

## Chemical composition, actividad larvicide, insecticide and repellent of essential oil

### *Aedes aegypti*

Composição química, atividade larvívica, insetívica e repelente e larvívica de óleos essenciais frente ao *Aedes aegypti*

Composición química, actividad larvívica, insectívica y repelente de los aceites esenciales contra *Aedes aegypti*

Received: 01/13/2022 | Reviewed: 01/21/2022 | Accept: 01/27/2022 | Published: 01/28/2022

#### **Antônia Laíres da Silva Santos**

ORCID: <https://orcid.org/0000-0001-6233-6173>  
Federal University of Piauí, Brazil  
E-mail: serialufpi@gmail.com

#### **Felipe Pereira da Silva Santos**

ORCID: <https://orcid.org/0000-0001-9079-952X>  
Federal University of Piauí, Brazil  
E-mail: felipe.p.santos1@hotmail.com

#### **Alyandra de Sousa Nascimento**

ORCID: <https://orcid.org/0000-0001-5059-7595>  
Federal University of Piauí, Brazil  
E-mail: alyandra.ufpi@gmail.com

#### **Layana Karine Farias Lima**

ORCID: <https://orcid.org/0000-0002-1431-2422>  
Federal University of Piauí, Brazil  
E-mail: layana\_farias@hotmail.com

#### **Lucas Mendes Feitosa Dias**

ORCID: <https://orcid.org/0000-0002-8706-9945>  
Federal University of Piauí, Brazil  
E-mail: lucas.mendes1610@hotmail.com

#### **Geovanna Trajano Oliveira da Silva**

ORCID: <https://orcid.org/0000-0003-2549-6703>  
Federal University of Piauí, Brazil  
E-mail: geovannatrajano@gmail.com

#### **Mahendra Rai**

ORCID: <https://orcid.org/0000-0001-7645-9801>  
University Sant. Gadge Baba Amravati, India  
E-mail: indobraz77@gmail.com

#### **Chistiane Mendes Feitosa**

ORCID: <https://orcid.org/0000-0001-8013-1761>  
Federal University of Piauí, Brazil  
E-mail: chistiane@ufpi.edu.br

### **Abstract**

Dengue is transmitted by the mosquito *Aedes aegypti*, which is controlled by insecticides and repellents. The plant-based essential oils are used as excellent repellents. Therefore, the present review is essential for understanding the efficacy of essential oils against mosquitoes. The articles related to essential oils were searched from 2014 to 2022 in Pubmed, Science Direct, LILACS, Scielo, and Google Scholar using the following keywords-essential oil, *Aedes aegypti*, and repellents. A total of 280 plants were extracted for EOs from 33 families. The most plants belong to Lamiaceae (45.4%), followed by Myrtaceae (38.3%) and Rutaceae (28.4%). The metabolites in EOs with the maximum repellent/larvicidal activity include  $\beta$  - caryophyllene,  $\alpha$  - pinene, 1,8 - cineol, linalool, and eugenol, the lethal concentrations ranged from 40 to 120 ppm. These results support the view that essential oils are promising in the formulation of repellents, larvicides, insecticides, and pesticides.

**Keywords:** *Aedes aegypti*; Insecticide; Essential oil; Larvicidal; Repellent.

### **Resumo**

A dengue transmitida pelo mosquito *Aedes aegypti* é controlada por larvívica, insetívica e repelente. Os óleos essenciais à base de plantas são usados como excelentes repelentes. Portanto, a presente revisão é essencial para o entendimento da eficácia dos óleos essenciais contra os mosquitos. Os artigos relacionados a óleos essenciais foram

pesquisados de 2014 a 2022 no Pubmed, Science Direct, LILACS, Scielo e Google Scholar usando as seguintes palavras-chave: óleo essencial, *Aedes aegypti* e repelentes. Um total de 280 plantas foram extraídas para EOs de 33 famílias. A maioria das plantas pertence a Lamiaceae (45,4%), seguida por Myrtaceae (38,3%) e Rutaceae (28,4%). Os metabólitos em OE com atividade repelente / larvicida máxima incluem  $\beta$ -cariofileno,  $\alpha$ -pineno, 1,8-cineol, linalol e eugenol, as concentrações letais variaram de 40 a 120 ppm. Esses resultados apóiam a visão de que os óleos essenciais são promissores na formulação de repelentes, larvicidas, inseticidas e pesticidas.

**Palavras-chave:** *Aedes aegypti*; Inseticida; Óleo essencial; Larvicida; Repelente.

### Resumen

El dengue es transmitido por el mosquito *Aedes aegypti*, que es controlado por insecticidas y repelentes. Los aceites esenciales de origen vegetal se utilizan como excelentes repelentes. Por lo tanto, la presente revisión es esencial para comprender la eficacia de los aceites esenciales contra los mosquitos. Los artículos relacionados con los aceites esenciales se buscaron entre 2014 y 2022 en Pubmed, Science Direct, LILACS, Scielo y Google Scholar utilizando las siguientes palabras clave: aceite esencial, *Aedes aegypti* y repelentes. Se extrajeron un total de 280 plantas para OE de 33 familias. La mayoría de plantas pertenecen a Lamiaceae (45,4%), seguidas de Myrtaceae (38,3%) y Rutaceae (28,4%). Los metabolitos en los AE con la máxima actividad repelente / larvicida incluyen  $\beta$ -cariofileno,  $\alpha$ -pineno, 1,8-cineol, linalol y eugenol; las concentraciones letales oscilaron entre 40 y 120 ppm. Estos resultados apoyan la opinión de que los aceites esenciales son prometedores en la formulación de repelentes, larvicidas, insecticidas y pesticidas.

