Larvicidal potential of plant-based extracts against dengue vector: A short review

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ABSTRACT

Introduction. Dengue fever, a vector borne disease transmitted primarily by Aedes albopictus and Aedes aegypti mosquitoes, has triggered a significant global resurgence. While many vector control programs depend on the use of chemical insecticides to curb outbreaks, its heavy reliance raises environmental concerns and the risk of insecticide resistance. Alternatively, botanically derived insecticidal agents with larvicidal properties offer an eco-friendlier option. This review aims to analyze scientific reports that described the effectiveness of plant-derived extracts for vector control.

Materials and Methods: A literature search was performed to analyze studies that focused on plant-based extracts used for larvicidal purposes using databases such as Science Direct. Springer, PubMed, and Scopus. The inclusion criteria for publications were larvicidal effects, published in English from the year 2017 and availability of full-text articles. The available literature was further characterized by the value of larvicidal activities of LC50 and LC90 (< 50 ppm), of 22 different parts of plant species from 7 plant families namely Apiaceae, Asteraceae, Lauraceae, Magnoliaceae, Myrtaceae, Piperaceae and Rubiaceae.

Results: When comparing the values of LC50, 12 plants species (Artemisia vulgaris, Crassocephalum crepidioides, Echinops grijsii, Melaleuca leucadendra, Neolitsea ellipsoidea, Pavetta tomentosa, Piper betle, Piper caninum, Piper Montium, Piper muntabile, Piper ovatum, Tarenna asiatica) showed promising larvicidal efficacies with LC50 < 10 ppm.

Conclusion: This review emphasizes the effective alternatives of plant extracts for the potential production of larvicides. Piper betle extract and chloroform extract of Tarenna asiatica reported the most significant larvicidal activity (LC50 < 1 ppm) against mosquito vectors. Further reviews focusing on the mode of actions of its phytochemically constituents are essential for the future development of potentially significant plant-based larvicides.

KEYWORDS:
Plant extract, larvicide, dengue, mosquito

INTRODUCTION

The incidence of dengue has increased precipitously, with a 30-fold increase in incidence during the past five decades.[1] New emerging outbreaks continue to pose threats in endemic countries, exerting catastrophic burdens on populations, health systems and economies.[2,3] The Ministry of Health Malaysia has documented a total of 19,450 cumulative dengue fever cases in the first two months of 2023, which demonstrates an alarming increase of 212% (6229 cases) compared to the same period in 2022. Similarly, to date, a total of 15 dengue-related fatalities have been reported in Malaysia in the first few months of 2023, compared to two deaths during the same period in the previous year.

At present, a licensed and commercially available vaccine for public health use against dengue remains elusive. Reducing dengue transmission is therefore dependent on sustainable vector control approaches, including various environmental, biological, plant-based and chemical control strategies.[4] Chemical control using synthetic formulation is predominantly one of the primary means to combat dengue, which has adversely resulted in the development of insecticide resistance, target site and metabolic resistance.[5] As such, reports of resistance against malathion, dieldrin, pyrethroid DDT and temephos, of local mosquitoes have been documented in the local settings.[6,7]

The rampant use of insecticides has been associated with detrimental ecological impacts including agrochemical poisoning, the death of non-target organisms, reduced biodiversity, and ecosystem functions as well as endangering public health.[8]

Studies utilizing various natural products suggest the utilization of botanical insecticides as a safer and eco-friendly alternative measure of vector control.[9,10,11] Plant-derived phytochemicals constitute a rich source of bioactive insecticidal compounds such as alkaloids, alkamides, sesquiterpenes, triterpenes, sterols, flavonoids, coumarins,

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anthraquinones, xanthones, acetogenonins and aliphatics. Such compounds can act as biodegradable larvicides, insect growth regulators, repellents and ovipositional attractants based on ethnomedical evidence.[12,13] Pavela et al.[12] reviewed numerous plant species for their larvicidal efficacy against major vectors belonging to the genera Anopheles, Aedes and Culex. Similarly, Pani et al.[13] reviewed fifty (50) medicinal plants for larvicidal properties against various mosquitoes namely *Anopheles stephensi, Aedes aegypti* and *Culex quinquefasciatus, Phlebotomus duboscqi, An. gambiae* and *An. fluviatilis.* This study aims to further review the larvicidal activities of different plant extracts specifically against dengue vectors *Ae. albopictus* and *Ae. aegypti.*

