PLANT SCIENCE TODAY
ISSN 2348-1900 (online)
Vol x(x): xx–xx
https://doi.org/10.14719/pst.1594

HORIZON
e-Publishing Group
HePG

REVIEW ARTICLE

A review on chemical profiles and biological activities of essential oil from some plants belonging to family Scrophulariaceae

Thao Nguyen Luu & Hong Thien Van*

Institute of Biotechnology and Food Technology, Industrial University of Ho Chi Minh City, No. 12 Nguyen Van Bao, Ward 4, Go Vap District, Ho Chi Minh City, Vietnam

*Email: vanhongthien@iuh.edu.vn

OPEN ACCESS

ARTICLE HISTORY

Received: 13 November 2021
Accepted: 02 April 2022

Available online
Version 1.0: 11 May 2022

Check for updates

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at https://horizonepublishing.com/journals/index.php/PST/open_access_policy

Publisher's Note: Horizon e-Publishing Group remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Indexing: Plant Science Today, published by Horizon e-Publishing Group, is covered by Scopus, Web of Science, BIOSIS Previews, Clarivate Analytics, etc. See https://horizonepublishing.com/journals/index.php/PST/indexing_abstracting

CITE THIS ARTICLE

Luu T N, Van H T . A review on chemical profiles and biological activities of essential oil from some plants belonging to family Scrophulariaceae. Plant Science Today (Early Access). https://doi.org/10.14719/pst.1594

Abstract

Scrophulariaceae is a large family, many species of which have been reported to have a wide range of biological activities and uses as folk medicines. The essential oils from species belonging to this family mainly contain monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons, oxygenated sesquiterpenes and non-terpenes. Furthermore, their essential oils have been reported to have a variety of biological activities such as antimicrobial, antioxidant, insecticidal etc. The objective of this review is to provide a brief overview of the chemical composition and biological activities of the essential oils isolated from different parts of species included in the Scrophulariaceae family. In addition, this paper also introduces the therapeutic potentials and provides the evidence for future medicinal applications of those species.

Keywords

Biological activity, chemical components, essential oil, Scrophulariaceae

Introduction

For thousands of years, humans have been using plants for many purposes, such as flavors, foods and medicines, in which medicinal herbs are the main sources of antimicrobial agents and potential and highly potent drugs. Many chemical compounds from medicinal herbs are also potent in treating some infectious diseases (1-3). The potential supply for the new drugs of Vascular herbs are still far from being fully explored. Of 500000 species found and identified, only a minority were phytochemically recorded in some researches (4) which studied on the medicinal aspects, chemical constituents and bioactivities of *Scrophulariaceae* species (5-7).

Essential oils are a complex of volatile compounds extracted from the aromatic plants, many parts of which contain essential oils, such as leaves, seed, flower, peel, berries, rhizome, root, bark, wood, resin and petals (8). Bioactive compounds found in the essential oils belong to different chemical groups, including alkanes, alcohols, aldehydes, ketones, esters and acids (9). The fact that many natural products are valuable in many fields such as pharmaceutics, perfumes, cosmetics, aromatherapy, phytotherapy, spices and nutrition, insecticides has also been shown by many previous studies (10).

Scrophulariaceae is a large family with over 3000 species belonging to 292 genera worldwide distributed. The family mainly consists of herbs while the rest are shrubs and lianas. Bilateral symmetric tubular flowers, (±

actinomorphic in *Verbascum*) and many- seeded capsular fruits are the 2 features characterizing the species in this family. As reported in some previous studies, some Scrophulariaceae species exhibit many biological activities and a highly diverse phytochemistry with a variety of chemical classes, such as terpenes, flavonoids and phenolic acids. Recently, *in vivo* and *in vitro* examinations of neuroprotective activity were conducted in some Scrophulariaceae species (11-17). However, given the above positive information, there are still a restriction on their economic uses and the limited information in terms of chemical profiles and biological activities involving the essential oils of Scrophulariaceae species. This review, therefore, aims to provide a short comprehensive picture of the chemical compositions and biological activities of the essential oils from different parts of some Scrophulariaceae species.

Chemical profiles of essential oils in the plants belonging to Scrophulariaceae

Across a certain previous studies involving the essential oils of Scrophulariaceae species, the chemical compounds in their essential oils mainly belong to the four chemical groups, including monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons and oxygenated sesquiterpenes and oxygenated monoterpenes. In those studies, a variety of plant parts, such as leaves, stems, aerial parts or the whole plants, were used for the essential oil extraction (11-17). The major compounds identified in the essential oils from different parts of Scrophulariaceae were presented in SupplementaryTable

Oxygenated monoterpenes are the group of substances contributing to the largest part of the essential oils of the *Scrophulariaceae* species. Many recent studies have shown the essential oils of *Limnophila rugosa* contained two main components, including methyl chavicol and trans-anethole accounting for 95% of the total essential oil content. The results were relatively similar among those studies, although *L. rugosa* specimens were collected in different regions of Vietnam or India (18-20). The essential oils from the leafs of *Adenosma bracteosa* collected in Vietnam contained carvacrol, another oxygenated monoterpene, as the most major constituent (21) while thymol was found as the most abundant constituent in the essential oil of *Conobea scoparioides* collected from Brazil (22).

The three *Scrophularia* species in Iran, including *S. amplexicaulis, S. frigida* and *S. subaphylla,* had eugenol and linalool as the highest portions found of the essential oils from their aerial parts (23-25). In addition, mentha-1, 5, 8-triene was the highest constituent found in the essential oils from the leaves of *Limnophila micrantha* in Vietnam (21). 1, 8-cineole was also the second highest constituent in *Adenosma indiana* (leaf) and *Adenosma glutinosum* (aerial part) essential oils (26). Similarly, fenchone and pulegone were the two main constituents found in the essential oils of *Adenosma capitatum* in Bangladesh (27) and *Limnophila aromatica* in Vietnam (19). The essential oils from the aerial parts of *Adenosma indianum* in China had fenchone as the highest percentage (28). Moreover, bornyl acetate, fenchyl acetate and camphene were identified as the three other major oxygenated monoterpenes in the essential oils from the leaves of the *Eremophila bignoniiflora* collected in three different locations in Australia, including New South Wales, Queensland and Adelaide (29).