**Palabras clave:** *Aedes aegypti*; Insecticida; Aceite esencial; Larvicida; Repelente.

## 1. Introduction

*Aedes aegypti* (Diptera: Culicidae) is the main vector responsible for diseases such as Dengue, Chikungunya and Zika. Such diseases have contributed to the increase in significant human morbidity and mortality in many countries with different economic, climatic and social characteristics. Mosquito control and personal protection are currently the most important measures to control the diseases caused. The use of larvicides, repellants and insecticides is a more practical and economical way to prevent the transmission of these diseases to human beings. Although synthetic insecticides and repellants are still the main means of protecting crops, the use of alternative methods has increased, due to the current need to overcome problems such as resistance and reducing the risks of environmental contamination caused by non-biodegradable synthetic products; one of these searches is based on plants (Pichersky & Gershenson, 2002; Drewes et al., 2006).

The use of substances extracted from plants (Essential Oils – EOs) with repellent and insecticidal action, originated in China, later expanding to the West. Due to the difference in volatility between the components of the liquid, distillation is the main process for separating these constituents, as it is based on the difference in composition of the constituents in the liquid and vapor phase in equilibrium (Almeida, 2005; Latyki, 2017).

During World War II some synthetic repellants were developed to protect humans from mosquito bites, with DEET (N,N-diethyl-m-toluamide) not only being a broad-looking repellent, but also the most effective and persistent on the skin. Herbal repellants, even with comparable or even better activities, tend to be short-lived and their effectiveness depends on their volatility, which makes synthetics more effective and more durable than natural products (Dethier, 1956; Isman, 2006; Nerio et al., 2010).

With 46,781 plant species, Brazil has the richest flora in the world (about 19% of the world's flora). In number of species, Legumes (2,144), Myrtaceae (1,038) and Rubiaceae (1,000) are the largest families, with about 750 and 500 species being also notable for Apocynaceae and Lamiaceae, respectively (Giulietti et al., 2005; Flora of Brazil, 2020). In recent years, these families have been intensively studied regarding their morphology, anatomy, cytogenetics, ecology and mainly phytochemistry, as they make a significant contribution to the drug industry and a vast number of products and extracts with high pharmacological and therapeutic activities (Figuereido et al., 2007).

Larvicidal, repellent and insecticide properties have been targets for the development of new products, as since 2008 Brazil has become the largest consumer of pesticides in the world, using around 700 thousand tons of synthetic products.

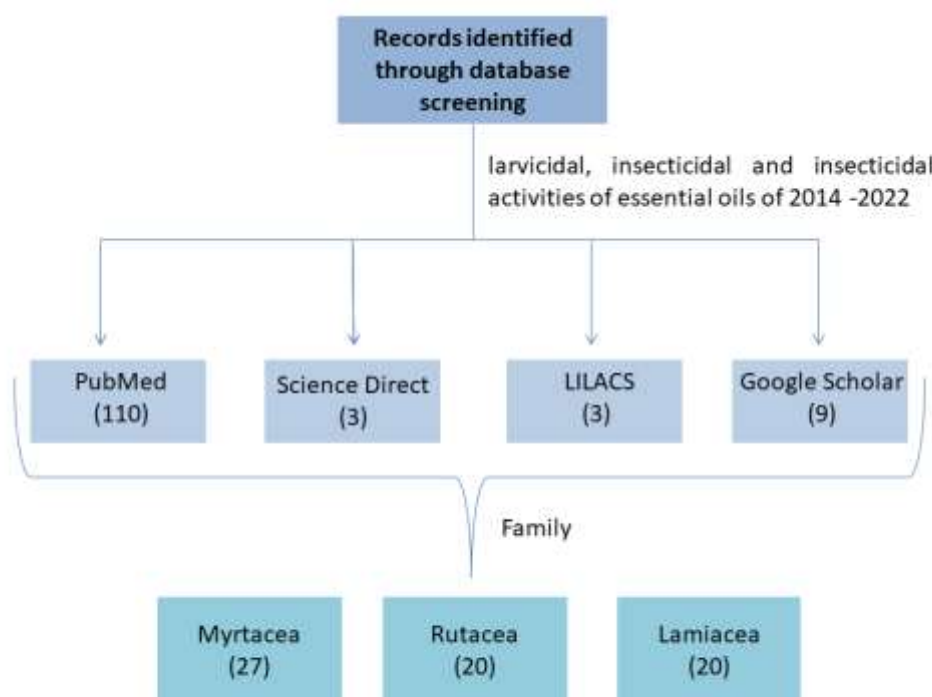
Significant restructuring in the industrial sector due to the growth in the number of active substances extracted from plants present in the market has contributed for this change to happen. Because nature has several substances that play a defensive role, among these substances we can mention: pyrethroids, extracted from chrysanthemum (*Chrysanthemum c.*) (Trev.), nicotine from *Nicotiana tabacum* L., rotenone, extracted from *Derris* sp., *Lonchocarpus* sp. and azadirachtin, isolated from *Azadirachta indica* A. Juss. Monoterpenes and sesquiterpenes also stand out (Ootani, 2010; Morais & Marinho, 2016).

