REVIEW

Essential Oils and Biological Activities of the Genus Vitex (Lamiaceae) – A Review

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Abstract

The genus Vitex which includes approximately 270 species, and is an important genus of the Lamiaceae family due to its production of secondary compounds. The plants are generally used in preventing women's complaints such as aging, menstrual, menopausal, breast disease, and infertility. The objective of this study was to carry out a review of essential oils of the genus Vitex and their biological activities. The data were collected from the scientific electronic databases including SciFinder, Scopus, Elsevier, PubMed, and Google Scholar, within miscellaneous scopes of the Vitex include either medicinal uses or essential oil studies from a different region of countries. A total of nineteen Vitex species have been reported for their essential oils and biological activities. It can be observed that the major components were caryophyllene, germacrene D, limonene, cis-calamenene, 1,8-cineole, and spathulenol. Pharmacological studies indicated that the essential oil exhibited antioxidant, antimicrobial, anti-inflammatory, antifungal, acaricidal, antibiofilm, larvicidal, cytotoxic, and acetylcholinesterase activities. This review is mainly meant to provide relevant information on the phytochemical features of Vitex species, with emphasis on the essential oil, providing guidance, or the selection of accessions or species with the best chemical profiles. Nonetheless, it seems clear that more clinical evaluations are required until essential oils can be considered as possible applications in pharmacy or as adjuvants to current medications.

Keywords: Essential oils, Vitex, Lamiaceae, caryophyllene, antimicrobial

Introduction

Essential oils are complex mixtures of volatile compounds that are produced by aromatic plants as secondary metabolites. They are responsible for the aromatic plant’s properties, and for this reason, they are characterized by their strong smells (Salleh et al., 2011, 2012). In general, essential oils are liquid, volatile, and soluble in lipids and organic solvents. They can be present in all plant organs, including buds, flowers, leaves, seeds, stems, flowers, fruits, roots, wood, or bark. Different extraction techniques are widely employed for the extraction of essential oils such as steam distillation, solvent extraction, and supercritical fluid extraction (Salleh et al., 2014a, 2014b, 2014c). These essential oils are characterized by the presence of variable mixtures of bioactive compounds, mainly terpenoids, especially monoterpenes and sesquiterpenes. In contrast, the essential oils have been commercialized as a source of potential herbicides and pesticides, aromatherapy and perfumes, foods and beverages, valuable dyes, and petro crops besides being used as health care products (Salleh et al., 2015a, 2015b, 2015c). Nowadays, researchers around the world produce medicines from the essential oils of natural products such as plants. The Lamiaceae plant species have diverse biological activities in their essential oils. Within 236 genera in the Lamiaceae family, the Vitex genus has been subjected to the most abundant available studies on its ethnobotanical profiles to discover the priceless potentials.

The genus Vitex constitutes approximately 270 species generally are trees and shrubs, with woody stems about 3 meters in height (Wang & Weller, 2006). They are widely distributed in tropical and subtropical regions such as Brazil, Nigeria, Turkey, Thailand, Vietnam, Algeria, and South Africa. Moreover, there are some species growing in the temperate zone as Iran, Montenegro, and all Europe countries (Devi and Singh,
The Vitex plant with the local name of Five-Finger and as a female herb has been used in traditional medicine and reported to have a variety of biological activities (Li et al., 2002). For instance, Vitex species broadly practiced for medicinal purposes are V. negundo, V. agnus castus, and V. trifolia. The leaves and seeds of V. negundo are extensively helpful for the treatment of rheumatism and inflammatory joint conditions (Callmander et al., 2014). The fruits of V. agnus castus fruits in Turkey are established in the effectiveness of women complaints such as female hormonal disorder, pre-menstrual disorder, menopausal remedy, treat aging and to improve vaginal lubrication (Ahangarpour et al., 2016). Besides, the leaves of V. trifolia are used to treat intestinal ailments, tuberculosis, amenorrhea, rheumatic, inflammation, sprains, wound healing, and fevers (Devi & Singh, 2014).

