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REVIEW: PLANTS WITH REPELLENT ACTIVITY

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ABSTRACT

Mosquitoes are vectors of illnesses, such as encephalitis, dengue, filariasis, intestinal sickness, and encephalitis. These diseases have become epidemics in Indonesia and around the world. Natural repellents are alternatives for preventing mosquito-borne diseases that are safe, easily degradable, and eco-friendly. This review aimed to identify compounds in plants with mosquito repellent activity. Data were obtained from national and international journals using search platforms, including PubMed, Scholar, SciDirect, and Hindawi. This review focuses on plants with repellent activity, their resulting repellent activity, the content of bioactive compounds, and the mosquito species used. Many plants contain naturally occurring compounds that can repel mosquitoes. Following scientific research, 14 bioactive compounds have been shown to have repellent activity in plants.

Keywords: repellent, volatile oil, mosquitos, bioactive compounds, narrative literature review

INTRODUCTION

Many types of insects, including mosquitoes, can be disease vectors. Every year, more than 700 million people suffer from diseases transmitted by mosquitoes (El-Sheikh *et al*., 2016). As a tropical region, Indonesia has several endemic mosquito species. Mosquito bites not only cause pain, but can also transmit diseases, not only in Indonesia, but worldwide (Nufus *et al.*, 2018). Filariasis, malaria, dengue fever, and encephalitis are diseases caused by mosquitoes (Das *et al.*, 2015). For example, 9, 906 chronic filariasis cases were reported in Indonesia in 2021, especially in 236 districts/cities in 28 provinces, which are endemic areas of filariasis transmitted by larvae found in mosquitoes (P2P, 2023). By the end of 2022, there were 143 thousand cases of dengue fever, with the highest incidence in the provinces of West Java, East Java, and Central Java (Samad *et al*., 2022). In 2019, the WHO mentioned that 229 million malaria cases spread across 87 countries, with 409,000 deaths caused by *Anopheles* sp. mosquitoes (Villena *et al*., 2022).

Several methods have been used to reduce mosquito populations, including insecticides, nets for sleep treatment with insecticides, and artificial repelling agents against mosquitoes. This could reduce the number of mosquito populations. However, the continued use of synthetic pesticides can induce mosquitoes to develop resistance, and mosquito sprays might trigger respiratory issues, especially in children (Azeem *et al*., 2019). Another method to avoid mosquitoes, especially their bites, is to use repellents. Repellents are essential in preventing mosquitoes from coming into contact with us, but if they are synthetic, unwanted effects will occur (Das *et al*., 2015). Most people have now switched to using plants to repel mosquitoes due to their abundant availability in connection with the conditions (Ardiana *et al*., 2022). Natural ingredients are believed to be safer than synthetic ingredients, and essential oils from these natural ingredients can be used as mosquito repellents (Azeem *et al*., 2019). In addition, plant-derived materials are biodegradable, safe for humans, slow the development of opposition, and easy and inexpensive for residents and tiny businesses. (Ogban *et al*., 2020). This review aimed to identify the beneficial substances that plants contain as repelling agents for mosquitoes.

RESEARCH METHOD

Data were obtained from national and international journals using search platforms such as PubMed, Scholar, SciDirect, and Hindawi. Literature others searches are taken from 2013 to 2023 using keywords "repellent mosquito," "repellent natural product," "repellent mosquito," "repellent" "repellent mosquito extract," "mosquito," "*Aedes aegypti*," "*Aedes albopictus*," "*Culex* sp," "*Culex quinquefasciatus*," "*Anopheles* sp," "*pipperaceae* repellent," "serai wangi repellent," "*Zingiber cassumunar*," "*Zingiber cassumunar* repellent," "*Ocimum sanctum*," "*Ocimum sanctum* repellent," "*Evodia Suaveolens*," "*Evodia Suaveolens* repellent", "*zodia*," "nyamuk" and "life of mosquitos." Primary data from 132 international and national journals were screened, and 43 journals that matched the requirements were acquired. The conditions for inclusion included the type of plant utilized, concentration of bioactive substances, outcomes of repellent activity testing, and mosquito species employed. Journals published before 2012 were excluded. The journal search process is illustrated in **Figure 1.**