Aiming at a better assessment of the larvicidal and repellent activities of substances extracted from EOs against the *Aedes aegypti* mosquito, this review focuses on the evaluation of the main sources of EOs and main compounds that have activities against larvae and mosquitoes in the period between 2014 to 2022.

## 2. Methodology

In this study, an integrative review was performed from 2014 to 2022 using Web-based databases, including PubMed, Science Direct, LILACS and Google Scholar using the following keywords: essential oil, *Aedes aegypti*, larvicidal, insecticidal and repellents (Figure 1 and Table 1).

**Figure 1:** Article search and selection strategy.



Source: Authors.

**Table 1:** Works selection.

Platform	Found works	Selected works
PubMed	110	56
Science Direct	3	3
LILACS	3	2
Google Scholar	9	6

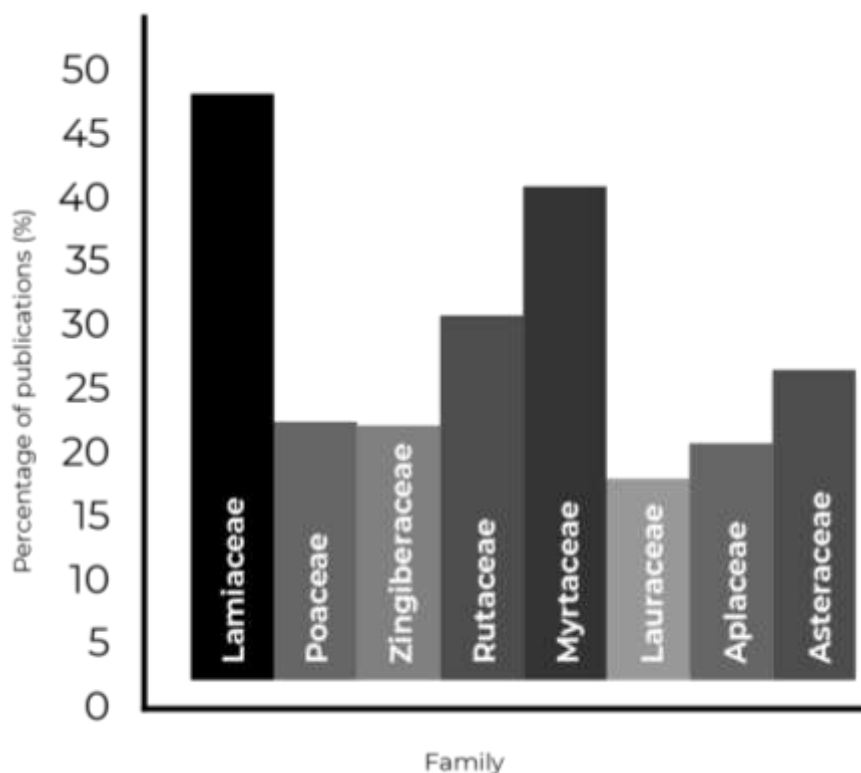
Source: Prepared by the research authors (2022).

### 3. Results and Discussion

#### 3.1 Botanical Description

About 280 EOs extracted from 33 different families have shown repellency against *Aedes aegypti*. Among the EO-producing plants, some families such as Lamiaceae (45.4%), Myrtaceae (38.3%) and Rutaceae (28.4%) were widely studied (Graph 1).

**Graph 1.** Families with the highest number of published works between 2014 and 2022.



Source: Authors.

The Lamiaceae (Figure 2) family, also known as *Labiatae*, is composed of several plant species of economic and medicinal interest. It covers 258 genera and 7,193 species, which can be found in both tropical and temperate regions, and in Brazil, there are on average 23 genera and 232 native species (Carréra et al., 2015; Trindade et al., 2016). Because they have important biosynthesized compounds due to secondary metabolism, the Lamiaceae family is known for its biological activities already reported in the literature and for its use as a spice (Lima & Cardoso, 2007).

**Figure 2.** Species of the Lamiaceae family (A - *Mentha longifolia*; B - *Lamium purpureum*; C - *Scutellaria galericulata*; D - *Ajuga reptans* and E - *Ocimum basilicum*).



Source: Authors.

