

## A systematic review of plant-based mosquito repellents and their activity

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Received 21 September 2022; revised received 07 July 2023; accepted 27 July 2023

Deadly pathogens and parasites can be transmitted through many vectors, and the mosquito is considered one of the most threatening vectors in public health, transmitting various diseases to humans such as zika fever, west Nile fever, chikungunya, dengue fever, hemorrhagic dengue, malaria and many more all over the world causing millions of deaths every year. Mosquito-borne diseases can be prevented with the use of 'mosquito repellents'; thus, it plays a crucial role in minimising the possibility of getting infections and its adverse effects. To prevent mosquito-borne diseases, synthetic mosquito repellent became a handy and preferred measurement. However, over time, it became incompetent because mosquitoes acquired immunity to them, and since synthetic repellent are chemicals, causes more harm to the ecosystem by contamination. So, there is a sore need for natural alternatives to synthetic repellents. Our ancient texts have mentioned that some important plant genera, such as *Azadirachta*, *Calotropis*, *Cinnamomum*, *Citrus*, *Eucalyptus*, *Geranium*, *Mentha*, *Lantana*, *Ocimum*, *Piper*, *Zingiber*, have anti-larval and insecticidal properties and their essential oils and extracts have been used in traditional practice form generations against host-seeking mosquitoes as a personal protection measure. Keeping these aspects in view, the main focus of this review is to demonstrate and analyse the mosquito-repellent activities of essential oils and extracts derived from different plant families and to understand their mode of action better.

**Keywords:** Essential oils, Mosquito-repellent plants, Mosquito-borne diseases, Pathogens, Vectors

**IPC code; Int. cl. (2021.01)**– A01N 65/00, A01P 17/00

### Introduction

Mosquito-borne diseases like dengue fever, malaria, yellow fever, filariasis, and chikungunya are major health problems all around the world<sup>1</sup>. There are more than a hundred species of mosquitoes throughout the world that can act as vectors to transmit various types of diseases in humans and other vertebrates<sup>2</sup>. Over the past three decades, the encounter of humans with mosquito-borne viruses (MBV) such as Zika virus, Flavivirus, Yellow fever virus, Dengue virus, West Nile virus and Chikungunya virus to become frequent, and these viruses greatly expanded their distribution range, causing large epidemics, responsible for millions of human cases with significant morbidity and mortality<sup>3</sup>. According to the recent data provided by the World Health Organisation (WHO), 241 million cases of malaria were estimated in 2020, which resulted in more than 400,000 deaths due to this disease. The data also showed that 40,000 deaths were recorded due to dengue fever alone every year globally.

Malaria is the most prevalent mosquito-borne illness caused by the *Plasmodium* parasite, which spreads through the bite of female *Anopheles*. On the other hand, chikungunya and dengue are mosquito-mediated viral infections caused by the same mosquito species, i.e. *Aedes aegypti* and *Aedes albopictus*. Another common mosquito-borne disease is lymphatic filariasis, commonly known as elephantiasis, caused by infection with filial worms which enter the human body through the bite of the *Culex quinquefasciatus* mosquito<sup>4</sup>. Another most common mosquito-borne infectious disease, West Nile, is caused by the arbovirus transmitted to humans through the bite of the *Cx. pipiens* mosquito.

As mosquitoes and diseases from them are spreading globally and affecting different regions, mosquito control and personal protection from mosquito bites is the most meaningful measure for controlling several life-threatening diseases transmitted by bites of blood-seeking mosquitoes. Properly selecting and applying mosquito repellents are essential to reduce mosquito-borne disease. Mosquito repellents are volatile chemicals which

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repel the mosquito in the opposite direction from its source<sup>5</sup>. An ideal insect repellent must be effective, safe, non-toxic, and not produce any adverse effect when used in houses or applied to children, adults and women during pregnancy<sup>6</sup>.

Chemical repellents such as allethrin, dimethyl phthalate (DMP), IR3535 [ethyl butyl acetylamino propionate (EBAAP)], N, N-diethyl-meta-toluamide (DEET) and picaridin and are utilised in most the commercially produced mosquito repellent. However, these chemical repellents contain harmful and poisonous compounds and are non-biodegradable, which can hamper the ecosystem and cause various other health-related issues<sup>7,8</sup>.

So, the best alternative is to use plant-based mosquito repellents to control mosquitoes and treat

mosquito-borne illnesses. The plant-based compounds are eco-friendly, species-specific, biodegradable and have lesser or no harmful effects on human beings<sup>9</sup>. Further, these natural plant-based products are considered safer than synthetic or chemical mosquito repellent. Several studies have reported the mosquito-repellent activities of plant extracts and their essential oils (Table 1). They have greatly increased our understanding of the behavioural mode of action of these plant-based repellants for mosquito control<sup>10-12</sup>.

The present systematic review was carried out through an extensive literature survey to reveal the scientific knowledge, research and development that have taken place on plant-derived mosquito repellent over the years to provide us with a better perspective on mosquito control.

