of *Garcinia* are oblong, 5-8 cm in length, and 2-3 cm thick. They are shiny deep-green in colour. The flowers in the cluster are spreading, dark pink, solitary and fleshy. Generally, the size of *Garcinia* fruits is similar to oranges. They are brownish or purple marbled with yellow colour. The fruits are juicy, with delightful fragrances and flavours. The fruit pulps consist of 6-8 seeds. The plants of this genus are locally known as mangosteens, sap trees, *Garcinia*, kokum, and monkey fruit ambiguously (18, 20-22).

The plant parts of *Garcinia*, such as barks, fruit rinds, flowers, leaves, and stems are used in folk medicine (18). In traditional herbal medical practice, plants from *Garcinia* are commonly used to treat pain, suppuration, infection, ulcer, dysentery, and diarrhea (23,24). Plants of *Garcinia* are rich in organic acids, primarily *garcinia* acid and hydroxycitric acid (20). According to literature, hydroxycitric acid is a potential hypocholesterolaemic and anti-obesity agent. It is primarily found in the leaves and fruits of *Garcinia*. The dietary supplements containing hydroxycitric acid are often used in reducing body weight (25,26). Several investigations have shown that *Garcinia* species possess oxygenated and prenylated xanthenes, benzophenones, flavonoids, biflavonoids, triterpenes and depsidones. These bioactive compounds showed a broad spectrum of biological and pharmacological activities including antioxidant, antitumor, anti-inflammatory, anticancer, anti-HIV, antidepressant, antimalarial, hepatoprotective activities, anti-tuberculosis, antimicrobial, antiulcer, antiplasmodial and cytotoxic (14, 23-24, 27-29).

### Essential Oils

EOs are volatile constituents derived from medicinal and aromatic plants (30). They are characterised by a complex mixture of organic volatile constituents. They are extracted from various parts of plant, such as fruits, buds, flowers, stems, roots, leaves, bark and seeds (31, 32). Generally, the volatile chemical constituents of plant EOs are classified into two major chemical classes, namely, terpenoids and phenylpropanoids.

Terpenoids comprise monoterpenes, sesquiterpenes and their oxygenated forms. Meanwhile, phenylpropanoids consist mainly phenols and their derivatives. They have different biosynthetic routes and characterised by low molecular weight constituents (33, 34). These volatile constituents are responsible for the distinctive odours and flavours of EOs (35). EOs play a key role in fighting infection, initiating cellular regeneration, and act as plant defense against fungus, virus, insect, and herbivore attack (36, 37). Owing to its broad range of biological activities, EOs are widely used in flavour and fragrance, food, cosmetic, aromatherapy, medicinal, agricultural and pharmaceutical industries (32, 35, 36, 38).

The common techniques used for EOs extraction include hydrodistillation, steam-distillation, cold pressing, supercritical fluid extraction, solvent extraction, and microwave-assisted extraction (32, 38). Among them, hydrodistillation is the most widely used method to extract EOs due to simplicity, low cost, and environmental friendly. Hydrodistillation using Clevenger apparatus is a recommended circulatory distillation apparatus described by European Pharmacopoeia (39-41). During hydrodistillation, the plant material is submerged in distilled water. A direct heat is then applied to boil it. The volatile constituents are vaporised and condensed on cooling to produce an immiscible mixture of EOs and aqueous phase (42, 43).

### EOs from *Garcinia* spp.

Many EO investigations have been performed on *Garcinia* plants. The major chemical constituents of the EOs from *Garcinia* spp. is listed in Table I. *G. atroviridis* is a popularly known fruit tree in the Clusiaceae family. The tree is endemic to Malaysia (44, 45). *G. atroviridis* is widely used in food preservative, seasoning and for medicinal purposes. It has been recorded that the local community use the plant to treat cough, earache, throat discomfort, and stomach ache. The leaves are made into juice for woman after childbirth. Meanwhile, the fruit is usually mixed with vinegar to make as a lotion for woman after confinement. EOs from the fruits, barks and leaves of *G. atroviridis* were extracted using hydrodistillation. Gas chromatography (GC) and gas chromatography-mass spectrometry (GC-MS) were employed to identify their chemical constituents. The fruit EO was mainly consisted  $\beta$ -caryophyllene (23.8%),  $\beta$ -caryophyllene alcohol (15.6%),  $\alpha$ -humulene (10.7%), palmitic acid (8.8%), and clovanol (5.2%). Meanwhile, (E)- $\beta$ -farnesene (58.5%) and  $\beta$ -caryophyllene (16.9%) were dominated in the leaf EO. The stem bark EO composed mainly palmitoleic acid (51.9%), followed by palmitic acid (21.9%), and 3-methoxy-5-pentylphenol (5.5%) (8, 9).

