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The Potential Of Secondary Metabolites From Cinnamomum SP. As Natural Insecticide Against Mosquitoes

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Abstract—Mosquitoes are the primary vectors of various infectious diseases such as dengue fever, malaria, and filariasis, making their control a crucial public health concern. One environmentally friendly alternative for mosquito control is the use of plant-based natural insecticides, such as Cinnamomum sp., which is known to contain bioactive compounds like cinnamaldehyde, eugenol, and linalool. These compounds exhibit insecticidal activity through neurotoxic mechanisms, repellency, antifeedant effects, and inhibition of mosquito larval growth. This study is a literature review that collects and analyzes various studies on the effectiveness of Cinnamomum sp. extract against mosquitoes. The review findings indicate that Cinnamomum sp. extract has high potential as a natural insecticide, demonstrating toxic effects on both mosquito larvae and adults while also act as an effective repellent. Additionally, the use of this extract is safer for the environment compared to synthetic insecticides. Therefore, Cinnamomum sp. could serve as a viable alternative for biological vector control, although further research is needed to optimize its formulation and field application.

Keywords—Bioactive compounds, Cinnamomum sp., mosquitoes, natural insecticide, vector control

I. INTRODUCTION

Mosquito-borne diseases are a health problem that occurs in several countries, especially tropical countries such as India and Thailand [1]. Some of the mosquito-borne diseases include dengue [2], malaria [3], yellow fever [4], west nile [5], rift valley fever [6], and zika [7]. In Indonesia, dengue fever and malaria are the diseases with the most cases. Dengue fever caused by dengue virus (DENV) was first identified in 1968 in the cities of Jakarta and Surabaya. Dengue fever caused by DENV increases during the rainy season (usually occurs between October and April). Since 2004, Indonesia has been among the countries with the highest DENV cases. Four serotypes of DENV (DENV1-4) have been identified, with DENV3 being known as the most severe disease-causing strain [8].

The use of synthetic pesticides in mosquito population control has long been the primary choice in an effort to reduce the risk of transmission of vector-borne diseases. However, concerns over the impact of persistence, resistance, high cost, as well as harmful effects on humans and non-target organisms, have prompted the search for safer alternatives. One interesting approach is the use of natural pesticides from plants containing bioactive compounds, such as those found in the genus *Cinnamomum* sp. [9]. *Cinnamomum* sp. is a group of plants known for its essential oils that accumulate in the bark. These compounds have been shown to have strong insecticidal activity against various types of mosquitoes, including Aedes aegypti which is a major vector for diseases such as dengue fever, as well as *Anopheles* sp. which spreads malaria [10].

The use of natural insecticides from *Cinnamomum* sp. offers several advantages over synthetic pesticides. First, the active compounds in these plants tend to have lower toxicity to humans and non-target organisms, reducing the risk of undesirable health effects. Second, their use is also more environmentally friendly as these compounds tend to degrade more easily in the natural environment, reducing environmental pollution caused by pesticide residues [11]. Bioactive compounds in *Cinnamomum* sp. have the potential to disrupt the mosquito life cycle by various complex mechanisms. For example, they can inhibit egg development by disrupting the reproductive process or affecting the ability of eggs to hatch. At the larval stage, the compounds can act as growth disruptors or interfere with the nervous system, inhibiting larval development into adults. At the pupa stage, these bioactive compounds can affect the metamorphosis process or organ development, thus slowing or inhibiting the development into adult mosquitoes that can infect humans [12].

The purpose of this review is to present in-depth information on the utilization of natural insecticides derived from *Cinnamomum* sp. The main focus of this review is to explain the bioactive compounds of *Cinnamomum* sp. as natural insecticides for mosquitoes. In addition, this review also explores the effectiveness of these natural insecticides in controlling mosquito populations, based on both experimental evidence and field observations. The mechanism of action of the bioactive compounds and other components in the target organisms, such as mosquitoes and larvae, is also analyzed in depth. By examining the bioactive compounds, efficacy, and mechanisms of action of natural insecticides derived from *Cinnamomum* species, this review aims to guide the development of more sustainable and eco-friendly pest control strategies.