Table 1 — Mosquito repellent plants and their activities against various mosquito species

Plant name	Common name	Plant part used	Active compound	Tested mosquito species	Reference
<i>Ageratum conyzoides</i>	Goat weed plant	Leave, flower, stem and root	Chromene, precocene I, precocene II with others	<i>An. gambiae</i> , <i>Ae. aegypti</i>	84, 85
<i>Ageratum houstonianum</i>	Floss flower	Leaves	Bioactive phytochemical constituents	<i>An. stephensi</i> , <i>Ae. aegypti</i> and <i>Cx. quinquefasciatus</i>	86
<i>Azadirachta indica</i>	Neem	Leaves and Seed oil	Azadirachtin, salanin, gedunin and deacetylnimbin	<i>An. stephensi</i>	87
<i>Calendula officinalis</i>	Marigold	Aerial parts	Phytochemicals	<i>An. stephensi</i>	88
<i>Calotropis procera</i>	Milk weed, Aak	Leaf	Saponins, flavonoids, tannin	<i>An. aerabiansis</i> , <i>Cx. quinquefasciatus</i>	35
<i>Carica papaya</i>	Papaya	Leaves	Phytochemicals	<i>Aedes</i> spp.	89
<i>Carica pubescens</i>	Mountain papaya	Seeds	Oleic acid and palmitic acid	<i>Ae. aegypti</i>	90
<i>Cinnamomum osmophloeum</i>	pseudocinnamomum	Leaves	Alpha-methyl cinnamaldehyde, benzaldehyde and trans-cinnamaldehyde	<i>Ae. albopictus</i> , <i>Cx. quinquefasciatus</i> and <i>Armigeres subalbatus</i>	91
<i>Cinnamomum verum</i>	Ceylon cinnamon tree or true cinnamon tree	Bark	Cinnamaldehyde	<i>Cx. quinquefasciatus</i>	92
<i>Cinnamomum zeylanicum</i>	Ceylon cinnamon	Leaves and Barks	Cinnamaldehyde	<i>Cx. quinquefasciatus</i> , <i>An. tessellatus</i> and <i>Ae. aegypti</i>	93
<i>Citrus aurantifolia</i>	Key lime	Stems and leaves	Geijerene, limonene and germacerene D	<i>Ae. aegypti</i> , <i>An. stephensi</i>	94
<i>Citrus reticulata</i>	Mandarin orange	Fruit peel	D-limonene and $\gamma$ -terpinene	<i>Ae. aegypti</i>	95
<i>Citrus sinensis</i>	Sweet orange	Fruit peel	Limonene	<i>Cx. pipiens</i>	96
<i>Cymbopogon citartus</i>	Lemongrass	Leaves	Citral, neral and $\beta$ -myrcene	<i>Ae. aegypti</i>	97
<i>Cymbopogon giganteus</i>	Kachi grass	Leaves	Limonene	<i>An. gambiae</i>	98
<i>Cymbopogon winterianus</i>	Java citronella	Leaves	Citronellol and geraniol	<i>Ae. aegypti</i>	76
<i>Eucalyptus globulus</i>	Blue gum	Leaf	1,8-Cineol, $\alpha$ -pinene	<i>An. stephensi</i>	99
<i>Eucalyptus tereticornis</i>	Forest red gum	Leaf	$\beta$ -pinene	<i>Cx. quinquefasciatus</i>	80

(Contd.)

Table 1 — Mosquito repellent plants and their activities against various mosquito species (*Contd.*)