**Table 1 : Essential Oils of *Garcinia* spp. and Their Biological Activities**

<i>Garcinia</i> spp.	Plant part	Major constituents	Chemical class	Biological activity	Reference
<i>G. atroviridis</i>	Fruit	$\beta$ -Caryophyllene (23.8%), $\beta$ -caryophyllene alcohol (15.6%), $\alpha$ -humulene (10.7%), palmitic acid (8.8%), clovanol (5.2%)	Sesquiterpene, sesquiterpenoid, fatty acid	Antibacterial, Anti-inflammatory	(8)
	Leaf	( <i>E</i> )- $\beta$ -Farnesene (58.5%), $\beta$ -caryophyllene (16.9%)	Sesquiterpene	Cytotoxic	(9)
	Bark	Palmitoleic acid (51.9%), palmitic acid (21.9%), 3-methoxy-5-pentylphenol (5.5%)	Fatty acid, alcohol	-	(9)
<i>G. celebica</i>	Leaf	$\alpha$ -Copaene (61.25%), germacrene D (6.72%), $\beta$ -caryophyllene (5.85%)	Sesquiterpene	Cytotoxic, anti-microbial	(10)
<i>G. gummi-gutta</i>	Leaf	$\beta$ -Caryophyllene (53.82%), ( <i>E</i> )- $\beta$ -farnesene (22.62%)	Sesquiterpene	Cytotoxic, anti-microbial	(11)
	Leaf	$\delta$ -cadinene (32.4%), $\alpha$ -copaene (30.2%), $\beta$ -caryophyllene (5.7%)	Sesquiterpene	-	(48)
<i>G. huillensis</i>	Fruit	$\alpha$ -Humulene (23.0%), valencene (18.2%), $\beta$ -caryophyllene (12.6%), caryophyllene oxide (6.3%), $\delta$ -selinene (5.0%)	Sesquiterpene, sesquiterpenoid	-	(49)
<i>G. kola</i>	Leaf	Citronellic acid (48.3%), dihydropseudoionone (5.12%)	Monoterpenoid	Antimicrobial	(12)
<i>G. imberti</i>	Leaf	$\beta$ -Caryophyllene (38.1%), $\alpha$ -humulene (30.5%), alloaromadendrene (5.5%)	Sesquiterpene	-	(48)
<i>G. indica</i>	Leaf	$\beta$ -Caryophyllene (18.6%), $\alpha$ -selinene (18.2%), $\alpha$ -humulene (17.6%), $\beta$ -selinene (12.3%), $\gamma$ -muurolene (5.9%), $\delta$ -cadinene (5.3%)	Sesquiterpene,	-	(48)
<i>G. mangostana</i>	Leaf	$\beta$ -Caryophyllene (21.1%), $\beta$ -elemene (9.7%), germacrene D (7.9%), $\alpha$ -selinene (7.4%), $\alpha$ -humulene (7.3%), $\beta$ -selinene (7.1%)	Sesquiterpene	Antibacterial, Toxicity	(13)
	Bark	$\beta$ -Caryophyllene (17.3%), $\beta$ -selinene (10.7%), $\alpha$ -humulene (6.4%), $\alpha$ -selinene (6.4%), $\beta$ -elemene (5.3%), $\delta$ -cadinene (5.3%), germacrene D (5.0%)		Antibacterial, Toxicity	(13)
<i>G. morella</i>	Leaf	$\beta$ -Copaene (49.4%), $\alpha$ -humulene (18.5%), caryophyllene oxide (6.7%)	Sesquiterpene, sesquiterpenoid	-	(48)
<i>G. nigrolineata</i>	Leaf	$\beta$ -Caryophyllene (25.2%), $\alpha$ -humulene (12.8%), valencene (6.2%), $\alpha$ -cadinol (5.8%), germacrene D (5.5%)	Sesquiterpene, sesquiterpenoid	-	(53)
<i>G. pushpangadaniana</i>	Leaf	$\delta$ -Cadinene (13.1%), $\gamma$ -cadinene (12.4%), $\gamma$ -muurolene (11.7%), $\beta$ -caryophyllene (11.4%), $\beta$ -bourbonene (6.8%)	Sesquiterpene	-	(48)
<i>G. rubro-echinata</i>	Leaf	$\alpha$ -Humulene (40.6%), $\beta$ -caryophyllene (37.9%), $\gamma$ -muurolene (7.2%)	Sesquiterpene	-	(48)
<i>G. talbotii</i>	Leaf	$\beta$ -Caryophyllene (30.4%), $\alpha$ -copaene (27.0%), $\alpha$ -humulene (10.7%)	Sesquiterpene	-	(48)
<i>G. travancorica</i>	Leaf	<i>n</i> -Undecane (40.1%), $\alpha$ -copaene (15.8%), $\delta$ -amorphene (7.0%)	Hydrocarbon, sesquiterpene	-	(48)
<i>G. wightii</i>	Leaf	Bicyclogermacrene (22.6%), $\beta$ -caryophyllene (19.0%), aromadendrene (6.8%), globulol (6.0%), viridiflorol (5.5%)	Sesquiterpene, sesquiterpenoid	-	(48)

