# Patent Literature on Mosquito Repellent Inventions which Contain Plant Essential Oils – A Review

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## Abstract

Bites of mosquitoes belonging to the genera *Anopheles* Meigen, *Aedes* Meigen, *Culex* L. and *Haemagogus* L. are a general nuisance and are responsible for the transmission of important tropical diseases such as malaria, hemorrhagic dengue and yellow fevers and filariasis (elephantiasis). Plants are traditional sources of mosquito repelling essential oils (EOs), glyceridic oils and repellent and synergistic chemicals. A Chemical Abstracts search on mosquito repellent inventions containing plant-derived EOs revealed 144 active patents mostly from Asia. Chinese, Japanese and Korean language patents and those of India (in English) accounted for roughly 3/4 of all patents. Since 1998 patents on EO-containing mosquito repellent inventions have almost doubled about every 4 years. In general, these patents describe repellent compositions for use in topical agents, cosmetic products, incense, fumigants, indoor and outdoor sprays, fibers, textiles among other applications. 67 EOs and 9 glyceridic oils were individually cited in at least 2 patents. Over 1/2 of all patents named just one EO. Citronella [*Cymbopogon nardus* (L.) Rendle, *C.winterianus* Jowitt ex Bor] and eucalyptus (*Eucalyptus* L'Hér. spp.) EOs were each cited in approximately 1/3 of all patents. Camphor [*Cinnamomum camphora* (L.) J. Presl], cinnamon (*Cinnamomum zeylanicum* Blume), clove [*Syzygium aromaticum* (L.) Merr. & L.M. Perry], geranium (*Pelargonium graveolens* L'Hér.), lavender (*Lavandula angustifolia* Mill.), lemon [*Citrus* × *limon* (L.) Osbeck], lemongrass [*Cymbopogon citratus* (DC.) Stapf] and peppermint (*Mentha* × *piperita* L.) EOs were each cited in > 10% of patents. Repellent chemicals present in EO compositions or added as pure "natural" ingredients such as geraniol, limonene, *p*-menthane-3,8-diol, nepetalactone and vanillin were described in approximately 40% of all patents. About 25% of EO-containing inventions included or were made to be used with synthetic insect control agents having mosquito repellent properties such as pyrethroids, *N,N*-diethyl-*m*-toluamide (DEET), (±)-*p*-menthane-3,8-diol (PMD) and dialkyl phthalates. Synergistic effects involving one or more EOs and synthetic and/or natural components were claimed in about 10% of all patents. Scientific literature sources provide evidence for the mosquito repellency of many of the EOs and individual chemical components found in EOs used in patented repellent inventions.

## Introduction

### Mosquito vectors of severe tropical diseases

Severe human tropical diseases such as malaria, dengue and yellow fevers and filariasis are transmitted by the bites of infected hematophagous female mosquitoes belonging to the genera *Aedes* Meigen, *Anopheles* Meigen, *Culex* L. and *Haemagogus* L. (Diptera: Culicidae). For example, about 3.3 billion people – 1/2 of the world's population – are at risk of contracting malaria. In 2008, there were more than 247 million cases and more than 1 million deaths caused by malaria mainly in African children [1]. Human malaria is caused by infections by unicellular protozoan parasites *Plasmodium falciparum* Welch, *P. vivax* Grassi & Feletti, *P. malariae* Feletti & Grassi and *P. ovale* Stephens which are transmitted by about 20 *Anopheles* spp. Another important disease is dengue hemorrhagic fever which is a viral infection caused by several *Flavivirus* spp. (Flaviviridae) whose most important vector is *Aedes* (*Stegomyia*) *aegypti* L. Dengue and dengue hemorrhagic fevers threaten an estimated 2.5 billion people – 2/5 of the world's population – and an estimated

50 million people contract the disease per year. Around 500 000 dengue patients, most of whom are children, require hospitalization each year and around 2.5% of those affected die [2]. Another serious tropical disease which threatens about 1 billion people in 80 countries is filariasis or elephantiasis. This disease already affects an estimated 120 million people and severely incapacitates and deforms 40 million people worldwide. Filariasis is caused by infections by several roundworm species of which *Wuchereria bancrofti* Cobbold (Filariidea: Onchocercidae) is the most important and is transmitted by the bites of the common house mosquito *Cx. pipiens* L. complex, *Cx. quinquefaciatus* Say, *Aedes* and *Anopheles* spp. [3,4]. Yellow fever is an arbovirus of the *Flavivirus* genus (Flaviviridae) which is transmitted from monkeys in the jungle to humans and then from human to human by mosquitoes. The most significant yellow fever mosquito vector is *Ae. aegypti*. Despite the existence of effective vaccines, there are an estimated 200 000 cases of yellow fever and approximately 30 000 deaths attributed to this disease each year [5]. In public health initiatives which aim to limit or eradicate these and other tropical diseases, mosquito vector control methods such as repellence figure prominently among those which are employed.

### Synthetic mosquito repellents DEET and alkyl phthalates

For more than 50 years, the synthetic compound DEET (*N,N*-diethyl-*m*-toluamide), has been the most effective single repellent for mosquito species and is the basis for many commercial repellent products on the market. Despite reports of severe toxic properties which can dramatically affect adults and especially young children including dermatitis, allergic reactions, neurological (seizures, coma) and cardiovascular toxicity, the risk of serious toxic effects from DEET is considered slight. Nevertheless, DEET should always be used at the lowest effective dose possible. Also, dimethyl and di-*n*-butyl phthalates (DMP and DBP, respectively), which are effective mosquito repellents and were widely used in the last century, are no longer generally recommended for use as mosquito repellents due to their toxicity [6].

### Plants as sources of mosquito control agents

Plants have historically been valuable sources of agents for the control of insects [3,7]. They are the sources of the natural insecticidal and larvicidal substances nicotine (*Nicotiana* L. spp.), quassin (*Quassia amara* L.), rotenone and rotenoids (*Derris* Lour. spp. and *Lonchocarpus* Kunth spp. roots), pyrethrins like chrysanthamic acid and its derivatives present in pyrethrum [extracts of *Chrysanthemum cinerariifolium* (Trevir.) Vis. flowers] and azadirachtin (*Azadirachta indica* A. Juss. seed kernel). These and other natural insect control agents have served as the basis for the development of the structurally-related synthetic pyrethroid, nicotinoid and rotenoid classes of insecticides and piperonyl butoxide synergist. Also, pyrethroids and piperonyl butoxide synergism are the basis for a number of commercially available mosquito control products in use today [3].

### Botanical repellents

Citronella essential oils (EOs) are obtained mainly from varieties of *Cymbopogon nardus* (L.) Rendle (Ceylon citronella) and *C. winterianus* Jowitt ex Bor (Java citronella). They have been used in mosquito repellency for more than a century in much of the world and are the most widely used natural repellents today [3]. Also, EOs of *Eucalyptus* L'Hér. spp. are widely used to repel insects, including mosquitoes, and contain insecticidal and repellent components *p*-menthane-3,8-diol (PMD), 1,8-cineole, α-pinene, *p*-cymene and γ-terpinene among other active compounds [8]. According to a recent review of the scientific literature, the most frequently studied repellent EOs are those obtained from species belonging to the genera *Cymbopogon* Spreng., *Ocimum* L. and *Eucalyptus* L'Hér. spp. and a number of mosquito repellent EOs have been identified in recent years having known active repellent chemical components [7]. Mosquito repellency is believed to be due to the synergistic interactions of the chemical components in EOs. Furthermore, strong synergistic effects between EOs and isolated natural or synthetic substances have been reported [7].

The United States Environmental Protection Agency [9] has registered citronella EO, eucalyptus EO and other plant oils as safe and effective ingredients for use in topical insect repellents. However, caution is recommended in the use of EOs in general due to a number of potential toxic effects [7]. Among the important toxic effects of EOs are mutagenicity and genotoxicity. Another toxic effect is the allergenicity of EO chemical components which are controlled in the European Community and elsewhere. Interestingly, a number of repellent and insecticidal plant EOs and their chemical constituents have been evaluated using a variety of methods and are believed to be non-mutagenic [10].

A number of commercial repellent products have been developed over the past decades which utilize derivatives of plants such as EOs, fractions and their isolated chemical components and synthetic components. Thus, it is important to have a comprehensive knowledge of the commercially significant uses of EOs in mosquito repellent inventions and to the best of our knowledge the patent literature on this topic has not been reviewed. The aim of the present review is to explore and analyze patent literature on mosquito repellent inventions which make use of or are based wholly on plant EOs and/or their chemical components. A secondary aim is to analyze the scientific bases and relevancy of the use of plant EOs and chemical components of these oils in patented mosquito repellent formulations.

## Chemical Abstracts Search Criteria

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A Chemical Abstracts search of the patent literature for the period of 1991 through May, 2010 was performed using SciFinder Scholar® [11]. Combinations of the key words "repellent", "mosquito" and "essential oil" generated an initial set of approximately 160 patents. This set was further refined. Patents describing mosquitocidal/larvicidal inventions, but having no stated claim or use as mosquito repellents were eliminated. Also, patented mosquito repellent inventions which did not make use of at least one commercially-obtained, plant-derived oil [a volatile (essential) oil, a concrete, or a pressed oil] or which did not describe the preparation of an EO by physical means for use within the patent were eliminated. This approach eliminated patents presenting solvent extraction performed on mixtures of several plant materials followed, for example, by distillation and evaporation as a means of obtaining the mosquito repellent invention. Also, by this criterion, incense and other smoke-generating inventions made from mosquito repellent plants but having no (added) EO in the composition were eliminated. Applying the above criteria led to a data set of 144 patents describing plant oil-containing mosquito repellent inventions which was the basis for the analysis presented below.

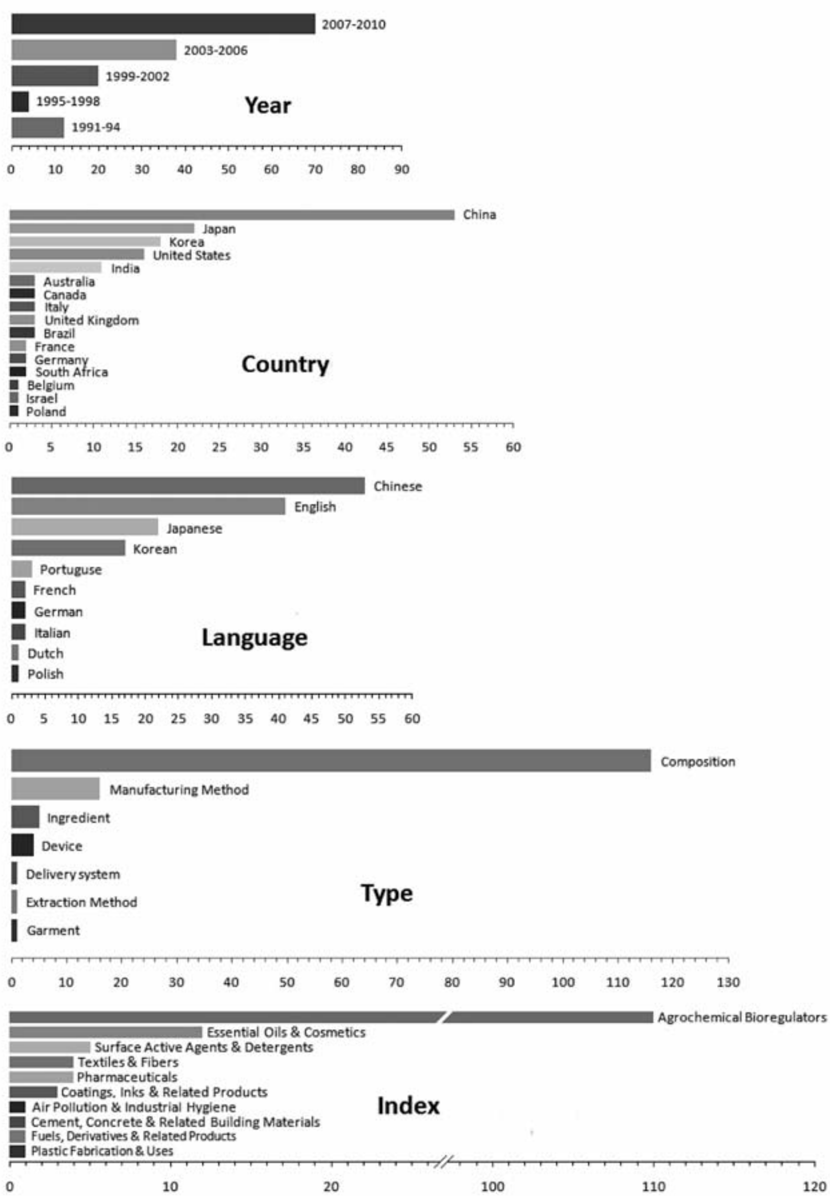


**Fig. 1** Analysis of EO-containing patented mosquito repellent inventions by patenting country, patent language, patent type and utility.