Another group of chemical components found in Scrophulariaceae essential oils was Monoterpene hydrocarbons. Limonene was found as the most abundant constituent in the essential oils of *Adenosma indiana* (leaf) collected in Vietnam (21), *Adenosma capitatum* (aerial parts) in Bangladesh (27), *Eremophila longifolia* (Leaf) in Australia (30), *Limnophila aromatica* (aerial part) in Vietnam and Thailand (19, 31). α-pinene was found as the most major constituent in the essential oil from the aerial part of *Adenosma glutinosum* and *Scrophularia deserti* collected in Vietnam and Iran (26, 31) while it was the second and the third highest percentage ones found in the leaf oils of *Eremophila longifolia* (Australia) and *Adenosma indiana* (Vietnam), respectively (21, 33). The essential oil extracted from the aerial parts of *L. aromatica* grown in Bangladesh was dominated by Z-ocimene (27). Some other monoterpene hydrocarbons groups, such as 2-carene, γ-terpinene, α-phellandrene, terpinolene, 3-carene, β-myrcene, β-Phellandrene were also mainly found in the essential oils of the *A. capitatum, A. glutinosum, C. scoparioides, L. aromatica, L. chinensis, L. micrantha* and *S. deserti* (19, 21, 22, 26, 27, 32).

Another group of chemical components found in the essential oils of Scrophulariaceae species was sesquiterpene hydrocarbons. α-humulene and β-Caryophyllene were recorded as the two constituents accounting for the highest proportions in the essential oils from the leaf of *Capraria biflora* in Brazil (34) while the essential oils of *Stemodia viscosa* in India contained β-caryophyllene and endo-fenchol as the two main constituents (35). Similarly, β-Caryophyllene was also a major constituent found in the leaf oils of *Stemodia maritima* in Brazil (36). α-cubebene was another main constituent recorded in the essential oil of *Rhinanthus angustifolius* collected in Turkey (37). The presence of oxygenated sesquiterpenes in the essential oils of Scrophulariaceae has been reported in a study which caryophyllene oxide was identified as the second highest percentage of essential oil from the leaf of *Stemodia maritima* in Brazil (36).

Aside from the four chemical groups of components belonging to terpenes, including monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons and oxygenated sesquiterpenes, the essential oils of Scrophulariaceae species also contain non-terpenes. Methyl thymol was the main constituent found in the essential oils of *Conobea scoparioides* in Brazil. 6α-hydroxymanoyl oxide and 6α-acetoxymanoyl oxide were the two main constituents in the essential oils from the leafs of *Stemodia trifoliate* (38) and *Stemodia foliosa* in Brazil (39). n-hexadecanoic acid; methyl benzoate; 2,3-dihydro -5-methyl-1H-indene and hexahydrofarnesyl acetone were the constituents with the highest proportions in the essential oils of *Euphrasia rostkoviana* (Czech Republic) (40), *Limnophila aromatica* (Vietnam) (19), *Rhinanthus angustifolius* (Turkey) (37) and *Scrophularia umbrosa*. (Iran) respectively (41). Phytol, 2-Pentadecanone and 1-Octen-3-ol were the 3 main constituents recorded in the aerial part of the *Scrophularia kotschyana* and *S. olympica* species in Turkey (42).

Biological activities of essential oils in the plants belonging to Scrophulariaceae

Antimicrobial activity

The antibacterial activity of essential oil extracted from the aerial parts of *Scrophularia amplexicaulis* collected in Iran against *Staphylococcus aureus* was conducted (23). In this study, the essential oil showed relatively low antibacterial activity using agar diffusion method, with the diameters of the zone of inhibition of 8 mm and 13 mm at the essential oil concentrations of 80 mg / ml and 100 mg /ml respectively. *Buddleja americana* is another species of Scrophulariaceae in America, the essential of which has been shown to be effective against to *Streptococcus mutans* with a minimum inhibitory concentration (MIC) of 0.63. µl/ml (48). In another study, it was showed that essential oil from *Euphrasia rostkoviana* collected in the Czech Republic was effective against many different strains of microorganisms (40). Accordingly, this study determined the MIC and IC50 values of antimicrobial activity against Enterococcus faecalis (512 µl/ml, 128 µl/ml), *Staphylococcus aureus* (512 µl/ml, 128 µl/ml), *Staphylococcus epidermidis* (512 µl / ml, 256 µl/ml), *Klebsiella pneumonia (*2048 µl/ml, 1024 µl/ml*), Escherichia coli (*2048 µl/ml, 1024 µl/ml), *Pseudomonas aeruginosa* (> 2048 µl/ml > 2048 µl/ml) and *Candida albicans* (128 µl/ml, 128 µl/ml).

In a study using agar diffusion method, it was demonstrated that the essential oil extracted from the whole plant of *Rhinanthus angustifolius* in Turkey was found to be effective against some pathogenic bacteria strains at different concentrations (37). For instance, 1% and 2% essential oil were all resistant to *Bacillus cereus*, *E. coli, E. coli* O157: H7 with the diameters of the zone of inhibition of 12.01 ± 0.1 mm and 10.24 ± 0.1 mm; 10.64 ± 0.10 mm and 8.19 ± 0.15 mm; 13.13 ± 0.10 mm and 10.20 ± 0.1 mm respectively. Meanwhile, *Staphylococcus aureus, Sacharomyces cerevisiae* and *Candida albicans* were only inhibited by the essential oil from *Rhinanthus angustifolius* at a concentration of 1% with the the diameters of the zone of inhibition of 8.14. ± 0.10 mm, 5.01 ± 0.15 mm and 7.19 ± 0.10 mm respectively (37).

Furthermore, the essential oils from the leaves of *Eremophila longifolia* in Australia displayed the antibacterial activity against many tested microorganisms, such as *Staphylococcus aureus, S. epidermidis, Salmonella typhimirium, Klebsielia aerogenes, Escherichia coli, Streptococcus pneumoniae, Bacillus subtilis* and *Candida. albicans* (30). *E. bignoniflora* is another species belonging to genus *Eremophila* and was endemic to Australia, the essential oil of which has been shown to be active against many strains of bacteria and fungi, such as *E. coli, Pseudomonas aeruginosa, Staphylococcus epidermidis, S. aureus, Bacillus subtilis, Klebsiella aerogenes, Salmonella typhimirium* and *Candida albicans* (29). In a study, the essential oils from the aerial parts of 5 *Scrophularia* species collected in Turkey, including *S. chrysantha, S. kotschyana, S. olympica, S. cinerascens* and *S. zuvandica* were reportedly active against *Mycobacterium smegmatis* and *Bacillus cereus* (42).