In Malaysia, *G. celebica* is known as “manggis hutan”. It is widely used in traditional medicine to cure ailments and health disorders. The leaf is used to treat itches while the root decoction is used against infection. According to literature, the leaf EO of *G. celebica* yielded 22 volatile constituents.  $\alpha$ -Copaene (61.25%) was predominated, followed by germacrene D (6.72%) and  $\beta$ -caryophyllene (5.85%). The major constituents,  $\alpha$ -copaene and  $\beta$ -caryophyllene possess woody and spicy aroma. These constituents are commonly used as a fragrance additive in cosmetics, toiletries, food and beverages (10, 46). Meanwhile, *G. gummi-gutta* is sometimes known as Malabar tamarind. It is a popular folk remedy and cuisine ingredient. In a study performed by Tan et al. (2020), 19 constituents were identified in the leaf EO of *G. gummi-gutta*.  $\beta$ -Caryophyllene and (E)- $\beta$ -farnesene were dominated in the leaf EO, accounting for 53.82% and 22.62%, respectively (11, 47). However, in a study conducted by Rameshkumar et al. (2017), the leaf EO of *G. gummi-gutta* were found to possess primarily  $\delta$ -cadinene (32.4%),  $\alpha$ -copaene (30.2%), and  $\beta$ -caryophyllene (5.7%) (48).

*G. huillensis* grown in Zimbabwe has been investigated for its fruit EO composition. The tree of *G. huillensis* can be grow up to 8 m in height. The flowers of *G. huillensis* are greenish-yellow while the leaves are often in tinged red. In traditional medicine, the bark is used as an aphrodisiac. The lotion made from the plant is used to treat septic sores and peptic ulcers. The fruit EO of *G. huillensis* was found to possess mainly  $\alpha$ -humulene, valencene, and  $\beta$ -caryophyllene, with relative area percentages of 23.0, 18.2, and 12.6, respectively (49). In Nigeria, *G. kola* is known as “namijin goro”. Various medicinal properties have been reported from the plant, particularly in the treatment of infection, asthma, rheumatism, throat and menstrual discomforts, bronchitis, cold, cough, and liver disorders. The seed and leaf of *G. kola* were documented to be effective against viral and bacterial infections, flu, dysentery and diarrhea. In addition to that, the leaves are used to treat stomach ache and typhoid. The fruit EO of *G. kola* obtained by hydrodistillation was predominated by citronellic acid (48.3%). Citronellic acid is an acyclic monoterpene carboxylic acid. It is commonly used as a flavor and fragrance agent (12, 50).