## Patenting Countries and Patent Families: Trends

The contribution of China, Japan, Korea and India to the overall number of patented EO-containing mosquito repellent inventions is significant. These countries accounted for, respectively, 37, 15, 13 and 8% (73%) of all patents (**Fig. 1**). An interesting trend is that all 53 Chinese, 17 of 18 Korean, 20 of 22 Japanese and 9 of 11 Indian patents have only been deposited in their countries of origin and in general have not been followed-up by later patents. Also, all Belgian, Brazilian, German and Polish patents followed the rule of single deposits without follow-up patents. In contrast, industrial, academic and other patents originating in Australia, Canada, the United Kingdom and the United States gave rise to larger patent families, made greater use of the World Patent System and led to deposits of patents on EO-containing repellents in multiple countries as a rule. Finally, more than 75% of all patented repellent inventions are indexed as agrochemical bioregulators and over 80% describe chemical compositions (often together with preparation details) (**Fig. 1**).

## EOs Used in Patented Mosquito Repellent Inventions

Plant taxonomic information [12], extraction methods, chemical composition, literature sources [8, 10, 13–115] and frequency of use for 67 EOs and 9 glyceridic oils which were individually cited in at least 2 (1.4%) of the total number of patents are presented in **Table 1**. Approximately 60% of all patents named just one plant EO. One patent claimed to use up to 44 plant oils in formulations. Citronella (34.7%) and eucalyptus (30.6%) EOs were each named in about 1/3 of all patented repellent inventions followed by (species, % of patents): lavender (*Lavandula angustifolia* Mill., 21.5%), peppermint (*Mentha × piperita* L., 16.7%), clove [*Syzygium aromaticum* (L.) Merr. & L.M. Perry, 15.3%], lemongrass [*Cymbopogon citratus* (DC.) Stapf, 14.6%], cinnamon (*Cinnamomum zeylanicum* Blume, 12.5%), geranium (*Pelargonium graveolens* L'Hér., 11.8%), camphor [*Cinnamomum camphora* (L.) J. Presl, 11.1%] and lemon [*Citrus × limon* (L.) Osbeck, 11.1%] EOs.

A number of EOs were cited in only one patented repellent invention (and were not included in **Table 1**). Given the importance

**Table 1** Botanic information, extraction methods, major chemical components, literature sources and frequency (%) of use of plant essential and glyceridic oils in patented mosquito repellent inventions, 1991 – May, 2010.

| Oil | Species | Family | Part | Method | Major components | Lit. | % Patents |
|---|---|---|---|---|---|---|---|
| **Essential Oils** | | | | | | | |
| Ambrette | *Abelmoschus moschatus* Medik. | Malvaceae | whole seed | steam distilled | *2E,6E*-farnesyl acetate, *Z*-7-hexadecen-16-olide, *β*-farnesene | [13, 14] | 1.4 |
| Angelica | *Angelica archangelica* L. | Apiaceae | root | steam distilled | ligustilide, ***α*** **&** ***β*****-pinene, carvacrol, 3-carene, limonene**, *β*-phellandrene, 15-pentadecanolide | [15, 16] | 1.4 |
| Anise | *Pimpinella anisum* L. | Apiaceae | fruit, seed | steam distilled | *trans*-anethole | [17] | 4.2 |
| Artemisia | *Artemisia argyi* H. Lév. & Vaniot | Asteraceae | leaf | steam distilled | germacrene D, *α*-phellandrene, ***α*****-myrcene, 1,8-cineole, borneol**, terpinol, **spathulenol** | [18, 19] | 4.9 |
| Basil | *Ocimum basilicum* L. | Lamiaceae | leaf, flower top | steam distilled | estragole, **limonene, fenchone, linalool, eugenol** *E*-methyl cinnamate, **1,8-cineole** | [20–22] | 4.9 |
| Bay laurel | *Laurus nobilis* L. | Lauraceae | leaf | steam distilled | **1,8-cineole**, sabinene, *α*-terpinyl acetate, **linalool** | [23, 24] | 1.4 |
| Bergamot | *Citrus* × *bergamia* Risso | Rutaceae | fresh or dried peel | pressed | **limonene**, linalyl acetate, ***β*****–pinene, *γ*-terpinene, linalool** | [24] | 1.4 |
| Camphor | *Cinnamomum camphora* (L.) J. Presl | Lauraceae | wood, bark, leaf | steam distilled | **1,8-cineole, *α*-terpineol, *α*-pinene, linalool, camphor,** sabinene | [10] | 11.1 |
| Cassia | *Cinnamomum cassia* (L.) C. Presl | Lauraceae | leaf, bark, stalk | steam distilled | *bark*: ***E*****-cinnamaldehyde, methyl *o*-salicylate**; *leaf*: 3-methoxy-1,2-propanediol, ***E*****-cinnamaldehyde**, *o*-methoxy-cinnamaldehyde | [25, 26] | 2.1 |
| Catnip, catmint | *Nepeta cataria* L. | Lamiaceae | dry leaf, stem | steam distilled | **nepetalactone, 1,8-cineole,** *α*-humulene, *α*-pinene, ***E*****-geraniol**, *β*-caryophyllene, **citronellol** | [20, 27, 28] | 4.9 |
| Cedar | *Cedrus* Trew (*Cupressus* L., *Juniperus* L.) spp. | Pinaceae (Cupressaceae) | wood | steam distilled | thujopsene, eudesmol, E-(+)-*α*-atlantone; *α,β* & *γ*-himachalenes; *α*- & *β*-cedrenes; **limonene**, *β*-phellandrene, ***α*** **&** ***β*****-pinene, 3-carene**; *p*-methyl-*Δ*-3-tetrahydro & *p*-methyl acetophenones; hinokitiol, **carvacrol** | [29] | 9.7 |
| Chamomile | *Chamaemelum nobile* (L.) All. *Matricaria recutita* L. | Asteraceae | seed, leaf, flower | steam distilled | *Roman*: isobutyl, isoamyl & 2-methylpentyl angelates, ***α*****-pinene** *German: E-β*-farnesene, *E,E-α*-farnesene, ***α*****-bisabolol**, *α*-bisabolol oxides A & B | [20, 28, 30] | 2.1 |
| Chrysanthemum | *Chrysanthemum indicum* L. | Asteraceae | dry flower | steam distilled | **verbenol**, 2-(2,4-hexadiynylidene)-1,6-dioxaspiro[4.4]non-3-ene, **1,8-cineole, *α*-pinene, camphor, borneol, bornyl acetate** | [31, 32] | 2.8 |
| Cinnamon | *Cinnamomum zeylanicum* Blume | Lauraceae | bark, leaf | steam distilled | **eugenol, cinnamaldehyde** | [25, 33, 34] | 12.5 |
| Citronella | *Cymbopogon nardus* (L.) Rendle, *C. winterianus* Jowitt ex Bor | Poaceae | leaf | steam distilled | **citronellal, geraniol, citronellol, geranyl acetate** | [35, 36] | 34.7 |
| Citrus | *Citrus* × *limon* (L.) Osbeck, *C.* × *sinensis* (L.) Osbeck, *C.* × *aurantifolia* L. | Rutaceae | peel | pressed, steam distilled | see orange, lemon, lime oil compositions | – | 1.4 |
| Clove | *Syzygium aromaticum* (L.) Merr. & L. M. Perry | Myrtaceae | flower bud | steam distilled | **eugenol**, caryophyllene, eugenyl acetate | [37] | 15.3 |
| Coriander | *Coriandrum sativum* L. | Apiaceae | fruit, seed | steam distilled | **linalool, geraniol, geranyl acetate**, 2-decenal, 3-dodecenal | [20, 38, 39] | 2.1 |
| Cypress | *Cupressus sempervirens* L. | Cupressaceae | needle, twig | steam distilled | sabinene, ***α*****-pinene, terpinen-4-ol, limonene** | [40, 41] | 4.2 |
| Dill | *Anethum graveolens* L. | Apiaceae | seed, leaf, stem | steam distilled | **carvone, limonene**, *α*-phellandrene, ***α*****-pinene**, *cis*-dihydrocarvone | [42, 43] | 1.4 |
| Eucalyptus | *Eucalyptus* L'Hér. spp. | Myrtaceae | leaf | steam distilled | **1,8-cineole, *p*-menthane-3,8-diol, *α*-pinene, *p*-cymene, *γ*-terpinene**, eucamalol, *allo*-ocimene, **citronellol, *α*-terpineol** | [8] | 30.6 |
| Fennel | *Foeniculum vulgare* Mill. | Apiaceae | fruit | steam distilled | *E*-anethole, **(+)-fenchone**, *α*-phellandrene, **(±)-limonene**, estragole | [24] | 4.9 |
| Garlic | *Allium sativum* L. | Amaryllidaceae | bulb | steam distilled | diallyl disulfide, diallyl trisulfide, methyl allyl trisulfide | [44, 45] | 6.3 |
| Geranium | *Pelargonium graveolens* L'Hér. | Geraniaceae | leaf, stem | steam distilled | 2-phenylethanol, **geraniol, citronellol, geranyl acetate** | [46] | 11.8 |

*continued next page*

**Table 1** Botanic information, extraction methods, major chemical components, literature sources and frequency (%) of use of plant essential and glyceridic oils in patented mosquito repellent inventions, 1991 – May, 2010. *(continued)*

