ISSN 1978-6743
E-ISSN 2477-3948
Jurnal Ilmiah Kesehatan
(Journal of Health Science)
Fakultas Keperawatan dan Kebidanan | Universitas Nahdlatul Ulama Surabaya

Effectiveness of *Areca Catechu* (Betel Nut) Extract on the Mortality of *Aedes Aegypti* and *Anopheles* Larvae: A Laboratory Experimental Study

Rolyn Frisca Djamanmona[1], Yowel Kambu[2], Nurul Kartikasari[3], Alva Cherry Mustamu[4]

[1,2,3,4] *Departement of Nursing, Health Polytechnic of Health Ministry, Sorong, Southwest Papua, Indonesia*

ARTICLE INFORMATION

Received: May 15, 2025
Revised: July 11, 2025
Available online: August 2025

KEYWORDS

Aedes aegypti; Anopheles spp.; *Areca catechu;* botanical insecticide; natural larvicide

CORRESPONDENCE

E-mail: rolyndjamanmona@poltekkessorong.ac.id

A B S T R A C T

Vector-borne diseases such as dengue fever and malaria continue to pose significant global public health challenges. The increasing resistance of mosquito vectors to synthetic insecticides underscores the urgency for exploring plant-based larvicidal alternatives. This study evaluates the effectiveness of *Areca catechu* (betel nut) extract on the mortality of *Aedes aegypti* and *Anopheles* spp. In addition, it analyzes the concentration at which its toxic effect is most optimal. Furthermore, it compares the extract's efficacy against *Aedes aegypti* and *Anopheles* spp. This investigation was a laboratory-based experimental study employing a post-test only control group design. One thousand two hundred third-instar larvae (600 A. aegypti, 600 Anopheles spp.) were randomly assigned to six groups: five treatment groups (from 1000to 10,000 ppm concentrations) and one negative control. Larvae were exposed to *Areca catechu* seed extract for 24 hours. Mortality data were analysed using one-way ANOVA with Bonferroni post-hoc tests, and LC_{50} and LC_{90} values were estimated via probit regression. Larval mortality increased significantly with extract concentration (p<0.001). At a 10,000-ppm concentration, mortality reached 100% in A. aegypti and 98% in Anopheles spp. Notably, *A. aegypti* exhibited greater susceptibility, with lower LC_{50} values (3180.42 ppm vs 3536.55 ppm). These differences were statistically significant across nearly all concentration levels. Thus, *Areca catechu* extract demonstrates potent, dose-dependent larvicidal activity against *Aedes aegypti* and *Anopheles spp*. The extract at 10,000 ppm within 24 hours achieved 100% mortality in *Aedes aegypti* and 98% in *Anopheles* spp. Furthermore, *Aedes aegypti* indicates a higher susceptibility to the extract.

INTRODUCTION

Mosquito-borne diseases, such as dengue hemorrhagic fever (DHF) and malaria, persist as significant global public health challenges. According to the World Health Organization (WHO), over 390 million dengue infections occur annually. At the same time, approximately 241 million cases of malaria were reported worldwide in 2021, with most cases concentrated in tropical and subtropical regions (WHO, 2022). The primary vectors of these diseases are *Aedes aegypti* and *Anopheles* spp., which thrive in stagnant and unhygienic aquatic environments. The increasing resistance to synthetic insecticides, along with their ecological and toxicological consequences, highlights the urgent need for the development of eco-friendly and effective plant-based vector control alternatives (Onen *et al.*, 2023; de Oliveira *et al.*, 2025; Kasman *et al.*, 2025).

One promising approach is the utilization of botanical insecticides derived from bioactive plant compounds. In recent years, scientific interest has grown in phytochemicals such as alkaloids, flavonoids, tannins, and saponins as potential natural larvicides. *Areca catechu* L. (betel nut) contains these compounds. It has demonstrated potential as an efficient biopesticide. Experimental studies reported that

https://doi.org/10.33086/jhs.v18.i03.7309

betel nut extract could induce significant mortality in *Aedes aegypti* larvae, with death rates reaching 100% at a 10% concentration within 12 hours of exposure (Martianasari and Hamid, 2019; Bharathithasan *et al.*, 2021; Aziz, Badruttamam and Rikadyanti, 2023).