*G. imberti* and *G. indica* distributed in Western Ghats were investigated for their leaf EOs composition. In total, 19 and 21 constituents were identified from the leaf EOs of *G. imberti* and *G. indica*, respectively. The leaf EOs of *G. imberti* was primarily composed of  $\beta$ -caryophyllene (38.1%),  $\alpha$ -humulene (30.5%), and alloaromadendrene (5.5%). Meanwhile, *G. indica* yielded mainly  $\beta$ -caryophyllene (18.6%),  $\alpha$ -selinene (18.2%),  $\alpha$ -humulene (17.6%),  $\beta$ -selinene (12.3%),  $\gamma$ -muurolene (5.9%), and  $\delta$ -cadinene (5.3%) [48].

*G. mangostana* is a popular tropical fruit tree. It is commonly known as mangosteen in Southeast Asia. The tree can grow up to 25 m in height with characteristic fragrance. Traditionally, *G. mangostana* is used to treat diarrhea, dysentery, infection, ulcer and enteritis. Hydrodistillation has been carried out to extract the leaf and stem bark EOs of *G. mangostana*. Based on the findings, 64 and 101 constituents have been identified in the leaf and stem bark EOs of *G. mangostana*, respectively. In the leaf EO,  $\beta$ -caryophyllene,  $\beta$ -elemene, germacrene D,  $\alpha$ -selinene,  $\alpha$ -humulene, and  $\beta$ -selinene were found as the major constituents, accounting for 21.1%, 9.7%, 7.9%, 7.4%, 7.3%, and 7.1%, respectively. Meanwhile, the stem bark EO was mainly composed of  $\beta$ -caryophyllene and  $\beta$ -selinene, with relative area percentages of 17.3 and 10.7, respectively (13, 51).

*G. morella* is known as an Indian gamboge. Generally, the tree can grow up to 12 m in height. Leaves of *G. morella* are simple and decussate. The bark of the tree is smooth with dark brown colour. The size of the fruits is similar to berries and contain four seeds. The plant is occasionally used as a base for mangosteen (52). Leaves of *G. morella* collected in Agastyamala forest were hydrodistilled using a Clevenger-type apparatus.  $\beta$ -Copaene (49.4%),  $\alpha$ -humulene (18.5%), and caryophyllene oxide (6.7%) were found as dominant constituents (48). On the contrary, *G. nigrolineata* is widely distributed in Malaysia, Singapore, Thailand, and Myanmar. It is a tropical tree known for its tasteful fruits. Hydrodistillation was conducted to extract the leaf EOs of *G. nigrolineata*. In total, 37 constituents were identified.  $\beta$ -Caryophyllene,  $\alpha$ -humulene, valencene,  $\alpha$ -cadinol, and germacrene D were the representative constituents, accounting for 25.2%, 12.8%, 6.2%, 5.8%, and 5.5%, respectively (53).

Five *Garcinia* species, namely, *G. pushpangadaniana*, *G. rubro-echinata*, *G. talbotii*, *G. travancorica*, and *G. wightii* are endemic species to the forest of Western Ghats. The leaves of the plants were extracted for their EOs using hydrodistillation. Among the detected volatile constituents, sesquiterpenes was found as the predominant chemical class.  $\delta$ -Cadinene (13.1%),  $\gamma$ -cadinene (12.4%),  $\gamma$ -muurolene (11.7%),  $\beta$ -caryophyllene (11.4%), and  $\beta$ -bourbonene (6.8%) were detected in the leaf EO of *G. pushpangadaniana*. Meanwhile,  $\alpha$ -humulene (40.6%),  $\beta$ -caryophyllene (37.9%), and  $\gamma$ -muurolene (7.2%) were found as major constituents in the leaf EO of *G. rubro-echinata*. Sesquiterpenes  $\beta$ -caryophyllene,  $\alpha$ -copaene, and  $\alpha$ -humulene were detected at 30.4%, 27.0% and 10.7%, respectively, in the leaf EO of *G. talbotii*. *G. travancorica* was found to possess n-undecane (40.1%),  $\alpha$ -copaene (15.8%), and  $\delta$ -amorphene (7.0%) as the dominant volatile constituents. In the leaf

EO of *G. wightii*, 23 constituents were detected. Bicyclogermacrene (22.6%),  $\beta$ -caryophyllene (19.0%), aromadendrene (6.8%), globulol (6.0%), and viridiflorol (5.5%) were found as the major constituents (48, 54).