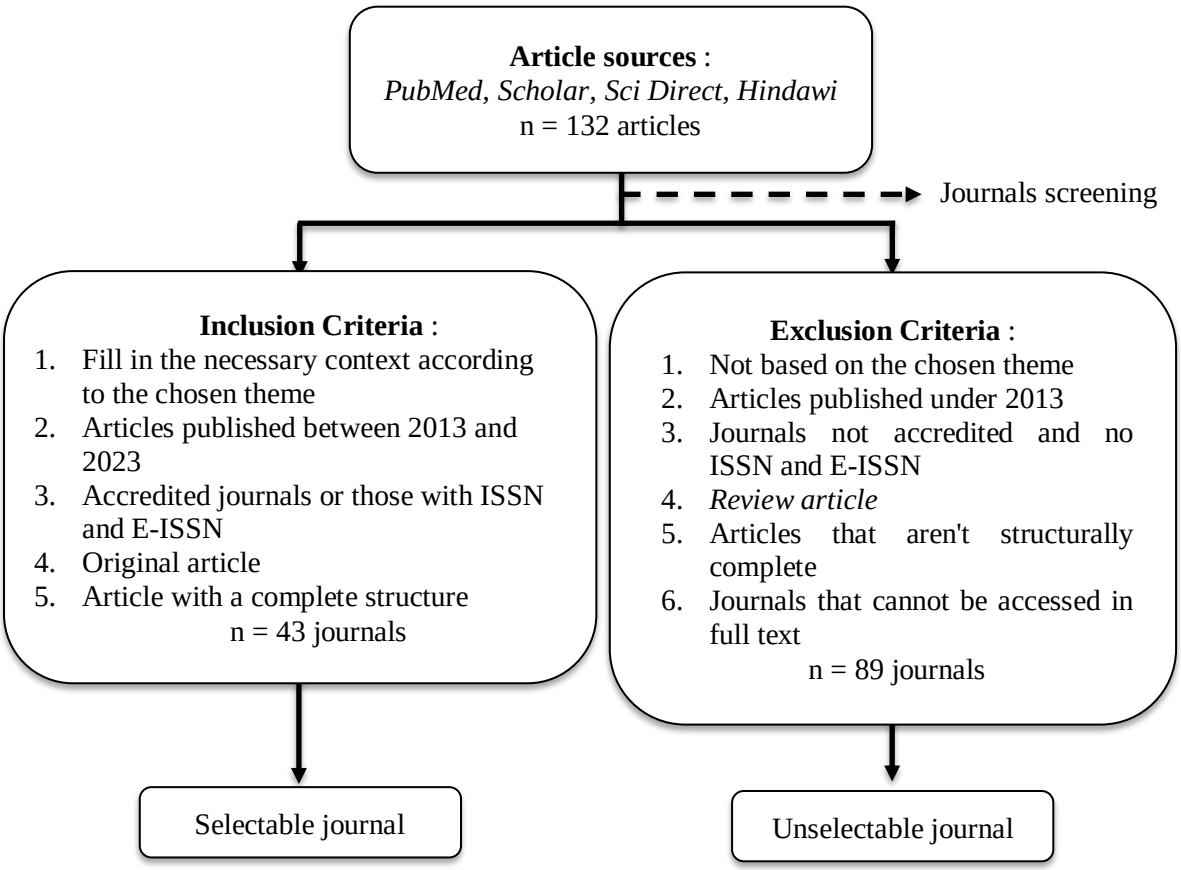


Figure 1. Flow Chart of Publishing Search Method

RESULTS AND DISCUSSION

Mosquito Vectors

The main transmitters of diseases, including chikungunya, yellow fever, malaria, and dengue, are mosquitoes, which pose a significant threat to human health. By feeding on blood, mosquitoes can transmit diseases to humans (Aini *et al*., 2017).

A. aegypti is the leading cause of dengue fever. Because of changing environmental conditions, this mosquito is adapting to its breeding sites, such as stagnant water on the ground and other places after rain, drains, and even puddles, which are places where the number of mosquito eggs is very high and where they begin to breed, not just in clean water (Yulianti *et al*., 2020). Aedes albopictus, also known as the tiger mosquito, is a mosquito

vector of dengue fever. This mosquito often lays eggs in temporary water sources, such as puddles, after rain. Before hatching, the eggs must undergo a wet-dry-wet cycle. They can survive for a long time, as they have adapted to avoid predation by larvae (Reed *et al*., 2022).