Among the species with the highest repellent, larvicidal and oviposition activity from 2014 to 2022 were: *Ocimum americanum* (Field alfava), *Salvia apiana*, *S. elegans*, *S. leucanta*, *S. officinalis*, *Ocimum basilicum* (basil), *O. americanum* (Majericium - white), *Nepeta cataria* (cat weed), *Dracocephalum heterophyllum*, *Hyssopus officinalis* (holy herb), *Origanum scabrum* (Oregano), *Lavendula angustifolia* (Lavender), *Mentha piperita* (Peppermint), *Rosmarinus officinalis* (Rosemary), *Thymus serpyllum* (Dandelion herb), *Dracocephalum ruyschiana*, *D. foetidum*, *D. ruyschiana*, *D. fruticosum*, *D. peregrinum*, *Nepeta rтанjensens*, *Ocimum sanctum* (Majerica - saint), *Plectranthus amboinicus* (Spearment), *Lavandula angustifolia* (Lavender), *Origanum vulgare* (Oregano), *Vitex negundo* (Tree re chastity), *Stachys tmolea*, *Vitex trifolia* (Pepper), *Ocimum campechianum* (Basil - large), *Pogostemon cablin* (Patchouli) and *Mentha requienii*.

Among the species mentioned, the genera *Ocimum*, *Salvia* and *Origanum* presented higher activity against *Aedes aegypti* with lethal concentrations ranging from 6.2 to 80 ppm. Many plants of the Lamiaceae family produce OEs with insecticidal activity, the presence of many substances is related to this activity, acting as a larval growth inhibitor. Among them are  $\gamma$ -terpinene,  $\alpha$ -terpinene, linalool, methyl-eugenol, eugenol,  $\beta$ -pinene,  $\alpha$ -pinene, 1,8-cineol, and citronellol (Table 2). Such compounds may cause toxic interference with biochemical and physiological functions, thus acting as a repellent. The processes of absorption, inhalation, and ingestion of toxins can cause an adverse effect on insects (Lima & Cardoso, 2007; Simões et al., 2004).

**Table 2.** Substances and activities against *Aedes aegypti* reported in the literature.

SUBSTANCE	MOLECULAR FORMULA AND MASS (g.mol <sup>-1</sup> )	SPECIES	ACTIVITY	REFERENCE				
γ-terpinene	C <sub>10</sub> H <sub>16</sub> (136.23)	<i>Petroselinum crispum</i>	Larvicide and adulticide	Intirach et al. (2016); Raj et al. (2017); Huang et al. (2019); Galvão et al. (2019); Silva et al. (2019).				
		<i>Pleiospermium alatum</i>						
		<i>Mentha requienii</i>						
		<i>Vitex rotundifolia</i>						
		<i>Crossostephium chinense</i>						
		<i>Lippia gracilis</i>						
		<i>Piper hispidinervum</i>						
		<i>Piper aduncum</i>						
		Linalool			C <sub>10</sub> H <sub>18</sub> O (154.25)	<i>Curcuma longa</i>	Insecticide, larvicide, adulticide and repellent	Auysawasdi et al. (2016); ÖZEK et al. (2016); Araujo et al., (2016); Santana et al. (2016); Demirci et a. (2017); Carroll et al. (2017); Demirci et al. (2017); Nascimento et al. (2017); Ramos et al. (2017); Silva et al., (2018); Satyal et al. (2019); Huang et al. (2019); Silva et al. (2019); Huang et al. (2020); Bailão, E. F. L. C., (2022).
						<i>Eucalyptus globulus</i>		
<i>Citrus aurantium</i>								
<i>Dracocephalum ruyschiana</i>								
<i>D. foetidum</i>								
<i>D. moldavica</i>								
<i>D. fruticosum</i>								
<i>D. peregrinum</i>								
<i>Syzygium aromaticum</i>								
<i>Citrus sinensis</i>								
<i>Piper augustum</i>								
<i>P. corrugatum</i>								
<i>P. curtispicum</i>								
<i>P. darianense</i>								
<i>P. grande</i>								
<i>Curcuma longa</i>								
<i>Eucalyptus globulus</i>								
<i>Citrus aurantium</i>								
<i>Rhanterium epapposum</i>								
<i>Origanum onites L</i>								
<i>Origanum onites L.</i>								
<i>Xylopi laevigata</i>								
<i>Xylopi frutescens</i>								
<i>Lippia pedunculosa</i>								
<i>Mentha piperita</i>								
<i>Aristolochia trilobata</i>								
<i>Severinia monophylla</i>								
<i>Arisaema fargesii</i>								
<i>Piper hispidinervum</i>								
<i>Piper aduncum</i>								
<i>Illicium verum</i>								
<i>Pimenta dioica</i>								
<i>Myristica fragrans</i>								
Methyl-eugenol	C <sub>11</sub> H <sub>14</sub> O <sub>2</sub> (178.23)	<i>Mentha piperita</i>	Insecticide, larvicide and adulticide	Voriss et al. (2018); Sarma et al., (2019).				
		<i>Allium sativum</i>						
		<i>Ocimum sanctum</i>						
		<i>Callistemon linearis</i>						
		<i>Eucalyptus maculata</i>						
		Eugenol			C <sub>10</sub> H <sub>12</sub> O <sub>2</sub> (164.20)	<i>Plectranthus barbatus</i>	Larvicide, adulticide and repellent	Govindarajan et al. (2016); Özek et al. (2016); Araujo et al. (2016); Soonwera et al. (2016); Affonso et al. (2018); Muturi et al. (2017); Tyagi et al. (2017); Voriss et al. (2018); Huang et al. (2019); Sarma et al. (2019); Scalvenzi et al. (2019); Pandiyan et al. (2019); Harikampakdee et al. (2018); Lucia et al. (2020); Oliveira et al. (2020); Almadiy et al. (2020); Santos et al. (2020).
<i>Dracocephalum ruyschiana</i>								
<i>D. foetidum</i>								
<i>D. moldavica</i>								
<i>D. fruticosum</i>								
<i>D. peregrinum</i>								
<i>Syzygium aromaticum</i>								
<i>Citrus sinensis</i>								
<i>Cymbopogon citratus</i>								
<i>Angelica archangelica</i>								
<i>Ferula assafoetida</i>								
<i>Citrus bergamia</i>								
<i>Cedrus deodora</i>								
<i>Cymbopogon nardus</i>								
<i>Syzygium aromaticum</i>								
<i>Eucalyptus globulus</i>								
<i>Allium sativum</i>								
<i>Pelargonium graveolens</i>								
<i>Citrus paradisi</i>								
<i>Dipterocarpus jourdainii</i>								
<i>Lavandula angustifolia</i>								
<i>Cymbopogon flexuosus</i>								
<i>Leptospermum scoparium</i>								