Reports are on the antibacterial activities of the essential oils from the aerial parts of *Limnophila geoffrayii* (45). They were all active against a certain bacterial and fungal strains. Accordingly, the corresponding MIC values of antimicrobial activity of essential oils against the tested microorganism were *Staphylococcus aureus* (0.1%), *E. coli* (0.2%), *Pseudomonas aeruginosa* (0.2%), *Salmonella typhimurium* (0.2 %), *Candida albicans* (0.1%) and *Aspergillus niger* (0.3%) (45). Recently, the antibacterial activity of the essential oils from aerial parts of 3 species belonging to genus *Limnophila* has been recorded in Vietnam (19). In the study, the essential oil of *L. aromatica* was effective against the 5 tested bacterial strains, including *Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa, Salmonella enteritidis* and *Salmonella typhimurium* with the inhibition zone diameters of 11.3 mm, 12.7 mm., 9.7 mm, 17.2 mm and 18.3 mm respectively. The essential oil from *L. rugosa* was active against 4 strains, including *B. cereus* (13.8 mm), *E. coli* (11.6 mm), *P. aeruginosa* (14.2 mm) and *S. enteritidis* (14.3 mm), while *B. cereus* (13.2 mm), *E. coli* (15.3 mm) and *S. enteritidis* (16.3 mm) were reportedly inhibited by the essential oils from *L. chinensis* (19).

Antioxidant capacity

To investigate the antioxidant activity of natural compounds, DPPH method has been one of the most common methods to be used so far. Reports are on a weak antioxidant activity of the essential oil extracted from the aerial part of *Scrophularia umbrosa* collected in Iran with the RC_{50} value of 13.71 mg/ml (41). In another study, the essential oil from *Rhinanthus angustifolius* subsp. *grandiflorus* collected in Turkey have shown antioxidant activity against DPPH radical (37). In a study, also based on DPPH method showed the antioxidant activity of twelve essential oil samples extracted from the leafs of *Eremophila longifolia* collected in Australia (30). Those twelve oil samples with concentrations ranging from 9 to 1929 ml/mM all possessed the antioxidant property (30). In another study, the essential oil of *Limnophila aromatica* in Thailand also showed the antioxidant activity with an IC_{50} value of 7.8 µg / ml. And aother major constituent found in essential oil of *L. aromatica*, eugenol, also had an antioxidant capacity with IC_{50} of 6.89 µg/ml (44).

Larvicidal activity

Aedes aegypti is a mosquito species endemic to South East Asia, the Pacific Islands area, Africa and the Americas. The organism has been known to be able to spread both the yellow fever in Central and South America and in west Africa, and dengue hemorrhagic fever. Due to the fact that the mosquito population in the larval stage is much easier to control than that in the adult stage, the strategy to control the proliferation of the larvae of *A. aegypti* is a must do. And hence, the natural products used as insecticides to control *aegypti* larvae have drawn much attention from many scientists (49-53). In a study, the essential oils extracted from the leaves and stems of *Stemodia maritima* collected in Brazil were reportedly active against larvae of *A. aegypti* with the LC_{50} values of 55.4 ppm and 22.9 ppm respectively (36). Moreover, caryophyllene oxide, a major constituent of the stem oils of *S. maritima,* was reported to be active against larvae of *A. aegypti* with the LC_{50} value of 50.4 ppm (36). Similarly, reports are on the larvicidal activity against the larvae of *A. aegypti* of the essential oil from the leaves of Capraria biflora in Brazil with the LC50 value (34).

Other bioactivities

Aside from the aforesaid bioactivites, the essential oils from Scrophulariaceae species were also proven to be potentially used as relaxation agent, antiparasitics, insecticide etc. As in a recent study, the inhalation of the essential oil from *Limnophila aromatica* was able to result in the relaxing effects on positive mood states and the relaxation of brain state (31). In another study, related to the use of the essential oils as antiparasitics, the water fraction containing terpenoids (84.6%) and non-terpenoid (11%) compounds of the essential oil extracted from the aerial parts of *Scrophularia striata* was employed to *in vitro* evaluate their effect on *Leishmania tropica* and *Leishmania major* promastigotes and axenic amastigotes. And as a result, the essential oil was proven to be an effective anti-leishmanial agent (47). The potential use as insecticide of the essential oils from Scrophulariaceae species was also investigated in a study using a bioassay with impregnated filter paper in which the essential oil from the aerial parts of *Limnophila geoffrayi* containing mainly d-Pulegone (27.14%), perillaldehyde (19.13%) and limonene (9.00%) was used. The essential oil was experimentally demonstrated to be a strong insecticide against the Oriental fruit fly *Bactrocera dorsalis* when an essential oil dose of 5 µl/disc was used and a high fruit fly mortality of 94% was recorded (45).

Bioactivities of key components of essential oils in the plants belonging to Scrophulariaceae

The biological activities of the essential oil extracted from Scrophulariaceae plants may be attributed to the chemical components present in their essential oils. For instance, eugenol, a major component in the essential oils of many Scrophulariaceae species, is a commonly constituent and was isolated for the first time in 1929 (54, 55). The antimicrobial and antioxidant properties of this compound have been reported by previous study. Eugenol was found to be effective against many pathogenic bacteria, including *Pseudomonas aeruginosa, Staphylococcus aureus, Enterobacter aerogenes, Listeria monocytogenes, Streptococcus agalactiae* and *Escherichia coli*. Studies demonstrated that the antibacterial effects of this compound are contributed by hydroxyl group which prevents the activities of histidine carboxylase, amylase and protease of bacteria (55, 56). In addition, cytoplasmic membrane of Gram-negative bacteria was damaged by eugenol. Because of hydrophobic molecule, lipopolysaccharide cell membrane is easily penetrated by this compound and altering the cell structure and causing the leak of intracellular components (57).