MATERIALS AND METHODS

Methods and Criteria for Literature Selection

The review is based on original articles obtained by searching online literature in major scientific database such as Science Direct, Springer, PubMed, and Scopus. The selected research studies focused on larvicidal activity of plant extracts against dengue vectors *Aedes albopictus* and *Aedes aegypti.* The terms ("plant extract"), ("larvicidal"), ("mosquito"), *("Aedes albopictus")*, and *("Aedes aegypti")* were considered as a means of selecting articles from 2017-2020. The keywords were used as is or in combination with other terms, using an "and" "or" during the search. In the initial screening process, an analysis of the information available in the title, running head, abstract and keywords was performed. Articles that failed to match the theme were excluded. Articles were then read in full text to elucidate the year, object, method of larvicidal assay and research fundings. Articles in languages other than English, and unpublished data were excluded. This study was conducted to compare the result of LC_{50} and LC_{90} of the numerous plant extracts as larvicide agents, with a reading value of < 50 ppm. A total of twenty-two (22) different parts of plant species from 7 families namely Apiaceae, Asteraceae, Lauraceae, Magnoliaceae, Myrtaceae, Piperaceae and Rubiaceae were selected for this study.

RESULTS AND DISCUSSION

Various factors including differences in plant components, chemical composition, bioactive compound concentration, extraction methods, age, maturity, and inherence chemistry may influence larvicidal potential. Plant extracts can be classified as strong larvicidal agents (LC_{50}< 50 ppm), a moderate (50 ppm < LC_{50} < 100 ppm) or a weak larvicidal agent (LC_{50} > 100 ppm).[14].Table I summarizes the different parts of 22 selected plants from 7 families namely Apiaceae, Asteraceae, Lauraceae, Magnoliaceae, Myrtaceae, Piperaceae and Rubiaceae that exhibited larvicidal properties (LC_{50} < 50 ppm) against dengue vector, *Ae. albopictus* and *Ae. aegypti.*

Apiaceae

Apiaceae (formerly Umbelliferae) is one of the largest plant families in the order Apiales. Apiaceae species are a valuable source of secondary metabolite compounds with a broad spectrum of biological activities including antithrombotic, antioxidant, hypotensive, antibacterial, antifungal and insecticidal abilities.[32,33] A study conducted by Sheng et al.[22] screened 53 essential oil for their larvicidal activity, the results of which demonstrated the ability of Foeniculum vulgar essential oil in exerting 100% mortality at the concentration of 100 ppm against 4th instar larvae of Ae. albopictus. Moreover, fennel was also recorded as the most potent essential oil from all the plants tested with the value of LC_{50} 27.50 ppm and LC_{90} at 33.90 ppm. In another study, Balasubramani et al.15 explored the larvicidal activities of Artemisia vulgaris essential oil against 3rd instar larvae of *Ae. aegypti,* with an LC50 at 6.87 ppm and LC_{90} at 59.10 ppm. Such activities could be attributed to the actions of photoactive compounds in *Ar. vulgaris* such as β-caryophyllene, α-humulene, and β- caryophyllene oxide.

Asteraceae

The genus *Echinops* belongs to the Asteraceae family. Many species contain a plethora of secondary metabolites and have been used traditionally as therapeutic agents with ethnomedicinal claims, mainly in Asian and African countries.[34] Zhao et al.[19] extracted essential oils from the roots of Echinops grijsii via hydrodistillation, and bioassay results demonstrated an LC_{50} at 2.65 ppm and LC90 at 4.65 ppm against *Aedes albopictus* larvae. Moreover, researchers also isolated main constituents from this herb plant, 5-(3-buten-1-yn-1-yl)-2,2'-bithiophene (5-BBT) and 5-(4-isovaleroyloxybut-1-ynyl)-2,2'-bithiophene (5-IBT) which revealed effective larvicidal activity against the fourth instar larvae of *Aedes albopictus* with LC50 values of 0.34 ppm and 0.45 ppm. In another study, petroleum benzene crude extract of *Acanthospermum hispidum* leaves showed larvicidal activity of LC_{50} values at 15.22 ppm and LC90 at 27.75 ppm.[16] Hung et al.[18] tested the crude extracts of Crassocephalum crepidioides against both dengue vector larvae, *Ae. albopictus* and *Ae. aegypti.* The result implied that 3rd instar larvae of *Ae. aegypti* showed higher larvicidal impacts compared to *Ae. albopictus* with LC_{50} values at 4.95 ppm and 14.4 ppm, respectively.