		<p><i>Citrus sinensis</i>  <i>Origanum vulgare</i>  <i>Cymbopogon martinii</i>  <i>Mentha piperita</i>  <i>Phoebe porosa</i>  <i>Rosmarinus officinalis</i>  <i>Melaleuca alternifolia</i>  <i>Jasminum officinale</i>  <i>Cinnamomum camphora</i>  <i>Cedrus deodara</i>  <i>Illicium verum</i>  <i>Pimenta dioica</i>  <i>Myristica fragrans</i>  <i>Arisaema fargesii</i>  <i>Mentha piperita</i>  <i>Allium sativum</i>  <i>Ocimum sanctum</i>  <i>Callistemon linearis</i>  <i>Eucalyptus maculata</i>  <i>Ocimum campechianum</i>  <i>Ocotea quixos</i>  <i>Piper aduncum</i>  <i>Illicium verum</i>  <i>Trachyspermum ammi</i>  <i>Ocimum gratissimum</i></p>		
		<p><i>Lippia microphylla</i>  <i>Dracocephalum heterophyllum</i>  <i>Hyssopus officinalis</i>  <i>Eucalyptus globulus</i>  <i>Citrus aurantium</i>  <i>Curcuma longa</i>  <i>Piper augustum</i>  <i>P. corrugatum</i>  <i>P. curtispicum</i>  <i>P. darienense</i>  <i>P. grande</i>  <i>P. hispidum</i>  <i>P. jacquemontianum</i>  <i>P. longispicum</i>  <i>P. multiplinervium</i>  <i>P. reticulatum</i>  <i>P. trigonum</i>  <i>Pinus kesiya</i>  <i>Curcuma longa</i>  <i>Eucalyptus globulus</i>  <i>Citrus aurantium</i>  <i>Boswellia ovalifoliolata</i>  <i>Daucus carota</i></p>		
$\beta$ -pinene	C <sub>10</sub> H <sub>16</sub> (136.23)	<p><i>Lippia microphylla</i>  <i>Eugenia piauhiensis</i>  <i>Myrcia erythroxylon</i>  <i>Psidium myrsinites</i>  <i>Siparuna camporum</i>  <i>Curcuma longa</i>  <i>Croton jacobinensis</i>  <i>Amomum subulatum</i>  <i>Eucalyptus nitens</i>  <i>Lippia gracilis</i>  <i>Eucalyptus globulus</i>  <i>Azadirachta indica</i>  <i>Salvia officinalis</i>  <i>Eucalyptus globulus</i></p>	Repellent, larvicide and insecticide	<p>Simões et al. (2015); Stappen et al. (2015); Auysawasdi et al., (2016); Santana et al. (2016); Govindarajan et al. (2016); Auysawasdi et al. (2016); Benelli et al. (2018); Muturi et al. (2019).</p>
1,8-cineol	C <sub>10</sub> H <sub>18</sub> O (154.25)	<p><i>Lippia microphylla</i>  <i>Eugenia piauhiensis</i>  <i>Myrcia erythroxylon</i>  <i>Psidium myrsinites</i>  <i>Siparuna camporum</i>  <i>Curcuma longa</i>  <i>Croton jacobinensis</i>  <i>Amomum subulatum</i>  <i>Eucalyptus nitens</i>  <i>Lippia gracilis</i>  <i>Eucalyptus globulus</i>  <i>Azadirachta indica</i>  <i>Salvia officinalis</i>  <i>Eucalyptus globulus</i></p>	Repellent, larvicide and insecticide	<p>Simões et al. (2015); Dias et al., (2015); Auysawasdi et al. (2016); Pinto et al. (2016); Costa et al., (2017); Govindarajan et al. (2019); VIVEKANANDHAN et al. (2019); Morales et al. (2019); <u>Yang</u> et al. (2020).</p>