Developing broad-spectrum botanical larvicides is essential to support integrated vector management (IVM) strategies. Prior investigations examined the larvicidal properties of *Areca catechu* extract against mosquito larvae. However, comparative studies assessing its efficacy against the primary vector species—*Aedes aegypti* and *Anopheles* spp.—are limited. Moreover, the lack of comprehensive data on the toxicity and effective concentration of *Areca catechu* extract for *Anopheles* larvae needs further investigation. Previous studies were often limited in scale and scope, with only a few studies employing robust randomized controlled experimental designs or testing a wide range of extract concentrations. For instance, Sembiring et al documented the larvicidal effects of young betel nut fruit on *Aedes* spp., but did not assess its impact on *Anopheles* spp. (Sembiring and Hasan, 2020).

Previous literature has demonstrated that bioactive compounds in plant extracts such as betel nut, soursop leaves, and citronella may serve as effective larvicides. However, the degree of efficacy and optimal concentrations vary across studies (Hossain *et al.*, 2021; Rahman, Naday and Utami, 2021; Kuka *et al.*, 2023; Syahputra and Ginting, 2024). Ongoing debates also concern the standardization of toxicity thresholds and the duration of exposure required to achieve maximal larvicidal effects.

Thus, there is a need for research that broadens the spectrum of target mosquito species and enhances methodological rigor to produce findings that can be practically implemented in community settings. The primary objective of this study is to evaluate the effectiveness of *Areca catechu* (betel nut) extract on the mortality of *Aedes aegypti* and *Anopheles* spp. larvae through a laboratory-based experimental design involving varying extract concentrations. In addition, it analyzes the concentration at which its toxic effect is most optimal. Identifying an optimal concentration of *Areca catechu* extract capable of inducing maximum larval mortality within a short exposure time can be a recommendation for developing sustainable, plant-based larvicide formulations. Furthermore, this paper compares the efficacy of the extract against *Aedes aegypti* and *Anopheles* spp.

This research can contribute to the literature on the larvicidal efficacy of *Areca catechu* while supporting ecologically based vector control strategies. It potentially provides a foundation for formulating plant-derived larvicides that are both effective and community-applicable. Its innovative contribution lies in the comparative approach across two vector species and the efficacy assessment under controlled laboratory conditions, thereby ensuring replicability and field evaluation potential.

https://doi.org/10.33086/jhs.v18.i03.7309

METHOD

The study employed a laboratory-based experimental design, specifically a post-test only control group design. This design was selected to facilitate identifying causal relationships between administering the *Areca catechu* extract (intervention) and measurable outcomes, while minimizing measurement bias due to prior observation. The independent variable in this study was the concentration of areca nut seed extract, with variations of 1000 ppm, 3000 ppm, 5000 ppm, 7000 ppm, and 10,000 ppm. The dependent variable was the mortality rate of *Aedes aegypti* and *Anopheles* spp. larvae after 24 hours of treatment. The authors used a Single-Blind approach, wherein the larval observers were unaware of the treatment groups to prevent information bias. A simple randomization procedure was employed to assign larvae to treatment groups to minimize selection bias.

The study focused on third instar larvae of *Aedes aegypti* and *Anopheles* spp., sourced from laboratory-reared colonies at the Integrated Laboratory, Poltekkes Kemenkes Sorong. Inclusion criteria specified active larvae aged 5–7 days (Third Instar) without morphological abnormalities. Exclusion criteria encompassed immobile larvae before treatment and those with bodily deformities. The sample size was calculated using Federer's formula for experiments with a completely randomized design (CRD):

$$(t-1)(r-1) \geq 15,$$

where t represents the number of treatments (five concentrations of *Areca catechu* extract plus one control, totaling 6), necessitating a minimum of 4 replications. Each group comprised 25 larvae, resulting in 6 groups × 4 replications × 25 larvae = 600 larvae per mosquito species. A randomized block design sampling technique was employed to control inter-batch variability. Larval recruitment adhered to a standardized schedule for incubation and development. The research was conducted at the Microbiology Laboratory of Poltekkes Kemenkes Sorong in a single center setting from January to March 2025. This site was selected due to its compliance with biosafety standards and the availability of mosquito culture units.