Lauracaea

The genus *Cinnamomum* is classified in the family of Lauraceae. Dai et al.[17] screened the larvicidal activity from the essential oil of five species of *Cinnamomum* against *Ae.s aegypti.* and *Ae. albopictus*. From the overall findings, *Cinnamomum ovatum* leaves essential oil showed notable larvicidal activity against *Ae. aegypti* larvae with the LC_{50} at 13.76 ppm and LC_{90} at 30.17 ppm, In the same study, it was found that *Cinnamomum polyadelphum* leaf essential oil exhibit larvicidal toxicity with the LC_{50} at 20.66 ppm and LC_{90} at 37.21 ppm against *Ae. albopictus*. In a study reported by Chau et al.[23], essential oil from 11 species of Lauraceae family were analysed for their larvicidal efficacy. The results are indicative of strong larvicidal activities of *Machilus grandifolia* essential oil with LC_{50} of 16.48 ppm against *Aedes albopictus* while the LC_{50} values is slightly higher, 20.23 ppm when tested with *Aedes aegypti* larvae. Moreover, Neolitsea ellipsoidea essential oil displayed the greatest larvicidal activity against *Ae. aegypti* with LC_{50} 6.59 ppm and LC90 at 14.00 ppm particularly after being exposed for 24 hours. *Neolitsea ellipsoidea* is deemed to be rich in (E)-β-ocimene (87.6%), a bioactive compound that could be directly correlated with its strong larvicidal efficacy.

Magnoliaceae

Several taxa of the genus Magnolia (family Magnoliaceae) have long been used traditionally especially in the Far East, due to its wide concoction of biologically active compounds

Table I: Plant extracts with potential larvicidal activity

Plant	Family	Part	Solvent	Host /stages	LC_{50} (ppm)	LC_{90} (ppm)	References
Artemisia vulgaris	Apiaceae	Leaf	Distilled water	Ae.aegypti (3rd instar)	6.87	59.1	Balasubramani et al. [15]
Acanthospermum hispidum	Asteraceae	Leaf	Petroleum benzene	Ae.aegypti (4th instar)	15.22	22.75	Vivekanandhan et al. [16]
Cinnamomum ovatum	Lauraceae	Leaf	Distilled water	Ae.aegypti (3rd instar)	13.76	30.17	Dai et al.[17]
Cinnamomum polyadelphum	Lauraceae	Leaf	Distilled water	Ae. albopictus /Ae.aegypti (3rd instar)	20.66/ 23.41	37.21/ 36.69	Dai et al.[17]
Crassocephalum crepidioides	Asteraceae	Stem & Leaf	Distilled water	Ae.albopictus /Ae.aegypti (3rd instar)	14.3/ 4.95	20.86/ 10.28	Hung et al.[18]
Echinops grijsii	Asteraceae	Root	Distilled water	Ae.albopictus (4th instar)	2.65	4.65	Zhao et al.[19]
Eucalyptus camaldulensis	Myrtaceae	Leaf	Distilled water	Ae.aegypti (3nd and 4th instar)	33.7	-	Manh et al.[20]
Eucalyptus nitens	Myrtaceae	Leaf	Distilled water	Ae.albopictus / Ae. Aegypti (3rd instar)	28.19/ 50.83	-	Costa et al.[21]
Foeniculum vulgare	Apiaceae	Seed	Acetone	Ae.albopictus (4th instar)	27.5	33.9	Sheng et al.[22]
Machilus grandifolia	Lauraceae	Leaf	Distilled water	Ae.aegypti/ Ae.albopictus	20.23/ 16.48	29.29/ 25.00	Chau et al.[23]
Magnolia coco	Magnoliaceae	Leaf	Ethanol	Ae.albopictus /Ae.aegypti	11.01/ 46.46	-	Chung et al.[24]
Manglietia Dandyi	Magnoliaceae	Leaf	Ethanol	Ae.albopictus	29.57	46.21	Ban et al.[25]
Magnolia kobus	Magnoliaceae	Flower	Acetone	Ae.albopictus (3rd instar)	45.06 (Early) 22.63 (Full bloom)	-	Kim et al.[26]
Melaleuca leucadendra	Myrtaceae	Fruit	Distilled water	Ae.albopictus /Ae. aegypti	19.17/ 13.90	39.08/ 31.76	Giang An et al.[27]
Melaleuca leucadendra	Myrtaceae	Leaf (Old)	Distilled water	Ae.aegypti	7.40	8.29	Giang An et al.[27]
Neolitsea ellipsoidea	Lauraceae	Leaf	Distilled water	Ae.aegypti (3rd instar)	6.59	14.00	Chau et al.[23]
Pavetta tomentosa	Rubiaceae	Leaf	Ethanol/ hexane	Ae.aegypti (4th instar)	1.03/ 1.43	1.44/ 1.97	Pratheeba et al.[28]
Piper betle	Piperaceae	Leaf	Distilled water	Ae.aegypti (4th instar)	0.72	-	Vasantha-Srinivasan et al.[29]
Piper caninum	Piperaceae	Leaf & Stem	Distilled water	Ae.aegypti (3rd instar)	1.38	2.42	Huong et al.[30]
Piper montium	Piperaceae	Leaf & Stem	Distilled water	Ae. aegypti (3rd instar)	1.93	3.18	Huong et al.[30]
Piper muntabile	Piperaceae	Leaf & Stem	Distilled water	Ae. aegypti (3rd instar)	1.85	2.70	Huong et al.[30]
Piper ovatum	Piperaceae	Root	Ethanol	Ae .aegypti (3rd instar)	2.57	3.8	Kanis et al.[31]
Tarenna asiatica	Rubiaceae	Leaf	Acetone/ methanol	Ae. aegypti (4th instar)	1.29	1.99	Pratheeba et al.[28]
Tarenna asiatica	Rubiaceae	Leaf	Chloroform	Ae. aegypti (4th instar)	0.952	-	Pratheeba et al. [28]