| Oil | Species | Family | Part | Method | Major components | Lit. | % Patents |
|---|---|---|---|---|---|---|---|
| **Essential Oils** | | | | | | | |
| Ginger | *Zingiber officinale* Roscoe | Zingiberaceae | rhizome | steam distilled | **geranial**, *α*-zingiberene, *E,E*-*α*-farnesene, neral, ar-curcumene, **geraniol** | [47,48] | 1.4 |
| Grapefruit | *Citrus reticulata* Blanco | Rutaceae | peel | pressed | **limonene, geranial**, neral | [49] | 2.1 |
| Guaiac wood | *Bulnesia sarmientoi* Lorentz ex Griseb. | Zygophyllaceae | wood | steam distilled | bulnesol, guaiol, *α*-bulnesene | [50] | 1.4 |
| Hiba | *Thujopsis dolabrata* (Thunb. ex L. f.) Siebold & Zucc. | Cupressaceae | wood | steam distilled | sabinene, 4-terpineol, thujopsene, hinokitiol, *α*-thujaplicine, **carvacrol** | [51–53] | 2.1 |
| Ho leaf | *Cinnamomum camphora* (L.) J. Presl | Lauraceae | leaf | steam distilled | **1,8-cineole, *α*-terpineol, linalool, camphor**, safrole, sabinene, **nerolidol** | [10,54,55] | 1.4 |
| Hyssop | *Hyssopus officinalis* L. | Lamiaceae | leaf, flower | steam distilled | sabinene, pinocamphene, isopinocamphene, isopinocamphone, pinocarvone, *cis* & *trans*-pinocamphones, ***β*-pinene, 1,8-cineole, camphor, linalool** | [56–58] | 1.4 |
| Jasmine | *Jasminum officinale* L. | Oleaceae | flower | solvent extracted | **linalool**, benzyl acetate, methyl & benzyl benzoates, methyl anthranilate, *Z*-jasmone, **eugenol** | [59,60] | 3.5 |
| Juniper | *Juniperus communis* L. | Cupressaceae | fruit | steam distilled | ***α*-pinene, myrcene**, sabinene, germacrene D | [61] | 1.4 |
| Lady-of-the-night | *Cestrum nocturnum* L. | Solanaceae | flower | solvent extracted, steam distilled | phenylethyl alcohol, benzyl alcohol, **eugenol** | [62] | 2.1 |
| Lavender | *Lavandula angustifolia* Mill. | Lamiaceae | flower | steam distilled | **linalool**, linalyl acetate, lavandulyl acetate, ***α*-terpineol, geranyl acetate, terpinen-4-ol, 1,8-cineole** | [63,64] | 21.5 |
| Lemon | *Citrus × limon* (L.) Osbeck | Rutaceae | peel | pressed | limonene, *β*-pinene, *γ*-terpinene | [65] | 11.1 |
| Lemon eucalyptus | *Eucalyptus citriodora* Hook. | Myrtaceae | leaf, twig | steam distilled | **citronellal, citronellol** | [8,66] | 8.3 |
| Lemongrass | *Cymbopogon citratus* (DC.) Stapf | Poaceae | leaf | steam distilled | **geranial,** neral, **myrcene** | [41] | 14.6 |
| Lemon tea tree | *Leptospermum petersonii* F. M. Bailey | Myrtaceae | leaf | steam distilled | neral, **geranial, *γ*-terpinene, geraniol, geranyl acetate, *α*-pinene, citronellal, terpinolene** | [67] | 1.4 |
| Lime | *Citrus × aurantifolia* L. | Rutaceae | peel | steam distilled, pressed | *D*-dihydrocarvone, ***D*-limonene, *α*-terpineol** | [68] | 2.1 |
| Manuka | *Leptospermum scoparium* Forst. & Forst. | Myrtaceae | leaf, stem | steam distilled | leptospermone, *trans*-calamenene, flavesone, **1,8-cineole**, ***α*-pinene** | [69,70] | 1.4 |
| Marjoram | *Origanum majorana* L. | Lamiaceae | leaf, flower | steam distilled | ***p*-cymene, *γ*-terpinene, terpinen-4-ol, linalool**, *cis*-sabinene hydrate | [71,72] | 2.1 |
| May chang/ Litsea | *Litsea cubeba* (Lour.) Pers. | Lauraceae | fruit | steam distilled | neral, **R-(+)-limonene, geranial, citronellal** | [46,73,74] | 4.9 |
| Melaleuca/ Tea tree | *Melaleuca alternifolia* Cheel | Myrtaceae | leaf | steam distilled | **terpinen-4-ol, *γ*-terpinene, *α*-terpinene, 1,8-cineole** | [75] | 9.7 |
| Mint, mentha | *Mentha* L. spp. | Lamiaceae | leaf, flower | steam distilled | **menthone, menthol, 1,8-cineole**, 4-terpineol | [76] | 9.7 |
| Orange | *Citrus × sinensis* (L.) Osbeck | Rutaceae | peel | pressed | **limonene, myrcene** | [77] | 4.2 |
| Palmarosa | *Cymbopogon martini* (Roxb.) Will.Watson | Poaceae | dry leaf | steam distilled | **geraniol, geranyl acetate, geranial** | [78] | 4.9 |
| Parsley (Curl leaf) | *Petroselinum crispum* (Mill.) Fuss | Apiaceae | leaf, stem, seed | steam distilled | *β*-phellandrene, myristicin, ***α* & *β*-pinene, myrcene** | [79] | 1.4 |
| Patchouli | *Pogostemon cablin* (Blanco) Benth. | Lamiaceae | dry, fermented leaf | steam distilled | (−)-patchoulol, *α*-guaiene, seychellene, *β*-caryophyllene, *α* & *β*-patchoulenes, selinene, *α*-bulnesene, norpatchoulenol, pogostol | [80] | 4.2 |
| Pepper | *Piper nigrum* L. | Piperaceae | fruit | steam distilled | *E*-*β*-caryophyllene, **limonene, *β*-pinene** | [81,82] | 2.1 |
| Peppermint | *Mentha × piperita* L. | Lamiaceae | aerial part | steam distilled | isomenthol, ***p*-menthone**, isomenthyl & menthyl acetates | [83,84] | 16.7 |
| Pine | *Pinus sylvestris* L. | Pinaceae | twig, bud | steam distilled | **3-carene, *α* & *β*-pinene**, *α*-cadinol, camphene | [85,86] | 8.3 |
| Rose | *Rosa × damascena* Mill., *R. × centifolia* L. | Rosaceae | petal | steam distilled, solvent extracted | 2-phenethyl alcohol, **citronellol, geraniol, linalool**, nonadecane | [30,87] | 6.3 |

*continued next page*

**Table 1** Botanic information, extraction methods, major chemical components, literature sources and frequency (%) of use of plant essential and glyceridic oils in patented mosquito repellent inventions, 1991 – May, 2010. *(continued)*

| Oil | Species | Family | Part | Method | Major components | Lit. | % Patents |
|---|---|---|---|---|---|---|---|
| **Essential Oils** | | | | | | | |
| Rosemary | *Rosmarinus officinalis* L. | Lamiaceae | flower | steam distilled | **verbenone, camphor, borneol, bornyl acetate, α-terpineol, terpinen-4-ol** | [41, 88] | 9.0 |
| Salvia (Sage) | *Salvia* L. spp. | Lamiaceae | leaf, flower, aerial part | steam distilled | **camphor, 1,8-cineole, α-pinene, camphene, limonene, linalool, myrcene**, β-caryophyllene, caryophyllene oxide, spathulenol, viridiflorol, **3-carene, α-bisabolol, geraniol**, linalyl acetate, γ-muurolene, **α-thujone**, manool | [89–92] | 1.4 |
| Sandalwood | *Santalum* L. spp. | Santalaceae | heartwood | steam distilled | α, β & *epi-β*-santalenes; α, β & *epi-β*-santalals; **α−santalol**; spiro, β, *E-β* & *epi-β* santalols, *trans-α*-bergamotene, *trans-α*-bergamotol | [80, 93] | 3.5 |
| Sour (bitter) orange | *Citrus × aurantium* L. | Rutaceae | peel | pressed | **limonene** | [94] | 3.5 |
| Spearmint | *Mentha spicata* L. | Lamiaceae | flower | steam distilled | **carvone, limonene** | [95] | 2.8 |
| Star anise | *Illicium verum* Hook. f. | Schisandraceae | seed | steam distilled | *E*-anethole, 4-allylanisole | [96, 97] | see anise* |
| Tagetes | *Tagetes minuta* L. | Asteraceae | leaf, stalk, flower | steam distilled, solvent extracted | *E* & *Z-β*-ocimenes, **limonene**, **α-terpineol**, dihydrotagetenone, *Z*-tagetone, *E* & *Z*-tagetenones | [98] | 2.1 |
| Tarragon | *Artemisia dracunculus* L. | Asteraceae | leaf, flower | steam distilled | sabinene, elemicine, methyl eugenol | [99] | 1.4 |
| Thyme | *Thymus vulgaris* L. | Lamiaceae | flower, leaf | steam distilled | ***p*-cymene, geraniol, *cis*-thujone, thymol, carvacrol** | [41] | 7.6 |
| Turmeric | *Curcuma longa* L. | Zingiberaceae | rhizome | steam distilled, solvent extracted | α-phellandrene, **1,8-cineole, terpinolene**, zingiberene, β-sesquiphellandrene, α & β-turmerones | [41] | 2.8 |
| Verbena | *Lippia triphylla* (L'Hér.) Kuntze | Verbenaceae | leaf | steam distilled | **geranial**, neral, **limonene, geraniol** | [100] | 1.4 |
| Vetiver | *Vetiveria zizanioides* (L.) Nash | Poaceae | root | steam distilled | khusimol, isonootkatool, β-vetivenene, α & β-vetivones | [101] | 2.1 |
| Violet | *Viola odorata* L. | Violaceae | leaf, flower | solvent extracted | nona-2,6-dienal, *cis*-hex-3-en-1-ol, hexadec-1-ene, pentadec-3-enal, octadec-1-ene, hexadecanoic & **octadeca-9,12-dienoic** acids | [102] | 1.4 |
| Wintergreen | *Gaultheria procumbens* L. | Ericaceae | leaf | steam distilled | **methyl salicylate** | [103] | 6.3 |
| Ylang-Ylang | *Cananga odorata* (Lam.) Hook. f. & Thomson | Annonaceae | flower | steam distilled | **linalool**, benzyl acetate, benzyl benzoate, benzyl salicylate | [41] | 2.8 |
| **Glyceridic Oils** | | | | | | | |
| Castor | *Ricinus communis* L. | Euphorbiaceae | seed | pressed | ricinolic, linoleic, **oleic** acids | [104] | 4.9 |
| Evening primrose | *Oenothera biennis* L. | Onagraceae | seed | pressed | **linalool**; palmitic, stearic, **oleic**, linoleic & γ-linolenic acids | [105, 106] | 1.4 |
| Ligusticum/ Chuanxiong | *Ligusticum chuanxiong* Hortorum ex Qiu, et al. in Qiu | Apiaceae | root | $CO_2$ extracted | butylphthalide, 2-propenyl phenoxyacetate, 3-isobutyliden phthalide, palmitic & **octadecenoic** acids | [107] | 1.4 |
| Mustard | *Brassica* L. spp. | Brassicaceae | seed | Pressed | erucic, **oleic**, linoleic, linolenic, palmitic & stearic acids | [108] | 2.1 |
| Neem | *Azadirachta indica* A. Juss. | Meliaceae | seed | pressed | salanin, nimbinin, nimbin, nimbidiol, azadirachtin; palmitic, stearic, **oleic**, linoleic acids | [104, 109] | 8.3 |
| Olive | *Olea europaea* L. | Oleaceae | fruit | pressed | **oleic**, palmitic, linoleic & stearic acids | [110] | 2.1 |
| Perilla | *Perilla frutescens* (L.) Britton | Lamiaceae | seed | pressed | **oleic**, linoleic & linolenic acids, **S-limonene, perillaldehyde**, elsholzia- ketone, naginataketone, perillaketone, myristicin, dillapiol, elemicin, isoegomaketone, perillene, egomaketone, shisofuran | [111–113] | 1.4 |
| Sesame | *Sesamum indicum* L. | Pedaliaceae | seed | pressed | linoleic, **oleic**, palmitic & stearic acids | [114] | 3.5 |
| Soybean | *Glycine max* (L.) Merr. | Fabaceae | seed | solvent extracted | linoleic, **oleic**, palmitic, α-linolenic & stearic acids | [115] | 4.2 |

Note: chemical components in **bold text** have proven mosquito repellent and deterrent properties according to literature and patent sources which are summarized in **Table 4**). Tropicos, botanical information system at the Missouri Botanical Garden [12] was used as a general reference on taxonomic information in this table

of potentially novel sources of mosquito repellent botanicals it is important to mention the following EOs: abies [*Abies spectabilis* (D. Don) Spach], almond [*Prunus dulcis* (Mill.) D. A.Webb], Australian yuzu (*Citrus junos* Siebold ex Tanaka), black pine (*Pinus nigra* Arnold), *Blumea lacera* (Burm. f.) DC., calamus (*Acorus calamus* L.), Canada fleabane [*Conyza canadensis* (L.) Cronquist], carda-

**Table 2** Uses and applications, EOs and other components of patented mosquito repellent inventions which claimed synergist effects.

| Use or technology | Plant EO | Plant species | Non-EO component | Source |
|---|---|---|---|---|
| Applied films | – | *Backhousia citriodora* F. Muell. | – | [116] |
| | | *Melaleuca ericifolia* Sm. | | |
| Coatings | Wintergreen | *Gaultheria procumbens L.* | pyrethroids | [117] |
| | Camphor | *Cinnamomum camphora* (L.) J. Presl | | |
| Floor wash | Eucalyptus | *Eucalyptus* L'Hér. spp. | – | [118] |
| | Lemon eucalyptus | *Eucalyptus citriodora* Hook. | | |
| | Citronella | *Cymbopogon winterianus* Jowitt ex Bor | | |
| Incense | Eucalyptus | *Eucalyptus* L'Hér. spp. | pyrethroids | [119] |
| | Cassia | *Cinnamomum cassia* (L.) C. Presl | | |
| Microcapsules for textiles | Eucalyptus | *Eucalyptus* L'Hér. spp. | DEET, isobornyl derivatives | [120] |
| Not specified | Rose | *Rosa* L. sp. | natural pyrethrins | [121] |
| | Jasmine | *Jasminum officinale* L. | | |
| | Limonene | synergist natural product | | |
| Spray/Fumigation on grass, shrubs, trees | Citronella | *Cymbopogon* Spreng. sp. | dimethyl phthalate, allyl sulfate | [122] |
| | Neem | *Azadirachta indica* A. Juss. | | |
| | Eucalyptus | *Eucalyptus* L'Hér. spp. | | |
| Vaporizer/Fumigant | Lippia | *Lippia* L. sp.+: | – | [123] |
| | Geranium | *Pelargonium graveolens* L'Hér. | | |
| | Lemon eucalyptus | *Eucalyptus citriodora* Hook. | | |
| | Basil etc. | *Ocimum basilicum* L. | | |

mom [*Elettaria cardamomum* (L.) Maton], cork tree (*Phellodendron amurense* Rupr.), *Elsholtzia hunanensis* Hand.-Mazz., flos lonicerae japonicae or jin yin hua (*Lonicera japonica* Thunb. ex Murray flower), fructus forsythiae [*Forsythia suspensa* (Thunb.) Vahl], galbanum (*Ferula galbaniflua* Boiss. & Buhse), herba schizonepetae [*Schizonepeta* (Benth.) Briq. sp.], hibiscus (*Hibiscus* L. sp.), larch (*Larix* Mill. sp.), lemon balm (*Melissa officinalis* L.), lovage (*Levisticum officinale* W. D. J. Koch), lilac (*Syringa vulgaris* L.), *Limnanthes alba* Hartw. ex Benth. seed, linaloe wood (*Bursera delpechiana* Poiss. ex Engl.), *Michelia × alba* DC. leaf, myrtle (*Myrtus communis* L.), *Ocimum canum* Sims, onion (*Allium cepa* L.), oregano (*Origanum vulgare* L.), peach [*Prunus persica* (L.) Batsch], pennyroyal (*Mentha pulegium* L.), pepper (*Capsicum annuum* L. var. *annuum*), petitgrain (*Citrus aurantium* L. var. *amara*), pimento [*Pimenta dioica* (L.) Merr.], pine needle (*Pinus* L. sp.), *Rhodomyrtus tomentosa* (Aiton) Hassk., rue (*Ruta graveolens* L.), *Stephania sinica* Diels, tansy (*Tanacetum* L. sp.), *Torreya grandis* Fortune ex Lindl. and valerian (*Valeriana* L. sp.). Nevertheless, we will not systematically go into details of the composition and repellency of these EOs in this review.