Hence, the review regarding Vitex essential oils has to be done to simplify and compile the information. However, V. negundo, V. agnus castus, and V. trifolia essential oils have been subject to the recent review, which will not be repeated here (Khan et al., 2019; Haghighi et al., 2019; Niazi et al., 2019; Niroumand et al., 2018; Suchitra & Cheriyan, 2018; Agalar et al., 2016; Toplan et al., 2015; Duymus et al., 2014; Rani & Sharma, 2013). The available information about Vitex essential oils of various species was searched thoroughly via electronic search (Pubmed, SciFinder, Scopus, Google Scholar, and Web of Science) and the articles published in peer-reviewed journals were collected via library search. The review aims to compile the information regarding their medicinal uses, chemical composition, and bioactivities of the essential oils from the genus Vitex.

### Medicinal uses of the genus Vitex

This review emphasizes the traditional uses and clinical potential of several Vitex species. Through this review, the authors intend to highlight the unexplored potential of the Vitex species. This genus needs to be investigated systematically so that potential species can be exploited as therapeutic agents. Various medicinal plants had been analysed by the plant researchers to match their therapeutic values and to divine the safety to human consumption. The genus Vitex is generally well-known for the treatment of female disorders, sexual dysfunctions, and inflammations. Table 1 shows the medicinal uses of several Vitex species.

<table>
<thead>
<tr>
<th>Species</th>
<th>Part</th>
<th>Medicinal uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>V. altissima</td>
<td>Fruits</td>
<td>To treat stomatitis, cardiac diseases, anorexia, blindness, leprosy, worm infestation (Yoganarasimhan, 2000)</td>
</tr>
<tr>
<td>V. buchananii</td>
<td>Leaves</td>
<td>To treat venereal diseases (Cabral et al., 2009)</td>
</tr>
<tr>
<td>V. cannabifolia</td>
<td>Fruits</td>
<td>To treat analgesia, cough, used as anti-tussive (Yamasaki et al., 2008)</td>
</tr>
<tr>
<td>V. congolensis</td>
<td>Leaves</td>
<td>To cure cicatrisation (Cabral et al., 2009)</td>
</tr>
<tr>
<td>V. diversifolia</td>
<td>Barks</td>
<td>To cure tooth and skin diseases, headache, intestinal bilharzias (Zerbo et al., 2011)</td>
</tr>
<tr>
<td>V. doniana</td>
<td>Barks</td>
<td>To treat gastroenteritis, diarrhea, and dysentery (Kilani, 2006)</td>
</tr>
<tr>
<td>V. ferruginea</td>
<td>Leaves</td>
<td>To cure skin diseases, mouth sore, snake-bite (Cabral et al., 2008)</td>
</tr>
<tr>
<td>V. gaumeri</td>
<td>Leaves</td>
<td>To treat colds, cough spelling, diarrhea, gastrointestinal affections (Damayanti et al., 1996)</td>
</tr>
<tr>
<td>V. leucoxylon</td>
<td>Leaves</td>
<td>To relieve headache, catarac, as a medicinal bath for fever and anemia, reduced cholesterol, anti-inflammatory (Makwana et al., 1994)</td>
</tr>
<tr>
<td>V. lucens</td>
<td>Leaves</td>
<td>To relieve sprains, backache, treating ear ulcers, sore throats, for dead’s people body wash (Dykgraaf, 1992)</td>
</tr>
<tr>
<td>V. madiensis</td>
<td>Leaves</td>
<td>To treat skin disease (Cabral et al., 2009)</td>
</tr>
<tr>
<td>V. madiensis</td>
<td>Leaves</td>
<td>To prevent malaria (Onedo et al., 2012)</td>
</tr>
</tbody>
</table>
V. megapotamica Leaves Used as a diuretic, hypocholesterolemic, recover skin problems, for treating hemorrhoids, uric acid problem, high blood pressure, inflammation of the uterus, bladder and prostate disorder (Alice et al., 1995)

V. mollis Leaves As a remedy to alleviate dysentery, analgesic, anti-inflammatory medicine, relieve scorpion stings, diarrhea, stomach ache (Rahman & Bhattacharya, 1982)

