

# Efficacy and Safety of Essential Oils in The Control of Mosquito: A Review of Research Findings

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## Abstract

For millennia, people have utilized essential oil-rich plants to control mosquitoes and other hematophagous insects. A review of the literature found that terpenoids and "sesquiterpenoid-rich oils" were effective in mosquito control. Due to the benign impression and successful prevention of mosquito bites, there has been a recent surge in the acceptance of biobased agents as mosquito control solutions, in conjunction with the worldwide demand to take action to battle climate change and its consequences. *Materials for this review, which included works published for the last decade and even earlier, were sourced from the research databases Scopus, Web of Science, PubMed, ERIC, IEEE Xplore, ScienceDirect, Directory of Open Access Journals (DOAJ), and JSTOR using the keywords "essential oils," "larvicidal activity," "oviposition deterrent," "repellents," "toxicity," "safety," and "efficacy."* Recent research has found that low and middle-income African populations prefer plant-based repellents over manufactured chemical repellents such as N, N-diethyl-m-toluamide and N, N-diethyl phenylacetamide. Although ethnobotanical studies have demonstrated that biobased repellents are effective, environmentally friendly, and have almost no biohazard impact, they are also a source of bioactive substances for the creation of novel mosquito repellent products. The World Health Organization and other relevant agencies have yet to certify and accept the bulk of these plants with potential viability. Furthermore, there is a very limited comparison list of the efficiency and safety of these plant-based repellents. As a result, there is a need to further investigate these bio-based natural repellents and their formulations for successful mosquito control, allowing for the production of novel repellents that deliver high repellence while also ensuring consumer safety.

**Keywords:** essential oils, repellent, mosquito, efficacy, safety, larvicidal activity, oviposition deterrent

## 1. Introduction

Mosquitoes pose a significant threat to millions of people worldwide, vectoring diseases such as malaria, dengue fever, yellow fever, filariasis, Japanese encephalitis, and Zika virus (Benelli & Mehlhorn, 2016; Patula *et al.* 2016; Saxena *et al.* 2016) which cause widespread morbidity, mortality and significant economic burden (Nyawira *et al.* 2020). Malaria is the most serious risk factor, and it is caused by *Plasmodium falciparum*, which is carried by female *Anopheles* mosquitoes. There are around 3500 mosquito species throughout the tropical and subtropical regions of the world (Prabakaran *et al.* 2017).

Dengue fever is a viral virus that slowly spread over the Western Hemisphere, grew more aggressively in the 1990s, and is mostly vectored by *Aedes mosquitos* (*Aedes aegypti* and, to a lesser degree, *Aedes albopictus*). Dengue fever instances are underreported, and many cases are misclassified. Dengue viruses pose a threat to about 390 million individuals in 128 countries (Beatty, 2007). Recent outbreaks of Zika virus infections in South America, Central America, and the Caribbean (Sujitha *et al.*, 2015) reflect the most recent arrivals of the Western Hemisphere's four arboviruses, dengue, West Nile virus, and chikungunya (Benelli & Mehlhorn, 2016; Fauci & Morens, 2016; Musso & Gubler, 2016). Unfortunately, there is no current therapy for the majority of arboviruses transmitted by mosquitoes, particularly the dengue and Zika viruses (Sujitha *et al.*, 2015).

Yellow fever is a viral hemorrhagic illness that is prevalent in tropical Africa, and Central and South America. It is spread by *Aedes aegypti*. Few individuals who get the virus experience severe symptoms, and around half of those infected die within 7–10 days. Yellow fever may be avoided with a very efficient, safe, and inexpensive vaccination. Within 30 days, the vaccine delivers effective protection in 99 % of immunized individuals (Katia, 2021).

Malaria, particularly *P. falciparum* infections, is a serious public health concern in underdeveloped nations such as Nigeria. Malaria morbidity and death influenced economic growth. Attempts to control or eliminate the illness, however, have mostly failed due to the rise of insecticide-resistant vectors and drug-resistant strains caused by *P. falciparum* kelch13 gene (PfKelch13) mutations (Amaratunga *et al.*, 2019). A global effort has always been and will continue to be made to use plants for disease prevention, vector control, and treatment where the traditional method is unsuccessful, costly, and unaffordable. The hunt for plant essential oils (EOs) as bio-insecticides for mosquito control is commonly thought to be a viable alternative to synthetic ones. According to research data available in the literature, essential oils from plant origins are used as mosquito repellants with high efficacy in terms of protection period and mortality rate of the vector species (Kweka *et al.*, 2008; Ghosh *et al.*, 2012).

Toxicology, on the other hand, is a major concern for the skin, neurological, and immune systems of humans and other animal species (Choochote *et al.*, 2007). Despite the claimed effectiveness of synthetic insecticides with long-lasting, it has however been implicated to exhibiting toxicity concerns resulting in skin irritation and breathing difficulties. However, EOs derived from plants, like lemon, are less hazardous than synthetic repellants (Nerio *et al.*, 2010). Essential oils from plants such as *Eucalyptus camaldulensis*, *Nepeta cataria*, and *Vitex negundo* have been shown to exhibit strong mosquito-repellent properties (Asadollahi *et al.*, 2019; Huang *et al.*, 2012; Patience *et al.*, 2018; Mohammadi & Saharkhiz, 2011; Moudachirou *et al.*, 1999; Singh *et al.*, 2011) with very low toxicity. The effectiveness and safety of EOs as mosquito larvicides, repellents, and oviposition deterrents, as well as the toxicity of EOs on non-target species, are the subject of this review.

## 2. Conventional Methods for Mosquito Control

There is rising awareness about the negative consequences of mosquito control compounds using synthetic insecticides which have led to a greater desire to seek natural and ecologically friendly insect repellants (Singh *et al.*, 2011). The use of repellents to protect humans from mosquito bites has previously been recognized as a crucial component of a fully integrated insect-borne disease control program (Amer & Mehlhorn, 2006). Commercial synthetic repellents frequently contain chemicals such as N, N-diethyl-meta-toluamide (DEET), Allethrin, N, N-diethyl mandelic acid amide, and dimethyl phthalate (Asadollahi *et al.*, 2019). These chemical repellents are hazardous to public health and should be avoided due to their negative effects on synthetic fabric and plastic, as well as toxic reactions such as allergy, dermatitis, and cardiovascular and neurological side effects that have been reported following widespread misuse and regular usage (Govindarajan *et al.*, 2016). The increased and constant use of synthetic repellents for mosquito control has disrupted natural ecosystems, resulting in pesticide resistance, mosquito population resurgence, and negative effects on non-target species (Govindarajan *et al.*, 2016; Sanghong *et al.*, 2015). As a result, employing natural mosquito repellent as an alternative to new synthetic repellents should be a cooperative option to reduce the negative impacts on the environment and human health.

## 3. Synergistic Action of Essential Oils

In terms of pesticide action, the goal of designing synergistic combinations is to minimize the dose of potentially polluting compounds while also lowering the possibility of resistance development. The ethnic-repellent formulation allows for the employment of a diverse variety of pest-repellent materials, such as plant extracts, fermentation products, and commercial clay and rock powder products. Nonetheless, due to the commercialization of standardized industrial items, the use of handmade products has diminished in recent years (Kyotosh, 2005). Also, it was discovered that combining extracts of *Azadirachta indica*, *Khya senegalensis*, and *Hyptis suaveolens* with conventional insecticides at one-half the recommended rate reduced cotton damage caused by the *Helicoverpa armigera* (bollworm), and provided greater efficacy than the conventional product alone at their recommended rate (Sinzogan *et al.* 2006). This led to an increase in farmers' confidence in indigenous technologies as a result of such a direct demonstration of the usability and value of botanical treatments (Chorianopoulos *et al.* 2006; Kithva, 2009).

The synergistic thinking that underpins the usage of combination products aims to create a dynamic product with several modes of action while maintaining the concept that the combined product's effect is greater than the sum of its known and unknown chemical components and should be optimized. The positive and negative synergy between the essential oil or its components and the other substances in the mix might occur (Harris, 2002). This is a crucial consideration since EOs may create a synergy that is subsequently nullified by the base product. The pH and salinity of the base may affect the activity of the EO. It has been observed that a low pH and salty environment may boost the formula's overall repellent activity (Chorianopoulos *et al.*, 2006). Synergistic effects have been demonstrated for EO combinations such as thyme,

anise, and saffron (Youssef, 1997). Khater, 2012 discovered that monoterpene mixes had a synergistic impact on mortality, thus he and his colleagues developed a one-of-a-kind monoterpene mixture with a 0.9 percent active component for use against foliar-feeding pests (Khater, 2012). Monoterpenoids bind to the octopaminergic receptor, which is found only in insects. Based on insect selectivity, a mixture of EOs containing hexahydroxyl was produced from various combinations of unique plant EOs to dramatically boost the effectiveness of these oils against insects (Sarma *et al.*, 2019). By combining oils with a common molecular structure (a six-membered carbon ring with an oxygenated functional group attached), this patented technology demonstrates rapid insecticidal activity, and because it is directed at octopaminergic sites, it is also classified as Generally Recognized as Safe (GRAS) and has been approved by the US Food and Drug Administration (FDA) (Tripathi *et al.*, 2009).