Ae. aegypti and *Ae. albopictus* are anthropophilic, meaning that they only develop on human hosts and transmit diseases through direct contact. Because of this characteristic, their lives are closely intertwined with humans. Both mosquito species are primarily active during the day, with two distinct periods of activity, in the morning and afternoon. Both the endophilic and exophagic forms were observed. However, *Ae. albopictus* mainly feeds as an opportunistic sucker that lives outside human houses, meaning it feeds on various hosts, including cold-blooded and warm-blooded animals, to transmit its pathogens. The life cycle and gonotropic cycle of both species are shown in **Figure 2** (Reinhold *et al*. 2018).

Culex mosquitoes are a parasitic zoonotic species. They are the leading cause of the largest filariasis outbreak in Indonesia. The highest estimated number of worm transmissions occurs in adult *Culex* mosquitoes. After the rainy season, *Culex* larvae are usually abundant. After the rainy season, *Culex* larvae are usually abundant. Although some predators can reduce their populations, the number of *Culex* mosquitoes remains high, posing a problem for humans. After the rainy season, *Culex* larvae are usually abundant. *Culex* larvae can survive in various environments, including bathtubs, drains, rice fields, and in areas with high levels of organic pollution. Culex larvae can survive in various environments, including bathtubs, drains, rice fields, and in areas with high levels of organic pollution. Female *Culex* mosquitoes are active at night and have the potential to transmit parasitic worms to both animals and humans. *Culex* larvae can survive in various environments including bathtubs, drains, rice fields, and areas with high levels of organic pollution (Anggraini *et al*., 2022). The life cycle of *Culex* sp. mosquitoes is shown in **Figure 3** (C.D.C. 2022).

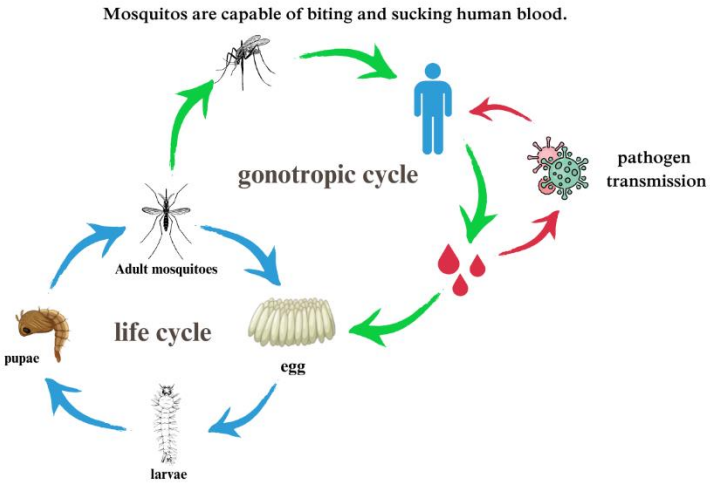


Figure 2. ***The life cycle of mosquitoes and gonotropic cycle of Aedes sp. serve as carriers of illness.***

Culex quinquefasciatus is a *Culex* species that causes lymphatic filariasis. Adult female *Cx. quinquefasciatus* mosquitoes require protein for 2-7 days, which they obtain from human or animal blood, and a sugar solution for 1-3 days. Female *C. quinquefasciatus* mosquitoes become active in the evening, and their bites can potentially transmit filarial worms (*Wuchereria bancrofti*) that cause lymphatic filariasis (Ramadhani *et al*., 2019).

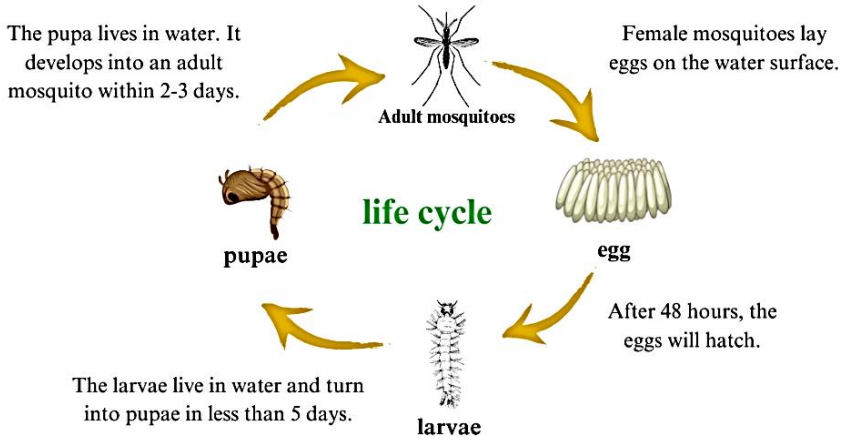


Figure 3. The life cycle of *Culex* sp.