V. mambassae Leaves To treat a snake bite (Cabral et al., 2009)

V. peduncularis Barks To treat malaria fever (Geetha Nambiar, 1999)

V. pinnata Roots To relieve backache, body ache and fatigue (Kok, 2008)

V. piramidata Leaves To treat diarrhea, gastrointestinal affections (Ahmad & Holdsworth, 1995)

V. polygama Leaves To block acyclovir-resistant herpes simplex virus from propagate (Gonçalves, 2001)

V. pubescens Leaves To treat diarrhea, gastrointestinal affections (Ahmad & Holdsworth, 1995)

V. rivularis Leaves To treat skin and nail problems, used as a tea (Cabral et al., 2009)

V. rotundifolia Fruits To calm headaches, fever, eye infection (Ono et al., 2002)

V. simplicifolia Leaves To cure malaria, infant tetanus, dermatoses, dermatitis, headaches, bilharzia, muscle aches, fever, toothache, colic, amoebiasis (Koudou et al., 2014)

V. strickeri Leaves To treat a snake bite (Cabral et al., 2009)

V. cymosa Leaves To prevent insect bite and sting (Tereza et al., 2001)

Chemical Composition of Vitex Essential Oils

Analysis of chemical components identified in Vitex essential oils shows that the oil consists of several groups of components, which are monoterpenic hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons, and oxygenated sesquiterpenes. Table 2 shows the major components identified in Vitex essential oils from various origins.