		<p><i>Salvia apiana</i>  <i>Salvia elegans</i>  <i>Salvia leucantha</i>  <i>Salvia officinalis</i>  <i>Nigella sativa</i>  <i>Murraya exótica</i>  <i>Plectranthus barbatus</i>  <i>Zingiber nimmonii</i>  <i>Lantana montevidensis</i>  <i>Syzygium lanceolatum</i>  <i>Piper augustum</i>  <i>P. corrugatum</i>  <i>P. curtipicum</i>  <i>P. darienense</i>  <i>P. grande</i>  <i>P. hispidum</i>  <i>P. jacquemontianum</i>  <i>P. longispicum</i>  <i>P. multiplinervium</i>  <i>P. reticulatum</i>  <i>P. trigonum</i>  <i>Cymbopogon citratus</i>  <i>Syzygium aromaticum</i>  <i>Syzygium aromaticum L</i>  <i>Xylopia laevigata</i>  <i>Xylopia frutescens</i>  <i>Lippia pedunculosa</i>  <i>Severinia monophylla</i>  <i>Salvia officinalis</i>  <i>Plectranthus amboinicus,</i>  <i>Mentha requienii</i>  <i>Vitex rotundifolia</i>  <i>Crossostephium chinense</i></p>	
$\beta$ -caryophyllene	C <sub>15</sub> H <sub>24</sub> (204.35)		Larvicide and repellent
			Ali et al. (2014); Raj et al. (2015); Krishnamoorthy et al. (2015); Govindarajan et al. (2016); Blythe et al. (2016); Benelli et al. (2016); Santana et al. (2016); Soonwera et al. (2016); Ffonso et al. (2017); Nascimento et al. (2017); Satyal et al., (2019); Morales et al., (2019); Huang et al., (2019); Borrero-landazabal et al., (2020).

Source: Authors.

Myrtaceae (Figure 3) is a very complex family that accounts for about 1.32% of all known Angiosperms, divided into two large subfamilies: Myrtoideae and Leptospermoideae and has 142 genera and over 5,500 species. In Brazil, it is among the most important families in most vegetation formations (Lima et al., 2015; Stadnik et al., 2016).

**Figure 3.** Species of the Lamiaceae family (A - *Eucalyptus globulus*; B - *Syzygium aromaticum*; D - *Eucalyptus globulus*; E - *Psidium guajava*).



Source: Authors.



Its species have great economic potential because they are used as food, as the species of *Psidium guajava* L. of guava and *Eugenia uniflora* L. of "pitanga", consumed in the form of juice, sweets, jellies and ice cream. Some species such as *Eugenia sprengelii* and *Leptospermum scoparium* are used as ornamental plants and *Eucalyptus globulus* and *Myrciaria dubia* stand out in folk medicine for the treatment of influenza, nasal congestion and sinusitis (Lorenzi et al., 2006; Lorenzi & Matos, 2002; Lorenzi & Souza, 2001, Morais et al., 2014).

OEs extracted from species of the Myrtaceae family have a lethal concentration ranging from 7.9 to 106.9 ppm. Species include *Eucalyptus globulus* (Eucalyptus), *Melaleuca leucadendron* (Seven capotes), *Syzygium aromaticum* (Clove), *Eugenia piauhiensis* (Guava), *Eucalyptus grandis* (Pink Eucalyptus), *Eucalyptus camaldulensis* (Red Eucalyptus). *Myrcia sylvatica* (Cumatê), *Eucalyptus citriodora* (Eucalyptus lemon), *Syzygium lanceolatum* (Jambo), *Melaleuca quinquenervia* (myrtle), *Eucalyptus nitens* (Eucalypt robusta), *Leptospermum scoparium* (Erica), *Melaleuca alternifolia* Call (Tree) linearis (Bottle - brush) and *Eucalyptus maculata* (Spotted Eucalyptus). Eugenol, eugenyl acetate, and  $\beta$ -caryophyllene (Table 2) are the major compounds identified in EOs of the Myrtaceae family.

The family is recognized for its opposite leaves, summertime inflorescences, flowers with stamens arranged in a ring and variable fruits, the Rutaceae family (Figure 4) consists of 150-162 genera and 1500-2096 species, are widely distributed throughout the humid, tropical and temperate regions in the world; and about 29 genera 182 species are found in Brazil (Melo & Zickel, 2004; Albuquerque, 1976; Pirani et al., 2002).

**Figure 4.** Species of the Lamiaceae family (A - *Citrus aurantifolia*; B - *Murraya exotica*; C - *Citrus paradisi*; D - *Citrus sinensis*; E - *Pleiospermium alatum*).



Source: Authors.

An important feature of this family reported by Pirani et al. (2002) is the development of strong aromatic oil-producing glands, which contributes to the genera of this family being responsible for several aromas, thus having a great economic importance. Several secondary metabolites are commonly found, such as alkaloids, especially those derived from

anthranilic acid, coumarins, lignans, flavonoids, terpenes and limonoids with a broad-spectrum of biological activities (Albarici et al., 2010).