#### 4. Plant-Based Alternatives for Mosquito Control

Plant-based repellents have recently gained popularity due to their high concentration of insecticidal secondary metabolites, which are both safe and biodegradable into benign by-products. EOs are complex combinations of volatile organic molecules generated as secondary metabolites by plants, which include terpenes, sesquiterpenes, and oxygenated substances (Dhifi *et al.*, 2016). They are often responsible for a plant's particular odor, with around 3,000 known EOs having a commercial value in the pharmaceutical, beverage, agriculture, food, and cosmetic industries (FAO, 2020). As a result, the Food and Drug Administration of the United States deems them to be generally safe (Trongtokit *et al.*, 2005).

Their composition can vary greatly across aromatic plant species and variations, as well as between geographical locations within the same variety (Juliani *et al.*, 2007). The oils are mostly utilized in the perfume business, but some are also used in the food sector to make pharmaceuticals, soaps, shampoos, cosmetics, paints, and so on. Aside from the purposes described above, research has revealed that certain EOs have antibacterial and antifungal properties against specific pathogenic organisms, making them helpful in the pharmaceutical business (DeLisser *et al.*, 1997; Bennisir & Sridhar, 2012). The yield of EOs is inherently limited, ranging from 0.5 to 6% by weight (except clove buds, which produce 11–15 %) (Jones, 1994). Further, *E. camaldulensis*, *N. cataria*, and *V. negundo* with EO yields of 5.9 % v/w, 4.7 % v/w, and 1.0 % v/w, respectively, have been found to exhibit substantial mosquito-repellent potential (Asadollahi *et al.* 2019; Patience *et al.* 2018; Moudachirou *et al.* 1999; Hebbalkar *et al.* 1992; Mohammadi & Saharkhiz, 2011; Singh *et al.* 2015).

#### 5. Chemical Composition of Essential Oil Used in Mosquito Control

The chemical composition of some essential oils with mosquito repellent activities is shown (table 1). Essential oils are complex blends of volatile organic compounds derived from secondary plant metabolites. According to Zomorodian *et al.*, 2012, the chemical makeup of the essential oils tested by gas chromatography/mass spectrometry, the primary constituents of the *N. cataria* essential oil were 4 $\alpha$ - $\alpha$ ,7- $\alpha$ ,7 $\beta$ -nepetalactone (58%) and 4 $\alpha$ - $\alpha$ ,7- $\beta$ ,7 $\alpha$ -nepetalactone (31.2%). The principal compounds discovered in the leaves oil of *V. negundo* were  $\delta$ -guaiene (1.3 %), Epiglobulol (30.3 %),  $\beta$ -caryophyllene epoxide (10.2 %),  $\alpha/\beta$ -selinene (22%), germacrene-4ofl (9.0 %), (E)-nerolidol (3.0 %),  $\delta$ -cedrene (14%), germacrene (2.33%) (Singh *et al.* 2011; Kheder *et al.* 2020). *E. camaldulensis* essential oil had significant amounts of 1,8-cineole (37.1%),  $\beta$  -pinene (0.1%), eucalyptol (11.07%), terpinene-4-ol (5.5%), globulol (9.6%),  $\gamma$ -terpinene (10.4%), p-cymene (11.6%), Limonene (9.22%), Geraniol (5.20%),  $\alpha$ -Pinene (0.10%), Iso-carveol (0.49%), (Okoli *et al.*, 2021). The oils isolated from these plants (Table 1) suggest the presence of unique chemicals that are most likely responsible for the repellent effect of mosquitos. However, due to oxidation, plant-based repellents only give short-term protection. Fortunately, these disadvantages can be minimized by using inclusion complexes (Torres-Alvarez *et al.* 2020) or oil microencapsulation (Okoli *et al.*, 2021; Aguiar *et al.*, 2020).

Table 1. Some of the chemical constituents of essential oils with mosquito repellency

<i>Plectranthus incanus</i> (Pal, M., <i>et al.</i> 2011)		<i>Citrus aurantium</i> (Sanei-Dehkordi, A., <i>et al.</i> 2017)		<i>Vitex negundo</i> (Singh, P. K., <i>et al.</i> 2011)		<i>Eucalyptus camaduelensis</i> (Okoli, J.B., <i>et al.</i> 2021)	
cis-Piperitone oxide,	32.40	$\alpha$ -Pinene	0.30	$\alpha$ - Thujene	9.86	Eucalyptol	11.07
Fenchone	6.00	$\beta$ -Pinene	0.65	$\alpha$ - Pinene	7.74	<b>1,8-cineole</b>	<b>37.10</b>
Limonene	0.10	$\beta$ -Myrcene	1.00	Camphene	21.10	p-cymene	11.60
Borneol	1.40	DI-Limonene	94.81	Sabinene	3.11	Limonene	9.22
Piperitenone	3.00	Trans-Ocimene	0.19	Linalool	3.60	$\alpha$ -Pinene	0.10
Hydroxyl piperitone	0.50	Gamma-Terpinene	0.01	$\alpha$ - Copaene	25.26	Geraniol	5.20
Piperitenone oxide	41.50	Linalool Oxide	0.04	$\beta$ - Elemene	19.16	$\gamma$ -terpinene	<b>10.40</b>
$\alpha$ -Copaene	0.80	1-Octanol	0.13	t-Caryophyllene	2.72	<b>globulol</b>	<b>9.60</b>
$\beta$ -Cubebene	0.60	Linalool Oxide	0.02	Stearic acid	5.84	<b>terpinen-4-ol</b>	<b>5.50</b>
Caryophyllene oxide	0.80	Isoterpinolene	0.01	Behenic acid	1.52	Iso-carveol	0.49
$\beta$ -Caryophyllene	2.90	Nonanal	0.02	viridiflorol	26.52	<b><math>\beta</math>-pinene</b>	<b>0.10</b>
$\alpha$ -Humulene	0.80	$\alpha$ -Terpinolene	0.44	p-caryophyllene	13.20		
$\beta$ -Bisabolene	0.80	Linalyl acetate	0.32	4-terpineol	4.46		
$\alpha$ -Cadinene	1.00	Sabinene Hydrate Acetate	0.03	linalool	2.04		
$\delta$ -Cadinene	0.80	Neryl Acetate	0.03	Globulol	1.82		
		geranyl acetate	0.13	elemol	1.48		
		trans-Caryophyllene	0.03	fJ-farnesene	1.38		
		Germacrene-D	0.08	aromadendrene	1.04		
		Nerolidol	0.06				
		Palmitic Acid	0.06				
		Trans-Oleic Acid	0.26				

## 6. Repellant Activity of Essential Oils

Repellants are compounds that keep insects from flying or biting humans or animals. Some monoterpenes, such as cineole,  $\alpha$ -pinene, eugenol, limonene, terpinolene, citronellol, cineole, citronellal, thymol, and camphor, are frequent components of many EOs that have been found to have mosquito repellent properties (Yang *et al.* 2003; Vongsombath *et al.* 2012; Park, 2005).  $\beta$ -caryophyllene is the most commonly referenced sesquiterpene as a powerful repellent against *Aedes aegypti* (Gillij *et al.* 2007). Even though the presence of monoterpenoids and sesquiterpenes appears to be related to the repellent properties of several EO (Vongsombath *et al.* 2012; Ravi & Sita, 2007; Sukumar *et al.*, 1991; Hassanali, 2005. Luo *et al.*, 2022) observed that phytol had a strong repellent effect on *Anopheles Sinensis*. Toloza *et al.* (2006) investigated the repellent efficacy of 16 essential oils derived from indigenous and exotic Argentine plants, as well as 21 isolated secondary metabolites, and reported that benzyl alcohol, menthol, and thymol were the most effective against *Pediculus humanus capitis*. Furthermore, the tick's repellent properties of  $\alpha$ -pinene,  $\beta$ -citronellol, geraniol, and cinnamyl alcohol extracted from *Dianthus Calophyllum* essential oil are effective in controlling ticks on animals. Odalo *et al.* (2005) and Omolo *et al.* (2004) studied the repellent properties of 12 Kenyan plants from various genera against *A. gambiae*, as well as some metabolites isolated from these plants. The most efficient repellent substances were perillaldehyde, *cis*-verbenol, *cis*-carveol, myrcene, citronellal, perillyl alcohol, caryophyllene oxide, thymol, 3-carene, carvacrol, 4-isopropylbenzenemethanol, and geraniol. Sesquiterpenoid, diterpenoid, acyclic, monocyclic, and bicyclic monoterpenoids are among the many structural kinds.