<table>
<thead>
<tr>
<th>Species</th>
<th>Country</th>
<th>Part</th>
<th>Total identified (%)</th>
<th>Major components</th>
</tr>
</thead>
<tbody>
<tr>
<td>V. capitata</td>
<td>Brazil</td>
<td>Leaves</td>
<td>95.2</td>
<td>δ-Cadinene (7.1%), viridiflorene (5.2%) (De Sena Filho et al., 2017)</td>
</tr>
<tr>
<td>V. cymosa</td>
<td>Brazil</td>
<td>Leaves</td>
<td>40.96</td>
<td>β-Copaene-4-α-ol (9.78%), caryophyllene oxide (6.46%), β-bisabolene (5.16%), cubenol (5.09%) (Leitao et al., 1999)</td>
</tr>
<tr>
<td>V. diversifolia</td>
<td>South Africa</td>
<td>Leaves</td>
<td>99.4</td>
<td>Limonene (74.2%), caryophyllene oxide (3.2%) (Ch. Nebie et al., 2005)</td>
</tr>
<tr>
<td>V. doniana</td>
<td>Nigeria</td>
<td>Leaves</td>
<td>92.6</td>
<td>β-Phellandrene (31.3 %), phytol (28.3 %), β-caryophyllene (12.6 %) (Sonibare et al., 2009)</td>
</tr>
<tr>
<td>V. ferruginea</td>
<td>South Africa</td>
<td>Aerial parts</td>
<td>83.4-90.8</td>
<td>Germacrene D (26.8-34.9%), β-phellandrene (3.0-10.7%), β-caryophyllene (4.0-6.9%) (Cabral et al., 2008)</td>
</tr>
<tr>
<td>V. gardneriana</td>
<td>Brazil</td>
<td>Leaves</td>
<td>95.9</td>
<td>cis-Calamenene (29.7%), 6,9-guaiadiene (14.5%), caryophyllene oxide (14.0%) (Vale et al., 2019)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>94.71-95.20</td>
<td>cis-Calamenene (24.45-35.62%), 6,9-guaiadiene (12.47-28.86%), caryophyllene oxide (16.06-10.13%) (Silva et al., 2019)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>91.4-94.7</td>
<td>cis-Calamenene (29.7%), 6,9-guaiadiene (14.5%), caryophyllene oxide (14.0%) (Pereira et al. 2018)</td>
</tr>
<tr>
<td>V. kwangsiensis</td>
<td>China</td>
<td>Seeds</td>
<td>93.1</td>
<td>Methyl linoleate (11.2%), caryophyllene oxide(10.3%), β-eudesmol (9.1%), methyl palmitate (8.1%) (Tian &amp; Liu, 2018)</td>
</tr>
<tr>
<td>V. limonifolia</td>
<td>Thailand</td>
<td>Leaves</td>
<td>97.31</td>
<td>Caryophyllene (43%), caryophyllene oxide (13%) (Suksamrann et al., 1990)</td>
</tr>
<tr>
<td>Species</td>
<td>Country</td>
<td>Part</td>
<td>Component(s)</td>
<td>Value(s)</td>
</tr>
<tr>
<td>-------------------------</td>
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</tr>
<tr>
<td><em>V. megapotamica</em></td>
<td>Brazil</td>
<td>Leaves</td>
<td>Butylated hydroxytoluene, phytol, α-caryophyllene, δ-elemene, β-caryophyllene</td>
<td>92.36, 34.17%, 12.66%, 11.84%, 10.65%, 7.82%</td>
</tr>
<tr>
<td><em>V. obovata</em></td>
<td>South Africa</td>
<td>Aerial parts</td>
<td>(E)-Caryophyllene, γ-murolene, α-copaene, (10.8%)</td>
<td>96.8, 16.2%, 13.5%, 10.8%</td>
</tr>
<tr>
<td><em>V. obovate ssp. wilmssii</em></td>
<td>South Africa</td>
<td>Aerial parts</td>
<td>1,8-Cineole, α-copaene (7.39%), carvophyllyene oxide (5.94%)</td>
<td>82.83, 11.69%, 7.39%, 5.94%</td>
</tr>
<tr>
<td><em>V. pooara</em></td>
<td>South Africa</td>
<td>Aerial parts</td>
<td>α-Copaene (11.79%), 1,8-cineole (7.18%)</td>
<td>82.23, 11.79%, 7.18%</td>
</tr>
<tr>
<td><em>V. polygama</em></td>
<td>Brazil</td>
<td>Leaves</td>
<td>(E)-Caryophyllene, α-elemene (5.03%), α-pinene (4.06%)</td>
<td>37.71, 11.27%, 5.03%, 4.06%</td>
</tr>
<tr>
<td><em>V. quinata</em></td>
<td>Vietnam</td>
<td>Leaves</td>
<td>β-Pinene (30.1%), β-caryophyllene (26.9%), β-elemene (7.4%)</td>
<td>92.1, 30.1%, 26.9%, 7.4%</td>
</tr>
<tr>
<td><em>V. rehmannii</em></td>
<td>South Africa</td>
<td>Aerial parts</td>
<td>Germacrene D, ar-curcume, γ-curcumene, β-caryophyllene, α-copaene</td>
<td>80.65, 9.1-5.5%, 7.8-9.7%, 7.3-6.6%, 6.4-5.0%</td>
</tr>
<tr>
<td><em>V. rivularis</em></td>
<td>Cameroon</td>
<td>Leaves</td>
<td>Germacrene D, ar-curcume, γ-curcumene, β-caryophyllene, α-copaene</td>
<td>88.1-90.6, 9.1-5.5%, 7.8-9.7%, 7.3-6.6%, 6.4-5.0%</td>
</tr>
<tr>
<td><em>V. rondifolia</em></td>
<td>Korea</td>
<td>Leaves</td>
<td>α-Pinene (13.2%), α-terpineol (10.6%), 1,8-cineole (4.4%), manoyl oxide (4.0%)</td>
<td>70.7, 13.2%, 10.6%, 4.4%, 4.0%</td>
</tr>
<tr>
<td><em>V. rufescens</em></td>
<td>Brazil</td>
<td>Leaves</td>
<td>(E)-Caryophyllene, ledol, α-humulene, allo-aromadendrene, viridiflorene, β-elemene</td>
<td>97.8, 21.0%, 15.7%, 6.9%, 5.8%</td>
</tr>
<tr>
<td><em>V. zeyheri</em></td>
<td>South Africa</td>
<td>Aerial parts</td>
<td>1,8-Cineole, globulol, linalool</td>
<td>82.27, 15.29%, 5.46%, 5.24%</td>
</tr>
</tbody>
</table>