Among the groups of plants with positive insecticidal activity are citrus fruits with a lethal concentration ranging from 43.7 to 538 ppm, among which are *Citrus aurantifolia* (Lemon), *C. hystrix* (combava), *Fortunella japonica* (Ximxim), *C. sinensis* (Orange), *Exotic Murraya* (Jasmin - Orange), *C. grandis* (Cimbo), *Amyris balsamifera* (Torch Wood), *C. aurantium* (Bitter Orange), *Swinglea glutinosa* (Lemon Swinglea), *C. bergamia* (Orange - Clove), *C. paradisi* (Grapefruit), *Zanthoxylum limonella* (Cat's hand), *Pleiospermium alatum* (lime orange), *Severinia monophylla* and *Zanthoxylum limoncello*. The genus Citrus is the most prominent in larvicidal activity, such property may be linked to the abundance of limonene (Table 2) present in the EO.

Pavela (2015) presented a bibliographic review from 2003 to 2014, in which the OEs of best lethal activity against mosquitoes are reported in five families: Lamiaceae, Cupressaceae, Rutaceae, Apiaceae, and Myrtaceae, confirming the results presented here.

### 3.2 Metabolites responsible for activity against *Aedes aegypti*

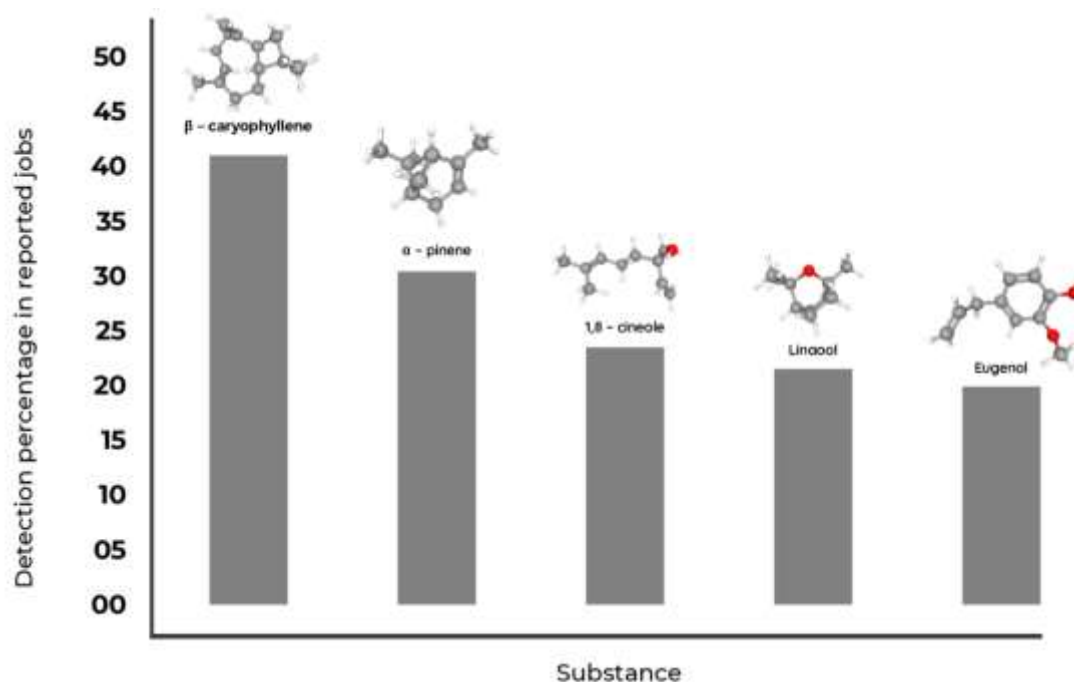
The secondary metabolites in plants are composed of hydrocarbons (terpenes and sesquiterpenes) and oxygenated compounds (alcohols, esters, ethers, aldehydes, ketones, lactones, phenols, and phenolic ethers) that have pharmaceutical properties and are responsible for the characteristic odor of plants. Such compounds present high vapor pressures under atmospheric conditions, which favors their significant release into the air (Pichersky & Gershenzon, 2002; Edris, 2007).

The basic route of biosynthesis of these volatile constituents is conveniently treated in three stages. The first is the formation of the C<sub>5</sub> basic unit by two alternative pathways: the mevalonate pathway from acetyl-CoA located on the cytosol and is responsible for providing C<sub>5</sub> units for sesquiterpenes and the methylthritol phosphate pathway. from pyruvate and glyceraldehyde-3-phosphate located on plastids, providing IPP (isopentyl diphosphate) and DMAPP (dimethylallyl diphosphate) for hemiterpene, monoterpene and diterpene biosynthesis (Dudareva et al., 2004; Dewick, 2009).

In the second phase of terpene biosynthesis, condensation reactions of prenyltransferases catalyzed IPP and DMAPP units form the precursors of monoterpenes (geranyl diphosphate - GPP), sesquiterpenes (farnesyl diphosphate - FPP) and diterpenes (geranylgeranyl diphosphate). And in the third stage of formation of volatile terpenes involves the conversion of the various prenyl diphosphates, DMAPP (C<sub>5</sub>), GPP (C<sub>10</sub>), FPP (C<sub>15</sub>) and GGPP (C<sub>20</sub>), to hemiterpenes (isoprene and 2-methyl-3-butenes). 2-ol), monoterpenes, sesquiterpenes, and diterpenes, respectively. Terpene synthase enzymes are responsible for such reactions. Many terpene volatiles are direct products, but others are formed by transforming the starting products by oxidation, dehydrogenation, acylation, and other types of reactions (Edris, 2007; Dudareva et al., 2004).