Eugenol has been also reported to possess antifungal activities against many fungal strains, including *Penicillum italicum, Aspergillus niger, Saccharomyces cerevisiae, Trichophyton rubrum, Penicillum glabrum, Candida albicans, Laetiporus sulphureus, Trichophyton mentagrophytes, Fusaria oxysporum* and *Lenzites betulina* (55, 56, 58). With fungi, eugenol is the cause of the disturbance to the function of cell membrane, the inhibition of virulence factors, and preventing the formation of fungal biofilm (55, 56, 58). In addition, eugenol is a compound characterized by antioxidant and neuroprotective properties and monoamine oxidase (MAO) inhibitor (59). The component is able to scavenge free radicals, inhibit the reactive oxygen species generation, stop the formation of reactive forms of nitrogen, enhance cyto-antioxidant capacity and help secure the function of microbial DNA and proteins. Eugenol is also known to help repair oxidative damage, destroy damaged molecules, and stop the formation of mutations developing into cancer (54, 60, 61). Eugenol structure is known to be responsible for the antioxidative potential of eugenol, the structure facilitates the fixation of eugenol to phenoxy radicals by receiving donated hydrogen atoms (62).

β-caryophyllene, another component in the essential oils of Scrophulariaceae plants, had an inhibitory effect on many bacterial and fungal strains, including *Staphylococcos aureus, Klebsiella pneumonia, Bacillus subtilis, B. cereus, Escherichia coli, Pseudomonas aeruginosa, Penicillium citrinum, Aspergillus niger, Trichoderma reesei* and *Rhizopus oryzae* (63). Furthermore, β-caryophyllene also possessed the antioxidant activity with IC_{50} values of 3.23 and 1.25 µM for FRAP and DPPH assays respectively (63). The larvicidal property of β-caryophyllene against *Aedes aegypti* has been reported by recent studies. Accordingly, this compound displayed active against *A. aegypti* with 3.3, 3.3, 3.3, 5.0 and 3.3% of mortality at dose of 150, 200, 250, 300 and 400 ppm (64).

A variety of terpene mixtures have been used as a cheap and non-invasive treatment for cholesterol stones in the gall bladder and bile ducts (65) and for ureteric stones (65), in which limonene was included. This compound has been reported to possess antibacterial and antifungal effects against *Listeria momocytogenes, Aspergillus niger, A. ochraecus, A. flavus, A. parasiticus, Alternaria alternata, Chaetomium sp., Fusarium culmorum and Penicillum citratum* (65). Moreover, this compound was also found to be effective against several bacterial pathogens such as *Bacillus cereus, Salmonella typhimurium, Escheriachia coli* and *Staphylococcus aureus* (66).

Another compound in the essential oil of Scrophulariaceae plants, α-pinene, possessed antimicrobial and larvicidal properties. This compound was active against many bacterial pathogens such as *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, S. epidermidis, Streptococcus faecalis, S. pyogenes* and *S. pneumonia*. Moreover, some fungal strains such as *Candida albicans, Sclerotinia sclerotiorum,* followed by *Mycobacterium smegmatis, Cylindrocarpon mali, Aspergillus niger, Stereum purpureum, Cryptococcus neoformans* and *Rhizopus oryzae* were also inhibited by this compound (67-69). In addition, α-pinene has been reported to possess larvicidal effects against fourth stage larvae of *Aedes aegypti*. The mortality

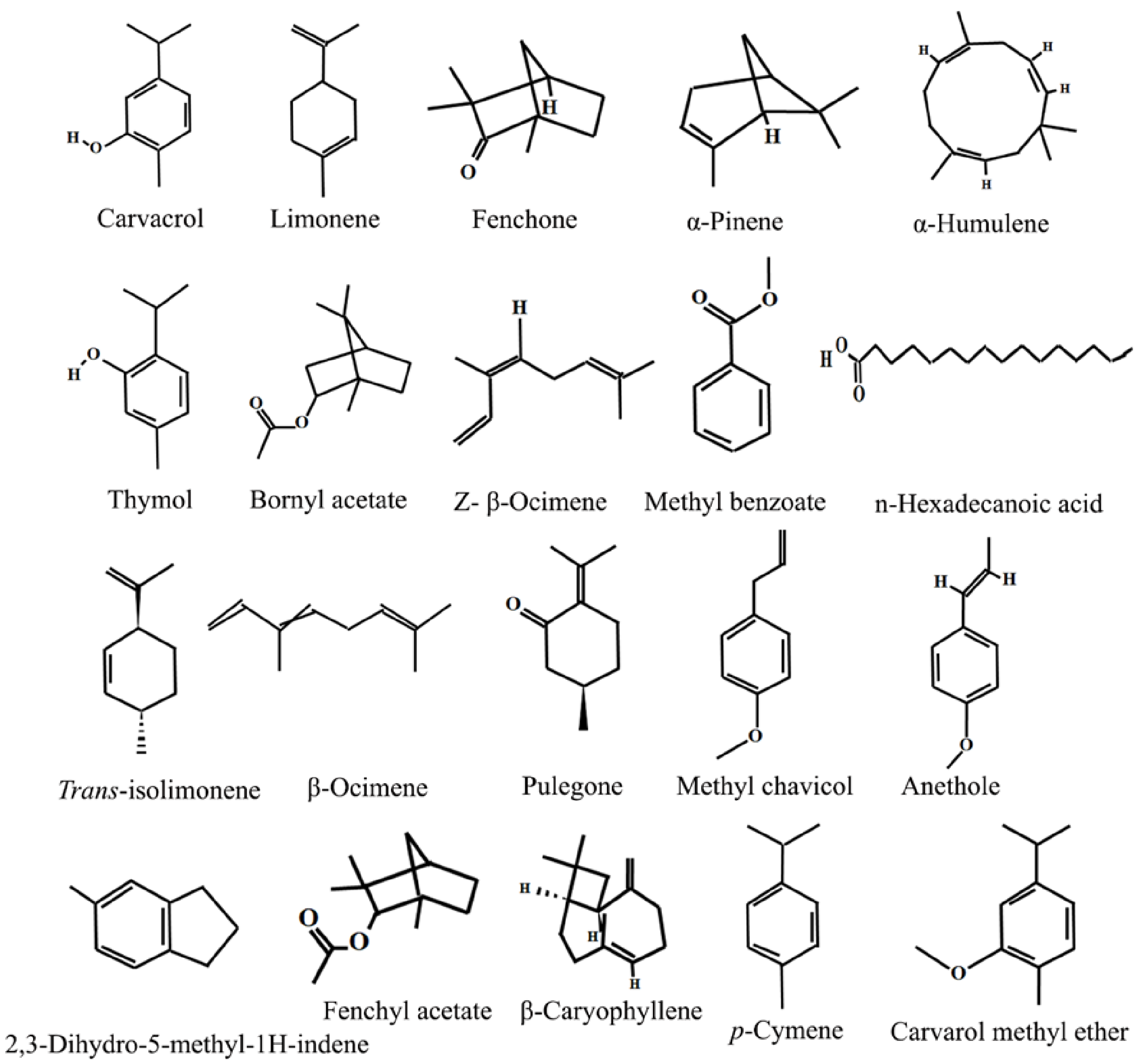

Fig. 1. Some chemical components of Scrophulariaceae essential oils.