The major components of *Vitex* essential oils mainly consist of sesquiterpene hydrocarbons. Caryophyllene was identified as the major component of four *Vitex* species which are; *V. limonifolia* (Thailand) (Sukasamrarn et al., 1990), *V. polygama* (Brazil) (Leitao et al., 1999), *V. rufescens* (Brazil), and *V. megapotamica* (De Sena Filho et al., 2017). Besides, germacrene D was found in two different *Vitex* species which are; *V. ferruginea* (South Africa) (Cabral et al., 2008) and *V. rivularis* (Cameroon) (Cabral et al., 2009). In addition, the other sesquiterpene hydrocarbons were δ-cadinene (De Sena Filho et al., 2017), cis-calamenene (Vale et al., 2019; Silva et al., 2019; Pereira et al., 2018), 6,9-guaiadiene (De Sena Filho et al., 2017), which were found in the leaf oil of Brazilian *V. capitata*, *V. gardneriana*, and *V. gardneriana*, respectively. Meanwhile, spathulenol was found its richness in the oil of *V. rehmannii* (Nyiligira et al., 2004). Monoterpene hydrocarbons were also reported in *Vitex* essential oils. They were limonene (Ch. Nebie et al., 2005), β-phellandrene (Sonibare et al., 2009), α-copaene (Nyiligira et al., 2004), β-pinene (Dai et al., 2015), and α-pinene (Kim et al., 2014) which were extracted as high percentage in *V. diversifolia*, *V. doniana*, *V. obovata wilmsii*, *V. quinata*, and *V. rondifolia* essential oils, respectively. In addition, the oxygenated monoterpenes were identified in *V. cymosa* (β-copaene-4-α-ol) (Leitao et al., 1999), *V. obovata* (1,8-cineole) (Nyiligira et al., 2004), and *V. zeyheri* (1,8-cineole) (Nyiligira et al., 2004) essential oils. On the other hand, another group of components that presents in *Vitex* essential oils were butylated hydroxytoluene and methyl linoleate, which were identified in the oils of *V. megapotamica* (De Brum et al., 2013) and *V. kwangsiensis* (Tian and Liu, 2018). It must be mentioned here that butylated hydroxytoluene is not a natural compound but an impurity.
Biological Activities of Vitex Essential Oils

**Antioxidant activity**

The antioxidant activity of *V. kwangsiensis* was tested by DPPH• method and it showed weak antioxidant activity. A maximum concentration 1 mg/mL of oil was conducted and the radical scavenging activity was 26.76% (Tian & Liu, 2018). In another study, the ferrous ion chelating activity of the *V. gardneriana* essential oil showed the best activity at 7.81 μg/mL. Besides, the oil showed a dose-response relationship in β-carotene oxidation with the best activity at 500 μg/mL (Vale et al., 2019). De Brum et al., (2013) reported the *V. megapotamica* essential oil showed percentage inhibition of 35.62% and 75.25% at concentrations of 76 and 101.6 mg/mL against DPPH free-radical scavenging assay. However, this report should be read with caution since the main component in the oil is an antioxidant added to diethyl ether for protection.

**Antimicrobial activity**

The essential oil of *V. gardneriana* was able to inhibit the growth of *S. aureus* with a MIC of 0.31% v/v. However, no MIC was determined on *P. aeruginosa*. In addition, the essential oil showed about 70% to 9% and 30% - 3% of growth reduction on *C. albicans* and *C. tropicalis*, respectively (Vale et al., 2019). In another study, *V. gardneriana* essential oil gave value of 4.0 mg/mL against dermatophytes and yeasts; *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. kruzei*, and *T. rubrum* (Pereira et al., 2018). The *V. doniana* essential oil exhibited antimicrobial activity against *Proteus mirabilis*, *Bacillus subtilis*, and *Candida albicans* with inhibition zones of 11, 4 and 12 mm, respectively (Sonibare et al., 2009). The essential oils of *V. obovata* ssp. *obovata*, *V. obovata* ssp. *wilmsii*, and *V. zeyheri* showed MIC value 32.0 and 16.0 mg/mL, respectively. In addition, *V. zeyheri* essential oil showed the best activity for *B. cereus* with MIC value 4.0 mg/mL (Nyiligira et al., 2004).