II. METHODS

This review is based on research articles related to the use of *Cinnamomum* sp. as a larvicide. The data sources for this review were obtained from Google Scholar. The keywords used for this search were “Cinnamaldehyde as insecticide,” “Cinnamomum as larvicide,” and “Cinnamomum as mosquito larvicide.” The articles will be analyzed and selected based on inclusion and exclusion criteria. The inclusion criteria are aligned with the objectives of this review article. The selected journal articles must be original research studies that provide primary data on the use of *Cinnamomum* sp. as a mosquito larvicide. Additionally, only original, full-text, and international articles will be considered. The exclusion criteria for article selection include original articles discussing the use of *Cinnamomum* sp. without detailing its metabolites or its application as a mosquito insecticide. Articles that are not international journals, not open access, or categorized as review articles, clinical trial reports, short reports, or case reports will also be excluded. Articles that meet the criteria based on title, keywords, and abstract will be reviewed in full text to assess their content and relevance to the research topic. The article selection process follows a systematic search while considering the inclusion and exclusion criteria. The analysis in this review article is conducted descriptively. The PRISMA diagram illustrating the review methodology is presented in Figure 1.

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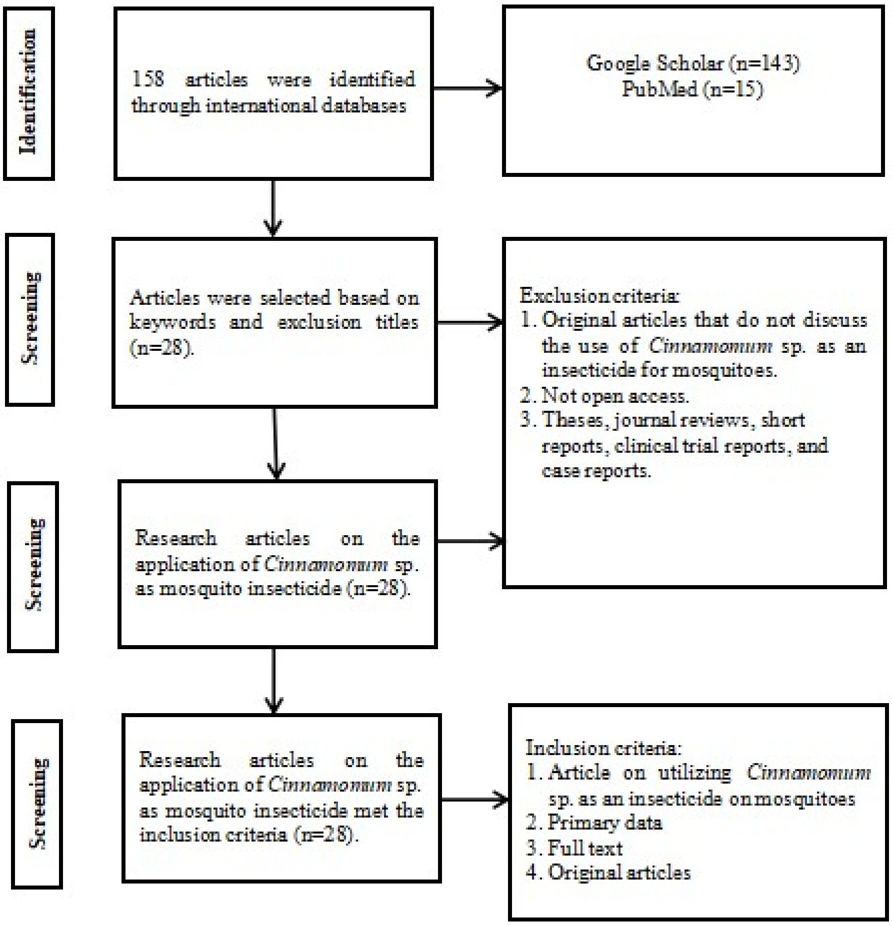

Figure 1. PRISMA diagram for article selection

III. RESULTS AND DISCUSSION

3.1. Bioactive Compounds in *Cinnamomum* sp. as Insecticide

The bioactive compounds found in *Cinnamomum* sp. are highly diverse. As shown in Table 1, cinnamaldehyde is the most abundant bioactive compound in *Cinnamomum* sp. This in line with the findings of [13], which state that cinnamaldehyde is the primary constituent of *Cinnamomum cassia*, accounting for 80% of its total composition. Similarly, research by [14] identified cinnamaldehyde as the most prevalent compound (49.33% of the total constituents), followed by cetophenone (6.94%), trans-cinnamic acid (5.45%), cis-cinnamaldehyde (4.44%), o-methoxycinnamaldehyde (3.48%), coumarin (3.42%), and (E)-cinnamyl alcohol (3.21%). Cinnamaldehyde is a phenolic essential oil and is recognized as a bioactive compound with potential as a natural mosquito insecticide [15]. These bioactive compounds can be extracted using various methods, including maceration (e.g., with methanol [16], ethanol [17], DCM [18], EtOAc [19], and EtOH [20], hydrodistillation [21], thermosyphon distillation [22], and steam distillation [23].