percentages of 12, 27, 33, 45 and 67% were recorded at doses of 150, 200, 250, 300 and 400 ppm (64).

It was demonstrated that the *Ocimum ciliatum* essential oil contained methyl chavicol as the most abundant compound (87.6%) had an inhibitory effect on many bacterial strains, including *Rhodococcus fascians, Brenneria nigrifluens, Agrobacterium vitis, Xanthomonas oryzae pv. oryzae, Ralstonia solanacearum, Pseudomonas tolaasii, P. syringae pv. syringae, P. syringae pv. lachrymans, Pantoea stewartii subsp. indologenes* and *Xanthomonas citri* (70). DPPH, cooxidation β-carotene/linoleic acid and thiobarbituric acid assays were commonly used to study the antioxidant activity of methyl chavicolMethyl chavicol (IC50 = 312.50 ± 2.28 µg/ml) was reported to be able to inhibit the DPPH free radical. The compound was able to diminish the lipid peroxidation at the level of 73.08 ± 4.79. It also caused the reduction in the malonaldehyde content and the inhibition of the pancreatic lipase (71). In addition, methyl benzoate has been reported to possess antimicrobial activities against some bacterial and funfal strains, including *Staphylococcus aureus, Escherichia coli, Bacillus substilis, Salmonelle paratyphi, Aspergillus niger, A. fumigata* and *Candida albicans* (72). Furthermore, ocimene and camphene were found to be effective against *Candida albicans* (73).

Conclusion

In this study, several relevant scientific works were gathered and reviewed in order to provide the information related to both the biological activity and the chemical composition in the essential oils of species belonging to Scrophulariaceae. This review showed that the content and the chemical compositions of the essential oils from several species of Scrophulariaceae greatly varied with different regional locations where the specimens were collected. The bioactivities of some constituents of the essential oils from several species of Scrophulariaceae promise a potential use of these essential oils for the large – scale production of folk medicines in the near future.

GC-MS has been the technique mostly used in the analyses of the chemical compositions. Nevertheless, many works involved in these techniques have not used the n-alkane standard for the calculation of retention indices, neither have they analyzed and compared the retention indices. Hence, those works hardly got the accurate evaluation of the essential oil constituents. Furthermore, there have not been many studies investigating into the biological activities and the mechanism of action of the components in the essential oils of species of Scrophulariaceae. Therefore, the studies in the future should be oriented towards those topics to further explain the biological activities of essential oils of species of Scrophulariaceae.

Authors contributions

TNL and HTV designed this study. Two authors searched and handled the data, drafted the manuscript and resolved all the queries of editors and reviewers.

Compliance with ethical standards

Conflict of interest: No conflict of interest was declared by the authors.

Ethical issues: None

Suppplimentary data

Supplementary Table. Major components identifed from Scrophulariaceae essential oils