Generally, patent literature on mosquito repellent inventions treats fragrant extracts as EOs whether these extracts are produced using an initial solvent extraction step (such as in the production of concretes), by steam distillation, hydrodistillation, direct distillation or pressing (resulting in proper EOs). Herein, the term EO refers broadly to fragrant extracts obtained using these different extraction techniques. Importantly, fragrant oils and partially volatile balsamic oils which have volatile and non-volatile (glyceridic) chemical components in their compositions (▶ **Table 1**) and mosquito repellent properties, such as evening primrose (*Oenothera biennis* L.), perilla [*Perilla frutescens* (L.) Britton], ligusticum (*Ligusticum chuanxiong* Hortorum ex Qiu, et al. in Qiu) and copaiba (*Copaifera* L. spp.) oils are used in mosquito repellent patented formulations together with plant EOs.

## Glyceridic Oils Used in Patented Mosquito Repellent Inventions

▼

Importantly, plant glyceridic oils, several of which are known to possess mosquito repellency, were used in patented formulations as carriers or active ingredients which were associated with prolonged repellent action. The most used glyceridic oils in patented EO-containing repellent inventions were neem/margarosa (*Azadirachta indica* A. Juss., 8.3%), castor (*Ricinus communis* L., 4.9%), soybean [*Glycine max* (L.) Merr., 4.2%] and sesame (*Sesamum indicum* L., 3.5%) oils (▶ **Table 1**).

## Synergist Effects Associated with EO-Containing Compositions

▼

Synergist interactions were claimed to be operating in 8% of EO-containing patents (▶ **Table 2**) [116–123]. For example, EO of a species of *Lippia* L. and any one of a number of EOs formulated into a slowly evaporating hydrocarbon soluble composition was said to modify neuronal activity in invertebrates such as adult mosquitoes and produce repellent activity comparable to commercial pyrethroids [123]. Another example of a synergist formulation involved almost equal amounts of eucalyptus (*Eucalyptus* spp.) and cassia [*Cinnamomum cassia* (L.) C. Presl] EOs together with an emulsifying agent and butyl acetate solvent which was meant to be used with pyrethroids in incense formulations [119]. Still another example of a synergist repellent meant for use with pyrethroids (allethrin, dimefluthrin) used EOs of wintergreen (*Gaultheria procumbens* L.) 30–50 (w/w) and camphor (*Cinnamomum camphora* (L.) J. Presl) 10–35 (w/w), emulsifier and solvent [117] (▶ **Table 2**).

## Scientific Basis for Mosquito Repellency of EOs in Patented Inventions

The scientific literature on the mosquito repellence of EOs used in patents provides important insights (**Table 3**) [8,37,41,46,61, 68,73,85,88,93,124–177]. Firstly, citronella (*Cymbopogon nardus, C. winterianus*), eucalyptus (*Eucalyptus* spp.) and lemon eucalyptus (*E. citriodora* Hook.) EOs which were cited in many patented inventions have been the subject of a number of studies in which repellency against species of *Culex, Anopheles* and *Aedes* in some cases comparable to DEET have been reported for these oils alone or in formulations [138,140,143,178]. Furthermore, many EOs used in patented inventions have quite significant repellent properties according to published studies such as: bay laurel (*Laurus nobilis* L.) [137], camphor (*Cinnamomum camphora*) [132], cassia (*Cinnamomum cassia*) [132] EOs against *Ae. aegypti*; lemon (*Citrus × limon*) EO [128,152] against *An. stephensi* Liston, catnip (*Nepeta cataria* L.) EO [128], lemongrass (*Cymbopogon citratus*) [128], may chong/litsea [*Litsea cubeba* (Lour.) Pers.] [128, 179], tagetes (*Tagetes minuta* L.) [128], violet (*Viola odorata* L.) EOs [128] against *Ae. aegypti, An. stephensi* and *Cx. quinquefasciatus*; peppermint (*Mentha × piperita*) EO on human skin against *An. annularis* van der Wulp*, An. culicifacies* Giles and *Cx. quinquefasciatus* [160]; sandalwood (*Santalum* L. spp.) EO formulations against a *Culex* sp. [177]; geranium (*Pelargonium graveolens*) oil formulations [137,144,147,148] against species of *Culex, Anopheles* and *Aedes*; thyme (*Thymus vulgaris* L.) EO against *Cx. quinquefasciatus* [128,137,162]; marjoram (*Origanum majorana* L.) and juniper (*Juniperus communis* L.) EOs against *Cx. pipiens pallens* Coquillet [151]; and wintergreen (*Gaultheria procumbens*) EO against species of *Culex* and *Aedes* [131].

A broad-scale screening of plant oils against *Ae. aegypti, An. stephensi* and *Cx. quinquefasciatus* evaluated protection periods and percent of repellence on human skin as compared to 20% DEET [128]. In general, *Ae. aegypti* was the most difficult species to repel, followed by *An. stephensi* and finally *Cx. quinquefasciatus* for both oils and controls. The control (DEET) exhibited a protection period (PP) of 6 h and percent repellency (R%) of 46% against *Ae. aegypti*, whereas against *An. stephensi* and *Cx. quinquefasciatus* protection was for 8 h at 100% repellency [128] (**Table 3**). While the most active EOs against all three mosquito species were cited above, the following oils were active against *An. stephensi* and *Cx. quinquefasciatus*, but not significantly active against *Ae. aegypti*: chamomile (*Chamaemelum nobile*), cinnamon (*Cinnamomum verum*), galbanum (*Ferula galbaniflua*), jasmine (*Jasminum grandiflorum*), lavender (*Lavandula angustifolia*), pepper (*Piper nigrum*), rosemary (*Rosmarinus officinalis*), sandalwood (*Santalum album*) and soybean (*Glycine max*) [128]. Another group of oils in this study actively repelled only *Cx. quinquefasciatus*: cedar (*Cedrus, Cupressus* and *Juniperus* spp.), citronella (*Cymbopogon nardus, C. winterianus*), eucalyptus (*Eucalyptus globulus*), broad and narrow-leaved eucalyptus (*E. dives* and *E. radiata*, respectively), geranium (*Pelargonium graveolens*), juniper (*Juniperus communis*), lemon (*Citrus × limon*), lemon eucalyptus (*Eucalyptus citriodora*), myrtle (*Myrtus communis*), peppermint (*Mentha × piperita*), sage (*Salvia sclarea*), thyme (*Thymus serpyllum*) verbena (*Lippia triphylla*) and wild soybean (*Glycine soja*) [128]. Differences in the species specificity of the repellence profiles of these and other EOs may explain their use in repellent mosquito products. This may have to do with differences in the local and regional profiles of mosquito species populations and explain the use of mixtures of these EOs to generate broad spectrum formulations for simultaneous repellency of multiple mosquito species.

While *Ae. aegypti* and other adults may in general be difficult to repel using plant-based products or synthetic repellents, a number of plant EOs have been identified which are effective against this species (**Table 3**). The following repellency effects of EOs against adult *Ae. aegypti* have been observed: hairy basil (*Ocimum basilicum*) in stable nanoemulsions with vetiver (*Vetiveria zizanioides*) and citronella (*Cymbopogon nardus* and *C.winterianus*) EOs are a good repellent [129], bay laurel (*Laurus nobilis*) EO is an acceptable smelling, good spatial repellent [130], camphor (*Cinnamomum camphora*) EO and cassia (*C. cassia*) bark extract on human skin are repellents comparable to DEET [137], catmint (*Nepeta cataria*) EO exhibited 8 h of protection on human skin, cinnamon (*Cinnamomum zeylanicum, C. verum*) EOs exhibit moderate to good repellency [128], citronella (*C. winterianus*) EO exhibits knockdown repellency at 1–2% [141] and *C. winterianus* EO + vanillin exhibits 8 h of repellency [138], fennel (*Foeniculum vulgare*) fruit extract/fractions offer complete repellency [145] and EO as an aerosol or cream has comparable repellency to other EO repellents [144], geranium (*Pelargonium graveolens*) + citronella EO in a cream product exhibited good repellency in the field [46], lemon eucalyptus (*E. citriodora*) has knockdown repellency/adulticide activity [46], may chang/litsea (*Litsea cubeba*) EO exhibits contact and noncontact repellency and is a good/excellent repellent in formulations on the human forearm providing protection over 8 h [73,128], turmeric (*Curcuma longa*) EO + 5% vanillin exhibits 8 h of repellency and in formulations with other EOs + 5% vanillin offers protection from DEET and IR3535-resistant strains of *Ae. aegypti* over 4.5 h [138,156] and violet (*Viola odorata*) EO on human skin exhibited 8 h protection at a good level of repellency [128] (**Table 3**).

Several EOs from *Zanthoxylum* L. spp. (*Z. piperitum* DC., *Z. armatum* DC., *Z. bungei* Planch. & Linden ex Hance) were cited in patented mosquito repellent inventions. According to recent literature, *Zanthoxylum* L. spp. EOs have mosquito repellent activity [159,180]. Also, besides *A. argyi* H. Lév. & Vaniot (artemisia) EO, which is known to repel mosquitoes [127], the EOs of several other *Artemisia* L. spp. were used in patented formulations such as *A. annua* L. (wormwood), *A. vulgaris* L. and *A. apiacea* Hance. This is interesting given that *A. annua* EO has proven insect repellent properties [165].

The Amazon region is a source of plant-derived mosquito repellent oils. For example, *Carapa guianensis* Aubl. (andiroba) pressed fruit oils or extracts are formulated preferentially into candles during manufacturing as fumigant mosquito repellents [124], burned in kerosene lamps or used in topical repellent formulations which are commercially available in Brazil. *Copaifera* L. spp. (copaiba) balsam oils or extracts are used in mosquito repellency in Brazil especially in the Amazon region (**Table 3**). Furthermore, a formulation of andiroba, copaiba and baby oils exhibited repellency to mosquitoes in an Amazon field study [125].