For the analysis of secondary metabolites in *Cinnamomum* sp., the most commonly used instruments are GC-MS and HPLC. Gas Chromatography-Mass Spectrometry (GC-MS) is an analytical technique that combines two separate methods: Gas Chromatography (GC) and Mass Spectrometry (MS). GC is used to separate compound mixtures into individual components based on their physicochemical properties, while MS identifies these compounds based on their mass and fragmentation patterns [24]. High-Performance Liquid Chromatography (HPLC) is an instrumental technique used to separate, identify, and quantify compounds in a solution. This method employs a liquid mobile phase and a highly sensitive stationary phase column to separate

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compounds based on their affinity for the stationary and mobile phases [25]. For volatile compound analysis, GC-MS is the preferred technique due to its high sensitivity, allowing the detection of volatile compounds at extremely low concentrations, typically at parts per million (ppm) or even parts per billion (ppb) levels. Additionally, GC-MS analysis is generally non-destructive to volatile compounds, enabling accurate measurements without sample degradation [26].

Table 1. Utilization of Bioactive Compounds from *Cinnamomum* sp. as Mosquito Insecticides

No	Species	Bioactive Compounds	Extraction Method/Detection Method	Target	Results	References
1	*Cinnamomum verum*	Cinnamaldehyde	Maceration (ethanol)/ GC-MS	*Aedes aegypti*	The extract at 7% concentration achieves 100% mortality	[27]
2	*Cinnamomum osmophloeum*	Cinnamaldehyde	Hydrodistillation/ GC-MS	*Anopheles gambiae*	The extract at 200 µg/mL concentration achieves 100% larval mortality	[12]
3	*Cinnamomum subavenium*	Eugenol	Hydrodistillation/ GC-MS	*Anopheles sinensis*	LC_{50} = 79.63 µg/mL	[28]
4	*Cinnamomum tonkinense*	Citral	Hydrodistillation/ GC-MS	*Aedes albopictus* dan *Aedes aegypti*	LC_{50} = 16.7 µg/mL	[29]
5	*Cinnamomum verum*	Cinnamaldehyde	Steam distillation/ GC-MS	*Aedes aegypti*	LC_{50} = 41.56 µg/mL	[30]
6	*Cinnamomum verum*	Cinnamaldehyde	Hydrodistillation/ GC-MS	*Culex quinquefasciatus*	LC_{50} = 24,5 µg/mL	[31]
7	*Cinnamomum zeylanicum*	Cinnamaldehyde	Steam distillation/ GC-MS	*Aedes aegypti*	LC_{50} = 0,03 µg/mL	[23]
8	*Cinnamomum tamala*	Cinnamaldehyde	Water/ GC-MS	*Culex quinquefasciatus*	The extract at 5% concentration achieves 100% larval mortality	[32]
9	*Cinnamomum zeylanicum*	Linalool	Steam distillation/ GC-MS	*Anopheles stephensi, Aedes aegypti, Culex quinquefasciatus*	*Cinnamomum tamala* extract has an LC_{50} of 85.6 ppm for *Anopheles stephensi*, 65.10 ppm for *Aedes aegypti*, and 52.90 ppm for *Culex quinquefasciatus*.	[33]
10	*Cinnamomum zeylanicum*	Cinnamaldehyde	Water /N/A	*Aedes aegypti*	The extract at 10% concentration achieves 100% larval mortality	[34]
11	*Cinnamomum camphora*	Cinnamaldehyde	Hydrodistillation/ GC-MS	*Anopheles stephensi*	LC_{50} = 0,026%.	[10]
12	*Cinnamomum camphora*	Cinnamaldehyde	EtOH/ HPLC	*Culex pipiens*	LC_{50} = 0.009 µg/mL.	[35]
13	*Cinnamomum zeylanicum*	β-Cubebene	Hydrodistillation/ HPLC	*Anopheles gambiae*	LC_{50} = 98,95 ppm.	[36]
14	*Cinnamomum* sp.	Eugenol	Hydrodistillation/ GC-MS	*Anopheles gambiae*	LC_{50} = 10,46 µg/mL	[37]
15	*Cinnamomum verum*	Cinnamaldehyde	Thermosyphon Distillation/ GC-MS	*Culex quinquefasciatus*	Inhibits egg hatching by 100%	[1]
16	*Cinnamomum verum*	Trans-cinnamaldehyde	Hydrodistillation/ GC-MS	*Aedes aegypti, Aedes albopictus*	Inhibits egg hatching by 91-93%	[38]
17	*Cinnamomum*	Eugenol	N/A	*Instar larvae of*	LC_{50} = 5,4 µg/mL	[39]