References

1. Silva NCC, Fernandes JA. Biological properties of medicinal plants: a review of their antimicrobial activity. The Journal of Venomous Animals and Toxins including Tropical Diseases. 2010;16(3):402-13. https://doi.org/10.1590/S1678-91992010000300006
2. Hemraj V, Anil J. Antimicrobial activities of medicinal plants-review. International Journal of Research in Pharmaceutical and Biomedical Sciences. 2012;3(1):222-30.
3. Marwa A, Abdelrhman A. Chemical diversity of essential oils from flowers, leaves and stems of *Rhanterium epapposum* Oliv. growing in northern border region of Saudi Arabia. Asian Pacific Journal of Tropical Biomedicine. 2016;6(9):767-70. https://doi.org/10.1016/j.apjtb.2016.07.010
4. Mahesh B, Satish S. Antimicrobial activity of some important medicinal plant against plant and human pathogens. World Journal of Agricultural Sciences. 2008;4:839-43.
5. Brahmachari G. *Limnophila* (Scrophulariaceae): Chemical and pharmaceutical aspects - an update. The Open Natural Products Journal. 2014;7(1):1-14. https://doi.org/10.2174/1874848101407010001
6. Pasdaran A, Hamedi A. The genus Scrophularia: a source of iridoids and terpenoids with a diverse biological activity. Pharmaceutical Biology. 2017;55(1):2211-33. https://doi.org/10.1080/13880209.2017.1397178
7. Roy R, Jash SK, Singh RK, Gorai D. *Limnophila (Scrophulariaceae):* chemical and pharmacological aspects. World Journal of Pharmaceutical Research. 2015;4(7):1269-300.
8. Hamid AA, Aiyelaagbe OO, Usman LA. Essential oils: its medicinal and pharmacological uses. International Journal of Current Research. 2011;33(2):86-98.
9. Neiro L, Olivero J, Stashenko E. Repellent activity of essential oils: a review. Bioresource Technology. 2010;101(1):372-78. https://doi.org/10.1016/j.biortech.2009.07.048
10. Glicerio LM, Nerlis PC, Enilson PC, Miladys TA, Adriana HB. Essential oils as a source of bioactive molecules. Rev Colomb Cienc Quím Farm. 2019;48(1):80-93. https://doi.org/10.15446/rcciquifa.v48n1.80067
11. Kim SR, Lee KY, Koo KA, Sung SH, Lee NG, Kim J, Kim YC. Four new neuroprotective iridoid glycosides from *Scrophularia buergeriana* roots. J Nat Prod. 2002;65(11):1696-99. https://doi.org/10.1021/np0202172
12. Roodsari R, Zamanian Azodi M, Salimpour F. Herbal remedies and medicines; introducing some Iranian plants. Journal of Paramedical Sciences. 2013;4(2):116-22.
13. Sohn SH, Ko E, Jeon SB, Lee BJ, Kim SH, Dong MS et al. The genomewide expression profile of *Scrophularia ningpoensis*-treated thapsigargin-stimulated U-87MG cells. Neurotoxicology. 2009;30(3):368-76. https://doi.org/10.1016/j.neuro.2009.02.006
14. Esposito E, Dal TR, Pressi G, Bramanti P, Meli R, Cuzzocrea S. Protective effect of verbascoside in activated C6 glioma cells: possible molecular mechanisms. Naunyn-Schmied Arch Pharmacol. 2010;381:93-105. https://doi.org/10.1007/s00210-009-0466-0
15. Adewusi EA, Moodley N, Steenkamp V. Antioxidant and acetylcholinesterase inhibitory activity of selected southern African medicinal plants. South African Journal of Botany. 2011;77(3):638-44. https://doi.org/10.1016/j.sajb.2010.12.009
16. Oh WJ, Jung U, Eom HS, Shin HJ, Park HR. Inhibition of lipopolysaccharide-induced proinflammatory responses by *Buddleja offcinalis* extract in BV-2 microglial cells via negative regulation of NF-κB and ERK1/2 signaling. Molecules. 2013;18(8):9195-9206. https://doi.org/10.3390/molecules18089195
17. Pendota SC, Aderogba MA, Ndhlala AR, Van SJ. Antimicrobial and acetylcholinesterase inhibitory activities of *Buddleja salviifolia* (L.) Lam. leaf extracts and isolated compounds. J Ethnopharmacol. 2013;148(2):515-20. https://doi.org/10.1016/j.jep.2013.04.047
18. Nguyen TL, Le NT. Study of the essential oil of *Limnophila rugosa* (Roth.) Merr. in the South of Vietnam. Journal of Essential Oil Bearing Plants. 2011;14(3):366-72. https://doi.org/10.1080/0972060X.2011.10643947
19. Van HT, Do TT, Luu TN, Le VS, Doan VD. Chemical constituents and antibacterial activities of essential oils from aerial parts of three *Limnophila* species (Scrophulariaceae) in Southern Vietnam. Research Journal of Chemistry and Environment. 2021;25(4):12-19.
20. Verma RS, Padaliaa RC, Chauhan A. Geographical impact on essential oil composition of *Limnophila rugosa (Roth.) Merr.* Journal of Essential Oil Research. 2014;26(5):338-41. https://doi.org/10.1080/10412905.2014.922510
21. Do ND, Tran DT, Tran HT, Ogunwande IA. Chemical constituents of leaf essential oils of four Scrophulariaceae species grown in Vietnam. Journal of Essential Oil Research. 2015. https://doi.org/10.1080/10412905.2015.1067650
22. Costa RG, Faria LJG, Gusmao SAL , Silva JKR, Andrade EHA, Maia JGS. Essential oil of Pataqueira (*Conobea scoparioides* Benth.): from natural occurrence and produced by hydroponics. Advances in Plants and Agriculture Research. 2014;1(3):90-94. http://doi.org/10.15406/apar.2014.01.00015

23. Pasdaran A, Delazar A, Nazemiyeh H, Nahar L, Sarker SD. Chemical composition and antibacterial (against *Staphylococcus aureus*) and free-radical-scavenging activities of the essential oil of *Scrophularia amplexicaulis* Benth. Rec Nat Prod. 2012;6(4):350-55.

24. Asgharian P, Afshar FH, Asnaashari S, Moghaddam SB, Ebrahimi A, Delazar A. Characterization of terpenoids in the essential oil extracted from the aerial parts of *Scrophularia subaphylla* growing in Iran. Advanced Pharmaceutical Bulletin. 2015;5(4):557-61. http://doi.org/10.15171/apb.2015.075

25. Asgharian P, Afshar FH, Asnaashari S, Moghaddam SB, Delazar A. The seasonal variations of the chemical composition of essential oil obtained from *Scrophularia frigida.* Jundishapur Journal of Natural Pharmaceutical Products. 2016;11(1):29742. http://doi.org/10.17795/ jjnpp-29742

26. Nguyen XD, Le VH, Leclercq PA. A new chemotype of *Adenosma glutinosum* (L.) Druce var. *caeruleum* (R.Br.) Tsoong from Vietnam. Journal of Essential Oil Research. 1996;8:359-62. https://doi.org/10.1080/10412905.1996.9700640

27. Bhuiyan MNI, Akter F, Chowdhury JU, Begum J. Chemical constituents of essential oils from aerial parts of *Adenosma capitatum* and *Limnophila aromatica*. Bangladesh J Pharmacol. 2010;5:13-16. https://doi.org/10.3329/bjp.v5i1.4019

28. Zeng Z, Meng C, Ye X, Zeng Z. Analysis of volatile components of *Adenosma indianum* (Lour.) Merr. by steam distillation and headspace solid-phase microextraction. Journal of Chemistry. 2013;545760. https://doi.org/10.1155/2013/545760

29. Sadgrove NJ, Hitchcock M, Watson K, Jones GL. Chemical and biological characterization of novel essential oils from *Eremophila bignoniiflora* (F. Muell) (Myoporaceae): A traditional aboriginal Australian bush medicine. Phytotherapy Research. 2013;27:1508-16. http://doi.org/10.1002 / ptr.4889

30. Sadgrove NJ, Mijajlovic S, Tucker DJ, Watson K, Jones GL. Characterization and bioactivity of essential oils from novel chemotypes of *Eremophila longifolia* (F. Muell) (Myoporaceae): a highly valued traditional Australian Medicine. Flavour Fragr J. 2011;26:341-50. https://doi.org/10.1002/ffj.2062

31. Thanatuskitti P, Siripornpanich V, Sayorwan W, Palanuve C, Ruangrungsi N. The effects of inhaled *Limnophila aromatica* essential oil on brain wave activities and emotional states in healthy volunteers: a randomized crossover study. Research Journal of Pharmacognosy. 2020;7(4):1-*9.* https://dx.doi.org/10.22127/rjp.2020.230400.1586