Previous research has shown that terpenoids with two functional groups are physiologically efficacious as mosquito repellents (Han, 2008; Hazarika *et al.*, 2022). Although the repellent effect of EOs is often attributed to specific molecules, some synergistic interactions among these metabolites may result in greater bioactivity than the single isolated components (Gillij *et al.* 2007; Omolo *et al.* 2004; Hummelbrunner & Isman, 2001). The repellent efficacy of a blend of EOs from *Artemisia princeps* and *Cinnamomum camphora* against adults of *Sitophilus oryzae* L. and *Bruchus rugimanus* was much greater than that of individual oils (Liu *et al.* 2006).

## 7. Improvement of Essential Oil Repellence Efficiency

Although essential oils are useful when applied freshly, their protective benefits generally wear off soon (Trongtokit *et al.* 2005). In the case of mosquitoes, essential oils often function in the vapor phase, which is only effective for a limited length of time. This is most likely due to their high volatility, which might be reduced by developing formulations that can maintain active chemicals on the skin for extended periods. The increase in repellence activity for EOs is heavily influenced by the product content.

Creams, polymer mixes, or microcapsules-based formulations for controlled release and improved repellency duration (Trongtokit *et al.*, 2005; Yuan & Ping Hu, 2011; Sharma & Ansari, 1994; Nentwig, 2003; Chang *et al.* 2020) have been

developed using nanotechnology. For example, to boost mosquito-repellent characteristics, *Zanthoxylum limoncello* oil was effectively microencapsulated in glutaraldehyde cross-linked gelatin (a polymer) (Maji *et al.*, 2007). The efficiency of a product in a topical application containing citrus oil in repelling mosquitos was evaluated on various formulations. The order of efficacy was hydrophilic base > emulsion base > oleaginous base (Oyedele *et al.* 2002). To increase the efficiency of the EO repellent, fixative elements such as liquid paraffin (Oyedele *et al.* 2002) vanillin (Tawatsin *et al.* 2001), salicylic acid (Blackwell *et al.*, 2003), mustard, and coconut oils were used. Vanillin is a common chemical that is combined with EO (Choochote *et al.*, 2007; Tawatsin *et al.* 2001; Chaithong *et al.* 2006). This chemical greatly boosts the protection times of EO, particularly when used against *A. aegypti* (Sritabutra & Soonwera, 2013), it has also been shown to function effectively with other mosquito species. When looking for techniques to improve the repellency of essential oils, many variables should be considered: new formulations, fixative additives, nanoencapsulation, and the manufacture of combination repellents are all potential for increasing the effectiveness and economic value of repellents generated from essential oils.

### 8. Larvicidal Activity and Safety of Plant Essential Oils

Plants and phytophagous insects have been in conflict for millennia, which has resulted in the selection of a multitude of secondary metabolites with insecticidal action across a wide variety of plant species. It is hardly unexpected, then, that EOs have an immediate toxic impact on mosquito larvae when given to water in a controlled laboratory context. According to Romi *et al.* (2003), the LC<sub>50</sub> of temephos on larvae of *Aedes albopictus* Skuse populations in Italy varied from 0.0026 to 0.0085 ppm, but the LC<sub>50</sub> of Bti for field-collected strains of *A. aegypti* differs.

Few EOs have LC<sub>50</sub> < 1 ppm and multiple investigations have revealed that more than 50 ppm is necessary to kill 50% of the larvae studied (Shaalán *et al.*, 2005; Dias & Moraes., 2014; Pavela, 2015). According to WHO recommendations, such high concentrations are impractical. Shaalan *et al.* (2005) suggested that extracts generating less than 100% larval death in laboratory circumstances at a dosage of 10 ppm be stopped. In addition to mosquito larvae activity, concerns of practicability must be addressed. Aside from mosquito larvae activity, problems of practicability must be addressed. Products based on essential oils should be useful in several conditions such as organic matter in the water, salinity, temperature, pH, etc. The different degrees of vulnerability among mosquito species must also be considered.

The insecticidal effect of essential oils on mosquito larvae has sparked considerable attention in recent scientific literature, with numerous studies envisioning EOs as possible alternatives to conventional larvicides (Masetti, 2016). Larval control is an important strategy in the integrated management of most mosquito species (Becker *et al.*, 2010), and numerous pesticides have been employed to eradicate mosquito larvae. In general, poorer nations apply less stringent regulatory limits (Bläsing *et al.*, 2012), but the relatively high cost of traditional larvicides, as well as the difficulty in obtaining such goods, impede larval control initiatives. For these reasons, there is a significant deal of interest in the development of novel larvicides that do not harm human health or aquatic habitats and should be freely accessible and cheap in underdeveloped nations. As a result, EOs have regained popularity as prospective low-risk pesticides (Hummelbrunner & Isman, 2001; Regnault-Roger *et al.*, 2012). Terpenoids and, to a lesser degree, phenylpropanoids are the most common elements of EOs (Bakkali *et al.*, 2008). Several reports have been reported on EOs from a wide range of plant species that show an insecticidal effect on mosquito larvae by either the whole extract or specific purified components (Shaalán *et al.* 2005; Pavela, 2015; Hunter *et al.* 1996; Liu *et al.* 2019). Aside from effectiveness, most research indicated that EOs had no influence on human health and have no environmental negative effects (Bhavaniramya *et al.* 2019; Maurya, A., *et al.* 2021; Okon *et al.* 2021).

### 9. Health Impact of Essential Oils

Many popular EOs and their primary components have been examined experimentally for a long time as additives for foods and drinks, perfumes for cosmetics, and pharmaceutical items (Hummelbrunner & Isman, 2001). In general, these EOs are not hazardous to mammals or other vertebrates when consumed orally (Regnault-Roger & Vincent, 2012; Trumble, 2002). Aside from contact dermatitis and allergic reactions caused by repeated skin applications of *Melaleuca alternifolia* (Maiden Betcher). Some EOs such as *Mentha pulegium* L., *Artemisia absinthium* L., and *Hedeoma pulegioides* (L.) Pers. can cause severe acute poisoning (Trumble, 2002). If probable larvicidal activity is discovered for an EO for which no health issues have previously been identified, mammalian toxicity testing should be done. Such testing should be necessary before the start of any field trials.

Table 2. Some major chemical constituents and biological activity of essential oils isolated from plants

<i>Plant</i>	<i>Chemical Constituents</i>	<i>Biological Activity</i>	<i>References</i>
<i>N. cataria</i>	4a- $\alpha$ ,7- $\alpha$ ,7a $\beta$ -nopetalactone (58%)	Mosquito Repellent	Zomorodian <i>et al.</i> , 2012
<i>V. negundo</i>	Epiglobulol(30.3%), $\beta$ -caryophyllene (10.2%), $\alpha$ / $\beta$ -selinene (22%)	Mosquito Repellent	Khokia <i>et al.</i> , 2008; Singh <i>et al.</i> , 2011
<i>E.camaduelensis</i>	1,8-cineole (37.10%), p-cynene (11.6%)	Mosquito Repellent	Khoder <i>et al.</i> , 2020
<i>H. spicigera</i>	1,8-cineole (24.0%),(E) – caryophyllene (22.2%)	Mosquito repellent, postharvest	Mishra <i>et al.</i> , 2021
<i>H. suaveolous</i>	Sabinene (15.99%), $\beta$ -caryophyllene (18.57%), E-spathulenol (11.09%).	Mosquito repellent, antibacterial, Antioxidant	Mishra <i>et al.</i> , 2021
<i>Citrus limon</i>	Monoterpenes, D-Limonène (57.8%)	Antifungal, antioxidant	Singh <i>et al.</i> , 2002
<i>Matricaria recutita</i>	Oxygenated $\alpha$ -Bisabolol (31.89%)	Anti-irritant, anti-microbial. anti-inflammatory,	Nwaniki, 2015
<i>Cinnamomum, Zeylanicum</i>	Cinnamaldehyde	Bactericide, fungicide, insecticide	Ye <i>et al.</i> , 2013

Table 2, showed some major chemical constituents and biological activity of essential oils isolated from plants. The complexity of essential oils chemical constituents isolated from plants which work in synergy may impact positively on the health of human, animals and organisms. The chemical constituents in these essential oils dominated by monoterpenes (oxygenated and hydrocarbons), accounted for 82.8% of the oil's content possessing antifungal, bactericidal, pesticidal, trypanocides, antimicrobial, antioxidant activities which promote good health and used for various medical applications. With the emergence of conventional drugs for the treatment of microbial resistance, and viral infections essential oils have shown to have potentials as alternative to these conventional drugs in the management of the emergence of microbial resistance, viral infections crop protection amongst others. Essential oil constituents have been implicated in possessing bactericidal, virucidal, and fungicidal activity in clinical trials (Deyno *et al.*; Valdivieso-Ugarte *et al.* 2019). As a result of these biological activities of these essential oils, it is suggested that it might not just be used to fight infections, but also can play a role in the preservation of food due to their antimicrobial activity combined with their antioxidant property (Deyno *et al.*; Valdivieso-Ugarte *et al.* 2019).