Anopheles sinensis, and *Anopheles gambiae* are *Anopheles* species that cause malaria (Pathak *et al.*, 2023). Adult female *Anopheles* mosquitoes are most active in the late afternoon or evening when they bite people and animals because they need blood to reproduce and lay eggs. The life cycle of *the Anopheles* sp. mosquitoes is shown in **Figure 4**. (C.D.C., 2016).

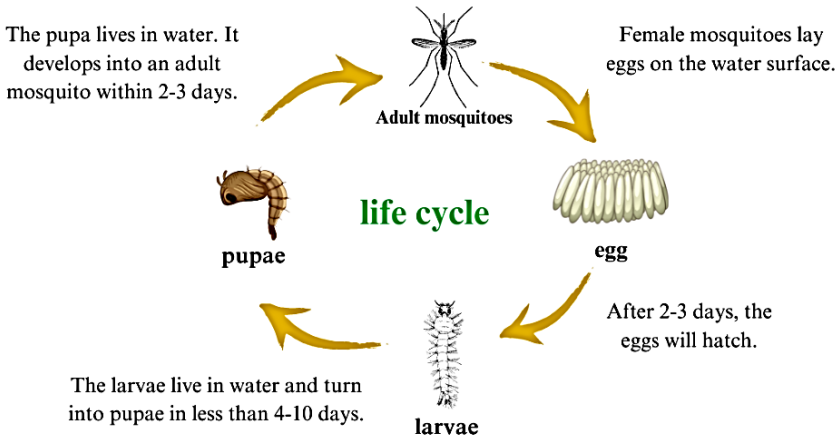


Figure 4. The life cycle of *Anopheles* sp.

Repellent

Mosquitoes can be dangerous, particularly in humans. Therefore, preventive measures are necessary to avoid bites. One such method is the use of repellents. One often used as a repellent is DEET, research has shown that it can have harmful effects on humans, such as urticaria syndrome, anaphylaxis, hypotension, and neurotoxins. Therefore, people are increasingly using plants as repellents, specifically the oils they contain, which have been proven to be biodegradable, eco-friendly, and safe for humans (Li *et al.*, 2021). The main bioactive components found in essential oils are citronellal, citronellol, and geraniol. They can be used as alternatives to repellents (Eden *et al.*, 2020).

Plants with Potential as Repellents

Piper aduncum L. belonging to the *Piperaceae* family and is frequently referred to as ‘sirih hutan’ / ‘lada berduri’ in Indonesia. This may be due to its repellent properties. It is a shrub with alternating leaves and pointy leaves. Traditionally, this plant has been used in

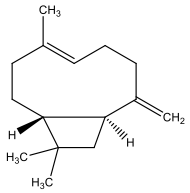
medicine and as a cuisine. The leaves of this plant contain caryophyllene, an agent with the potential to function as an ecological repellent owing to its unpleasant aroma for mosquitoes. This was proven in a study by Mamood in 2017, which reported a 100% repellency rate for 60 minutes when the essential oil was formulated into a cream or ointment (Mamood *et al.*, 2017). Research conducted by Wibawa et al. in 2019 supports the claim that *P. aduncum* L. leaves contain essential oils, particularly caryophyllene, which has the potential to be repellent (Wibawa *et al*., 2019).