32. Mardani M, Rezapour S, Eftekhari Z, Majid AS, Rashidipour M, Afsordeh O et al. Chemical composition of *Scrophularia deserti.* International Journal of Pharm. Tech Research. 2016;9(6):285-90. http://doi.org/10.13040/IJPSR.0975-8232.8 (5).1953-58

33. Sadgrove NJ, Jones GL. Cytogeography of essential oil chemotypes of *Eremophila longifolia* F. Muell (Scrophulariaceae). Phytochemistry. 2014. https://doi.org/10.1016/ j.phytochem.2014.05.005

34. Souza LGS, Almeida MCS, Monte FJQ, Santiago GMP, Braz-Filho R, Lemos TLG. Constituintes químicos de *Capraria biflora* (Scrophulariaceae) e atividade larvicida de seu óleo essencial. Quim Nova. 2012;35(11):2258-62. https://doi.org/10.1590/S0100-40422012001100032

35. Mammen D, Daniel M. Volatile oils and flavones of *Stemodia viscosa* Roxb. Journal of Advanced Pharmacy Education and Research. 2012;2(4):221-24.

36. Arriaga AMC, Rodrigues FEA, Lemos TLG, Oliveira MCF, Lima JQ, Santiago GMP, Raimundo BF, Mafezoli J. Composition and larvicidal activity of essential oil from *Stemodia maritima* L. Natural Product Communications. 2007;2(12):1237-39. https://doi.org/10.1177%2F1934578X0700201209

37. Kaya AA, Ucuncu O, Ilter SM, Baltaci C, Ozturk S. Chemical composition and bioactive properties of the essential oil of *Rhinanthus angustifolius* subsp. *grandiflora*. Bulgarian Chemical Communications. 2017;49(4):923-27.

38. Silva WMB, Assunção JCC, Araújo RM, Silveira ER, Pessoa ODL. New volatile constituents from leaves of *Stemodia trifoliata* (Link.) Reichb. (Schrophulariaceae). J Braz Chem Soc. 2009;20 (1):37-41. https://doi.org/10.1590/S0103-50532009000100007

39. Oliveira LLDSS, Rocha MKL, Oliveira JCS, Camara CAG. Chemical composition of essential oil from leaves of *Stemodia foliosa* growing wild in a fragment of the Atlantic forest of Pernambuco, Brazil. Chemistry of Natural Compounds. 2018;54(5):1000-01. https://doi.org/10.1007/s10600-018-2534-5

40. Novy P, Davidova H, Cecilia SSR, Rondevaldova J, Pulkrabek J, Kokoska L. Composition and antimicrobial activity of *Euphrasia rostkoviana* Hayne essential oil. Evidence-Based Complementary and Alternative Medicine Volume. 2015. https://doi.org/10.1155/2015/734101

41. Nikkhah E, Asnaashari S, Babaei H, Afshar FH, Delazar A. Chemical composition and biological activities of essential oil and methanol extract of *Scrophularia umbrosa.* Research Journal of Pharmacognosy. 2017;4(1):41-50.

42. Rend AG, Kalayci Y, Korkmaz B, Karaoglu SA, Yayh N. Chemical composition and antimicrobial activity of the essential oils of five *Scrophularia* L. species from Turkey. Records of Natural Products. 2017;11(6):521-31. http://doi.org/10.25135/ rnp.67.17.02.010

43. Maia JGS,- Zoghbi MGB, Andrade EHA. Silva MHL, Essential oils from *Conobea scoparioides* (Cham. & Schltdl.) Benth. Flavour and Fragrance Journal. 2000;15:413-14. https://doi.org/10.1002/1099-1026(200011/12)15:6<413::AID-FFJ931>3.0.CO;2-H

44. Arunya S, Nuntavan B, Opa V, Hiroshi W. Antioxidant activity of *Limnophila aromatica* Merr. Thai J Phytopharm. 2004;11:11-17.

45. Thongdon J, Inprakhon AP. Composition and biological activities of essential oils from *Limnophila geoffrayi* Bonati. World Journal of Microbiology and Biotechnology. 2009;25:1313-20. https://doi.org/10.1007/s11274-009-0016-4

46. Barati A, Sani AM. Chemical composition of the essential oil and antimicrobial activity of aqueous and methanolic extracts of *Scrophularia khorassanica.* Journal of Essential Oil Bearing Plants. 2017;20(3):662-71. https://doi.org/10.1080/0972060X.2017.1329668

47. Bahrami S, Jalali MHR, Ramezani Z, Janeh G. Anti-leishmanial activity and identification of chemical constituents of *Scrophularia striata* essential oil by head space solid phase micro extraction gas chromatography mass spectrometry (HS-SPME GC-MS). Boletín latinoamericano y del caribe de plantas medicinales y aromáticas. 2019;18(6):586-94.

48. Miller AB, Cates RG, Lawrence M, Soria AF, Espinoza LV, Martinez JV, Arbizú DA. The antibacterial and antifungal activity of essential oils extracted from Guatemalan medicinal plants. Pharmaceutical Biology. 2015;53(4):548-54. https://doi.org/10.3109/13880209.2014.932391

49. Mendonça FAC, Silva KFS, Santos KK, Ribeiro Júnior KAL, Sant'Ana AEG. Activities of some Brazilian plants against larvae of the mosquito *Aedes aegypti*. Fitoterapia. 2005;76:629-36. https://doi.org/10.1016/j.fitote.2005.06.013

50. Santiago GMP, Lemos TLG, Pessoa ODL, Arriaga AMC, Matos FJA, Lima MAS et al. Larvicidal actvity against *Aedes aegypti* L. (Díptera: Culicidae) of essential oils of *Lippia* species from Brazil. Natural Product Communications. 2006;1:573-76. https://doi.org/10.1177/1934578X0600100711

51. Santos RP, Nunes EP, Nascimento RF, Santiago GMP, Menezes GHA, Silveira ER, Pessoa OD. Chemical composition and larvicidal activity of the essential oils of *Cordia leucomalloides* and *Cor-*

dia curassavica from the Northeast of Brazil. Journal of Brazilian Chemical Society. 2006;17:1027-30. https://doi.org/10.1590/S0103-50532006000500030