The *Areca catechu* seed extract was prepared through maceration in 96% ethanol for 72 hours, followed by filtration and evaporation using a rotary evaporator at 45–50°C to obtain a concentrated extract. The intervention involved combining the extract with 100 ml of water in a glass beaker containing 25 test larvae, with concentrations varying from 1000 to 10,000 ppm. Each group underwent a single 24-hour exposure session. The intervention protocol was designed for the Template for Intervention Description and Replication (TIDieR), incorporating a single 24-hour exposure session, a one-time administration frequency, a standardized number of larvae (25 per unit), and consistent concentration and volume across groups. All larvae were obtained from the same batch to ensure biological homogeneity. Laboratory personnel were trained according to standard operating procedures (SOPs) that covered larval inoculation

https://doi.org/10.33086/jhs.v18.i03.7309

and mortality documentation. Protocol adherence was monitored through routine observations and daily data audits. Single blinding was implemented at the observer level to mitigate information bias. The negative control consisted of distilled water (Aquadest), while a synthetic larvicide, temephos 0.02 ppm, served as the positive control. The intervention timeline is depicted in Figure 1.

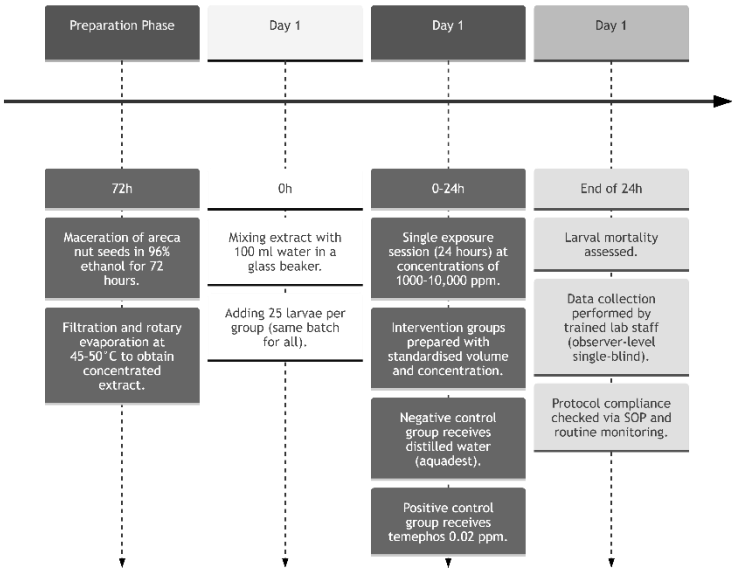

Figure 1. Timeline of Intervention Procedure with *Areca catechu* seed extract

Larval mortality data were systematically recorded using a standardized observation form, specifically a Case Report Form (CRF). Mortality was defined as the absence of movement or response to mechanical stimulation for 30 seconds or more. Observations were conducted with a 3× magnifying glass and sterile entomological tweezers. Data collection was carried out by two trained laboratory technicians and verified through a double-entry system. The procedural validity was benchmarked against the guidelines established by the World Health Organization (WHO, 2005), while interobserver reliability was evaluated using Cohen's Kappa, with a value exceeding 0.85. Quality control was maintained through daily audits and cross-verification. Data management was executed using Excel 365 software, incorporating password protection, encrypted cloud-based storage, and weekly backups on the internal server of Poltekkes Kemenkes Sorong. Instances of missing data that constituted less than 5% were addressed using complete case analysis. The data collection spanned four weeks, during which daily logbook entries were made, and hard copy forms were archived.