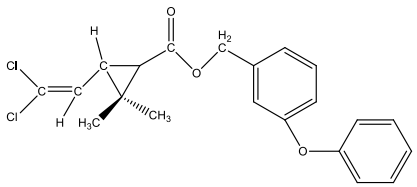
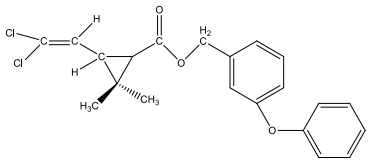
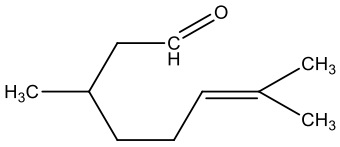
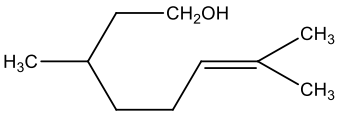
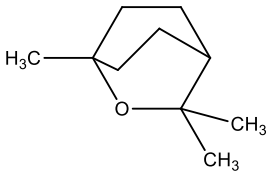
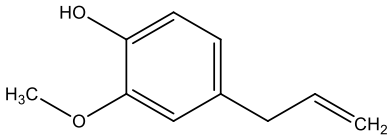
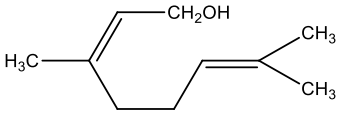
Cymbopogon nardus L. is a 'rumpus abadi', commonly known as 'serai wangi', belonging to the *Poaceae* family. It thrives in tropical and subtropical locations, including America, Asia, and Africa. These components can act as natural repellents. Citronella oil extracted from this grass contains three active components: citronellal, citronellol, and geraniol. Proof of the repelling action of the essential oil derived from *C. nardus* L. leaves with respect to *Ae. aegypti* mosquitoes at a concentration of 5% provided 100% protection for 2 hours and over 99% protection for more than 4 hours (Arpiwi *et al*., 2020). An investigation of the extraction of crucial oils from the leaves of *C. nardus* L. against *Culex* sp. mosquitoes was conducted by Ardian in 2022. This study found that the protective power was 97.91% after 2 hours.

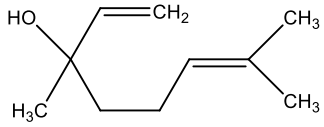
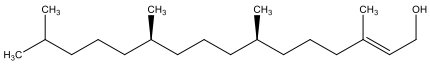
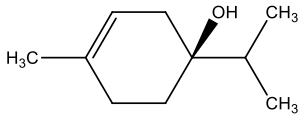
Additionally, other essential oils found in *C. nardus* L leaves have the potential to act as repellents, namely Deltamethrin and Permethrin (Trans-permethrin and Cis-permethrin), both of which are toxic to mosquitoes (Ardiana *et al*., 2022). *Cymbopogon winterianus* Jowitt is another species of the *Poaceae* family that has the potential to act as a mosquito repellent. It had a protection rate of 92.26% against *A. aegypti* mosquitoes at a concentration of 75% for 5 hours (Yanti *et al*., 2022).

Ocimum basilicum (L.), known as 'kemangi' in Indonesia, belongs to the *Lamiaceae* family and can repel. Fajarini demonstrated this in 2015 research on *O. basilicum* (L.) leaves. A concentration of 15% resulted in a repellent time of less than 1 hour, while concentrations of 25% and 35% resulted in repellent times of 1.2 and 1.5 hours, respectively (Fajarini *et al*., 2015). Other *Lamiaceae* families that have been studied include *Ocimum caninum* and *Ocimum gratissimum.* These findings demonstrated that at concentrations of 2–5 mg/l, the crude oil of *O. caninum* leaves had a 100% repellent percentage against *Anopheles gambiae*, indicating a repellency time of 90 minutes. Meanwhile, the essential oil of *O. gratissimum* at a concentration of 3-5 mg/l showed a repellency time of 120 minutes (Afolabi *et al*., 2018). The main components that act as repellents in the leaves of plants of the *Lamiaceae* family are linalool, eugenol, and 1,8 cineole (Fajarini *et al*., 2015).

Table I. Structure of Bioactive Compounds in Plants with Potential as Repellents

Plant Sources	Bioactive Compounds	Molecular Structure	Ref
Basil (*Ocimum basilicum*) Silvery wormwood (*Artemisia argyi*)	*β-caryophyllene*	 (1R,9S,E)-4,11,11-trimethyl-8-methylenebicyclo[7.2.0]undec-4-ene	(Ullah *et al*., 2021) (Luo *et al*., 2022)

Plant Sources	Bioactive Compounds	Molecular Structure	Ref
Serai Wangi (*Cymbopogon nardus* L.)	*Cis-permethrin*	 3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate	(Ardiana *et al*., 2022)
Serai Wangi (*Cymbopogon nardus* L.)	*Trans-pemethrin*	 3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate	(Ardiana *et al*., 2022)
Serai Wangi (*Cymbopogon nardus* L.)	*Citronellal*	 3,7-dimethyloct-6-enal	(Bota *et al*., 2015) (Arpiwi *et al*, 2020)
Serai Wangi (*Cymbopogon nardus* L.)	*Citronellol*	 3,7-dimethyloct-6-en-1-ol	(Bota *et al*., 2015) (Arpiwi *et al*, 2020)
Basil (*Ocimum* sp.) Silvery wormwood (*Artemisia argyi*) Kayu putih (*Eucalyptus globulus*)	*Eucalyptol (1-8 cineole)*	 1,3,3-trimethyl-2-oxabicyclo[2.2.2]octane	(Rassaeifar *et al*., 2013) *(Fajarini et al*., 2015) (Luo et al., 2022) (Sheikh *et al*., 2021)
Basil (*Ocimum* sp.)	*Eugenol*	 4-allyl-2-methoxyphenol	(Fajarini *et al*., 2015)
Serai Wangi (*Cymbopogon nardus* L.)	*Geraniol*	 (Z)-3,7-dimethylocta-2,6-dien-1-ol	(Bota *et al*., 2015) *(Arpiwi et al*, 2020)