## Scientific Basis for Mosquito Repellency of Glyceridic Oils

Neem or margarosa oil is obtained by pressing the fruit of the neem tree (*Azadirachta indica*). Neem oil is burned in 1% compositions in kerosene lamps as indoor mosquito emitters of chemical repellent-fumigant deterrents which have been evaluated and are considered to be safe [173,174]. Also, neem oil in mixtures

**Table 3** Scientific evidence for mosquito repellent and related properties of plant EOs and glyceridic oils used in patented repellent inventions.

| Plant oil | Plant species | Mosquito repellent properties | Source |
|---|---|---|---|
| **Essential oil** | | | |
| Andiroba | *Carapa guianensis* Aubl. | patented candles commercialized in Brazil as mosquito fumigant-repellents; repellency in Amazon field test of 1 : 1 : 1 andiroba, copaiba and baby oil mixture | [124, 125] |
| Anise | *Pimpinella anisum* L. | good repellent against *Cx. pipiens* | [126] |
| Artemisia | *Artemisia argyi* H. Lév. & Vaniot | repels mosquitoes | [127] |
| Basil | *Ocimum basilicum* L. | *Ae. aegypti* (PP 2 h, R% 81), *An. stephensi* (PP 3.5 h, R% 67), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; 5 % hairy basil + 5 % vetiver + 10 % citronella EOs in nanoemulsion repel *Ae. aegypti* 4.7 h; repels *Anopheles* sp. in human bait test & *Cx. pipiens* | [128, 129] |
| Bay laurel | *Laurus nobilis* L. | spatial repellence against *Ae. aegypti*, acceptable smell, definite mosquito repellence | [130] |
| Bergamot | *Citrus* × *bergamia* Risso | repellence against *Culex* & *Aedes* spp. is comparable to citronella oil | [131] |
| Camphor | *Cinnamomum camphora* (L.) J. Presl | *Ae. aegypti* (PP 2.5 h, R% 32), *An. stephensi* (PP 8 h, R% 43), *Cx. quinquefasciatus* (PP 8 h, R% 57)*; EO (0.1 $mg \cdot cm^{-2}$ on human skin): repellency and duration against *Ae. aegypti* comparable to DEET | [128, 132] |
| Cassia | *Cinnamomum cassia* (L.) C. Presl | bark extract (0.1 $mg \cdot cm^{-2}$): repels *Ae. aegypti* comparably to DEET (on human skin), 5 % EO in cream provided 50 min of protection to humans against female *Ae. aegypti* | [132] |
| Catnip, catmint | *Nepeta cataria* L. | *Ae. aegypti* (PP 8 h, R% 84), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; 1–6 h protection against *Ae. albopictus* (23 & 468 $\mu g \cdot cm^{-2}$); safety pharmacology evaluation: *N. cataria* oil is safe compared to DEET, *p*-menthane-3,8-diol, etc. May cause minor skin irritation | [128, 133, 134] |
| Cedar | *Cedrus* Trew (*Cupressus* L., *Juniperus* L.) spp. | *Ae. aegypti* (PP 3 h, R% 38), *An. stephensi* (PP 8 h, R% 38), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; repels *An. stephensi* | [127, 128, 135] |
| Chamomile | *Chamaemelum nobile* (L.) All. | *Ae. aegypti* (PP 4 h, R% 65), *An. stephensi* (PP 8 h, R% 76), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Cinnamon | *Cinnamomum zeylanicum* Blume | high repellency ($RD_{95}$ $mg \cdot mat^{-1}$) against *An. stephensi* (49.6), *Ae. aegypti* (53.9), *Cx. quinquefasciatus* (44.2) | [136] |
| | *C. verum* J. Presl | *Ae. aegypti* (PP 5.5 h, R% 70), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Citronella | *Cymbopogon nardus* (L.) Rendle, *C. winterianus* Jowitt ex Bor | repellency by 1 : 1 citronella & lavender EOs in 2 oz. castor oil; *Ae. aegypti* (PP 2 h, R% 76), *An. stephensi* (PP 8 h, R% 52), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; *C. winterianus* + vanillin repels *Ae. aegypti, An. dirus, Cx. quinquefasciatus* 8 h; + eucalyptus oil in floor cleaner, 6 h repellency; comparable to DEET & N,N-diethyl mandelic acid amide vs. *Aedes* spp.; 5 % hairy basil + 5 % vetiver + 10 % citronella EOs in nanoemulsion with 4.7 h protection against *Ae. aegypti; C. winterianus* $LC_{50}$ & $LC_{95}$ = 0.5 & 0.9 % for *Cx. quinquefasciatus*,1.0 & 2.0 % for *Ae. aegypti* | [37, 128, 129, 137–141] |
| Clove | *Syzygium aromaticum* (L.) Merr. & L. M. Perry | *Cx. pipiens pallens*: isoeugenol & eugenol (from clove oil) > repellency than citronella. Clove bud oil + vanillin (long-term protection) > DEET; repels *Ae. aegypti, An. dims, Cx. quinquefasciatus* for 2–4 h; knockdown $LC_{50}$ & $LC_{95}$=0.5 & 0.9 % for *Cx. quinquefasciatus*, 1.0 & 2.0 % for *Ae. aegypti* | [46, 61, 141] |
| Copaiba | *Copaifera* L. spp. | 1 : 1 : 1 andiroba, copaiba & baby oils repels mosquitoes in Amazon field test | [125] |
| Dill | *Anethum graveolens* L. | *Ae. aegypti* (PP 1.5 h, R% 78), *An. stephensi* (PP 3.5 h, R% 71), *Cx. quinquefasciatus* (PP 3 h, R% 57)* | [128] |
| Eucalyptus | *Eucalyptus globulus* Labill. | *Ae. aegypti* (PP 1 h, R% 57), *An. stephensi* (PP 5.5 h, R% 29), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| | *E. camaldulensis* Dehnh. | EO repels *Cx. pipiens* adult females | [8] |
| | *Eucalyptus* L'Hér. spp. | + citronella EO in floor cleaning product, 6 h protection; 15 % oil composition ≥ 3 h protection & composition + vanillin ≥ 5 h protection to humans; EO contg 30 % *p*-menthanediol repels *An. darlingi* (97 %) | [126, 140, 142, 143] |
| Eucalyptus, broad-leaved | *E. dives* Schauer | *Ae. aegypti* (PP 3.5 h, R% 19), *An. stephensi* (PP 8 h, R% 38), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Eucalyptus, narrow-leaved | *E. radiata* Sieber ex DC. | *Ae. aegypti* (PP 2.5 h, R% 65), *An. stephensi* (PP 8 h, R% 43), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Fennel | *Foeniculum vulgare* Mill. | 5 % in aerosol or 8 % in cream repels *Ae. aegypti* comparably to citronella & geranium EOs; cream & EO repel *Culex, Anopheles* & *Aedes* spp. comparably to geranium & citronella EOs in field; hexane fraction (0.1 $mg \cdot cm^{-2}$ repels *Ae. aegypti* 99 %) of fruit methanol extract contains repellent (+)-fenchone & *E*-9-octadecenoic acid | [144, 145] |
| Galbanum | *Ferula galbaniflua* Boiss. & Buhse | *Ae. aegypti* (PP 2.5 h, R% 70), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Garlic | *Allium sativum* L. | EO and chemical components have strong repellent properties | [146] |
| Geranium | *Pelargonium graveolens* L'Hér. | *Ae. aegypti* (PP 2.5 h, R% 78), *An. stephensi* (PP 8 h, R% 62), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; geranium + lemongrass EOs repel *Aedes* spp.; geranium + sandalwood EOs + soybean oil in burned stick repellents; geranium (25 % geraniol) EO + lemongrass extract product protect against bites of *Ae. atlanticus* and *Ae. mitchellae* for 4 h; geranium + sandalwood EOs + soybean oil product repel *Culex* sp. & other mosquitoes for 3 h in the field; geranium + citronella EOs (1 : 1) in cream product repels *Ae. aegypti* and *Culex, Anopheles* & *Aedes* spp. in the field; in cold creams with repellency to *Cx. fatigans* in lab & on humans; various forms of EO definite promise as repellents | [46, 128, 137, 144, 147, 148] |
| Ginko | *Ginkgo biloba* L. | edulan (isolated from leaf extract) repels *Ae. albopictus* | [149] |
| Hibawood | *Thujopsis dolabrata* (Thunb. ex L. f.) Siebold & Zucc. | hinokitiol isolated from EO, highly repellent hinokitiol-containing non-woven polyester fabric & coated foot band | [150] |
| Jasmine | *Jasminum grandiflorum* L. | *Ae. aegypti* (PP 4.5 h, R% 14), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Juniper | *Juniperus communis* L. | *Ae. aegypti* (PP 3.5 h, R% 43), *An. stephensi* (PP 8 h, R% 76), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; good repellency at 5 $\mu g \cdot cm^{-2}$ against female *Cx. pipiens pallens* | [128, 151] |

*continued next page*

**Table 3** Scientific evidence for mosquito repellent and related properties of plant EOs and glyceridic oils used in patented repellent inventions. *(continued)*

| Plant oil | Plant species | Mosquito repellent properties | Source |
|---|---|---|---|
| **Essential oil** | | | |
| Lavender | *Lavandula angustifolia* Mill. | *Ae. aegypti* (PP 3 h, R% 24), *An. stephensi* (PP 8 h, R% 81), *Cx. quinquefasciatus* (PP 8 h, R% 86)*; mosquito repellent: citronella 1: lavender 1 & castor oil 2 oz. | [127, 128] |
| Lemon | *Citrus* × *limon* (L.) Osbeck | *Ae. aegypti* (PP 1.5 h, R% 68), *An. stephensi* (PP 7 h, R% 10), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; repellency to *An. stephensi* ~ DEET in animal & human tests | [128, 152] |
| Lemon eucalyptus | *Eucalyptus citriodora* Hook. | *Ae. aegypti* (PP 2.5 h, R% 59), *An. stephensi* (PP 8 h, R% 52), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; use (*p*-menthane-3,8-diol, PMD, as active ingredient) recommended by CDC (Center for Disease Control and Prevention, USA) against West Nile vector; adulticide activity against *Cx. quinquefasciatus* & *Ae. aegypti* | [8, 46, 128] |
| Lemongrass | *Cymbopogon citratus* (DC.) Stapf | *Ae. aegypti* (PP 3 h, R% 70), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; field test of 25 % geraniol oil & lemongrass ext. with 4 h repellency against *Ae. atlanticus* and *Ae. mitchellae*; mixture containing lemongrass EO + *p*-menthanediol (PMD) repels *An. darlingi* & other spp. 95–98 % for 5–6 h in field (repellency > 15–20 % DEET) | [128, 147, 153] |
| Lemon tea tree | *Leptospermum petersonii* F. M. Bailey | limited repellency (< DEET) of *Ae. aegypti, Cx. quinquefasciatus, Cx. annulirostris* | [154] |
| Lepto-spermum | *L. liversidgei* R. T. Baker & H. G. Sm. | repellent: blocks ability of mosquitoes to perceive $CO_2$ emitted by humans | [155] |
| Lime | *Citrus* × *aurantifolia* L. | + mustard oil carrier as effective mosquito repellent | [68] |
| Marjoram | *Origanum majorana* | 5 µg · $cm^{-2}$ good repellent against female *Cx. pipiens pallens* | [151] |
| May chang/ Litsea | *Litsea cubeba* (Lour.) Pers. | *Ae. aegypti* (PP 8 h, R% 73), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; high contact and noncontact repellency to female *Ae. aegypti in vitro* in cages; formulation to fix on skin with high repellency in human volunteers for up to 8 h & 100 % repellency to *An. stephensi, Cx. quinquefasciatus, Ae. aegypti*; greater repellence of night-biting mosquitoes *An. dirus, Cx. quinquefasciatus* and *Ae. albopictus* than *Ae. aegypti* | [73, 128, 132, 156] |
| Melaleuca | *Melaleuca alternifolia* Cheel | limited repellence of *Ae. aegypti, Cx. quinquefasciatus, Cx. annulirostris in lab* | [75] |
| Mint, mentha | *Mentha haplocalyx* Briq. | *d*-8-acetoxycarvotanacetone isolated mosquito repellent | [157] |
| Myrtle | *Myrtus communis* L. | *Ae. aegypti* (PP 2.5 h, R% 57), *An. stephensi* (PP 6.5 h, R% 43), *Cx. quinquefasciatus* (PP 8 h, R% 86)* | [128] |
| Palmarosa | *Cymbopogon martini* (Roxb.) Will.Watson | high geraniol content mosquito repellent | [158] |
| Patchouli | *Pogostemon cablin* (Blanco) Benth. | partially repels *Ae. aegypti, Cx. quinquefasciatus, An. dims* | [159] |
| Pepper, black | *Piper nigrum* L. | *Ae. aegypti* (PP 1.5 h, R% 65), An. stephensi (PP 3 h, R% 62), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; repels *An. dirus, Cx. quinquefasciatus, Ae. albopictus* (≥ 4.5 h) | [128, 156] |
| Peppermint | *Mentha* × *piperita* L. | *Ae. aegypti* (PP 2 h, R% 59), *An. stephensi* (PP 6.5 h, R% 57), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; on human skin strongly repels *An. annularis* (100 %), *An. culicifacies* (92 %), *Cx. quinquefasciatus* (85 %); comparable to mylol oil (di-butyl & di-methyl phthalates); repels adult female *Cx. pipiens* | [126, 128, 160] |
| Pine | *Pinus sylvestris* L. | good mosquito repellency | [85] |
| Rose | *Rosa* L. *sp.* | moderate mosquito repellency | [127] |
| Rosemary | *Rosmarinus officinalis* L. | *Ae. aegypti* (PP 5.5 h, R% 43), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; repels *An. stephensi, Ae. aegypti* & *Cx. quinquefasciatus*; low repellency against *Ae. aegypti* in lab, acceptable to humans as final fragrance in repellent formulation; repels *Ae. aegypti* (avg 90 min) | [88, 128, 130, 136] |
| Sage | *Salvia sclarea* L. | *Ae. aegypti* (PP 2 h, R% 46), *An. stephensi* (PP 5 h, R% 19), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Sandalwood | *Santalum album* L. | *Ae. aegypti* (PP 2.5 h, R% 59), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| | *Santalum* L. spp. | repels *Cx. pipiens pallens*; EO containing cold creams repel *Cx. fatigans* in the lab & on human skin; area repellency of *Culex* sp. by commercial sticks (contg 0.5 % EO) (3 h protection); botanical repellent (w/soybean and geranium oil) 100 % effective in field (3-h test period, comparable to DEET) | [93, 148, 151] |
| Sour (bitter) orange | *Citrus* × *aurantium* L. | limited protection (repellency) against mosquitoes | [137] |
| Spearmint | *Mentha spicata* L. | repellent; piperitone oxide from *M. spicata* (var. *viridis*) EO repels *An. stephensi* | [161] |
| Tagetes | *Tagetes minuta* L. | *Ae. aegypti* (PP 1 h, R% 84), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; repels *Ae. aegypti* (avg 90 min) | [88, 128] |
| Thyme | *Thymus serpyllum* L. | *Ae. aegypti* (PP 2.5 h, R% 57), *An. stephensi* (PP 7.5 h, R% 33), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| | *Thymus vulgaris* L. | repels lab-reared adult female *Ae. albopictus* for 2 h; 0.01 % totally repels *Cx. quinquefasciatus* | [134, 162] |
| Turmeric | *Curcuma longa* L. | + 5 % vanillin repels *Ae. aegypti, An. dirus* and *Cx. quinquefasciatus* in cage & large room for 8 h; turmeric, citronella & hairy basil EOs + vanillin provide substitute for DEET; repels DEET & IR3535-resistant *Ae. aegypti* for 4.5 h | [138, 156] |
| Verbena | *Lippia triphylla* (L'Hér.) Kuntze | *Ae. aegypti* (PP 2.5 h, R% 70), *An. stephensi* (PP 5.5 h, R% 38), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |
| Vetiver | *Vetiveria zizanioides* (L.) Nash | stable nanoemulsion of 5 % hairy basil, 5 % vetiver & 10 % citronella EO: repels *Ae. aegypti* for 4.7 h | [41] |
| Violet | *Viola odorata* L. | *Ae. aegypti* (PP 6 h, R% 68), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 86)* | [128] |
| Wild verbena (Lippie) | *Lippia sidoides*, L. *javanica*, *Lippia* spp. | sources of perillaldehyde (repels *An. gambiae*) & perillic acid (repels *An. arabiensis* & *Ae. aegypti*) | [163, 164] |
| Wintergreen | *Gaultheria procumbens* L. | strongly repels *Culex* and *Aedes* spp. in different tests | [131] |
| Wormwood | *Artemisia annua* L. | mosquito repellent properties | [165] |