Insect-repellent and Larvicidal activity of mosquito-borne diseases such as dengue fever, yellow fever, malaria, filariasis, and viral encephalitis affect large human populations. The bite causes serious allergy such as local skin reaction, and systemic reaction. Essential oils of *H. suaveolens* have shown larvicidal activity against yellow fever mosquito *Aedes aegypti* (L), and *Aedes albopictus* larvae. The larvicidal activity of the essential oils is due to the chemical constituents such as alpha-pinene, beta-pinene, sabinene, terpinolene, beta-caryophyllene, and 4-terpineol (Barbara *et al.* 2012) in the plant. Literature available on the scientific data of the biological activity of essential oils has demonstrated that they have contact and fumigant toxicity to a number of economically important insect and mite pests, as well as to plant pathogenic fungi. EOs have impact on human health in different ways. Many studies available in the literature has shown the essential oils to possess psychological effects for example, in reducing anxiety, treating depression, and aiding falling asleep. The essential oils have also been shown to possess antimicrobial, antiviral, antioxidant, anti-inflammatory properties and used as an alternative to synthetic insect repellents. As there are many proven health benefits to essential oils, there are also adverse effects. Altogether, there has been a great number of research investigations on the essential oil applications in health however, their complex chemical components and the spectrum of possible biological activities require more research findings on their true effects on human health,

## 10. Environmental Impact

One of the most appealing advantages of EOs over traditional synthetic pesticides is their low environmental persistence and lack of accumulation in food chains (Hummelbrunner & Isman, 2001). Several studies on the impact of EOs on aquatic biocoenosis have been reported. Most of these investigations, however, utilized fish as non-target creatures (Govindarajan, 2016; Pavela & Govindarajan, 2004), with arthropods being seldom examined. In general, EOs are neurotoxic contact insecticides that target  $\gamma$ -Aminobutyric acid and octopamine synapses as well as acetylcholinesterase (Regnault-Roger *et al.* 2012). Due to the existence of these molecular targets in all arthropods, there are low odds of

finding a significant degree of EO selectivity in non-targeted arthropods. EOs of *Piper klotzschianum* (Kunth) DC were found to have similar LC<sub>50</sub> values with *Artemia salina* L. nauplii and *Aedes aegypti* larvae (Sarmiento-Neto, *et al.* 2016).

Toxic effects of EOs and their components isolated from the Myrtaceae have also been observed in laboratory trials against *Daphnia Magna* Straus (Park *et al.* 2005). EOs from *Pinus kesiya* Royle ex Gordon, on the other hand, were generally nontoxic to *Rhynchota Notonectidae* (water bugs) (Govindarajan *et al.* 2017). On tested mosquito larvae, however, these extracts had LC<sub>50</sub> values greater than 50 ppm. Except for microbial larvicides, all other pesticides used to control mosquito larvae (IGRs, diflubenzuron, temephos, and pyrethroids) have been found to harm non-target aquatic insects and crustaceans (Pisa *et al.* 2014; Suchismita & Anilava, 2008; Lacey, 2007). EOs appear to lack selectivity in the amounts necessary to be effective on mosquito larvae. However, because EOs have a shorter environmental persistence, the final impact of EOs on non-target arthropods under real-world settings is anticipated to be smaller than that of chemical larvicides.

### 11. Insecticidal Activity and Safety of Plant Essential Oils

The majority of monoterpenes are cytotoxic to animal and plant tissue, reducing the number of undamaged Golgi bodies and mitochondria, decreasing cell membrane permeability, and interfering with respiration and photosynthesis (Stefano *et al.* 2015). They're also very flammable, and many of them serve as chemical messengers for insects and other animals. The EO quantities needed to remove insect pests, as well as their mechanisms of action, may have consequences for human and other vertebrate safety. Even though little is known about the physiological effects of EOs on insects, treatments with specific EOs or their components elicit symptoms that imply a neurotoxic mechanism of action. (Kostyukovsky *et al.* 2002; Shaaya *et al.* 1997). Linalool, a monoterpene, has been demonstrated to alter the neurological system in insects, influencing ion transport and the release of acetylcholine esterase (Rajashekar *et al.* 2014). In insects, octopamine performs several biological activities, including those of a neurotransmitter, neurohormone, and circulating neurohormone-neuromodulator (Magee *et al.* 1984; Orchard, 1982). Based on pharmacological criteria, octopamine operates by engaging with at least two types of receptors known as octopamine-1 and octopamine-2 (Kastner *et al.* 2014).

Interrupting the octopamine function causes a complete collapse of the nervous system in insects. As a result, the insect octopaminergic system is a bio-rational target for pest control. The absence of octopamine receptors in vertebrates is most likely responsible for EO's strong mammalian selectivity as insecticides. Some EO compounds have been shown to act on insects' octopaminergic systems (Jankowska *et al.* 2018). Cloned cells from the brains of *Periplaneta americana* and *Drosophila melanogaster* (Enan, 2005) demonstrated that eugenol mirrored octopamine in elevating intracellular calcium levels. It was also established that octopamine receptors play a role in this. Furthermore, eugenol toxicity was increased in mutant *Drosophila melanogaster* missing octopamine synthesis, showing that the toxicity is mediated through the octopaminergic system, although geraniol toxicity was not. It has been proposed that the insecticidal activities of eugenol are due to the cellular alterations generated by it (Tripathi *et al.* 2009). Kostyukovsky *et al.* (2002) discovered a similar result, suggesting that EO components may compete for octopaminergic receptor activation; they showed significant effects at low dosages in *Helicoverpa armigera* abdominal epidermal tissue (Tripathi & Tripathi, 2009).

### 12. Oviposition Deterrence and Safety of Essential Oils

Ovicides are chemicals that prevent insect pests from laying eggs. EOs derived from natural plants or nano-encapsulated EOs have been found to significantly reduce the number of eggs laid by insect pests such as *Bemisia tabaci* (Fortes *et al.* 2020; Younas *et al.* 2021). A study was carried out on *Bemisia tabaci* utilizing nano-encapsulated EO from the *Clematis aromatic* plant. The findings showed that EOs might potentially inhibit the egg production of *B. tabaci* in common bean leaves (Peres *et al.* 2013). The efficiency was 98%, and the concentration of the EO released from the nanocapsule increased. Essential oils from *Thymus Vulgaris*, *Pogostemon cablin*, and *Corymbia citriodora* significantly decreased oviposition, egg hatching, and nymph survival (Yang *et al.* 2003). The three essential oils from the plants reduced egg hatching by 50%, according to the findings. The oils caused development to be disrupted in certain eggs of the *B. tabaci* bug. Nonetheless, there is no experiment on the oviposition deterrence of EOs on mosquito vectors found in the literature. As a result, further research into mosquitoes and the oil's safety impact on non-target creatures is required.

### 13. Essential Oils Trends and Development

A review of recent essential oil patents indicated that the great majority of the advances were centered on home uses. Some patents are also related to domestic animal protection. A great number of patents have been awarded for the protection of garments against moths and beetles. EOs have been used in agriculture and the food sector, in addition to these home purposes. Essential oils have also been demonstrated to be beneficial in the manufacture of products. Eucalyptus EOs, pyrethroids, and borax were combined in a wood preservation solution (Urabe, 1992). By thoroughly impregnating the polymer layer with *Thujopsis dolobrata* EO, the insect resistance of veneer-faced panels is enhanced

(Akita *et al.* 1991; Sugimoto & Tsubochi, 1992). All of these examples highlight the adaptability of EOs in a variety of circumstances. Cockroaches, mosquitoes, mites, ticks, and other household insects are repelled by a bio-rational repellent based on nepetalactone and dihydro-nepetalactone from *N. cataria* (Hazarika *et al.* 2012; Scialdone & Liauw, 2008). Tetrahydronootkatone and 1,10-dihydro nootkatone, both derived from *Chrysopogon zizanioides* oil, have been patented as mosquito, cockroach, termite, and ant repellents (Baton *et al.* 2005; Henderson *et al.* 2005). Thyme oil, as well as monoterpenoid combinations such as thymol, anethole, eugenol, and citronellal, have all been trademarked for pesticide action against cockroaches and green peach aphids. Similarly, human louse insecticides, citronellal, citronellol, citronellyl, or a mixture of these have been patented (Tripathi *et al.* 2009; Sritabutra & Soonwera, 2013).

#### 14. Conclusion

The interest in developing plant herbs as an alternative to chemical insecticides has been piqued due to their ease of availability, low cost, and lower environmental impact. Numerous ethnobotanical studies have found that plants can be used as an alternative source of mosquito control measures. They have a long history of use in many parts of the world. Natural products are thought to be safer for human consumption than synthetic compounds. Furthermore, unlike synthetic repellents, which are harmful to the environment, lethal effects on non-target organisms and mosquito resistance to insecticides have increased over the last five decades. These issues have highlighted the need for alternative strategies to be developed.

This research examined the efficacy and safety of essential oil-rich plants used for mosquito control from a range of sources. Based on the research gaps discovered in the literature, it is, therefore, recommended that researchers, scientists, and educators to examine the mechanisms involved in how the interactions of the components of each essential oil result in increased repellent ability (for the synergistic phenomenon). More study on the effects of EOs on other aquatic arthropods that prey on mosquito larvae, such as dragonfly nymphs and water beetles, is also required. Despite the widespread usage of plants as repellents, scientific understanding of these plants is limited, necessitating the initial step of collecting ethnobotanical data on these species.