### Biological Activities

EOs are studied extensively owing to their significant biological activities. It is reported that the bioactivities of EOs are mainly depending on their chemical compositions (55). Findings from different studies have demonstrated the antimicrobial, anti-inflammatory, and cytotoxic properties of *Garcinia* EOs (Table I).

### Antimicrobial activity

The hydrophobicity of EOs has allow them to move through the cell membrane of bacteria. The bioactive constituents of EOs can disturb the cell structure of bacteria and caused the cell death (56). The fruit EO of *G. atroviridis* was active towards *Bacillus subtilis* and *Staphylococcus aureus* with minimum inhibitory concentration (MIC) of 4.8 mg/mL. Meanwhile, it showed weak activity on *Escherichia coli*, *Pseudomonas stutzeri* and *Salmonella typhimurium* (8). Regarding the leaf EO of *G. celebica*, it showed better inhibition on *B. subtilis* and MRSA than *Proteus mirabilis*. However, no evident inhibition was detected on yeasts and fungi. In microdilution assay, the leaf EO of *G. celebica* gave MIC ranging from 1.25 to 2.5 mg/mL. The recorded minimal lethality concentration (MLC) was higher than MIC, suggesting a high concentration of EOs was needed to kill the test bacteria (10). On the contrary, the leaf EO of *G. gummi-gutta* was active against Gram-positive bacteria when tested using agar diffusion method. The recorded zones of inhibition were ranging from 9.0 to 11.0 mm. Based on the results, the MIC was estimated at 0.156  $\mu$ g/mL against MRSA, 0.625  $\mu$ g/mL against *S. aureus* and *Candida utilis*, and 1.250  $\mu$ g/mL against *Bacillus cereus*, *B. subtilis*, *Acinetobacter anitratus* and *Shigella boydii* (11). In a study performed by Okhale et al. (2016), the leaf EO of *G. kola* showed inhibition towards *Klebsiella pneumonia* (MIC: 50  $\mu$ g/mL), *Candida albicans* (MIC: 100  $\mu$ g/mL), *E. coli* (MIC: 200  $\mu$ g/mL) and *Pseudomonas aeruginosa* (MIC: 200  $\mu$ g/mL) (12). Meanwhile, agar well diffusion assay was employed to assess the antibacterial activity of the leaf and stem bark EOs of *G. mangostana*. The stem bark EO showed significant antibacterial activity than the leaf EO. It gave zones of inhibition on *B. subtilis* (21.3 mm), *Staphylococcus epidermidis* (20.0 mm), *S. aureus* (18.0 mm), *Proteus spp.* (14.0 mm), and *E. coli* (9.0 mm) (13). Studies have shown that sesquiterpenes-rich EOs possess antimicrobial activity.  $\beta$ -Caryophyllene is a ubiquitous sesquiterpene (~5-40%) found in the EOs of *Garcinia* spp.. It was reported that to  $\beta$ -caryophyllene demonstrated better antibacterial effect against Gram-positive bacteria than Gram-negative bacteria.

Additionally, this constituent exhibited antifungal effects against *Aspergillus niger*, *Penicillium citrinum*, *Rhizopus oryzae*, and *Trichoderma reesei* (57). According to Maia et al. (2010), EOs of *Vernonia remotiflora* and *V. braziliiana* which constituted about 40% of  $\beta$ -caryophyllene showed antibacterial activity against both Gram-negative and Gram-positive bacteria (58).