such as lignans, neolignans, alkaloids and terpenoids.[35] Such compounds have been associated with its cytotoxic antitumor, antioxidant, antimicrobial and insecticidal effects and activities.[36] The acetone extract from the flower of *Magnolia kobus*, collected in Korea has been shown to exhibit higher larvicidal activity with an LC_{50} value of 22.63 ppm in full bloom floral compared to early bloom floral stage, with an LC_{50} value of 45.06 ppm against *Ae. albopictus* third instar larvae.[26] This study also reported efficacy in terms of adulticidal activity and fumigant toxicity of *Magnolia kobus* flower extract against adult female *Ae. albopictus*. Similarly, Chung et al.[24] isolated essential oils of Magnolia coco leaves and tested them on both dengue vectors. The bioassay for larvicidal activity revealed susceptibility against *Ae. albopictus* with an LC_{50} value of 11.01 ppm. In comparison, the larvicidal activity for *Ae.s aegypti* was observed to be slightly lower (LC_{50} 46.46 ppm) following 24 hours of exposure. Moreover, the essential oil showed 100 % mortality at 50 ppm against *Ae. albopictus* larvae while for *Ae. aegypti* at 100ppm.

In another study, Ban et al.[25] tested the ethanolic extract of *Manglietia dandyi* leaves against fourth instar larvae *Ae. albopictus* and it exhibited larvicidal efficacy with LC_{50} 29.57 ppm and LC_{90} at 46.21 ppm after 24 hours.

Myrtaceae

Eucalyptus is a genus belonging to the Myrtaceae family that is cultivated globally in countries with Mediterranean and subtropical climates. The genus displays a broad spectrum of actions including antioxidant, anti-inflammatory, wound healing and antiviral properties.[37] Costa et al.[21] reported Eucalyptus nitens leaves extracts showed higher toxicity against larvae of *Ae. albopictus* than *Ae. aegypti* with the value of LC_{50} 28.19 ppm and 52.83ppm respectively. Another genus, *Eucalyptus camaldulensis* essential oil reported a 50% mortality rate of 300 Aedes aegypti larvae tested at 33.7 ppm concentration. In a separate study performed by Giang et al.[27], four species of Myrtaceae namely *Baeckea frutescens, Callistemon citrinus, Melaleuca leucadendra, Syzygium nervosum* were evaluated, against larvae of dengue virus transmission vectors, *Ae. aegypti* and *Ae. albopictus*. The larvicidal activity of these plant was evident with LC_{50} values < 50 ppm. From the study, the essential oil of *Melaleuca leucadendra* fruit showed LC_{50} values at 19.17 ppm and LC_{90} at 39.08 ppm against larvae of *Ae. albopictus Ae. albopictus*. However, the result reported for the mortality of *Ae. aegypti* larvae showed lower value of LC_{50} and LC_{90} compared to *Ae. albopictus* with readings of 13.9 ppm and 31.76 ppm respectively. Among tested plants, essential oil of *Melaleuca leucadendra* showed potent larvicidal activity with LC_{50} at 7.40 ppm against *Ae. aegypti* larvae after 24 hours.