#### Conflict of Interest

The authors declare that they have no conflict of interest.

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#### References

- Aguiar, M. C. S., das Graças Fernandes da Silva, M. F., Fernandes, J. B., & Forum, M. R. (2020). Evaluation of the microencapsulation of orange essential oil in biopolymers by using a spray-drying process. *Sci. Rep.*, *10*(1), 1-11. <https://doi.org/10.1038/s41598-020-68823-4>.
- Akita, K. (1991). Fukubi Kagaku Kogyo K K, Japan. Insect-repellent and mildewcidal laminate boards.
- Amaratunga, C., & Andrianaranjaka, V. H., et al. (2019). Association of mutations in the Plasmodium falciparum Kelch13 gene (Pf3D7\_1343700) with parasite clearance rates after artemisinin-based treatments—a WWARN individual patient data meta-analysis. *BMC Med.*, *17*(1), 1. <https://doi.org/10.1186/s12916-018-1207-3>
- Amer, A., & Mehlhorn, H. (2006). Repellency effect of forty-one essential oils against Aedes, Anopheles, and Culex mosquitoes. *Parasitol. Res.*, *99*(4), 478-490. <https://doi.org/10.1007/s00436-006-0184-1>
- Asadollahi, A., Khoobdel, M., Zahraei-Ramazani, A., Azarmi, S., & Mosawi, S. H., (2019). Effectiveness of plant-based repellents against different Anopheles species: A systematic review. *Malar. J.*, *18*(1), 436. <https://doi.org/10.1186/s12936-019-3064-8>
- Bakkali, F., Averbeck, S., Averbeck, D., & Idaomar, M. (2008). Biological effects of essential oils - A review. *Food Chem. Toxicol.*, *46*(2), 446-475. <https://doi.org/10.1016/j.fct.2007.09.106>
- Baton, L. A., & Ranford-Cartwright, L. C. (2005). Dihydronootkatone and Tetrahydronootkatone As Repellents To Arthropods.
- Beatty, M. E. (2007). Estimating the total world population at risk for locally acquired dengue infection. Abstract presented at the 56th Annual Meeting of the American Society of Tropical Medicine and Hygiene. *Am J Trop Med Hyg.* *77*(Suppl 5), 170-257.
- Becker, R. A., Janus, E. R., White, R. D., Kruszewski, F. H., & Brackett, R. E. (2010). Good laboratory practices: Becker et al. Respond. *Environ. Health Perspect.*, *118*(5), A194-A195. <https://doi.org/10.1289/ehp.0901755R>



- Benelli, G., & Mehlhorn, H. (2016). Declining malaria, rising of dengue and Zika virus: insights for mosquito vector control. *Parasitology Research*, 115(5). Springer Verlag, 1747-1754. <https://doi.org/10.1007/s00436-016-4971-z>
- Bennasir, A. H., and Sridhar, S., (2012). Toxicity due to exposure of cobalt and its inorganic salts on human and animal. *World J. Pharm. Res.*, (2), 16-32.
- Bhavaniramy, S., Vishnupriya, S., Al-Aboody, M. S., Vijayakumar, R., & Baskaran, D. (2019). Role of essential oils in food safety: Antimicrobial and antioxidant applications. *Grain Oil Sci. Technol.*, 2(2), 49-55. <https://doi.org/10.1016/j.gaost.2019.03.001>
- Blackwell, A., Stuart, A. E., & Estambale, B. A. (2003). The repellent and antifeedant activity of oil of *Myrica gale* against *Aedes aegypti* mosquitoes and its enhancement by the addition of salicylic acid. *Proc. R. Coll. Phys. Edinburgh*, 33, 209-214.
- Bläsing, B., Calvo-Merino, B., Cross, E. S., Jola, C., Honisch, J., & Stevens, C. J. (2012). Neurocognitive control in dance perception and performance. *Acta Psychol. (Amst.)*, 139(2), 300-308. <https://doi.org/10.1016/j.actpsy.2011.12.005>.
- Chaithong, U., Choochote, W., Kamsuk, K., Jitpakdi, A., & Dana, P. T. (2006). Larvicidal effect of pepper plants on *Aedes aegypti* (L.) (Diptera: Culicidae). *J. Vector Ecol.*, 31(1), 138-144. [https://doi.org/10.3376/1081-1710\(2006\)31\[138:leoppo\]2.0.co;2](https://doi.org/10.3376/1081-1710(2006)31[138:leoppo]2.0.co;2)
- Chang, M. M., Hong, S. Y., Yang, S. H., Wu, C. C., Wang, C. Y., & Huang, B. M. (2020). Anti-cancer effect of cordycepin on FGF9-induced testicular tumorigenesis. *Int. J. Mol. Sci.*, 21(21), 1-21. <https://doi.org/10.3390/ijms21218336>
- Choochote W., Chaithong, U., Kamsuk, K., Jitpakdi, A., Tippawangkosol, P., Tuetun, B., Champakaew, D., & Pitasawat, B. (2007). Repellent activity of selected essential oils against *Aedes aegypti*. *Fitoterapia*, 78(5), 359-364. <https://doi.org/10.1016/j.fitote.2007.02.006>.
- Chorianopoulos, N. G., Lambert, R. J. W., Skandamis, P. N., Evergetis, E. T., Haroutounian, S. A., & Nychas, G. J. E. (2006). A newly developed assay to study the minimum inhibitory concentration of *Satureja Spinosa* essential oil. *J. Appl. Microbiol.*, 100(4), 778-786. <https://doi.org/10.1111/j.1365-2672.2006.02827.x>
- DeLisser, H. M., Solomidou, M. C., Strieter, R. M., Burdick, M. D., Robinson C. S., Wexler, R. S., ... & Albelda, S. M. (1997). Involvement of endothelial PECAM-1/CD31 in angiogenesis. *Am. J. Pathol.*, 151(3), 671-7, [Online]. Available <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1857836&tool=pmcentrez&rendertype=abstract>
- Deyno, S., Mtewa, A. G., Abebe, A., Hymete, A., & Bazira, M. E. (2019). Essential oils as topical anti-effective agents: A systematic review and meta-analysis. *Complementary Ther. Med.*, 47, 102224. <https://doi.org/10.1016/j.ctim>
- Dhifi, W., Bellini, S., Jazi, S., Bahloul, N., & Mnif, W. (2016). Essential Oils' Chemical Characterization and Investigation of Some Biological Activities: A Critical Review. *Medicines*, 3(4), 25. <https://doi.org/10.3390/medicines3040025>
- Dias, C. N., & Moraes, D. F. C. (2014). Essential oils and their compounds as *Aedes aegypti* L. (Diptera: Culicidae) larvicides: Review. *Parasitol. Res.*, 113(2), 565-592. <https://doi.org/10.1007/s00436-013-3687-6>
- Enan, E. E. (2005). Molecular and pharmacological analysis of an octopamine receptor from American cockroach and fruit fly in response to plant essential oils. *Arch. Insect Biochem. Physiol.*, 59(3), 161-171. <https://doi.org/10.1002/arch.20076>
- FAO, (2020). World Programme for the Census of Agriculture 2020: Programme, concepts, and definitions [FAO Statistical Development Series], [Online]. Available: <https://www.fao.org/3/i4913e/i4913e.pdf>
- Fauci, A. S., & Morens, D. M. (2016). Zika Virus in the Americas - Yet Another Arbovirus Threat. *N. Engl. J. Med.*, 374(7), 601-604. <https://doi.org/10.1056/nejmp1600297>
- Fortes, I. M., Fernández-Muñoz, R., & Moriones, E. (2020). Host Plant Resistance to *Bemisia tabaci* to Control Damage Caused in Tomato Plants by the Emerging Crinivirus Tomato Chlorosis Virus. *Front. Plant Sci.*, 11. <https://doi.org/10.3389/fpls.2020.585510>
- Ghosh, A., Chowdhury, N., & Chandra, G. (2012). Plant extracts as potential mosquito larvicides. *Indian J. Med. Res.*, 135(5), 581-598.
- Gillij, Y. G., Gleiser, R. M., & Zygadlo, J. A. (2008). Mosquito repellent activity of essential oils of aromatic plants