*continued next page*

Table 3 Scientific evidence for mosquito repellent and related properties of plant EOs and glyceridic oils used in patented repellent inventions. (continued)

| Plant oil | Plant species | Mosquito repellent properties | Source |
|---|---|---|---|
| **Essential oil** | | | |
| Zanthoxylum | *Z. piperitum* DC., *Z. armatum* DC., *Z. bungei* Planch. & Linden ex Hance | repel mosquitoes | [159] |
| **Glyceridic oils** | | | |
| Castor | *Ricinus communis* L. | best carrier for pyrethrum extracts (long-lasting) | [137] |
| Mustard | *Brassica* L. spp. | longer protection (up to 5 h with *Zanthoxylum limonella* or lime oils) than coconut (*Cocus nocifera*) oil against *Ae. albopictus* | [166] |
| Neem/ Margosa | *Azadirachta indica* A. Juss. | knockdown repellency against *Ae. aegypti, Ae. albopictus, An. quadrimaculatus* Say; repels female *An. stephensi* ($ED_{50}$ 0.191–0.156 mg · $cm^{-2}$) in lab; low repellency against *Ae. albopictus* & *Cx. nigripalpus*; 2% in coconut (*Cocus nocifera*) oil on exposed body parts of human volunteers provided complete protection for 12 h from all *Anopheles* spp.; protection from *Anopheles* spp. (96–100%), *Aedes* (85%), *Culex* sp. (61–94%); significant protection by neem cream against adult *Ae. aegypti*; 1% in kerosene lamps in preclinical & clinical safety evaluation is safe to humans; 1% in kerosene burned in lamps effective in 2 field tests. Repellence: *Anopheles* > *Culex*; 1–4% in coconut oil on exposed body parts of humans: 81–91% protection for 12 h | [167–175] |
| Olive | *Olea europaea* L. | *Ae. aegypti* (PP 3.5 h, R% 68), *An. stephensi* (PP 8 h, R% 71), *Cx. quinquefasciatus* (PP 8 h, R% 71)*; 1 : 1 w/pyrethrum repels mosquitoes for 4 h | [128, 137] |
| Soybean | *Glycine max* (L.) Merr. | *Ae. aegypti* (PP 3 h, R% 54), *An. stephensi* (PP 8 h, R% 76), *Cx. quinquefasciatus* (PP 8 h, R% 100)*; oil-based product provided 1.5 h (low) repellency, 24% DEET provided 5 h protection; good repellency in product w/sandalwood + geranium in burned sticks vs. DEET; commercial product containing 2% oil repels *Ae. albopictus, Cx. nigripalpus, Ae. triseriatus* for 5, 8.5 & ≥ 7.3 h, respectively | [128, 169, 176, 177] |
| Soybean, wild (carotin) | *Glycine soja* Siebold & Zucc. | *Ae. aegypti* (PP 3 h, R% 16), *An. stephensi* (PP 8 h, R% 10), *Cx. quinquefasciatus* (PP 8 h, R% 100)* | [128] |

* PP = protection period (h), R% = percent repellency; 0.1 mL of a 20% EO solution (in 20% Genapol, 10% PEG, 20% ethanol, 50% water) applied to 30 $cm^2$ of human forearm; for 20% DEET solution (in same as above) these values were: *Ae. aegypti* (PP 6 h, R% 46), *An. stephensi* (PP 8 h, R% 100), *Cx. quinquefasciatus* (PP 8 h, R% 100) [24]

with coconut (*Cocos nucifera* L.) oil provides good protection for very long periods against *Anopheles* and *Aedes* spp. [170, 171, 175]. Castor (*Ricinus communis* L.), mustard (*Brassica* spp.), olive (*Olea europaea*) and other glyceridic oils have important roles in several patented repellent compositions containing pyrethrum extracts and EOs where they act as carriers and can extend the duration of repellent effects for several hours perhaps by slowing the release or evaporation of EOs from surfaces.

There are mixed scientific reports on the effective mosquito repellency of several glyceridic oils. Thus, for soybean (*Glycine max*) oil low repellency was observed as compared to 24% DEET formulations [176] and good repellency was observed for the smoke generated from burned sticks which contained soybean oil. Especially interesting is a report from a United States Department of Agriculture laboratory where 4 well-known synthetic mosquito repellents based on 10% KBR3023 [1-piperidinecarboxylic acid 2-(2-hydroxyethyl)-1-methylpropyl ester], 7.5% IR3535 [3-(*N*-butyl-*N*-acetyl)-aminopropionic acid ethyl ester], 15% and 7% DEET and 8 natural product-based repellents based on 2% soybean oil, 10% citronella (*Cymbopogon* spp.) EO, neem oil (*Azadirachta indica*) and others were tested in the lab against *Ae. albopictus* Skuse, *Cx. nigripalpus* Theobald and *Ae. triseriatus* Say [169]. The 2% soybean oil formulation exhibited mosquito repellency comparable to both 10% KBR3023 and 15% DEET based products each of which provided estimated mean protection time (eMPT) responses averaged over all three mosquito species of ≥ 7.2 h [169]. This study is evidence for the potential of soybean oil as a stand-alone repellent and as a component oil of repellent formulations.

## Mosquito Repellent Chemical Components of EOs and Added Isolated Compounds

Approximately 20% of all EO-containing patents mentioned a non-EO plant derivative and 40% mentioned a specific EO repellent component or added isolated natural chemical ingredient. Chrysanthamic acid and its derivatives which are components of pyrethrum (*Chrysanthemum* L. spp. flower extracts) were cited in 12% of all patented formulations involving EOs. Also, patents cited many "natural" chemical constituents which were either added to formulations or were important chemical components of EOs comprising the formulations. The most widely cited chemicals of plant origin were (% of patents): camphor (8.3), geraniol (7.6), linalool (7.6), menthol (7.6), geranial (7.0), citronellal (6.9), limonene (4.9), citronellol (4.9), borneol (4.2), 1,8-cineole (4.2), *p*-menthane-3,8-diol (4.2), camphene (3.5) and nepetalactone and derivatives (3.5). Many of these and other chemical components of EOs are potent mosquito repellents (**Table 4**) [131, 137, 143, 145, 151, 163, 169, 181–193] and are discussed below.

### Vanillin in EO containing mosquito repellent inventions

Vanillin was cited as an additive in 4% of EO-containing patents. According to several scientific publications, it increases the duration and magnitude of the repellent effect of synthetic repellents such as DEET as well as plant EOs. For example, 5% vanillin in formulations of EOs of turmeric (*Curcuma longa* L.), citronella (*C. winterianus*) or hairy basil (*Ocimum americanum* L.) provided up to 8 h of protection against *Ae. aegypti, An. dirus* and *Cx. quinquefasciatus* under cage conditions. Interestingly, 5% vanillin in formulations with DEET increased the protection time as compared to DEET alone against these three mosquito species (≥ 8 h protec-

**Table 4** Mosquito repellency or deterrency effects of individual major chemical components of EOs used in patented inventions.