Biosynthesis normally occurs in plant tissue epidermal cells, from which compounds can escape into the atmosphere or rhizosphere after being synthesized, so a wide variety of secondary metabolites have a number of effects such as herbivore and pathogen repulsion (Dudareva et al., 2004). These include  $\beta$  - caryophyllene;  $\alpha$  - pinene; 1,8 - cineol; linalool and eugenol (Table 2) as the main compound that presents larvicidal and repellent activity against *Aedes aegypti* in the last seven years (Graph 2).

**Graph 2.** Percentage of detection of chemical substances present in essential oils.



Source: Authors.

The 42.32% of the published reports provide evidence that  $\beta$ -caryophyllene is the most common bicyclic sesquiterpene found in OEs of various plants, such as *Erechtites hieraciifolius*, *Psidium myrsinites* and *Plectranthus amboinicus*. Krishnamoorthy et al. (2015) reported that the significant larvicidal activity of *Murraya exotica* essential oil may be due to the presence of important chemical constituents such as  $\beta$ -humulene (40.62%), benzyl benzoate (23.96%) and  $\beta$ -caryophyllene (7.05%), presenting an  $LC_{50}$  of 74.7 ppm against the 3rd and 4th stage larvae after 12h of exposure. The same is true for *Plectranthus amboinicus* EO,  $LC_{50}$  values for  $\beta$ -caryophyllene against *Aedes aegypti* was 74.46 ppm, a better value than for *Culex quinquefasciatus* mosquito which was 146.58 ppm (Huang et al., 2019). Huang et al. (2019) reported values  $LC_{50}$  of larvicidal activity of  $\beta$ -caryophyllene against species of *Aedes aegypti*, *Aedes albopictus*, *Anopheles subpictus*, *Culex pipens pallens*, *Culex tritaeniorhynchus* and *Ochlerotatus togoi*. The activity values  $LC_{50}$  ranged from 38.58. ppm to 97.90 ppm, and for *Aedes aegypti*  $\beta$ -caryophyllene presented the best activity (Hung et al., 2019).

Hung et al. (2019) mentioned the presence of  $\alpha$ -pinene in *Erechtites hieraciifolius* with 14.5% abundance and in *Erechtites valerianifolius* with 30.2% abundance, 10.6 and 12.5 ppm for the death of 50% of the larvae, such values suggest that  $\alpha$ -pinene has a more significant effect against *Aedes aegypti*. Ali et al. (2015) performed larvicidal activity against *A. aegypti* and *A. quadrimaculatus* in *Salvia* species that did not show significant activity against larvae due to the low abundance of  $\alpha$ -pinene. In *Angelica dahurica* and *A. pubescent* species presented by Tabanca et al. (2014) the abundance of  $\alpha$ -pinene was 46.3 and 37.6%, but it was 1-dodecanol and 1-tridecanol that showed larvicidal activity. *Pinus kesiya* EO demonstrated 21.8%  $\alpha$ -pinene with the lethal death concentration of 50% of the 57 ppm larvae (Govindarajan et al., 2016). Studies published from 2014 to 2019 related good larvicidal activity, ranging from 2.3 to 86 ppm for oils with  $\alpha$ -pinene in their composition.

The constituent of several plants OEs used in folk medicine, 1,8-cineol acts on the respiratory, cardiovascular and bone systems. *Lippia microphylla* has a  $LC_{50}$  of 75.6 ppm against *A. aegypti*, which can be applied to the presence of 1,8-cineol in its chemical composition (Simões et al., 2015). The values of 43.8 and 52.8 ppm are presented by Costa et al. (2017) and Costa et al. (2018) with 1,8-cineol as the major compound in OEs. Linalol, even present in many published studies,

presents low abundance and low activity compared to *A. aegypti*, Silva et al. (2016) found a high linalol abundance of around 51.8% in *M. piperita* EO more than low potential with the LC<sub>50</sub> of 367.6 ppm. For eugenol, it is observed that the articles with the best relative abundance are *Syzygium* species of the Myrtaceae family, the relative abundance found is around 50% and an average lethal concentration activity of 60 ppm (Pandiyan et al., 2019). An important factor to be considered is the presence of synergistic interactions between the components, thus increasing bioavailability or reducing doses for activity evaluation.

#### 4. Conclusion

The essential oils of plants of the Lamiaceae, Myrtaceae, and Rutaceae families have shown great potential for repellent and larvicidal activity against various arthropod species, especially against *A. aegypti*. Most of the metabolites with the best repellent/larvicidal activity were  $\beta$  - caryophyllene,  $\alpha$  - pinene, 1,8 - cineol, linalol, and eugenol. These products when mixed presented excellent repellent potential, obtaining lower values than those found for DEET.

Carrying out this type of review is extremely important, as it makes it possible to identify what is being researched and discussed on a particular topic. After carrying out this review, a variety of compounds extracted from plants can be seen that have shown potential activity against the *Aedes aegypti* mosquito, becoming promising in this regard, as they are ecologically effective and generally have low toxicity. Understanding how and which compounds and plant families have shown such significant activities contributes to the production of drugs that prevent the transmission and spread of dengue in low-income countries.

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