Plant name	Common name	Plant part used	Active compound	Tested mosquito species	Reference
<i>Jatropha curcas</i>	Purging nut or barbados nut or physic nut or poison nut or bubble bush	Leaves and seed	Alkaloids, steroids, flavonoids, oleic acid and linolenic acid	<i>Cx. pipiens</i> and <i>Cx. quinquefasciatus</i>	100, 101
<i>Juniperus procera</i>	African pencil-cedar or African juniper or East African juniper or East African-cedar or Kenya-cedar	Leaves	Phytochemicals including alkaloids, carbohydrates, glycosides, proteins, phenols, phytosterols, saponins and tannins	<i>An. arabiensis</i>	102
<i>Juniperus virginiana</i>	Eastern red cedar	Aerial green parts	Essential oil	<i>An. gambiae</i>	103
<i>Lantana camara</i>	Sage	Leaves, flower	Caryophyllene, eucalyptol and bicyclogermacerene	<i>Ae. aegypti</i>	104
<i>Mentha arvensis</i>	Corn Mint	Leaves	Tannins, saponins, flavonoids and terpenoids	<i>Ae. aegypti</i>	105
<i>Mentha piperita</i>	Peppermint	Leaves	Phytochemical constituents	<i>Ae. aegypti</i>	106
<i>Mentha spicata</i>	Spearmint	Leaves	R-carvone and limonene	<i>Cx. quinquefasciatus</i> , <i>Ae. aegypti</i> and <i>An. stephensi</i>	107
<i>Myrtus communis</i>	Myrtle	Aerial parts	Phytochemicals	<i>An. stephensi</i>	88
<i>Nepeta cataria</i>	Catnip, or catwort or catmint	Leaves	Phytochemicals	<i>Ae. aegypti</i>	108
<i>Ocimum americanum</i>	Lime basil	Leaf	6-methyl cinnamate	<i>Ae. aegypti</i>	109
<i>Ocimum basilicum</i>	Sweet basil, common basil	Leaf	Linalool and methyleuganol	<i>Ae. albopictus</i> , <i>Cx. tritaeniorhynchus</i>	110
<i>Ocimum gratissicum</i>	African basil	Leaf and branches	Euganol	<i>Ae. aegypti</i>	110
<i>Olea europaea</i>	Common olive	Leaves	Phytochemicals	<i>An. arabiensis</i>	111
<i>Pelargonium graveolens</i>	Rose geranium	Leaves	Geraniol, citronellol	<i>Ae. aegypti</i>	73
<i>Pinus merkusii</i>	Sumatran pine	Bark	Phytochemicals	<i>Ae. aegypti</i>	112
<i>Pinus brutia</i> , <i>P. canariensis</i> , <i>P. halepensis</i> , <i>P. nigra</i> , <i>P. stankewiczii</i> , <i>P. strobus</i> and <i>Pinus pinaster</i>	Greek <i>Pinus</i>	Fresh needles from branches	Caryophyllene, K-terpineole, eugenyl acetate, eugenol, isoeugenol, camphor, K-pinene, $\beta$ -pinene and cineole	<i>Ae. albopictus</i>	113
<i>Piper aduncum</i> , <i>P. arboretum</i> , <i>P. crassinervium</i> , <i>P. gaudichaudianum</i> and <i>P. marginatum</i>	Brazilian pepper	Leaves	$\beta$ -asarone, (E)-anethole, (E)- $\beta$ -caryophyllene, $\gamma$ -terpinene, p-cymene, limonene, $\alpha$ -pinene and $\beta$ -pinene	<i>Ae. aegypti</i>	114
<i>Piper betle</i>	Betel pepper	Leaves	Alpha-cubebene, alpha-caryophyllene, caryophyllene, cyclohexane, 1,6-cyclodecadiene, 4,7-methanoazulene, benzene, 1H-cyclopropa(a)naphthalene, 2H-2,4a-methanonaphthalene, and 1H-cycloprop(e) azulene	<i>Cx. quinquefasciatus</i>	115

*(Contd.)*

Table 1 — Mosquito repellent plants and their activities against various mosquito species (*Contd.*)

Plant name	Common name	Plant part used	Active compound	Tested mosquito species	Reference
<i>Piper caninum</i> and <i>P. montium</i>	Wild pepper, Tiêu núi	Leaves and/or stems	$\beta$ -caryophyllene, $\beta$ -bisabolene, $\alpha$ -pinene, and $\beta$ -pinene	<i>Ae. aegypti</i>	116
<i>Piper crocatum</i>	Red betel	Leaves	Bioactive phytochemical constituents	<i>Ae. aegypti</i>	117
<i>Piper longum</i>	Long pepper	Fruits	Piperonaline	<i>Cx. pipiens pallens</i>	118
<i>Piper nigrum</i>	Black pepper	Fruits	Piperine	<i>An. arabiensis</i> , <i>An. coluzzii</i> , <i>An. funestus</i> , <i>An. gambiae</i> and <i>An. quadrimaculatus</i>	119
<i>Piper retrofractum</i>	Javanese long pepper or the Balinese long pepper	Fruits	Bioactive phytochemical constituents	<i>Cx. quinquefasciatus</i> and <i>Ae. aegypti</i>	120
<i>Rosmarinus officinalis</i>	Rosemary	Leaves	$\alpha$ -pinene, 1,8-Cineole, 1-Verbenon, Borneol, Geraniol	<i>Ae. aegypti</i>	121
<i>Solanum lycopersicum</i>	Tomato	Leaves	Phytochemicals	<i>Ae. aegypti</i>	122
<i>Solanum nigrum</i>	Makoi or black nightshade	Fruit/Berries	Phytochemicals	<i>Cx. quinquefasciatus</i>	123
<i>Solanum trilobatum</i>	Purple fruited pea egg plant	Leaves	Phytochemicals	<i>Cx. quinquefasciatus</i> and <i>Cx. tritaeniorhynchus</i>	124
<i>Solanum villosum</i>	Red nightshade or hairy nightshade or woolly nightshade	Fruit/Berries	Phytochemicals	<i>Ae. aegypti</i>	125
<i>Solanum xanthocarpum</i>	Yellow-berried Nightshade	Fruits	Phytochemicals	<i>An. stephensi</i> and <i>Cx. quinquefasciatus</i>	126
<i>Syzygium aromaticum</i>	Clove	Flower bud	Essential oil such as 2-methoxy-3-(2-propenyl)	<i>An. stephensi</i>	127
<i>Syzygium polyanthum</i>	Indonesian bay leaf or daun salam	Leaves	Saponins, triterpenes, alkaloids and essential oil	<i>Ae. aegypti</i>	128
<i>Tagetes erecta</i>	Mexican marigold	Leaves and stems	Piperitone, D-limonene and piperitenone	<i>Ae. aegypti</i>	129
<i>Tagetes minuta</i>	Wild marigold or stinking roger	Aerial parts	3,9-epoxy-p-metha-1,8(10) diene, AR-turmerone, $\beta$ -caryophyllene, bicyclogermacrene dihydrotagetone, ocimene, ocimenones, piperitenone and tagetones	<i>An. arabiensis</i>	130
<i>Thymus serrulatus</i> and <i>Thymus schimperi</i>	Ethiopian thyme	Aerial parts	Thymol, camphor, cineole, methyl eugenol, limonene and myrcene	<i>An. arabiensis</i>	131
<i>Thymus vulgaris</i>	Garden thyme or common thyme	Aerial parts	Carvacrol, p-cymene, linalool, $\alpha$ -terpinene, and thymol	<i>Cx. pipiens pallens</i>	132
<i>Zingiber officinale</i>	Ginger	Rhizome	Zingiberene, kaemferol and zingiberol	<i>Ae. aegypti</i>	133