- growing in Argentina. *Bioresour. Technol.*, 99(7), 2507-2515. <https://doi.org/doi:10.1016/j.biortech.2007.04.066>
- Govindarajan, M., Kadaikunnan, S., Alharbi, N. S., & Benelli, G. (2017). Single-step biological fabrication of colloidal silver nanoparticles using *Hugonia mystax*: larvicidal potential against Zika virus, dengue, and malaria vector mosquitoes. *Artif. Cells, Nanomedicine Biotechnol.*, 45(7), 1317-1325. <https://doi.org/10.1080/21691401.2016.1228664>
- Govindarajan, M., Rajeswary, M., Arivoli, S., Tennyson, S., & Benelli, G. (2016). Larvicidal and repellent potential of *Zingiber nimmonii* (J. Graham) Dalzell (Zingiberaceae) essential oil: an eco-friendly tool against malaria, dengue, and lymphatic filariasis mosquito vectors? *Parasitol. Res.*, 115(5), 1807-1816. <https://doi.org/10.1007/s00436-016-4920-x>
- Han, Z. W. S. S. C. (2008). QSAR study of mosquito repellents from terpenoid with a six-member-ring, *Bioorg. Med. Chem. Lett.*, 18(9), 2854-9.
- Harris, R. (2002). Synergism in the essential oil world. *Int. J. Aromather.*, 12(4), 179-186. [https://doi.org/10.1016/S0962-4562\(02\)00083-8](https://doi.org/10.1016/S0962-4562(02)00083-8)
- Hassanali, J. O. (2005). Repellency of essential oils of some plants from the Kenyan coast against *Anopheles Gambia*. *Acta Trop.*, 95(3), 210-8.
- Hazarika, Dhiman, S., Rabha, B., Bhola, R., & Singh, L. (2012). Repellent activity of some essential oils against *Simulium* species in India. *J. Insect Sci.*, 12. <https://doi.org/10.1673/031.012.0501>
- Hazarika, H., Krisnatreyya H., Tyagi, V., Islam, J., Gogoi, N., & Danswring. (2022). The fabrication and assessment of mosquito repellent cream for outdoor protection. *Sci. Rep.*, 12(1). <https://doi.org/10.1038/s41598-022-06185-9>
- Hebbalkar, D. S., Hebbalkar, G. D., Sharma, R. N., Joshi, V. S., & Bhat, V. S. (1992). Mosquito repellent activity of oils from *Vitex negundo* Linn. Leaves. *Indian J. Med. Res. - Sect. An Infect. Dis.*, 95, 200-203.
- Henderson, A. J. Z., Bartholomew, K., Trinke, S. J., & Kwong, M. J. (2005). When loving means hurting: An exploration of attachment and intimate abuse in a community sample. *J. Fam. Violence*, 20(4), 219-230. <https://doi.org/10.1007/s10896-005-5985-y>
- Huang, H. C., Chang, T. Y., Chang, L. Z., Wang, H. F., Yih, K. H., Hsieh, W. Y., & Chang, T. M. (2012). Inhibition of melanogenesis Versus antioxidant properties of essential oil extracted from leaves of *vitex negundo* Linn and chemical composition analysis by GC-MS. *Molecules*, 17(4), 3902-3916. <https://doi.org/10.3390/molecules17043902>
- Hummelbrunner, L. A., & Isman, M. B. (2001). Acute, sublethal, antifeedant, and synergistic effects of monoterpenoid essential oil compounds on the tobacco cutworm, *Spodoptera litura* (Lep., Noctuidae). *J. Agric. Food Chem.*, 49(2), 715-720. <https://doi.org/10.1021/jf000749t>
- Hunter, D. J., Spiegelman, D., & Adam, H. O. (1996). Cohort Studies of Fat Intake and the Risk of Breast Cancer-A Pooled Analysis. *N. Engl. J. Med.*, 334(6), 356-361. <https://doi.org/10.1056/nejm199602083340603>
- Jankowska, M., Rogalska, J., Wyszowska, J., & Stankiewicz, M. (2018). Molecular targets for components of essential oils in the insect nervous system-a review. *Molecules*, 23(1). <https://doi.org/10.3390/molecules23010034>
- Jones, K. C. (1994). International program on chemical safety (IPCS) environmental health criteria. *Environ. Pollut.*, 84(2), 203. [https://doi.org/10.1016/0269-7491\(94\)90105-8](https://doi.org/10.1016/0269-7491(94)90105-8)
- Juliani, H. R., Biurrun, F. N., Koroch, A., De Carli, A., & Zygadlo, J. A. (2007). The Production of Native and Exotic Herbs, Medicinal and Aromatic Plants in Argentina, in *new crops and new uses*, J. Janick and A. Whipkey, Eds. 316-321.
- Kastner, K. W., Shoue, D. A., Estia, G. L., Wolford, G. H., Fuerst, M. F., Markley, L. D., ... & McDowell, M. A. (2014). Characterization of the *Anopheles gambiae* octopamine receptor and discovery of potential agonists and antagonists using a combined computational-experimental approach. *Malar. J.*, 13(1). <https://doi.org/10.1186/1475-2875-13-434>
- Katia, V. (2021). Yellow fever. *Revista chilena de infectología*. <https://www.who.int/news-room/fact-sheets/detail/yellow-fever>
- Khater, H. F. (2012). Prospects of botanical biopesticides in insect pest management. *J. Appl. Pharm. Sci.*, 3, 641-656. <https://doi.org/10.7324/japs.2012.2546>
- Kheder, D. A., Al-Habib, O. A. M., Gilardoni, G., & Vidari, G. (2020). Components of Volatile Fractions from *Eucalyptus camaldulensis* Leaves from Iraqi-Kurdistan and Their Potent Spasmolytic Effects. *Molecules*, 25(4).

<https://doi.org/10.3390/molecules25040804>

- Kithva, P. H., Grøndahl, L., Kumar, R., Martin, D., & Trau, M. (2009). An organic matrix-mediated processing methodology to fabricate hydroxyapatite based nanostructured biocomposites. *Nanoscale*, 1(2), 229-232. <https://doi.org/10.1039/b9nr00062c>
- Kostyukovsky, M., Ravid, U., & Shaaya, E. (2002). The potential use of plant volatiles for the control of stored product insects and quarantine pests in cut flowers. *Acta Hort.*, 576, 347-358. <https://doi.org/10.17660/ActaHortic.2002.576.52>
- Kweka, E. J., Moshia, F., Lowassa, A., Mahande, A. M., Kitau, J., Matowo, J., ... & Temu, E. A. (2008). Ethnobotanical study of some of mosquito repellent plants in north-eastern Tanzania. *Malar. J.*, 7. <https://doi.org/10.1186/1475-2875-7-152>.
- Kyōtoshi Maizō Bunkazai Kenkyūjo, A. K., Bhuiyan, S. M., & Bhattacharya, P. R. (2005). Shirakawa gaiku ato okazaki iseki. *Journal of Pharmacognosy and Phytotherapy*, 1(5), 052-063, [Online]. <http://www.academicjournals.org/journal/JPP/article-abstract/370D4E01129>.
- Lacey, L. A. (2007). Bacillus thuringiensis zero variety Israelensis and bacillus sphaericus for mosquito control. *J. Am. Mosq. Control Assoc.*, 23(2), 133-163. [https://doi.org/10.2987/8756-971x\(2007\)23\[133:btsiab\]2.0.co;2](https://doi.org/10.2987/8756-971x(2007)23[133:btsiab]2.0.co;2)
- Liu, Mishchenko, M. I., Cairns, B., Carlson, B. E., & Travis, L. D. (2006). Modeling single-scattering properties of small cirrus particles by use of a size-shape distribution of ice spheroids and cylinders. *J. Quant. Spectrosc. Radiat. Transf.*, 101(3), 488-497. <https://doi.org/10.1016/j.jqsrt.2006.02.040>
- Liu, S. D., Song, M. H., Yun, W., Lee, J. H., Kim, H. B., & Cho, J. H. (2019). Effect of carvacrol essential oils on immune response and inflammation-related genes expression in broilers challenged by lipopolysaccharide. *Poult. Sci.*, 98(5), 2026-2033. <https://doi.org/10.3382/ps/pey575>
- Luo, D. Y., Yan, Z. T., Che, L. R., Zhu, J. J., & Chen, B. (2022). Repellency and insecticidal activity of seven Mugwort (*Artemisia argyi*) essential oils against the malaria vector *Anopheles Sinensis*. *Sci. Rep.*, 12(1), 5337. <https://doi.org/10.1038/s41598-022-09190-0>.
- Magee, P. S., Kohn, G. K., & Menn, J. J. (1984). American Chemical Society. Division of Pesticide Chemistry., and D. C. American Chemical Society. Meeting (186th : 1983 : Washington, Pesticide synthesis through rational approaches. in *In P. S. Magee, G. K. Kohn, & J. J. Menn (Eds.), ACS symposium series 255 (103-125). Washington, DC: American Chemical Society.*, p. 352.
- Maji, S. K., Pal, A., Pal, T., & Adak, A. (2007). Adsorption thermodynamics of arsenic on laterite soil. *J. Surf. Sci. Technol.*, 23(3-4), 161-176.
- Masetti, A. (2016). The potential use of essential oils against mosquito larvae: A short review. *Bull. Insectology*, 69(2), 307-310.
- Maurya, A., Prasad, J., Das, S., & Dwivedy, A. K. (2021). Essential Oils and Their Application in Food Safety. *Front. Sustain. Food Syst.*, 5. <https://doi.org/10.3389/fsufs.2021.653420>
- Mohammadi, S., & Saharkhiz, M. J. (2011). Changes in Essential Oil Content and Composition of Catnip (*Nepeta cataria* L.) During Different Developmental Stages. *J. Essent. Oil-Bearing Plants*, 14(4), 396-400. <https://doi.org/10.1080/0972060X.2011.10643592>.
- Moudachirou, M., Gbénou, J. D., Chalchat, J. C., Chabad, J. L., & Lartigue, C. (1999). Chemical composition of essential oils of eucalyptus from Bénin: *Eucalyptus citriodora* and *e. camaldulensis*. Influence of location, harvest time, storage of plants and time of steam distillation. *J. Essent. Oil Res.*, 11(1), 109-118. <https://doi.org/10.1080/10412905.1999.9701085>.
- Musso, D., & Gubler, D. J. (2016). Zika Virus. *Clin. Microbiol. Rev.*, 29(3), 487-524. <https://doi.org/10.1128/CMR.00072-15>
- Nentwig, G. (2003). Use of repellents as prophylactic agents. *Parasitol. Res.*, 90(SUPPL.1), S40-S48. <https://doi.org/10.1007/s00436-002-0755-8>
- Nerio, L., Olivero-Verbal, S. J., & Stashenko, E. (2010). Repellent activity of essential oils: A review. *Bioresour. Technol.*, 101(1), 372-378. <https://doi.org/10.1016/j.biortech.2009.07.048>
- Ngassoum, M. B., Jirovetz, L., & Buchbauer, G. (1999). Essential oil and headspace from *Hyptis suaveolens* (L.) Poit. leaves and flowers from Cameroon. *Journal of Essential Oil Research*, 11, 283-8.
- Nyawira, W. L., et al., (2020). Efficacy of Plant-based Repellents Against *Anopheles* Mosquitoes: A Systematic Review.