	sp.			*Anopheles stephensi*		
18	*Cinnamomum cassia* + *Cinnamomum loureiroi*	Cinnamaldehyde	Hydrodistillation/ GC-MS	*Aedes aegypti, Aedes albopictus dewasa*	Mortality rate of 100%	[40]
19	*Cinnamomum cassia*	Trans-cinnamaldehyde	Hydrodistillation/ GC-MS	*Aedes aegypti*	The repellent index of essential oil at concentrations of 25% after 90 minutes was 73,33%	[41]
20	*Cinnamomum verum*	Cinnamaldehyde	N/A	*Culex pipiens* larvae	LC_{50} = 754,30 ppm	[42]
21	*Cinnamomum* sp.	Cinnamaldehyde	N/A	*Aedes aegypti, Culex quinquefasciatus, Anopheles quadrimaculatus* adult	100% mortality after 4 hours of exposure	[43]
22	*Cinnamomum zeylanicum*	Cinnamaldehyde	N/A/ GC-MS	*Anopheles stephensi*	LC_{50} = 37 ppm	[44]
23	*Cinnamomum melastomaceum*	Linalool	Hydrodistillation/ GC-MS	*Aedes aegypti, Aedes albopictus, Culex quinquefasciatus*	LC_{50} values of less than 50 µg/mL	[45]
24	*Cinnamomum zeylanicum*	Cinnamaldehyde	Maceration (alcohol 70%)/GC-MS	*Culex pipiens* larvae	LC_{50} = 28,30 µg/mL.	[46]
25	*Cinnamomum* sp.	Cinnamaldehyde	N/A	*Aedes albopictus, Aedes aegypti* larvae	LC_{50} = 50-200 µg/mL	[47]
26	*Cinnamomum* sp.	Cinnamaldehyde	N/A/GC-MS	*Culex quinquefasciatus* larvae	LC_{50} = 29,24 µg/mL	[48]
27	*Cinnamomum burmannii* Blume	Cinnamaldehyde	Maceration (hexane)/N/A	*Culex pipiens* larvae	LC_{50} = 184,28 µg/mL	[49]
28	*Cinnamomum burmannii* Blume	Cinnamaldehyde	N/A	*Aedes aegypti* adult	Gel from *Cinnamomum burmannii* essential oil provides up to 96.85% protection against mosquito bites.	[50]
29	*Cinnamomum verum*	Cinnamaldehyde	N/A/GC-MS	*Culex pipiens* oviposition	Toxicity index = 75.00% at 24 h of exposure	[51]
30	*Cinnamomum iners*	Geraniol	Hydrodistillation/ GC-MS	*Aedes aegypti* adult	The repellency percentage was 12,33% at a concentration of 5%	[52]
31	*Cinnamomum burmannii*	Cinnamaldehyde	Hydrodistillation/ GC-MS	*Aedes aegypti* adult	Mortality = 100%	[53]
32	*Cinnamomum* sp.	Eugenol	Hydrodistillation/ GC-MS	*Anopheles gambiae*	Mortality = 89,3%	[54]
33	*Cinnamomum zeylanicum*	Cinnamaldehyde	N/A	*Anopheles stephensi* adult	Complete protection time in minutes provided by the nanoliposomal gel containing	[55]

					2.5% *Cinnamomum zeylanicum* essential oil against *Anopheles stephensi* mosquitoes	
34	*Cinnamomum burmannii*	Cinnamaldehyde	N/A	*Aedes aegypti* adult	5th minute after applying *Cinnamomum burmannii* extract, the protection power (or effectiveness) against whatever the extract is supposed to protect against was 88.3%.	[56]
35	*C. Sulphuratum, C. perotettii, C. verum, C. wightii, C. champora, C. glanduliferum, C. malabatrum*	Eugenol	Hydrodistillation/ GC-MS	Instar larvae of *Aedes aegypti*	All the oil samples demonstrated effective larvicidal activity against late-third instar larvae of *Aedes aegypti*	[57]