***Lantana camara***

*L. camara* is a 1-4 m tall perennial shrub which belongs to the family Verbenaceae. It has hairy, egg-shaped, opposite leaves with long petioles and oval blades. The flowers of *Lantana* are small, pink, white, orange, yellow coloured and dense in flat-topped clusters, and the fruits are drupaceous, sweet in taste,

fleshy, ovoid, purple, black in colour and 5 mm long<sup>13,14</sup>. This plant has therapeutic value because of the presence of flavonoids, triterpenoids, saponins, steroids, oligosaccharides, phenylpropanoid, glycosides, anthocyanin, isoflavones, coumarins and naphthoquinone<sup>13,15</sup>. In recent studies, the *L. camara* plant reported various medicinal properties like

antibacterial activity, wound healing activity, antifungal activity, antimotility activity, antiulcerogenic activity, hemolytic activity, antihyperglycemic activity, anti-inflammatory activity, anticancer and mosquito controlling activity<sup>16,17</sup>.

Many researchers have identified caryophyllene, eucalyptol,  $\alpha$ -humelene, germacrene,  $\alpha$ -copaene, aromadendrene,  $\alpha$ -cubebene,  $\alpha$ -humulene,  $\alpha$ -guaiene,  $\beta$ -elemene,  $\alpha$ -selinene,  $\beta$ -selinene,  $\delta$ -cadinene, caryophyllene oxide, nerolidol and spathulenol as a major constituents in the extract of *L. camara*. These components were found to have insecticidal, insect repellent, attractant and antimicrobial properties<sup>18,19</sup>.

According to Dua *et al.*<sup>18</sup>, the essential oil obtained from the leaves of *L. camara* showed adulticidal activity against vectors of malaria (*An. culicifacies*, *An. stephensi*), vector of dengue and chikungunya (*Ae. aegypti*) and vector of filariasis (*Cx. quinquefasciatus*). At a concentration of 400 ppm, the methanolic extract of *L. camara* leaves gave the highest protection against the bite of female *Anopheles* for more than five hours<sup>20</sup>. Further, the flower extract of *L. camara* provides 94.5% protection against *Ae. aegypti* and *Ae. albopictus*<sup>21</sup>.

#### *Azadirachta indica*

*A. indica* is a deciduous plant that can grow up to 15-20 meters tall. It belongs to the family Meliaceae, native to the Indian and African continents. It has pinnate leaves and white and fragrant flowers. The fruit is smooth and varies from oval to round in shape<sup>22</sup>.

According to the reports, its constituents have several positive health impacts, including hepatoprotective benefits, anti-parasitic, anti-inflammatory, and blood sugar-reducing qualities<sup>23</sup>. The leaves, seeds and seed oil of this plant contain sallanin, a compound which has effective mosquito repelling properties<sup>24</sup>. *A. indica* oil prevents feeding activities of mosquitoes due to the presence of various volatile and organic compounds, disrupts endocrine functioning and causes growth abbreviations<sup>25</sup>. Further, azadirachtin is effective in inhibiting the larva of mosquitoes, however, it does not affect their digestive and nervous system<sup>26</sup>. The plant has therapeutic values because of the presence of azadirachtin. A study shows that azadirachtin produces almost 100% larval mortality<sup>27</sup>.