- Biomed. Sci.*, 6(3), 44. <https://doi.org/0.11648/j.bs.20200603.11>
- Odalo, J. O., Omolo, M. O., Malebo, H., Angira, H., & Njeru, P. M. (2005). Repellency of essential oils Coast, of some plants from the Kenyan Tropica, against *Anopheles gambiae*. *Acta*, 95, 210-218.
- Okoli, B.J., Ladan, Z., Mtunzi, F., & Hosea, Y. C. (2021). Vitex negundo L. Essential Oil: Odorant Binding Protein Efficiency Using Molecular Docking Approach and Studies of the Mosquito Repellent. *Insects* 2021, 12, 1061. <https://doi.org/10.3390/insects12121061>
- Okon, E. M., Falana B. M., Solaja, S. O., Yakubu, S. O., & Alabi, O. O. (2021). Systematic review of climate change impact research in Nigeria: implication for sustainable development. *Heliyon*, 7(9). <https://doi.org/10.1016/j.heliyon.2021.e07941>
- Omolo, M. O., Okinyo, D., Ndiege, I. O., Lwande, W., & Hassanali, A. (2004). Repellency of essential oils of some Kenyan plants against *Anopheles Gambia*. *Phytochemistry*, 65(20), 2797-2802. <https://doi.org/10.1016/j.phytochem.2004.08.035>
- Orchard, I. (1982). Octopamine in insects: neurotransmitter, neurohormone, and neuromodulator, *Can. J. Zool.*, 60(4), 659-669. <https://doi.org/10.1139/z82-095>
- Oyedele, A. O., Gbolade, A. A., Sosan, M. B., Adewoyin, F. B., Soyelu, O. L., & Orafidiya, O. O. (2002). Formulation of an effective mosquito-repellent topical product from lemongrass oil. *Phytomedicine*, 9(3), 259-262. <https://doi.org/10.1078/0944-7113-00120>
- Pal, M., Kumar, A., & Tewari, S. K. (2011). Chemical composition and mosquito repellent activity of the essential oil of *Plectranthus Incanus* Link. *FACTA UNIVERSITATIS Series: Physics, Chemistry and Technology*, 9(1), 57-64. <https://doi.org/10.2298/FUPCT1101057P>
- Park, B. S., Choi, W. S., Kim, J. H., Kim, K. H., & Lee, S. E. (2005). Monoterpenes from thyme (*Thymus vulgaris*) as potential mosquito repellents. *J. Am. Mosq. Control Assoc.*, 21(1), 80-83. [https://doi.org/10.2987/8756-971X\(2005\)21\[80:MFTTVA\]2.0.CO;2](https://doi.org/10.2987/8756-971X(2005)21[80:MFTTVA]2.0.CO;2)
- Pastula, D. M., Smith, D. E., Beckham, J. D., & Tyler, K. L. (2016). Four emerging arboviral diseases in North America: Jamestown Canyon, Powassan, chikungunya, and Zika virus diseases. *Journal of NeuroVirology*, 22(3). Taylor and Francis Ltd, 257-260. <https://doi.org/10.1007/s13365-016-0428-5>
- Patience, G. S., Karirekinyana, G., Galli, F., Patience, N. A., Kubwabo, C., & Collin, G. (2018). Sustainable manufacture of insect repellents derived from *Nepeta cataria*. *Sci. Rep.*, 8(1), 1-9. <https://doi.org/10.1038/s41598-017-18141-z>
- Pavela, R. (2015). Essential oils for the development of eco-friendly mosquito larvicides: A review. *Ind. Crops Prod.*, 76, 174-187. <https://doi.org/10.1016/j.indcrop.2015.06.050>
- Pavela, R., & Govindarajan, M. (2017). The essential oil from *Zanthoxylum monophyllum* a potential mosquito larvicide with low toxicity to the non-target fish *Gambusia affinis*. *J. Pest Sci. (2004)*, 90(1), 369-378. <https://doi.org/10.1007/s10340-016-0763-6>
- Peres, H., Santos, S., & Oliva-Teles, A. (2013). Selected plasma biochemistry parameters in gilthead seabream (*Sparus aurata*) juveniles. *J. Appl. Ichthyol.*, 29(3), 630-636. <https://doi.org/10.1111/j.1439-0426.2012.02049.x>
- Pisa, L. W., Rogers, V. A., Belzunces, L. P., Bonmatin, J. M., Downs, C. A., Goulson, D., ... & Wiemers, M. (2014). Effects of neonicotinoids and fipronil on non-target invertebrates. *Environ. Sci. Pollut. Res.*, 22(1), 68-102. <https://doi.org/10.1007/s11356-014-3471-x>
- Prabakaran, P., Sivasubramanian, C., Veeramani, R., & Prabhu, S. (2017). Review Study on Larvicidal and Mosquito Repellent Activity of Volatile Oils Isolated from Medicinal Plants. *Int. J. Environ. Agric. Biotechnol.*, 2(6), 3132-3138. <https://doi.org/10.22161/jeans/2.6.46>
- Rajashekar, Y., Raghavendra, A., & Bakthavatsalam, N. (2014). Acetylcholinesterase inhibition by biofumigant (Coumarin) from leaves of lantana camera in stored grain and household insect pests. *Biomed Res. Int.* <https://doi.org/10.1155/2014/187019>
- Ravi, S., & Sita, P. (2007). Evaluation of the mosquitocidal activity of essential oil and sesquiterpenes from leaves of *Chloroxylon swietenia* DC. *Parasitol. Res.*, 101(2), 413-418. <https://doi.org/10.1007/s00436-007-0485-z>
- Regnault-Roger, C., Vincent, C., & Arnason, J. T. (2012). Essential oils in insect control: Low-risk products in a high-stakes world. *Annu. Rev. Entomol.*, 57, 405-424. <https://doi.org/10.1146/annurev-ento-120710-100554>
- Romi, R., Toma, L., Severini, F., & Di Luca, M. (2003). Susceptibility of Italian populations of *Aedes albopictus* to