Plant Sources	Bioactive Compounds	Molecular Structure	Ref
Basil (*Ocimum* sp.) Zodia (*Evodia sauveolens*)	*Linalool*	 3,7-dimethylocta-1,6-dien-3-ol	(Vieira *et al*., 2013) (Fajarini *et al*., 2015) (Yabansabra *et al*., 2023)
Mangroves (*Rhizophora mucronata*) Silvery wormwood (*Artemisia argyi*)	*Phytol*	 (7R,11R,E)-3,7,11,15-tetramethylhexadec-2-en-1-ol	(Moldoveanu, 2019) (Karthi *et al*., 2020) (Luo *et al*., 2022)
Bangle (*Zingiber cassumunar*)	*Terpinen-4-ol*	 (S)-1-isopropyl-4-methylcyclohex-3-enol	(Li *et al*., 2021)

Rhizophora mucronata is a red mangrove plant believed to be used as a repellent. According to Karthi's 2020 study, the extract from *R. mucronata* leaves contains 13 main bioactive compounds. Phytol is thought to have a repellent activity. The maximum activity duration was 210 minutes against all three mosquito species, with activity percentages of 96.4% for *Culex quinquefasciatus* and 94.32% for *Ae. aegypti* and 97.2% for *Anopheles stephensi* (Karthi *et al.*, 2020). The compounds were further strengthened in a subsequent study 2022 on *Artemisia argyi* plants, which contained four main compounds: eucalyptol, β-caryophyllene, caryophyllene oxide, and phytol. These compounds are repellents against mosquitoes, particularly eucalyptol (monoterpenoid) and phytol (diterpenoid), which are widely reported natural pesticides (Luo *et al.*, 2022).

According to the *Myrtaceae* family, *Eucalyptus globulus* is 'tanaman kayu putih' in Indonesia. In response to a study performed by Sheikh *et al*. in 2021 on *the repellant efficacy of E. globulus essential oil* against *Anopheles stephensi* bites, the highest repellency percentage of 83.33% was achieved after 2 hours of application at a concentration of 7%. Eucalyptol, or 1-8 cineole, is the bioactive compound responsible for this activity (Sheikh *et al*., 2021).

Plant *Zingiber cassumunar* is classified as part of the *Zingiberaceae* family. It is known as ‘Bangle’ in Indonesia,'while it is called Bulei in China. This plant is essential for medicinal purposes (Han *et al*., 2021). *Z. cassumunar* has many benefits, including its use as a repellent. It has modest repellent action as opposed to *albopictus* mosquitos, with a minimum effective dosage of 0.25 ± 0.01 mg/cm2 as opposed to the usual (DEET) with a minimum effective concentration of 0.03 ± 0.01 mg/cm2. Terpinen-4-ol and butadiene are the most common constituents of essential oils. One significant function of terpinen-4-ol is as a repellant. It is important to note that this statement is based on objective evidence rather than subjective evaluations (Li *et al*., 2021).

Tribulus terrestris, often known as ‘Rujak Polo,’ is an annual plant found worldwide and is a member of the *Zygophyllaceae* family. Observations have been made regarding the capacity to reject *Ae. aegypti* mosquitoes. This is due to the findings of El-Sheikh's 2016 study on The petroleum ether extract of T. terrestris leaves, which demonstrated 100% repellency at a dose of 1.5 mg/cm2 for a repellency span of 4 hours. This result is comparable to the standard (DEET), which was used as a reference for dose and time after delivery (El-Sheikh *et al*., 2016).