According to Ghosh *et al.*<sup>28</sup>, a phytochemical nimbin obtained from neem oil is effective against *An. gambiae*. Nimbin interacts directly with OBPs

(Odorant Binding Proteins), which play an important role in identifying a host for a blood meal. Hence, *A. indica* oil is considered an effective repellent. Essential oil from *A. indica* seeds with coconut oil as diluent provided 90.26 and 88.83% protection at 50 and 100% concentration against *Cx. quinquefasciatus*<sup>29</sup>.

#### *Calotropis species*

*Calotropis procera* and *Calotropis gigantea* are the two common species of the genus *Calotropis* that possess mosquito-repellent activity. *Calotropis* (also known as giant milkweed or calotrope) is an evergreen, xerophytic, perennial shrub of the subfamily Asclepiadaceae widely distributed in the tropical and sub-tropical regions of Africa and Asia<sup>30</sup>. *C. procera* exhibits antimicrobial effects, anthelmintic effects, anti-inflammatory effects, analgesic effects, antipyretic effects, anticancer effects, anti-angiogenic activity, antidiabetic effect, immunological effects, gastroprotective effect, and antioxidant effects<sup>31</sup> and also has been used in the treatment of eczema, ulcers, leprosy, asthma, fever, indigestion, diarrhoea, and skin diseases<sup>32</sup>. *C. gigantea* is used to treat paralysis, inflammation, intestinal worms, bronchitis and dyspepsia<sup>33</sup>. Several studies reported the presence of tannin, saponins, alkaloids, flavonoids, pregnanes, and cardenolides in *C. gigantea*<sup>33,34</sup>. Hitherto, studies have also reported that leaf and flower extracts of *C. procera* and *C. gigantea* exhibit larvicidal, ovicidal, and mosquito-repellent activity.

According to Elimam *et al.*<sup>35</sup>, the leaf extract of *C. procera* showed larvicidal activity against *An. arabiensis* and *Cx. quinquefasciatus*. Their study showed LC<sub>90</sub> values (lethal concentration that causes 90% mortality) at 783.43, 1018.59, 1224.62 ppm (parts per million) against 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> instar larvae of *An. arabiensis* and at 433.51, 538.27, and 763.13 ppm against 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup> instar larvae of *Cx. quinquefasciatus*. The aqueous leaf extract of *C. gigantea* exhibits 86±1.42% (LC<sub>50</sub>=137.90) larvicidal activity against *Cx. gelidus* and 94±1.31% (LC<sub>50</sub>=110.05) against *Cx. tritaeniorhynchus* at 1000 ppm dose<sup>36</sup>. At a concentration of 5.0 mg/cm<sup>2</sup>, the ethanol flower extract of *C. gigantea* showed 100% protection for 150 min, whereas chloroform flower extract provided 95.66% protection against *C. quinquefasciatus*<sup>37</sup>.

#### *Zingiber* and other related species

*Zingiber* spp. is a herbaceous perennial and flowering plant that grows up to 1 meter. They belong

to the family Zingiberaceae. It originated in maritime South East Asia and is commonly used as a spice and herb due to its medicinal properties<sup>38</sup>.

The essential oil derived from *Zingiber officinale* (English ginger), *Zingiber moran* (Cassumunar ginger), *Curcuma amanda* (Mango ginger) showed larvicidal and repellent properties<sup>9,39</sup>. 1, 8 epoxy-p-methane Bicyclo[2.2.1]heptan-2-one,1,7,77-trimethyl-, 1S and camphenein *C. amanda* oil; carbonic acid, carveol, careen, camphene, citral, D-limonene, succinic acid and thymol in *Z. moran* oil and alpha terpineol, careen, citral, endoborneol, geraniol, linalool, neocloven, thymol, terpineol in *Z. officinale* oil, respectively, are effective larvicidal and repellent activity<sup>9</sup>.

According to Hazarika *et al.*<sup>9</sup>, *Z. officinale* showed the highest larvicidal activity. It showed LC<sub>50</sub> values of 87.09 and 57.01 mg/L after 24 and 48 h. Moreover, *Z. officinale*, *Z. moran* and *C. amanda* showed 100, 87 and 83% repellency at 100 mg/L for 2 h against *An. stephensi*.

Essential oil of *Kaempferia galangal* (aromatic zinger) contains the active compound ethyl p-methoxy cinnamate at LC<sub>50</sub> below 50 ppm found to be a larvicidal agent against *Ae. vittatus* and *An. maculatus*<sup>40</sup>. Similarly, 4% of *Z. officinale* essential oil in telon oil was 91.95% effective for 60 minutes against mosquitoes<sup>41</sup>.