- temephos and other insecticides. *J. Am. Mosq. Control Assoc.*, 19(4), 419-423.
- Sanghong, R., Junkun, A., Chaithong, U., Jitpakdi, A., Riyong, D., Tuetun, B., ... & Pitasawat, B. (2015). Remarkable repellency of *Ligusticum sinense* (Umbelliferae), a herbal alternative against laboratory populations of *Anopheles minimus* and *Aedes aegypti* (Diptera: Culicidae). *Malar. J.*, 14(1), 307. <https://doi.org/10.1186/s12936-015-0816-y>
- Sarma, R., Adhikari, K., Mahanta, S., & Khanikor, B. (2019). Combinations of Plant Essential Oil Based Terpene Compounds as Larvicidal and Adulticidal Agent against *Aedes aegypti* (Diptera: Culicidae). *Sci. Rep.*, 9(1), 9471. <https://doi.org/10.1038/s41598-019-45908-3>
- Sarmiento-Neto, J. F., Do Nascimento, L. G., Felipe, C. F. B., & De Sousa, D. P. (2016). Analgesic potential of essential oils. *Molecules*, 21(1), 20. <https://doi.org/10.3390/molecules21010020>
- Saxena, S. K., Elahi, A., Gadugu, S., & Prasad, A. K. (2016). Zika virus outbreak: an overview of the experimental therapeutics and treatment. *VirusDisease*, 27(2), 111-115. <https://doi.org/10.1007/s13337-016-0307-y>
- Scialdone, M. A., & Liauw, A. Y. (2008). Acetals of Nepetalic Acid and Method of Preparation.
- Shaalán, E. A., Canyon, D., Younes M. W., Abdel-Wahab, H., & Mansour, A. H. (2005). A review of botanical phytochemicals with mosquitocidal potential. *Bioresour. Technol.*, 97, 1599-1604.
- Shaaya, E., Kostjukovski, M., Eilberg, J., & Sukprakarn, C. (1997). Plant oils as fumigants and contact insecticides for the control of stored-product insects. *J. Stored Prod. Res.*, 33(1), 7-15, [https://doi.org/10.1016/S0022-474X\(96\)00032-X](https://doi.org/10.1016/S0022-474X(96)00032-X)
- Sharma, V. P., & Ansari, M. A. (1994). Personal protection from mosquitoes (Diptera: Culicidae) by burning neem oil in kerosene. *J. Med. Entomol.*, 31(3), 505-507. <https://doi.org/10.1093/jmedent/31.3.505>.
- Singh, S. P., Garg, V., & Visit, S. (2021). Extraction and analysis of essential oil of Nirgundi (*Vitex negundo* L.). *Der Pharm. Sin.*, 2. [Online]. Available: [www.pelagiaresearchlibrary.com](http://www.pelagiaresearchlibrary.com)
- Singh, S., Parihar, P., Singh, R., Singh, V. P., & Prasad, S. M. (2016). Heavy Metal Tolerance in Plants: Role of Transcriptomics, Proteomics, Metabolomics, and Economics. *Front. Plant Sci.*, 6, 1143. <https://doi.org/10.3389/fpls.2015.01143>
- Singh, Sharma, P. K., Garg, V. K., & Visit, S. (2011). Extraction and analysis of essential oil of Nirgundi (*Vitex negundo* L.). *Der Pharm. Sin.*, 2. [Online]. Available: [www.pelagiaresearchlibrary.com](http://www.pelagiaresearchlibrary.com)
- Sinzogan, A. A. C., Kossou, D. K., Atachi, P., & Van, H. A. (2006). Participatory evaluation of synthetic and botanical pesticide mixtures for cotton bollworm control. *Int. J. Trop. Insect Sci.*, 26(4), 246-255. <https://doi.org/10.1017/S1742758406415691>
- Sritabutra, D., & Soonwera, M. (2013). Repellent activity of herbal essential oils against *Aedes aegypti* (Linn.) and *Culex quinquefasciatus* (Say.). *Asian Pacific J. Trop. Dis.*, 3(4), 271-276. [https://doi.org/10.1016/S2222-1808\(13\)60069-9](https://doi.org/10.1016/S2222-1808(13)60069-9)
- Stefano, G. B., Snyder, C., & Kream, R. M. (2015). Mitochondria, chloroplasts in animal and plant cells: Significance of conformational matching. *Med. Sci. Monit.*, 21, 2073-2078. <https://doi.org/10.12659/MSM.894758>.
- Suchismita, S., & Anilava, K. (2008). Acute Toxicity of Synthetic Pyrethroid Cypermethrin to Some Freshwater Organisms. *Bull. Environ. Contam. Toxicol.*, 80(1), 49-52.
- Sugimoto, K., & Tsubochi, H. (1992). Daiken Trade & Industry, Japan. An improved method for extending the insecticidal and mildewicidal performance of impregnated decorative panels.
- Sujitha, V., Murugan, K., Paulpandi, M., Panneerselvam, C., Suresh, U., Roni, M., .... & Benelli, G. (2015). Green-synthesized silver nanoparticles as a novel control tool against dengue virus (DEN-2) and its primary vector *Aedes aegypti*. *Parasitol. Res.*, 114(9), 3315-3325. <https://doi.org/10.1007/s00436-015-4556-2>
- Sukumar, K., Perich, M. J., & Boobar, L. R. (1991). Botanical derivatives in mosquito control: a review. *J. Am. Mosq. Control Assoc.*, 7(2), 210-237.
- Tawatsin, A., Wratten, S. D., Scott, R. R., Thavara, U., & Techadamrongsin, Y. (2001). Repellency of volatile oils from plants against three mosquito vectors. *J. Vector Ecol.*, 26(1), 76-82, [Online]. <http://www.ncbi.nlm.nih.gov/pubmed/11469188>
- Toloza, A. C., Zygodlo, J., Mougabure Cueto, G., Biurrún, F., Zerba, E., & Picollo, M. I. (2006). Fumigant and repellent properties of essential oils and component compounds against permethrin-resistant *Pediculus humanus capitis* (Anoplura: Pediculidae) from Argentina. *J. Med. Entomol.*, 43(5), 889-895. [https://doi.org/10.1603/0022-2585\(2006\)43\[889:FARPOE\]2.0.CO;2](https://doi.org/10.1603/0022-2585(2006)43[889:FARPOE]2.0.CO;2)

- Torres-Alvarez, C., Castillo, S., Sanchez-Garcia, E., Gonzalez, C. A., Galindo-Rodriguez, A. S., Gabaldon-Hernandez, J. A., & Baez-Gonzalez, J. (2020). Inclusion Complexes of Concentrated Orange Oils and  $\beta$ -Cyclodextrin: Physicochemical and Biological Characterizations. *Molecules*, 25(21). <https://doi.org/10.3390/molecules25215109>
- Tripathi, S., & Tripathi, J. N. (2009). Relative susceptibility of banana cultivars to *Xanthomonas campestris* PV. *Musacearum*. *African J. Biotechnol.*, 8(20), 5343-5350, [Online]. <http://www.academicjournals.org/AJB>
- Tripathi, Upadhyay, S., Bhuiyan, M., & Bhattacharya, P. R. (2009). A review on prospects of essential oils as a biopesticide in insect-pest management. *J. Pharmacogn. Phytother.*, 1(5), 52-63. <http://www.academicjournals.org/jpp>
- Trongtokit, Y., Rongsriyam, Y., Komalamisra, N., & Apiwathnasorn, C. (2005). Comparative repellency of 38 essential oils against mosquito bites. *Phytother. Res.*, 19(4), 303-309. <https://doi.org/10.1002/ptr.1637>
- Trumble, J. T. (2002). Caveat emptor: Safety considerations for natural products used in arthropod control. *Am. Entomol.*, 48(1), 7-13. <https://doi.org/10.1093/ae/48.1.7>
- Urabe, C., (1992). Ohtsu Tire Japan. Insect control in wood.
- Valdivieso-Ugarte, M., Gomez-Llorente, C., Plaza-Diaz, J., & Gil, A. (2019). Antimicrobial, Antioxidant, and Immunomodulatory Properties of Essential Oils: A Systematic Review. *Nutrients*, 11(11), <https://doi.org/10.3390/nu11112786>. doi: E2786 [pii]
- Vongsombath, C., Palsson, K., Bjrk, L., Borg-Karlson, A. K., & Jaenson, T. G. T. (2012). Mosquito (Diptera: Culicidae) repellency field tests of essential oils from plants traditionally used in Laos. *J. Med. Entomol.*, 49(6), 1398-1404, <https://doi.org/10.1603/ME12025>.
- Yang, Y. C., Lim, M. Y., & Lee, H. S. (2003). Emodin Isolated from *Cassia obtusifolia* (Leguminosae) Seed Show Larvicidal Activity against Three Mosquito Species. *J. Agric. Food Chem.*, 51(26), 7629-7631. <https://doi.org/10.1021/jf034727t>
- Younas, M., Zou, H., Laraib, T., Rajpoot, N. A., Khan, N.A., Zaidi, A. A., ... & Arit, M. (2021). The impact of insecticides and plant extracts on the suppression of insect vector (*Bemisia tabaci*) of Mungbean yellow mosaic virus (YMMV). *PLoS One*, 16(9). <https://doi.org/10.1371/journal.pone.0256449>
- Youssef, N. S. (1997). Toxic and synergistic properties of several volatile oils against larvae of the house fly, *Musca domestica vicina* Maquart (Diptera: Muscidae). *Journal-Egyptian Ger. Soc. Zool.*, 22, 131-150.
- Yuan, Z. & Ping Hu, X. (2011). Evaluation of differential antiseptic activities of *Lantana Camara* oven-dried tissues against *Reticulitermes virginicus* (Isoptera: Rhinotermitidae). *Insect Sci.*, 18(6), 671-681. <https://doi.org/10.1111/j.1744-7917.2010.01400.x>.
- Zomorodian, K., Saharkhiz, M. J., Shariati, S., Pakshir, K., Rahimi, M. J., & Khashei, R. (2012). Chemical Composition and Antimicrobial Activities of Essential Oils from *Nepeta cataria* L. against Common Causes of Food-Borne Infections. *ISRN Pharm.*, 2012, 1-6. <https://doi.org/10.5402/2012/591953>

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