3.2. Effectiveness and Mechanism of Action

The bioactive compounds of *Cinnamomum* sp. exhibit diverse toxicity and mechanisms of action, including larvicidal, ovicidal, adulticidal, pupicidal, repellent, oviposition inhibitory, and reproductive inhibitory effects. The effectiveness of *Cinnamomum* sp. extracts is presented in Table 1. The data indicate that cinnamaldehyde is the most dominant compound and highly toxic to various mosquito species. The toxicity of plant extracts on target organisms can be determined using LC_{50}. LC_{50} (Lethal Concentration 50%) is a measure of toxicity that describes the concentration of a substance required to kill 50% of a test organism population within a specific period. The LC_{50} value is typically represented in units of mass per volume (e.g., mg/L or ppm) and is commonly used in toxicological studies to assess the harmful effects of chemicals or pollutants on aquatic animals, insects, and other organisms. The lower the LC_{50} value, the more toxic the substance, as a lower concentration is required to achieve lethal effect on half of the test population.The study [58] showed that the chitin wall is destroyed by essential oil (cinnamaldehyde), which enters through the pores of the eggshell, causing embryotoxicity and inhibiting the hatching process. Reference [1] explains that the survival of *Culex quinquefasciatus* larvae after exposure to cinnamon oil at a concentration of 50 ppm for 24 hours showed 100% larval mortality. The dead larvae were characterized by a shriveled, pale white body, damaged respiratory tubes, and complete lack of movement. Larvae exposed to essential oil exhibited toxic effects, including loss of fine hairs on body segments, head damage, reduced exoskeleton thickness, and loss of peritrophic membrane integrity. This was indicated by shrinkage and loss of definition in internal organs, decreased exoskeleton thickness, and structural damage to the air siphon, Malpighian tubules, and gut. The study [59] found that the respiratory cavity of *Culex quinquefasciatus* larvae folded, narrowed, and the inner part of the siphon was damaged, while the body and head darkened. Oxygen deprivation in the larval tissue led to nervous system damage, and siphon damage caused irregular breathing, ultimately resulting in death.

Essential oils and their toxic compounds can increase cAMP and calcium levels in nerve cells. Essential oils disrupt metabolism and respiration in larvae, ultimately leading to death. This occurs because the enzyme acetylcholinesterase breaks down the neurotransmitter acetylcholine, causing paralysis in the larvae. Mosquitoes use five types of stimuli to locate a host: moisture, visual cues, CO_2, heat, and body odor. The sensilla that respond to these stimuli include compound eyes, grooved pegs, coeloconic sensilla, capped pegs, and trichoid sensilla. Natural compounds from *Cinnamomum* sp. can act on multiple targets within the insect central nervous system and also function as AChE (acetylcholinesterase) inhibitors. AChE is a crucial target of nerve agents, as it breaks down neurotransmitters in cholinergic nerve synapses. When inhibited, acetylcholine accumulates, keeping its receptors open, leading to paralysis and death—a mechanism similar to organophosphates and carbamates. Additionally, the repellent effect of cinnamaldehyde is attributed to its interaction with specific odor receptors and/or Nav channels [1].The effectiveness of natural insecticides is influenced by various factors, such as the target species, application method, chemical composition, temperature after application, and the ratio of key components in the plant extract [60].

The toxicity level of *Cinnamomum* sp. on non-target organisms was studied by [61] using zebrafish as test subjects. *Cinnamomum* sp. extract was added to water containing zebrafish, and the results showed that no zebrafish died, as the LC_{50} value was greater than 100 ppm. This finding indicates that *Cinnamomum* sp. extract has very low toxicity toward non-target organisms like zebrafish, making it safe and environmentally friendly alternative for pest control. Thus, using this extract as an insecticide can reduce negative impacts on aquatic ecosystems and the environment, offering sustainable solution for pest management. [62] stated that the essential oil of *Cinnamomum* sp. did not cause mortality in the earthworm *Eisenia fetida*, third-instar larvae, or adult beetles *Harmonia axyridis*. However, at a concentration of 5.5 mL/L, it caused 16.3% mortality in *H. axyridis* larvae. Additionally, [63] demonstrated that the non-target organism *Tenebrio molitor* L., when sprayed with *Cinnamomum* sp. extract at LC_{50} = 28.34, did not experience mortality. These findings indicate that *Cinnamomum* sp. extract is not toxic to non-target organisms when used at the recommended dosage.

IV. Conclusion

Based on this study, it can be concluded that cinnamaldehyde, the primary bioactive compound found in *Cinnamomum* sp., is a promising component for insecticide development. Cinnamaldehyde is not only a key constituent of essential oil that gives cinnamon its distinctive aroma but also exhibits significant insecticidal activity. This compound has been proven effective in disrupting the nervous system and metabolism of mosquitoes and their larvae, leading to neurological disturbances and death. Additionally, cinnamaldehyde demonstrates antimicrobial properties and the ability to damage insect cell membranes, further reinforcing its potential as an environmentally friendly mosquito control agent. These findings highlight the practical applications of cinnamaldehyde in developing safer and more effective vector control strategies, reducing reliance on chemical insecticides that may pose risks to the environment and human health.

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