#### **Mentha species**

*Mentha* spp. Is an aromatic and perennial herb that grows 10-120 cm<sup>42</sup>. They belong to the family Lamiaceae and commonly grow in damp and moist soils across Europe, Africa, Asia and Australia<sup>43</sup>. Around the world, essential oils from plants in the Lamiaceae (*Mentha* genus) are frequently utilised as insect repellents<sup>44</sup>. Essential oil from *Mentha* spp. has been reported to resist malaria, filarial, and yellow fever vectors for 60–180 min<sup>45</sup>. Due to its antioxidant and antimicrobial properties, *Mentha* spp. improves immunity and digestion<sup>46</sup>. Cineole, limonene, methone, methylacetate, and menthol are active compounds in their essential oil<sup>47</sup>. *Mentha* leaves consist of 0.5-4% essential oil. *Mentha* EO contains 25-78% methanol, 14-36% menthol, and 3.5-14% cineol, which show mosquito-repellent properties<sup>48</sup>. Cotton fabric treated with 25% *Mentha* plant extract for 90 min, dried for 5 min at 90°C, and mordanted with 10% citric acid showed 100% mosquito repellent activity<sup>43</sup>.

#### **Citrus species**

The genus *Citrus* (also known as agrumes) belongs to the family Rutaceae, and the subfamily Aurantioideae is one of the most popular crops throughout the world, which includes a large number of species. Southeastern Asia is believed to be the centre of origin of *Citrus*. *Citrus* fruits are a good source of nutrition with ample vitamin C, providing average vitamin C concentration ranging from 23-83 mg/100g fresh weight. Along with vitamin C, it also provides Vitamin B1 and Vitamin B6<sup>49</sup>. The components present in citrus food include sugars, organic acids, and several secondary metabolites such as carotenoids, limonoids, alkaloids, coumarins, flavonoids and essential oils<sup>50,51</sup>, among all these components, flavonoids are found in abundance<sup>52</sup>. The fruit of *Citrus* exhibits a number of biological activities, including anti-inflammatory activity, anticancer activity, antioxidant activity, anti-allergy activity, antimicrobial activity, cardiovascular effect, and neuroprotective effects<sup>53</sup>. The oil derived from the peel of *Citrus reticulata* (Mandarin orange) has 90-95% limonene, which has an effective potential to repel mosquito vectors and other insects<sup>54</sup>.

According to the study by Visakh *et al.*<sup>55</sup>, the essential oil of *Citrus maxima* peel showed effective larvicidal activity against *Ae. aegypti* and *Cx. tritaeniorhynchus* species of mosquitoes with LC<sub>50</sub> values of 47.07±2.4 mg/mL and 58.04±2.8 mg/mL. Similarly, in their study, Sarma *et al.*<sup>56</sup> reported that the essential oils extracted from the leaf and peel of *Citrus aurantifolia* possess ovicidal, larvicidal, and adulticidal activity against the mosquito *Ae. aegypti*.

Further, the ethanolic peel extract of *Citrus sinensis* was found to be highly effective against *Ae. aegypti* and *Cx. quinquefasciatus* with adulticidal and larval LC<sub>50</sub> value below 500 ppm with more than 50% repellency at 150 ppm concentration till 3 h<sup>57</sup>.

#### **Ocimum species**

The genus *Ocimum* is, well known for its nutritive and medicinal value, is a member of the family Lamiaceae. *Ocimum basilicum* (Common basil), *Ocimum sanctum* (Holy basil), *Ocimum canum* (Dulal Tulsi), *Ocimum micranthum* (Peru basil), *Ocimum gratissimum* (African basil), *Ocimum kilimandscharicum* (Camphor basil) are some known important species of the genus *Ocimum* that grow in different parts of the world including Asia, Africa, Central and Southern America<sup>58,59</sup>. The major chemical constituents present in *O. sanctum* are β-

caryophyllene,  $\beta$ -elemene, eugenol, germacrene, oleanolic acid, linalool, rosmarinic acid and ursolic acid<sup>60</sup> and in *O. basilicum* are linalool, cinnamic acid, and eucalyptol<sup>61</sup>. Various types of phytochemicals like phenolic compounds, saponins and flavonoids are reported to be present in *Ocimum* species that have various biological activities, including anticancer, antidiabetic, antioxidant, antimicrobial, anti-inflammatory, wound-healing, radioprotective effects and cardioprotective effects<sup>58,62</sup>. Many studies have reported the effective mosquito repellent and larvicidal activity of the plant within *Ocimum* against various species of mosquitoes<sup>63-65</sup>.

The lotion prepared from the essential oil of *O. basilicum* provides repellency of 2.30, 3, and 4 hours against *Anopheles* mosquito at 2, 4, and 6% concentration<sup>64</sup>. A study performed by Oparaocha *et al.*<sup>66</sup> showed that lotion prepared from the volatile oil of *O. gratissimum* provides effective protection against the bite of different mosquito vectors. On the other hand, a study reported that chloroform and methanol leaf extract of *O. sanctum* exhibits larvicidal activity against *Ae. aegypti* and *Cx. quinquefasciatus*.