Data were analyzed using Jamovi version 2.4.8, with statistical significance established at $p<0.05$. The primary analysis employed a One-Way ANOVA to evaluate differences in larval mortality among treatment groups, followed by Bonferroni post-hoc tests to identify significantly different groups. The Authors utilized the Kruskal–Wallis test for data not normally distributed. The secondary analysis

involved estimating LC_{50} and LC_{90} values through Probit regression. Missing data were addressed via listwise deletion due to their minimal proportion. No interim analysis was conducted, as the study design was short-term and involved a single intervention session. A per-protocol comparison approach was applied, as no dropouts or crossover interventions existed.

Ethical approval for this study was obtained from the Health Research Ethics Committee of Poltekkes Kemenkes Sorong, certificate number: 014/KEPK/FKM-UX/I/2025. As the research involved mosquito larvae and did not include human or vertebrate animal subjects, informed consent was deemed unnecessary. Experimental data was securely stored with encryption, ensuring the absence of identifiable information. The study was free from conflicts of interest and was self-funded by the authors. Raw data can be accessed upon request through the institutional repository, with access limited to scientific purposes. Any significant amendments to the protocol will be submitted to the ethics committee for approval. Safety monitoring procedures were not implemented due to the minimal risk and the exclusion of higher-order organisms in this study.

RESULT

The Number of the Samples

This study employed 1,200 mosquito larvae, comprising 600 *Aedes aegypti* larvae and 600 *Anopheles* spp. larvae. Each species was divided into six groups: five treatment groups exposed to varying concentrations of *Areca catechu* seed extract (1,000 ppm, 3,000 ppm, 5,000 ppm, 7,000 ppm, and 10,000 ppm), and one negative control group (without extract). Each group consisted of 25 larvae, with four replicates per group.

Table 1. The Number of the Samples

Mosquito Species	Number of Larvae per Group	Number of Groups	Total Larvae
Aedes aegypti	25	6	600
Anopheles spp.	25	6	600

Table 1 presents the distribution of larvae by species, the number of treatment groups, and the total number of larvae used in the study. Most larvae were in the third instar stage, exhibiting normal morphological features and motor activity before intervention. All larvae originated from the same laboratory colony to ensure biological homogeneity.

Larval Mortality After *Areca catechu* Seed Extract Exposure

The experiment assessed larval mortality after 24 hours of exposure to different *Areca catechu* seed extract concentrations. Statistical analysis was performed using one-way ANOVA and a Bonferroni post-hoc test to determine significant differences between groups.

https://doi.org/10.33086/jhs.v18.i03.7309

Table 2. Mean Larval Mortality (%) After 24 Hours of *Areca catechu* Seed Extract Exposure

Concentration (ppm)	*Aedes aegypti* (mean ± SD)	*Anopheles* spp. (mean ± SD)
1000	26% ± 4.08	22% ± 5.20
3000	48% ± 3.54	42% ± 4.15
5000	76% ± 2.94	70% ± 3.67
7000	92% ± 2.16	88% ± 2.92
10000	100% ± 0.00	98% ± 1.15
Control (0 ppm)	2% ± 0.88	3% ± 1.22

The ANOVA test revealed statistically significant differences ($p<0.001$) in larval mortality for *Aedes aegypti* and *Anopheles* in the treatment groups. Post-hoc comparisons indicated that the most pronounced differences occurred at 5,000 ppm and above compared to lower concentrations and the control (Table 2).

Subgroup Analysis by Mosquito Species

Further analysis was conducted to compare the response of each mosquito species to identical concentrations of the *Areca catechu* seed extract.

Table 3. Comparison of Larval Mortality Between Species and the Independent t-test Result

Concentration (ppm)	Mean Mortality Difference (%) *	*p*
1000	4.00	0.042
3000	6.00	0.015
5000	6.00	0.008
7000	4.00	0.021
10000	2.00	0.098

* Mean Mortality Difference = Mean Mortality of *Aedes aegypti* − *Anopheles* spp.

Aedes aegypti generally exhibited slightly higher larval mortality rates than *Anopheles* at all *Areca catechu* seed extract concentrations. These differences were statistically significant at nearly all concentration levels ($p<0.05$), except at the highest concentration of 10,000 ppm (Table 3).