**Anti-inflammatory activity**

The essential oils of *V. pooara*, *V. rehmannii*, *V. obovata* ssp. *obovata*, *V. obovata* ssp. *wilmsii* and *V. zeyheri* reported the anti-inflammatory against 5-lipoxygenase assay with IC50 values of 25.0, 40.5, 42.0, 48.0, and 64.0 ppm, respectively (Nyiligira et al., 2004). The essential oil of *V. rotundifolia* suppressed LPS induced NO formation significantly in a dose-dependent fashion, by providing about 60% decrease of nitric oxide production at 25.0 μg/mL concentration (Kim et al., 2014).

**Antifungal activity**

The essential oil of *V. ferruginea* exhibited significant antifungal activity against dermatophyte strains with MIC between 0.16-0.64 μL/mL against *Epidermophyton floccosum*, *Trichophyton rubrum*, *T. mentagrophytes*, *Microsporum canis*, and *M. gypseum* (Cabral et al., 2008). The essential oil of *V. rivularis* exhibited significant antifungal activity against dermatophyte strains (*E. floccosum*, *T. rubrum*, *T. mentagrophytes*, *M. canis*, and *M. gypseum*) with MIC and MLC values ranging from 0.16 to 0.64 μL/mL and 0.32 to 2.5 mL/mL, respectively (Cabral et al., 2009).

**Acaricidal activity**

The toxicity against the coconut mite *Aceria guerreronis* showed that *V. gardneriana* essential oil had strong acaricidal activity, with an LC50 of 0.85 mg/mL. However, the essential oils of *V. capitata*, *V. megapotamica*, and *V. rufescens* plant did not kill adults of *A. guerreronis* over a period of 24 h. As a way of toxicity comparison, the acaricide abamectin, sprayed at its label rate, inflicted 100% mortality to *A. guerreronis* (De Sena Filho et al., 2017).
Antibiofilm activity

Vale et al., (2019) reported that the biomass formation of *C. albicans* and *C. tropicalis* biofilm was inhibited after 24 h treatment with *V. gardneriana* essential oil. All concentrations tested were able to reduce *C. albicans* biomass. However, *C. tropicalis* biomass was inhibited at 2.5% to 0.312% oil concentrations. They concluded that the *V. gardneriana* essential oil reduced significantly the biofilm biomass and the number of viable cells of bacteria and yeasts, mainly on biofilm formation.

Larvicidal activity

The seasonal variation in essential oils of *V. gardneriana* was studied by Silva et al. (2019). The essential oils extracted in January (LC\textsubscript{50} 78.3 μg/mL), March (LC\textsubscript{50} 44.1 μg/mL), April (LC\textsubscript{50} 47.9 μg/mL), May (LC\textsubscript{50} 28.0 μg/mL), July (LC\textsubscript{50} 43.5 μg/mL), August (LC\textsubscript{50} 62.0 μg/mL), and December (LC\textsubscript{50} 84.3 μg/mL) exhibited significant larvicidal activity against third instar larvae of *Aedes aegypti*.

Cytotoxic activity

The *V. gardneriana* essential showed that 0.3-1.25% concentrations had cytotoxic effects in L929 cell lines, whereas no significant cytotoxic effects in HaCat cell lines was observed (Vale et al., 2019).

Acetylcholinesterase activity

The essential oil of *V. gardneriana* displayed IC\textsubscript{50} value of 11.2 mg/mL which was assessed using a thin layer chromatographic method (Pereira et al., 2018).

Conclusion

This review compiles the medicinal uses, chemical components, and biological activities of the *Vitex* essential oils. The studies managed to declare that the essential oils of *Vitex* genus contain monoterpenes and sesquiterpenes which potentially stimulate biological activities such as antioxidant, antimicrobial, anti-inflammatory, antifungal, acaricidal, antibiofilm, larvicidal, cytotoxic, and acetylcholinesterase properties. Undeniably, there are some current needs for other new plant-derived products to be tested for biological activity. The genus *Vitex* could be an imperative natural source for developing contemporary drugs and medicines.

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REFERENCES