52. Yu JQ, Liao ZX, Cai XQ, Lei JC, Zou GL. Composition, antimicrobial activity and cytotoxicity of essential oils from *Aristolochia mollissima*. Environmental Toxicology and Pharmacology. 2007;23:162-67. https://doi.org/10.1016/j.etap.2006.08.004
53. Murugan K, Murugan P, Noortheen A. Larvicidal and repellent potential of *Albizzia amara* Boivin and *Ocimum basilicum* Linn. against dengue vector, *Aedes aegypti* (Insecta: Díptera: Culicidae). Bioresource Technology. 2007;98:198-201. https://doi.org/10.1016/j.biortech.2005.12.009
54. Tammannavar P, Pushpalatha C, Jain S, Sowmya SV. An unexpected positive hypersensitive reaction to eugenol. Case Rep. 2013;bcr2013009464. https://doi.org/10.1136/bcr-2013-009464
55. Marchese A, Barbieri R, Coppo E, Orhan IE, Daglia M, Nabavi SF et al. Antimicrobial activity of eugenol and essential oils containing eugenol: A mechanistic viewpoint. Crit Rev Microbiol. 2017;43: 668-89. https://doi.org/10.1080/1040841X.2017.1295225
56. Devi KP, Nisha SA, Sakthivel R, Pandian SK. Eugenol (an essential oil of clove) acts as an antibacterial agent against *Salmonella typhi* by disrupting the cellular membrane. J. Ethnopharmacol. 2010;130:107-15. https://doi.org/10.1016/j.jep.2010.04.025
57. Ulanowska M, Olas B. Biological Properties and Prospects for the Application of Eugenol-A Review. Int J Mol Sci. 2021;22:3671. https://doi.org/10.3390/ijms22073671
58. Mak KK, Kamal MB, Ayuba SB, Sakirolla R, Kang YB, Mohandas K et al. A comprehensive review on eugenol's antimicrobial properties and industry applications: A transformation from ethnomedicine to industry. Phcog Rev. 2019;13:1-9. https://doi.org/10.4103/phrev.phrev_46_18
59. Kabuto H, Tada M, Kohno M. Eugenol [2-Methoxy-4-(2-propenyl) phenol] prevents 6-hydroxydopamine induced dopamine depression and lipid peroxidation inductivity in mouse striatum. Biol Pharm Bull. 2007;30:423-27. https://doi.org/10.1248/bpb.30.423
60. Khalil AA, Rahman U, Khan MR, Sahar A, Mehmood T, Khan M. Essential oil eugenol: sources, extraction techniques and nutraceutical perspectives. RSC Adv. 2017;7:32669-81. https://doi.org/10.1039/C7RA04803C
61. Pavithra B. Eugenol-A Review. J Pharm Sci Res. 2014;6:153-54.
62. Gülçin I. Antioxidant activity of eugenol: A structure-activity relationship study. J Med Food. 2011;14:975-85. https://doi.org/10.1089/jmf.2010.0197
63. Dahham SS, TabanaYM, Iqbal MA, Ahamed OBK, Ezzat MO, Majid ASA. The anticancer, antioxidant and antimicrobial properties of the sesquiterpene β-caryophyllene from the essential oil of *Aquilaria crassna*. Molecules. 2015;20:11808-29. https://doi.org/10.3390/molecules200711808.
64. Santos GKN, Dutra KA, Barros RA, Camara CAG, Lira DD, Gusmao NB. Essential oils from *Alpinia purpurata* (Zingiberaceae): Chemical composition, oviposition deterrence, larvicidal and antibacterial activity. Ind Crops Prod. 2012;40:254-60. https://doi.org/10.1016/j.indcrop.2012.03.020
65. Lis-Balchin M, Ochocka RJ, Deans SG, Asztemborska M, Hart S. Bioactivity of the enantiomers of limonene. Med Sci Res. 1996;24:309-10.
66. Guimarães AC, Meireles LM, Lemos MF, Guimarães MCC, Endringer DC, Fronza M, Scherer R. Antibacterial activity of terpenes and terpenoids present in essential oils. Molecules. 2019;24:2471. https://doi.org/10.3390/molecules24132471
67. Prudent D, Perineau F, Bessiere JM, Michel G, Bravo R. Chemical analysis, bacteriostatic and fungistatic properties of the essential oil of the atoumau from martinique (*Alpinia speciosa* K. schum.). J Essent Oil Res. 1993;5:255-64. https://doi.org/10.1080/10412905.1993.9698218
68. Leite AM, Lima EO, Souza EL, Diniz MFFM, Trajano VN, Medeiros IA. Inhibitory effect of β-pinene, α-pinene and eugenol on the growth of potential infectious endocarditis causing Gram-positive bacteria. Braz J Pharm Sci. 2007;43:122-26. https://doi.org/10.1590/S1516-93322007000100015
69. Rivas ACS, Lopes PM, Barros MMA, Machado DCC, Alviano CS, Alviano DS. Biological activities of α-pinene and β-pinene enantiomers. Molecules. 2012;17:6305-16. https://doi.org/10.3390/molecules17066305
70. Moghaddam M, Alymanesh MR, Mehdizadeh L, Mirzaei H, Pirbalouti AG. Chemical composition and antibacterial activity of essential oil of *Ocimum ciliatum*, as a new source of methyl chavicol, against ten phytopathogens. Industrial Crops and Products. 2014;59:144-48. https://doi.org/10.1016/j.indcrop.2014.05.006
71. Bouvier-Brown NC, Goldstein AH, Worton DR, Matross DM, Gilman JB, Kuster WC, Welsh-Bon D, Warneke C, Gouw JA, Cahill TM, Holzinger R. Methyl chavicol: characterization of its biogenic emission rate, abundance and oxidation products in the atmosphere. Atmos Chem Phys. 2009;9:2061-74. https://doi.org/10.5194/acp-9-2061-2009
72. Mohanapriya S, Muthukumaran, Vairam S. Synthesis, characterization, thermal behavior and antimicrobial activity of 3-methyl benzoate complexes of transition metal with hydrazine. Bull Chem Soc Ethiop. 2016;30(2):241-52. http://dx.doi.org/10.4314/bcse.v30i2.8
73. Thakre AD, Mulange SV, Kodgire SS, Zore GB, Karuppayil SM. Effects of cinnamaldehyde, ocimene, camphene, curcumin and farnesene on *Candida albicans*. Advances in Microbiology. 2016;6:627-43. http://dx.doi.org/10.4236/aim.2016.69062

§§§