On the other hand, the LC<sub>50</sub> values of chloroform and methanol plant leaf extracts against the larvae of *Ae. aegypti* were 150.40 and 175.26 ppm and against the larvae of *Cx. quinquefasciatus* were 93.92 and 82.12 ppm<sup>67</sup>. Baba *et al.*<sup>63</sup> studied the effectiveness of *O. basilicum* oil against *An. gambiae* and *Cx. quinquefasciatus*, and the results showed that a 100% concentration of its oil exhibits repellent potential against *An. gambiae* and *Cx. quinquefasciatus* with mean protection time of 303 and 249 min, respectively.

#### **Geranium and other related species**

*Geranium*, commonly known as cranesbill, is a plant commonly found in temperate and mountain regions. Geranium belongs to the family Geraniaceae. It attains a height of 1-3 feet<sup>68</sup>. The major constituents present in geranium oil are citronellol (38%), geraniol (16%), citronellyl formate (10.4%), and linalool (6.45%)<sup>69</sup>. Over 2% concentration of *Geranium* oil exhibit 100, 98, 94, and 90% larvicidal activity against 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> instar larvae of *Cx. quinquefasciatus*<sup>70</sup>. However, *Geranium* oil, along with lavender oil, exhibited weak repellency when diluted at 1% in 1, 2-propanediol but showed 100% repellency when diluted at 30% in 1, 2-propanediol<sup>71</sup>.

*Pelargonium citrosum* smells like citronella oil and is reported to repel the mosquitoes<sup>72</sup>. Homemade

fabric softener treated with geranium oil improved fabric quality and resulted in 24% mosquito repellency<sup>73</sup>.

#### **Cymbopogon species**

These plants are well known for their high essential oil content and effective repellent activity. The genus *Cymbopogon* belongs to the family Poaceae (Graminaceae) and consists of around 144 species distributed mainly in subtropical and tropical areas of America, Asia and Africa. The major bioactive components present in *Cymbopogon* species are limonene, geraniol, citronellol, neral, geranial, piperitone etc<sup>74</sup>. The constituents present in this plant have several health impacts, including antimicrobial activity, antioxidant activity, anti-inflammatory activity, insecticidal activity, hepatoprotective activity and anticancer activity<sup>75</sup>.

The active components in citronella oil, geraniol and citronellol showed 78 and 77% repellency for 60 min against the vector *A. aegypti*<sup>76</sup>. Essential oil of *Cymbopogon citratus* (Lemongrass) possesses 100% ovicidal activity at 300 ppm and larvicidal activity against 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> instar larvae of *Cx. quinquefasciatus* at LC<sub>50</sub> values of 144.54, 165.70 and 184.18<sup>77</sup>. A study conducted by George *et al.*<sup>7</sup> revealed that oil extracted from the leaves of *C. citratus* showed 43% repellency and 100% mortality against mosquito species after 18 min of its application. Similarly, the essential oil of *C. martini* was also reported for its 100% repellency for 2 h against *Ae. aegypti* at the concentration of 100 ppm<sup>78</sup>.

#### **Eucalyptus species**

The genus *Eucalyptus* belongs to the large myrtle family called Myrtaceae and includes more than 900 species. Some of the species of this genus have been reported to possess antimicrobial, antibacterial, antifungal and antioxidant activity<sup>79</sup>. Major chemical constituents present in *Eucalyptus* species are  $\alpha$ -terpineol,  $\alpha$ -pinene,  $\alpha$ -eudesmol,  $\alpha$ -humulene,  $\alpha$ -terpinyl acetate,  $\beta$ -myrcene,  $\beta$ -pinene,  $\beta$ -phellandrene, 1,8-cineole,  $\gamma$ -terpinene, benzene, borneol, benzene methanol, caryophyllene oxide, fenchyl alcohol, geraniol, globulol, guaiol, linalyl propionate, limonene, myrtenolnerolidol, pinocarvone, piperitone, etc<sup>80</sup>. *Eucalyptus* species are known for their high essential oil content and repellent activity. The oil prepared from *Eucalyptus* provides 93.37 and 92.04% protection against mosquito *Cx. quinquefasciatus*, at 50 and 100% (v/v) concentrations, respectively, with the protection time up to 240 min<sup>29</sup>.

A study showed that the 8% concentration (in 70% alcohol) of oil extracted from leaves of *Eucalyptus tereticornis* and *Eucalyptus deglupta* have an effective repellent activity of 91.91 and 94.05% against *Cx. quinquefasciatus* for 4 h<sup>80</sup>.

#### **Pinus species**

Pine trees are coniferous, evergreen and grow 3-80 meters tall. It belongs to the family Pinaceae. These trees are commonly found in the northern hemisphere. Pine trees are known to have mosquito-repellent properties as well<sup>81</sup>. Essential oil from *Pinus* showed larvicidal activity with LC<sub>50</sub> values between 82-112 ppm. Pine oil provides 100% protection for 11 h against *An. culicifacies* and 97% protection for 9h against *Cx. quinquefasciatus*<sup>82</sup>. Essential oils of *P. brutia*, *P. halepensis* and *P. stankeviczi* were able to inactive larvae and showed larvicidal activity (LC<sub>50</sub> values 67.04 mg/L and 70.21 mg/L). The essential oil from these species of *Pinus* showed high repellent activity at the dose of 0.2 µL/cm<sup>83</sup>.