### Anti-inflammatory activity

Generally, immune system adopt inflammation to safeguard the body from injuries and wounds. In this aspect, non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used to inhibit cyclooxygenase-2 (COX-2) (59, 60). In assessing anti-inflammatory activity, COX inhibitory assay was conducted on the fruit EO of *G. atroviridis*. It showed IC<sub>50</sub> values of 4.64 and 2.53  $\mu$ g/mL on COX-1 and COX-2, respectively. Indomethacin was used as a positive control with IC<sub>50</sub> values of 3.31  $\mu$ g/mL (COX-1) and 4.72  $\mu$ g/mL (COX-2). The fruit EO exhibited a selectivity index (COX-2/COX-1) of 0.54. It was reported that a lower ratio (<1) of selectivity index indicates a high selectivity of the sample towards COX-2. Hence, the fruit EO of *G. atroviridis* which comprised mainly sesquiterpenes may possess significant anti-inflammatory activity (8). The involvement of sesquiterpenes in anti-inflammatory activity was reported to occur through different pathways. According to da Silveira e Sa et al. (2015),  $\beta$ -caryophyllene and  $\alpha$ -humulene showed anti-inflammatory effects via expression of kinin B1 receptor. Kinins are produced during the inflammatory processes which governed by two receptors (B1 and B2). In regard to this, receptor B1 is known as the target for anti-inflammatory agents in the management of pain and inflammation (61).

### Cytotoxic activity

EOs of *Garcinia* have been studied for their cytotoxicity with the aim of assessing their anticancer potential. The cytotoxic effects of EOs might due to different mechanisms. Among them are cell cycle arrest, loss of essential organelle function, cell death by apoptosis and/or necrosis (62, 63). At a concentration of 100  $\mu$ g/mL, the leaf EO of *G. atroviridis* has caused more than 50% cell death on human breast MCF-7 cancer cells. Based on the findings, the leaf EO showed cytotoxic effects in a dose- and time-dependent manner. However, the stem bark EO of *G. atroviridis* did not induced significant cytotoxic effect on the tested cancer cells. The IC<sub>50</sub> of the leaf EO on MCF-7 cancer cells was estimated at 71  $\mu$ g/mL. According to the findings, the leaf EO was effective than the stem bark EO in inhibiting the proliferation of MCF-7 cancer cells. In a combination treatment using tamoxifen (anticancer drug) and the leaf EO, it has caused more cancer cell death than using the drug alone (9). Regarding the leaf EO of *G. celebica*,

it showed substantial cytotoxic effects on MCF-7 cancer cells in a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The recorded IC<sub>50</sub> value was 45.2 µg/mL (10). On the contrary, the leaf EO of *G. gummi-gutta* showed a significant cytotoxicity towards human breast MDA-MB-231 and MCF-7/TAM(R) cancer cells. The leaf EO exhibited a notable cytotoxic selectivity of 4.38 and 4.0 against MDA-MB-231 and MCF-7/TAM(R), respectively, implying its potential in anticancer treatment (11). The EOs of *G. mangostana* were toxic to *Artemia salina* when assessing using a brine shrimp lethality test. The lethal concentration at 50% of toxicity (LC<sub>50</sub>) gave 1.70 and 5.15 µg/mL from the leaf and stem bark EOs, respectively (13). Previous studies revealed that terpenes and its oxygenated derivatives are promising anticancer agents in triggering the cancer cell death. Various EO constituents have been shown as cytotoxic via different mechanisms, such as apoptosis, necrosis and cell cycle arrest. They have been reported in affecting the membrane fluidity of the cancer cell, decreasing the production of adenosine triphosphate (ATP), and causing the loss of mitochondrial potential (64, 65).

## CONCLUSION

Since ancient times, EOs have been employed in traditional medicine. Plants from *Garcinia* are a valuable source of EOs. The present review highlights the volatile chemical constituents of EOs extracted from various plant parts of *Garcinia* spp. Terpenes was a dominant chemical class in the EOs of *Garcinia*. Numerous terpenes and their derivatives have advantageous biological properties that can be used to treat diseases, such as inflammation, cancer, bacterial and fungal infections. Generally, EOs are non-mutagenic and non-genotoxic. The EOs extracted from *Garcinia* exhibited potent biological activities, suggesting their potential in the pharmaceutical sector. Nevertheless, EOs standardization is required as it is affected by geographical locations, seasonal variations and etc. Extensive investigations involving *in vivo* study, administration route, and side effects are warranted to evaluate the toxicity of EOs for clinical use.

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