| EO component | No. EOs† | Repellency | Mosquito | Source |
|---|---|---|---|---|
| α-Bisabolol | 2 | [d]84 % spatial repellency for 180 min, avoidance freq. (contact repellency) = DEET | female *Ae. aegypti* | [181] |
| Borneol | 3 | [b]1.4 mg (−)-borneol · $cm^{-2}$ = 70 % repellency | female *Ae. aegypti* | [182] |
| | | [b,c]$RD_{50} = 1.7 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| Bornyl acetate | 2 | [b]1.4 mg · $cm^{-2}$ = 15 % repellency | female *Ae. aegypti* | [182] |
| Camphene | 2 | [b,c]$RD_{50} = 2.2 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| Camphor | 6 | [b,c]$RD_{50} = 1.4 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| | | [b]1.4 mg · $cm^{-2}$ (±)-camphor, (+)-camphor, (−)-camphor = 36, 35 & 47 % repellencies, resp. | female *Ae. aegypti* | [182] |
| 3-Carene | 4 | [b,c]$RC_{50} = 8.6 \times 10^{-4}$ mg · $cm^{-2}$ | female *An. gambiae* | [183] |
| | | 1 h, 1.92 µg · $cm^{-2}$ = 68†, 65‡ % repellency | *Ae. aegypti, Ae. albopictus* | [163] |
| Carvacrol | 4 | [b,c]$RC_{50} = 2.4 \times 10^{-4}$ mg · $cm^{-2}$ | female *An. gambiae* | [183] |
| Carvone | 2 | [b,c]$RD_{50} = 1.3 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| | | *d*-carvone & *l*-carvone: feeding deterrents/repellents, good spatial repellents/ inhibitors, contact repellents/deterrents | – | [184] |
| Cinnamaldehyde | 2 | definite mosquito repellent potential | – | [137] |
| | | *E*-cinnamaldehyde (0.051 mg · $cm^{-2}$) & DEET (0.025 mg · $cm^{-2}$) provided 87 & 95 % protection, resp., after 30 min | female *Aedes aegypti* | [184] |
| 1,8-Cineole | 15 | [b]cineole 1.4 mg · $cm^{-2}$ = 21 % repellency | female *Ae. aegypti* | [182] |
| | | [b]3 % in vaseline or olive oil = 73 or 120 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| | | [b,c]$RD_{50} = 1.2 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| Citronellal | 4 | [b,c]$RD_{50} = 2.2 \times 10^{-4}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| | | feeding deterrent/repellent, spatial repellent/inhibitor, contact repellent/deterrent | – | [186] |
| Citronellol | 6 | repellent component | – | [145] |
| | | feeding deterrent/repellent, spatial repellent/inhibitor | – | [186] |
| *p*-Cymene | 3 | [b,c]$RD_{50} = 1.0 \times 10^{-5}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| Eugenol | 5 | high repellency | female *Cx. pipiens pallens* | [151] |
| | | [b,c]$RD_{50} = 1.3 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| Fenchone | 2 | [b,c]$RD_{50} = 1.9 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| | | 0.4 mg (+)-fenchone · $cm^{-2}$ = 51 % repellency after 1 h[b,f] | female *Ae. aegypti* | [145] |
| Geranial | 7 | at 0.2 mg · $cm^{-2}$, blood-sucking by mosquitoes reduced by 10, 15, and 18 % after 1, 2 and 3 h, respectively | *Cx. pipiens pallens, Cx. pipiens quinquefasciatus* | [187] |
| Geraniol | 11 | [b,c]$RD_{50} = 1.1 \times 10^{-4}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| | | spatial repellent: 0.25 µg · $cm^{-2}$ *ca*. 100 % (reversible) inhibition of host-seeking after 48 h exposure | female *Ae. albopictus* | [188] |
| Geranyl acetate | 6 | effective feeding deterrent/repellent, effective spatial repellent/inhibitor, contact repellent/deterrent | Mosquitoes | [186] |
| Limonene | 19 | [b]3 % in vaseline/olive oil = 61/78 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| | | 1 h, 1.92 µg · $cm^{-2}$ = 70†, 70‡ % repellency | *Ae. aegypti, Ae. albopictus* | [189] |
| | | [b,c]$RD_{50} = 1.8 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| Linalool | 14* | [b]1.4 mg (±)-linalool · $cm^{-2}$ = 67 % repellency | female *Ae. aegypti* | [182] |
| | | [b]3 % in vaseline/olive oil = 52/65 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| | | [b,c]$RD_{50} = 1.5 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| *p*-Menthane-3,8-diol | 1 | 26 % formula more repellent than 4 synthetic & 7 natural product repellents | *Ae. albopictus, Cx. nigripalpus, Ochlerotatus triseriatus* | [169] |
| | | 15 % formula with lemongrass EO (*Cymbopogon citratus*) = 99 % protection for 5 h in the field; [h]16 % formula with lemongrass EO = 95 % protection for 6 h in the field | *An.* darling, *Ae. ochlerotatus taeniorhynchus* | [143] |
| Menthone | 2 | [b]3 % in olive oil = 35 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| Methyl salicylate | 2 | most repellent (screening) | – | [131] |
| Myrcene | 6 | [b,c]$RC_{50} = 8.4 \times 10^{-4}$ mg · $cm^{-2}$ | female *An. gambiae* | [183] |
| | | [b]1.4 mg · $cm^{-2}$ = 20 % repellency | *Ae. aegypti* | [182] |
| Nepetalactone | 1 | mosquito repellent ingredient in formulations | – | [190] |
| *E*-Nerolidol | 1 | [d]67 % spatial repellency for 180 min, avoidance freq. (contact repellency) < DEET | female *Ae. aegypti* | [181] |
| Oleic acid | 8** | 0.4 mg · $cm^{-2}$ = 52 % repellency after 1 h[b,f] | female *Ae. aegypti* | [145] |
| Perillaldehyde | 1 | [b,c]$RD_{50} = 3.2 \times 10^{-4}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| α-Pinene | 15 | *d*-α-pinene, 2 h protection | Mosquito | [191, 192] |
| | | [b]3 % in vaseline/olive oil = 27/56 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| β-Pinene | 8 | [b]3 % in vaseline/olive oil = 22/39 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| | | [b,c]$RD_{50} = 1.6 \times 10^{-3}$ mg · $cm^{-2}$ | female *An. gambiae* | [163] |
| α-Santalol | 1 | [d]87 % spatial repellency for 180 min, avoidance freq. (contact repellency) = DEET | female *Ae. aegypti* | [181] |
| Spathulenol | 2 | [e]proportion not biting = 0.73, 0.75, respectively | *Ae. aegypti, An. stephensi* | [193] |

*continued next page*

**Table 4** Mosquito repellency or deterrency effects of individual major chemical components of EOs used in patented inventions. *(continued)*

| EO component | No. EOs† | Repellency | Mosquito | Source |
|---|---|---|---|---|
| α-Terpinene | 1 | 1 h, 1.92 µg $cm^2$ = 68†, 55‡ % repellency | *Ae. aegypti, Ae. albopictus* | [189] |
| | | [b]$1.4\ mg \cdot cm^{-2}$ = 15 % repellency | female *Ae. aegypti* | [182] |
| | | [b,c]$RD_{50} = 2.4 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |
| γ-Terpinene | 6 | 1 h, $1.92\ \mu g \cdot cm^{-2}$ = 60†, 72‡ % repellency | *Ae. aegypti, Ae. albopictus* | [189] |
| | | [b]3 % in vaseline/olive oil = 35/48 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| | | [b,c]$RD_{50} = 2.7 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |
| Terpinen-4-ol | 5 | 1 h, $1.92\ \mu g \cdot cm^{-2}$ = 92†, 85‡ % repellency | *Ae. aegypti, Ae. albopictus* | [189] |
| | | [b]$1.4\ mg \cdot cm^{-2}$ = 83 % repellency | *Ae. aegypti* | [182] |
| | | [b,c]$RD_{50} = 1.5 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |
| | | spatial repellent/inhibitor | – | [186] |
| α-Terpineol | 7 | [b]3 % in vaseline/olive oil = 78/99 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [185] |
| | | feeding deterrent/repellent, spatial repellents/inhibitor, contact repellent/deterrent | | [186] |
| | | [b,c]$RD_{50} = 1.3 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |
| Terpinolene | 2 | 1 h, $1.92\ \mu g \cdot cm^{-2}$ = 55†, 70‡ % repellency | *Ae. aegypti, Ae. albopictus* | [189] |
| | | [b,c]$RD_{50} = 2.6 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |
| (α + β)-Thujone | 2 | [b]$1.4\ mg \cdot cm^{-2}$ = 20 % repellency | *Ae. aegypti* | [182] |
| | | [b,c]$RD_{50} = 1.5 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |
| Thymol | 1 | [b,c]$RC_{50} = 1.9 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [183] |
| | | [b]3 % in vaseline/olive oil = 52/65 min protection | 1 : 1 male : female *Cx. pipiens molestus* | [186] |
| *cis*-Verbenol | 1 | [b,c]$RD_{50} = 7.5 \times 10^{-5}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |
| Verbenone | 1 | [b,c]$RD_{50} = 1.6 \times 10^{-3}\ mg \cdot cm^{-2}$ | female *An. gambiae* | [163] |

– = Information not found. † Number of oils in **Table 1** which contain this as their major component. *In evening primrose *(Oenothera biennia)* glyceridic oil. ** Mosquito repellent component of glyceridic oils. † DEET = 50 % repellency. ‡ DEET = 60 % repellency. [a] Used as additive in one patent. [b] Human-bait assay. [c] Positive control DEET exhibited $RC_{50} = 3.3 \times 10^{-4}\ mg \cdot cm^{-2}$. [d] Applied concentration $78.6\ \mu g \cdot cm^{-2}$. Repellency is statistically different from negative control. DEET and turmerone had 83 and 89 % repellencies, respectively. Contact repellency is defined as 100 % of individuals off treated surface. Avoidance frequency of DEET and turmerone = 0.8. [e] Substance was applied at $25\ nmol \cdot cm^{-2}$ cloth. Positive control was (1S,2′S)-2-methylpiperidinyl-3-cyclohexen-1-carboxamide (SS-220) at $25\ nmol \cdot cm^{-2}$ cloth (provided 0.80 and 0.78 non-biting mosquitoes, respectively, for *Ae. aegypti* and *An. stephensi*). [f] $0.2\ mg \cdot cm^{-2}$ DEET (positive control) provided 97 % repellency after 1 h. [g] Positive control 15 % DEET (in EtOH) = 92 % protection (average over trial period). [h] Positive control 20 % DEET (in EtOH) = 64 % protection (average over trial period)

tion). In another example, 15 % eucalyptus (*Eucalyptus* spp.) EO and 5 % vanillin provided 5 h of repellency against *Ae. albopictus* [18] and in other work involving human volunteers, clove (*Syzygium aromaticum*) bud EO and vanillin mixtures provided long acting repellency against adult female *Cx. pipiens pallens* [151]. Thus, combinations of vanillin with plant EOs can lead to formulations which are substitutes for DEET [138, 142, 151].

In patents, vanillin is cited as an ingredient in mosquito repellent formulations with: *Zanthoxylum armatum* DC. and/or *Z. piperitum* DC. EOs [194], clove bud and leaf (*Syzygium aromaticum*), juniper berry (*Juniperus communis*) and/or marjoram (*Origanum majorana*) EOs [195], lemongrass (*Cymbopogon citratus*) EO/*p*-menthane-3,8-diol formulations [196], combinations of citronella, clove, geranium (*Pelargonium graveolens*), lavender (*Lavandula angustifolia*), patchouli [*Pogostemon cablin* (Blanco) Benth.] and peppermint (*Mentha* × *piperita*) EOs [197] among others.

### Synthetic additives in EO-containing inventions

About 25 % of all EO-containing patented repellents had at least one synthetic repellent component. Thus, DEET (*N,N*-diethyl *m*-toluamide), the gold-standard synthetic mosquito repellent [11], was used in 10 % and dimethyl (dialkyl) phthalates were cited in 5 % of EO-containing patented inventions. Also, one or more synthetic pyrethroids (allethrin, cyhalothrin, deltamethrin, dimefluthrin, esbiothrin, metofluthrin, permethrin, tetramethrin and vaporthrin) were used in 10 % of EO-containing mosquito repellents. It must be stressed that pyrethroids can be strong mosquitocides (toxicity), spatial mosquito repellents and mosquito irritants as was shown, for example, for permethrin in field studies [6] and α-cypermethrin, deltamethrin, permethrin in a very recent publication [198]. Only about 3 % of patents made use of the synthetic synergist piperonyl butoxide.

## Chemical Composition of EOs Used in Patented Inventions

Information on the major chemical components of plant EOs used in mosquito repellent inventions is presented in **Table 1**. Among these are EOs which are concentrated sources of proven mosquito repellent monoterpenes and phenylpropanoids such as the EOs of angelica (*Angelica archangelica*), artemisia (*Artemisia argyi*), basil (*Ocimum basilicum*), bergamot (*Citrus* × *bergamia*), camphor (*Cinnamomum camphora*), cassia (*Cinnamomum cassia*), catnip (*Nepeta cataria*), chrysanthemum (*Chrysanthemum indicum*), cinnamon (*Cinnamomum zeylanicum*), citronella (*Cymbopogon nardus, C. winterianus*), coriander (*Coriandrum sativum*), cypress (*Cupressus sempervirens*), dill (*Anethum graveolens*), eucalyptus (*Eucalyptus* spp.), geranium (*Pelargonium graveolens*), grapefruit (*Citrus reticulata*), ho leaf (*Cinnamomum camphora*), hyssop (*Hyssopus officinalis*), juniper (*Juniperus communis*), lavender (*Lavandula angustifolia*), lemon (*Citrus* × *limon*), lemon eucalyptus (*Eucalyptus citriodora*), lemongrass (*Cymbopogon citratus*), lemon tea tree (*Leptospermum petersonii*), lime (*Citrus* × *aurantifolia*), marjoram (*Origanum majorana*), may chang/litsea (*Litsea cubeba*), melaleuca/tea tree (*Melaleuca alternifolia*), mint/mentha (*Mentha*), orange (*Citrus* × *sinensis*), palmarosa (*Cymbopogon martini*), curl leaf parsley (*Petroselinum crispum*), pepper (*Piper nigrum*), pine (*Pinus sylvestris*), rose (*Rosa* × *damascena, R.* × *centifolia*), rosemary (*Rosmarinus officinalis*), salvia/sage (*Salvia* spp.), sour (bitter) orange (*Citrus* × *aurantium*), spearmint (*Mentha spicata*), thyme (*Thymus vulgaris*), verbena (*Lippia triphylla*) and wintergreen (*Gaultheria procumbens*). In these EOs, proven mosquito repellent volatile components camphor, 1,8-cineole, citronellol, eugenol, geranial, geraniol, limonene, linalool, myrcene, α and *β*-pinenes, γ-terpinene, terpinen-4-ol and α-terpineol are well represented among the major components (▶ **Table 4**).