#### **Discussion**

According to recent estimates of the global total diversity of all land plants (bryophytes, lycophytes, ferns, gymnosperms and angiosperms) are now in the region of 450,000 known species<sup>134,135</sup> with diversity strongly concentrated in the humid tropics and around another 15% or so still estimated to be awaiting discovery<sup>136</sup>: of this total, vascular plants are estimated to represent around 383,671 species with 13,269 species of lycophytes and pteridophytes<sup>137</sup> while flowering plants are estimated to be 369,434 species and seed plants some 369,434 species<sup>135</sup>; of bryophytes there are 20,240 species (12,754 are mosses and 7,486 are hornworts and liverworts)<sup>138,139</sup>. Perhaps a third of all land plants are at risk of global extinction, including those that are undescribed so far or are described but otherwise data deficient. Therefore, it is vital to screen these plant species for their specific human use, especially in vector management, towards discovering new ovicides, larvicides, adulticides and repellents. However, in this regard, only a small fraction of plant species have been screened out and evaluated as an important strategy for controlling agricultural pests, urban viruses or vectors of medical-veterinary importance. Thus, these unscreened plant species are more likely to have unusual traits that could be useful in the future.

This systematic review was conducted to analyse the repellency effect of various plant extracts and essential oils against several mosquito species for their management. Some of the most commonly used botanical plant genera with their effective repellent properties include – *Ageratum*, *Azadirachta*, *Calendula*, *Calotropis*, *Carica*, *Cinnamomum*, *Citrus*, *Cymbopogon*, *Eucalyptus*, *Geranium*, *Jatropha*, *Juniperus*, *Lantana*, *Mentha*, *Myrtus*, *Nepeta*, *Ocimum*, *Olea*, *Pinus*, *Piper*, *Rosmarinus*, *Solanum*, *Syzygium*, *Tagetes*, *Thymus*, *Zingiber* and so on (Table 1). DEET (N,N-diethyl-3-methylbenzamide) is one of the most effective synthetic repellents widely used but has some potential risks to human health<sup>140</sup>. To tackle this problem, many recent studies have focused on non-toxic plant-based mosquito repellents compared to synthetic compounds, which are considered safer and prevent the accumulation of toxic chemicals in the environment. Recent studies have shown that long-term, unregulated, and disproportionate use of synthetic compounds has severe negative effects on the environment and can lead to mosquitoes developing resistance and insensitivity to these compounds<sup>141</sup>. Essential oil and volatile compounds derived from plants can provide sufficient protection time against mosquitoes. Several plants and their constituents have been studied from this prospective for their effective mosquito-repelling properties (Table 1). Essential oils from various plants have been thoroughly investigated, and their ability to keep mosquitoes away makes them a preferred natural compound (Table 1). Recently, Pavela<sup>142</sup>, reported that most essential oils with a value of LC<sub>50</sub> less than 100 ppm against mosquito larvae were derived from five botanical plant families: Apiaceae, Cupressaceae, Lamiaceae, Myrtaceae and Rutaceae.

Regarding the mode of action, essential oils can produce severe neurotoxic effects on insects through several targets, such as inhibiting acetylcholinesterase enzyme in the cholinergic system or acting on the Octopamine receptor and GABA receptor<sup>143-145</sup>. However, because they are volatile substances, this gives rise to the problem of their prolonged application in mosquito control. This issue has been solved in recent years by extending the effectiveness of essential oils with the help of innovative technologies like microencapsulation and Nano emulsion<sup>146</sup>. Overall, the review suggests that plant-based mosquito repellents have the potential to provide prolonged and expected protection against

various types of mosquitoes without causing any notable adverse effects on human health and the environment.

### Conclusion

The mosquito menace is faced worldwide as it leads to several diseases. Currently available chemical mosquito repellent has side effects as they are harmful to the body and can cause allergic reactions. Plant-based mosquito repellents are considered safe and eco-friendly means of prevention compared to long-established chemical repellents. In this regard, essential oils from plant species are envisaged to be more effective. Several plant species of the genera *Azadirachta*, *Citrus*, *Lantana*, *Ocimum*, *Calotropis*, *Zingiber*, *Mentha*, and *Pinus* contain certain active compounds that can be extracted and used as a repellent. Different repellents have different modes of action, and different mosquito species react differently to the same repellent. These plants are beneficial for preparing natural plant-based repellent, can also be used for preparing many medicines, and have scope for value-added products. The conclusion of our review study suggests that the development of natural or plant-based mosquito repellents will help to decrease the adverse effects or side effects of synthetic repellents and can be used as a cheap, safe, and eco-friendly alternative to synthetic repellents. However, more research is needed in this field, and we need to screen more plants for active compounds that contain repellent activities.

### Conflicts of interest

All the authors declare no conflict of interest.

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