Delonix elata (L.) belongs to the *Fabaceae* family, also known in Indonesia as 'Flamboyan kuning,' and has been reported to have repellent activity. In 2014, Govindarajan conducted a repellency test on the leaf and seed extracts of *Culex quinquefasciatus* using five different solvents: methanol, ethyl acetate, chloroform, benzene, and hexane. The best result in terms of duration was obtained when the leaves of *D. elata* (L.) were treated with methanol solvent at a rate of 5 mg/cm2 for 150 minutes, resulting in 100% repellency. Using the same solvent at an intake of 5 mg/cm2 and optimum duration of 120 minutes, 100% repellency was obtained. No research has been conducted on the active compounds that may act as repellents on *D. elata* (L.) leaves or seeds, as this is the first test (Govindarajan, 2014). However, in a 2014 study by Senthilkumar and Sami Veerappa, phytochemical screening was conducted on the methanol extract of the leaves and roots of *D. elata* (L.). Secondary metabolites found in *D. elata* (L.) include flavonoids, proteins, tannins, phenolics, saponins, alkaloids, glycosides, amino acids, and carbohydrates. (Senthilkumar and Veerappa, 2014). The study was continued by Govindarajan, Rajeswary, and Sivakumar in 2015 using the same plant, solvent, and solvent concentrations but with a different mosquito vector, *Anopheles stephensi*. The best result was achieved using methanol as the solvent at a concentration of 5 mg/cm2, which showed 100% repellency for an optimum duration of 210 minutes (Govindarajan *et al*., 2015).

Table II. Efficacy of Plants as Mosquito Repellents

Plant Sources	Mosquito Species	% Repellency	Effective Duration	Ref
Piper aduncum L.	*Ae. aegypti*	100%	60 minutes	(Mamood *et al.*, 2017)
Cymbopogon nardus L.	*Ae. aegypti*	99%	>4 hours	(Arpiwi *et al.*, 2020)
		92.26%	5 hours	(Yanti *et al.*, 2022)
Ocimum caninum	*Anopheles gambiae*	100%	90 minutes	(Afolabi et al., 2018)
Ocimum gratissimum	*Anopheles gambiae*	100%	120 minutes	(Afolabi *et al.*, 2018)
Rhizophora mucronata	*Culex quinquefasciatus* *Ae. aegypti* *Anopheles stephensi*	96.4% 94.32% 97.2%	210 minutes 210 minutes 210 minutes	(Karthi *et al.*, 2020)
Eucalyptus globulus	*Anopheles stephensi*	83.33%	2 hours	(Sheikh *et al.*, 2021)
Tribulus terrestris	*Ae. aegypti*	100%	4 hours	(El-Sheikh *et al*., 2016)
Delonix elata (L.)	*Culex quinquefasciatus*	100%	150 minutes	(Govindarajan, 2014)
	Anopheles stephensi	100%	210 minutes	(Govindarajan *et al*., 2015)
Evodia sauveolens	*Ae. aegypti*	93.33%	3 hours	(Yabansabra *et al*., 2023).

Evodia sauveolens belongs to the Rutaceae family, commonly known as 'zodia' in Indonesia. It is widely recognized as an effective mosquito repellent. According to research conducted by Yabansabra in 2023, the most significant bioactive substance in the essential oil of the plant's leaves is linalool, the main compound in sauveolens, which serves as a

repellant against *Ae. aegypti* mosquitoes. The obtained repellency results were 92.85% at a concentration of 25%, 91.66% at a concentration of 50%, and 93.33% at a concentration of 75%. These concentrations were applied for 3 hours (Yabansabra *et al.*, 2023). The concentration used was higher than that used in Sudiarti's study in 2021, which used the same plant and mosquito species at concentrations of 1%, 2%, and 3%. The best result was obtained at a concentration of 3%, with a repellent effect of 77.3% and a contact time of 15 minutes (Sudiarti *et al*., 2021). This demonstrates that the higher the concentration, the better is the repellent performance. However, this also has the disadvantage of requiring more raw materials to obtain the extract or essential oils.

CONCLUSION

Many plants contain biologically active substances that can function as insect repellents, specifically mosquitoes. Based on the literature search, the compounds β-caryophyllene, cis-permethrine, trans-pemethrine, citronellal, citronellol, eucalyptol (1-8 cineole), eugenol, geraniol, linalool, phytol, and terpinen-4-ol were identified., which are bioactive compounds found in plants, can be used as natural repellents. Scientific studies have proven their effectiveness, and they can be easily obtained as plants grow abundantly in our surroundings.

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