### Chemical composition of glyceridic oils used in patented EO-containing inventions

Glyceridic plant oils are important components of EO-containing mosquito repellent formulations not only for their carrier properties, but because they contain trace or larger amounts of free, long-chain mono- and polyunsaturated fatty acids and derivatives of these. It has been known for some time that insect antennae are highly sensitive to gas-phase long-chain fatty acids. For example, Hwang et al. [199] showed that gravid *Cx. quinquefasciatus* Say in an olfactometer in contact with room temperature vapors of $C_{14}$-$C_{24}$ mono-, di- and polyunsaturated fatty acids were significantly repelled. These authors also demonstrated that fatty acids having at least one *Z*-configuration olefin bond (analogous saturated and *E*-configuration fatty acids were less repellent or inactive) were especially effective repellents. One of the most repellent fatty acids was oleic acid (9*Z*-olefin) which is a common free fatty acid in vegetable oils whose 18 carbon chain was considered to be optimal within the group of fatty acids studied [199]. Independently, female *Ae. aegypti* were found to be moderately repelled by oleic acid as compared to DEET in a human-bait assay [145]. Thus, free, long-chain, unsaturated fatty acids which are present in glyceridic oils are sufficiently volatile to be mosquito repellent substances in formulations containing plant EOs. This is especially relevant given claims in several patents of the mosquito repellent effects of olive (*Olea europaea* L.), sesame (*Sesamum indicum* L.), mustard (*Brassica* L. spp.), soybean [*Glycine max* (L.) Merr.] and other oils (for examples, see [200] or [201]).

### Mosquito repellent major chemical components of EOs

Among the more widely distributed mosquito repellent major chemical components of EOs used in patented inventions are the cyclic and noncyclic monoterpenes limonene, α-pinene, 1,8-cineole and linalool (▶ **Table 4**). These are major components of, respectively, 28, 22 [including limonene-containing perilla (*Perilla frutescens*) oil], 22 and 21% [including linalool-containing evening primrose (*Oenothera biennis*) oil] of the EOs most used in patented repellent inventions (▶ **Table 1**).

EOs in patented mosquito repellent inventions are composed of a number of chemical components which individually exhibit important mosquito repellency, deterrency and inhibitory effects (▶ **Table 1** and **Table 4**). For example, α-bisabolol and α-santalol provided 3 h of high spatial repellency and contact repellency equivalent to DEET against female *Ae. aegypti* while *E*-nerolidol exhibited good spatial repellency for 3 h and less contact repellency than DEET [181]. Also, the following substances singly exhibited good repellency against the mosquito species indicated: carvacrol ($RC_{50} = 2.4 \times 10^{-4}$ mg·cm$^{-2}$, female *An. gambiae*) [183], cinnamaldehyde (0.051 mg·cm$^{-2}$ against female *Aedes aegypti*, repellency comparable to DEET) [184], citronellal ($RD_{50} = 2.2 \times 10^{-4}$ mg·cm$^{-2}$), *p*-cymene ($RD_{50} = 1.0 \times 10^{-5}$ mg·cm$^{-2}$) and *cis*-verbenol ($RD_{50} = 7.5 \times 10^{-5}$ mg·cm$^{-2}$) against female *An. gambiae* [163], geranial (0.2 mg·cm$^{-2}$, reduces blood-sucking by *Cx. pipiens pallens* and *Cx. pipiens quinquefasciatus* over 3 h). The following EO components provided reasonable repellency at *ca.* 2 µg·cm$^{-2}$ against adult *Ae. aegypti* and *Ae. albopictus*: 3-carene, limonene, α-terpinene, γ-terpinene, terpinen-4-ol and terpinolene [189].

Several interesting isolated repellent substances are described in patented EO-containing products (▶ **Table 3**). For example, hinokitiol-containing polyester non-woven fabric and hinokitiol-coated polyester foot band are said to provide 100% repellency against mosquitoes and hinokitiol from hibawood (*Thujopsis dolabrata*) EO (and other sources) is an important natural repellent [150]. Another example is the isolation of edulan from ginkgo (*Ginkgo biloba*) EO and the repellent activity of this compound and derivatives against *Ae. albopictus* are described in a patent in which it is also claimed that these compounds are safe to humans [149]. The mosquito repellent natural substance *d*-8-acetoxycarvotanacetone was isolated from *Mentha haplocalyx* Briq. [157]. Also, several *Lippia* spp. EOs were cited in patents [e.g., *L. sidoides* and *L. javanica* (wild verbena or lippie oil)] and are important sources of the mosquito repellent compounds perrilic acid and perillaldehyde [163, 164] (▶ **Table 3**). The latter compound is a component of perilla (*Perilla frutescens*) oil and exhibited good repellency ($RD_{50} = 3.2 \times 10^{-4}$ mg·cm$^{-2}$) against female *An. gambiae* [163] (▶ **Table 4**). In another patented invention, garlic (*Allium sativum*) EO and isolated component chemicals of garlic EO were tested for repellency against mosquitoes. More than a dozen allyl sulfide, allyl disulfide and allyl polysulfide components of garlic EO applied to human skin were found to deter *Ae. aegypti, An. gambiae* and *Cx. quinquefasciatus* landing and blood feeding [202].

### Geraniol

Geraniol is a major component of 16% of the more used EOs in patented inventions (▶ **Table 1**) and its mosquito repellency has been studied. As an isolated chemical, it exhibited good repellency on human skin in the lab [163] and reversible spatial repellency/protection from bites [188]. A 25% formulation of this substance was the basis for a commercial product which exhibited effective repellency in the lab [93, 167, 169] but was less effective as compared to other products at repelling mosquitoes according to an early field study [143]. In a recent field study, a 25% geraniol and lemongrass (*Cymbopogon citratus*) composition offered superior protection against the bites of *Ae. atlanticus* and *Ae. mitchellae* (4 h) than repellent formulations based on 12% EOs (1 h) and EOs, benzophenone-3, octinoxate and octisalate mixture (1.5 h) [147].

### *p*-Menthane-3,8-diol

The mosquito repellency of the component of *Eucalyptus* spp. EOs, *p*-menthane-3,8-diol (PMD), is firmly established [8, 143, 178]. As a repellent additive in formulations, 15–16% PMD/lemongrass formulations provided 5–6 h of excellent repellency (95–99%) against *Anopheles* and *Aedes* spp. [153]. Indeed, in a U.S. Dept. of Agriculture study, 26% PMD-containing product was more repellent in the lab to *Ae. albopictus, Cx. nigripalpus* and *Ae.triseriatus* than synthetic products based on 10% KBR3023, 7.5% IR3535, 15% and 7% DEET, and 7 natural product-based repellents based on 2% soybean oil, 10% citronella EO, neem oil, 25% geraniol, etc. [169].

### Mosquito repellent minor components of EOs

Some minor or lower concentration components of EOs are worth mentioning because they exhibit significant mosquito repellency. For example, citral (geranial + neral) and fenchyl alcohol are minor components of citronella (*Cymbopogon nardus, C. winterianus*) and rose (*Rosa damascena*) EOs, respectively, and exhibit moderate repellency to female *An. gambiae* ($RD_{50} = 1.3 \times 10^{-3}$ and $1.4 \times 10^{-3}$ mg · cm$^{-2}$, respectively) [163]. Also, linalool oxide, a minor component of lemon eucalyptus (*E. citriodora*) EO was found to be repellent ($RC_{50} = 6.5 \times 10^{-4}$ mg · cm$^{-2}$) to female *An. gambiae* [183] and Tripathi et al. [161] found that the peppermint (*Mentha × piperita*) EO component piperitone oxide was highly repellent to adult *An. stephensi*. In other works, farnesol [a component of chamomile, jasmine and rose (*Rosa damascena*) EOs], elemol (a component of catnip, citronella and hyssop EOs) and hedycaryol (a component of black pepper EO) exhibited 69, 89 and 95% spatial repellency over 180 min to adult female *Ae. aegypti* and avoidance frequency (contact repellency) greater than or equal to that of DEET [181]. Cinnamyl alcohol, a minor constituent of cassia (*Cinnamomum cassia*) EO, exhibits less repellency to female *Ae. aegypti* than the major component, cinnamaldehyde, but still this repellency is significant (at 0.051 mg · cm$^{-2}$, 86% protection after 30 min) and worth mentioning here [184]. Also, a minor component of EO of catmint (*Nepeta* L. spp.) EOs [28], dihydronepetalactone, exhibits important repellency against arthropods, including mosquitoes [203]. Citronellyl acetate is a minor component of eucalyptus (*Eucalyptus* spp.) [165], lemon eucalyptus (*E. citriodora*) [66], rose (*Rosa damascena*) [87] and tarragon (*Artemisia dracunculus*) [99] EOs and is a feeding deterrent/repellent and mosquito spatial repellent/inhibitor. Also, the minor component of salvia/sage EO [92], hydroxy-*p*-cymene, is both a feeding deterrent/repellent and mosquito contact repellent/deterrent [186]. Lastly, isoeugenol (a component of clove EO) was found to be highly repellent to female *Cx. pipiens pallens* [151].

## Synthetic EOs: Additive Effects/Synergism versus Suppression/Dilution

▼

In some cases, patented formulations in effect improve upon the natural repellency of an essential oil by mimicking or synthesizing an oil which ideally contains components which together contribute to the repellent effect and eliminates those which counteract (attract mosquitoes), make no contribution or suppress the repellency of other components. Work done by Odalo et al. [183] nicely illustrates this process. An initial observation was that major components of 6 EOs when tested singly were less repellent than the natural EOs in which these components are found. Synthetic EOs were prepared by mixing pure major components in the same proportion in which they occur in the natural EOs. Repellencies of synthetic EOs ranged from comparable to up to three times the activity of the corresponding natural EOs against *An. gambiae* in the human-bait test based on $RC_{75}$ values [183]. The activity of synthetic EOs substantiates the additive and/or synergistic nature of the interaction of blended EO components (and also suppressive or diluting/repellency diminishing effects of nonactive components). The same principles of addition/synergism and suppression/dilution are operational in the process of formulating EOs and isolated components into patented repellent inventions.

## Enantiomeric Composition of EOs

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Scientific (and patent) literature on the composition of EOs is often based on non-chiral column gas chromatography-mass spectrometry (GC-MS) and compound retention time/index analysis. Thus, information is not systematically available on the enantiomeric purity of the EO components in **Table 1**. Enantiospecificity in mosquito repellency is an important issue. For example, Gu et al. [189] found that commercial *R*-(−)-terpinen-4-ol exhibited > 90% repellency against *Ae. aegypti* and *Ae. albopictus* adults at a concentration of 1.92 µg · cm$^{-2}$ in a test lasting 1 h. *S*-(+)-terpinen-4-ol of high enantiomeric purity is found in lavender (*Lavandula angustifolia*) EOs [204]. No mosquito repellency data were found in the literature for *S*-(+)-terpinen-4-ol. In principle, enantiomers may not be equally repellent to mosquitoes and their organoleptic and other properties (toxic, allergic, etc.) are not equally desirable for use as repellents. More research is needed on the comparative mosquito repellency of enantiomerically pure EO components such as *S*-(+)-terpinen-4-ol and *R*-(−)-terpinen-4-ol against different mosquito species.

## Allergenicity of EO Chemical Components

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Limonene, benzyl alcohol, linalool, citronellol, geraniol, citral, anisyl alcohol, cinnamaldehyde, eugenol, isoeugenol, coumarin, farnesol, benzyl benzoate, benzyl salicylate among other volatile components are known allergens. As described above, these components are major or minor components of EOs used in repellent inventions (**Table 1** and references cited therein). These and other volatile allergens are easily detected by GC-MS and are controlled in the European Union and elsewhere.

## Conclusion

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Patents on plant EO and volatile component-containing mosquito repellent inventions make use of scientifically substantiated claims to repellency to mosquitoes based on lab and field experiences. Our experience is that mosquito repellents and other insect control products, must be evaluated in the environments and settings in which they are to be used. Repellents must be developed based on plant oils and isolated chemical components by targeting *Aedes, Anopheles, Culex* and other mosquito species which are found locally and regionally. Repellency approaches should be multipronged and make use of sprays, fumigants, paints and varnishes, incense, candles, etc. in domestic settings, fumigation and spraying in outdoor settings and topical repellents, clothes made of repellent fabrics, repellent wristbands among other available products for individual protection.

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