Piperaceae

Piper species belonging to the Piperaceae family are aromatic plants that are widely cultivated in tropical and subtropical countries. This includes *Piper betle* L. which is well known for its medicinal properties. Piper plants are rich with secondary metabolites in the leaves, seeds, stems, roots, and branches are associated with a wide range of health benefits, and has documented to possess anti-inflammatory, antioxidant, antibacterial, antifungal, and antimalarial properties.[38-39] Huong et al.[30] investigated the larvicidal activity of essential oil from 13 species of piper against third instar larvae of *Ae. aegypti*. Findings indicated that Piper caninum essential oil has substantial larvicidal promising capabilities with an LC_{50} value of 1.38 ppm and LC_{90} of 2.42 ppm after 24 hours of contact. *Piper montium* extracts from leaves and stems also demonstrated high mortality rates of larvae with LC_{50} at 1.93 ppm and LC_{90} at 3.18 ppm. Ethanolic extracts of *Piper ovatum* extracted from the root against larvae of *Aedes aegypti* displayed LC_{50} at 1.93 ppm.[31] Moreover, Vasantha-Srinivasan et al.[29] isolated the volatile crude oil from *Piper betle* leaves shows promising potency among their species with LC_{50} 0.72 ppm and 0.64 ppm against laboratory and wild strains of *Ae. aegypti* larvae respectively.

Rubiaceae

Anti-dengue capabilities of *Pavetta* tomentosa and *Tarenna asiatica from the Rubicea family leaf extracts* were studied by Pratheeba et al.[28] using five different types of solvent against *Ae. aegypti*. From the study, the hexane extract of *Pavetta tomentosa* leaves displayed a more effective larvicidal activity compared to the *Tarenna asiatica* with LC_{50} 1.43 ppm and 1.70 ppm respectively. Nevertheless, the acetone and the methanolic extract of *Tarenna asiatica leaves* showed promising larvicidal activity with the value of LC_{50} 1.29 ppm and 1.99 ppm upon exposure of 24 hours. From the overall solvent, the chloroform extract of *Tarenna asiatica* revealed the greatest larvicidal activity compared to five other different solvents, which displayed the lowest value of LC_{50} at 0.952 ppm. Moreover, the phytochemical tested in both plants showed the presence of saponins, flavonoids and alkaloids in all experimented extracts.

CONCLUSION

Concerns associated with the extensive usage of synthetic compounds have increased substantially over the past years, necessitating the search for alternative control measures for dengue vectors. Botanical or plant-based extracts shows promise as natural larvicides; one that is non - toxic and biodegradable. This short review summarizes the larvicidal abilities of plant-based extracts 2017-2020 which includes the plant species from seven families: Apiaceae, Asteraceae, Lauraceae, Magnoliaceae, Myrtaceae, Piperaceae and Rubiaceae that have demonstrated potential larvicidal properties with LC50 documented to be <50 ppm. Within all these family, extracts of 12 plants showed potent larvicidal activity with LC50 < 10 ppm. Among the plants with great larvicidal efficacy is the Piper genus (Pipiracea). Extracts of *Piper betle* and chloroform extract of *Tarenna asiatica* plant displayed the most effective larvicidal capabilities with 0.72 ppm and 0.952 ppm respectively (LC_{50} < 1 ppm). Similarly, many species of the Piperaceae family displayed larvicidal activities with LC50 < 10 ppm, rendering them potential candidates for the development of new eco-friendly bio-insecticidal formulations and the possibility for further investigations in the control of *Ae. Albopictus* and *Ae. aegypti*.

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CONFLICT OF INTEREST

The authors declare no conflict of interests.

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