Estimation of LC_{50} and LC_{90} Values

To assess the toxicological effectiveness of the *Areca catechu* seed extract, a Probit regression analysis was conducted to estimate the lethal concentration values required to induce 50% (LC_{50}) and 90% (LC_{90}) mortality among larvae.

Table 4. LC_{50} and LC_{90} Values for *Areca catechu* Seed extract

Species	LC_{50} (ppm)	LC_{90} (ppm)
Aedes aegypti	3180.42	5832.77
Anopheles spp.	3536.55	6248.93

The LC_{50} and LC_{90} values were lower in *Aedes aegypti*, indicating that this species was more sensitive to all concentrations *of catechu* seed extract than *Anopheles* spp (Table 4).

DISCUSSION

This study demonstrated that the *Areca catechu* extract exhibited significant larvicidal efficacy against *Aedes aegypti* and *Anopheles* spp. Larvae. The increasing concentrations of the extract directly correlated

https://doi.org/10.33086/jhs.v18.i03.7309

with elevated larval mortality. Mortality rates reached 100% for *Aedes aegypti* and 98% for *Anopheles* at a concentration of 10,000 ppm within 24 hours. This finding was statistically significant ($p<0.001$) and consistent across treatment groups (Table 2). Thus, the results of this study reinforce *Areca catechu*'s potential as a natural larvicide due to its bioactive compounds.

The LC_{50} and LC_{90} values confirmed that *Aedes aegypti* was more sensitive to the extract than *Anopheles* spp. (Table 4). The result aligns with the study's aim to compare the toxicity of *Areca catechu* seed extract against both tropical disease vectors. This study's aim is particularly relevant given the increasing resistance of mosquito vectors to synthetic larvicides and the growing demand for natural, biodegradable, and sustainable vector control agents. This finding strengthens the idea that *Areca catechu* is a competent and applicable phytolarvicide within environmentally based vector management strategies.

The substantial larvicidal efficacy of *Areca catechu* extract is likely attributable to its secondary metabolites, including arecoline, tannins, flavonoids, and saponins. Those are recognized for their insecticidal and neurotoxic properties. Arecoline, the principal alkaloid in the seed, has been demonstrated to disrupt the larval nervous system, resulting in paralysis and subsequent death. Tannins and saponins function as antinutrients and biological surfactants, damaging cell membranes and interfering with the larvae's osmoregulatory processes (Bharathithasan *et al.*, 2021; Sun *et al.*, 2024). These findings align with previous studies that reported the larvicidal activity of *Areca catechu* extracts against *Aedes* spp., where mortality rates reached 90–100% at higher concentrations (Noya, Rahardjo and Prakasita, 2022; Nawarathne and Dharmarathne, 2024).

This study's novel contribution demonstrated that such larvicidal effectiveness also extends to *Anopheles* spp., although with slightly reduced sensitivity. A noteworthy finding was the significant difference in mortality between the two species. *Aedes aegypti* exhibited higher mortality rates at equivalent concentrations compared to *Anopheles* spp. This discrepancy may be due to interspecies differences in cuticular physiology, integument permeability, and neural sensitivity.

Research by Lu et al. indicated that variability in the expression of detoxification enzymes, such as cytochrome P450, could influence larval tolerance to toxic agents (Lu, Song and Zeng, 2021). Several findings diverged from initial expectations, notably the inability of 10,000 ppm to achieve 100% mortality in *Anopheles* spp. It may be attributed to biological variability among larvae, microenvironmental resilience, or inconsistent exposure due to larval movement. Thus, ensuring uniform extract distribution and meticulously monitoring microenvironmental conditions during experiments is essential. Theoretically, this research enhances the understanding of plant-derived secondary metabolites as biological insecticidal agents.

https://doi.org/10.33086/jhs.v18.i03.7309

This paper corroborates ecotoxicological theories that phenolic compounds and alkaloids can induce significant physiological disruptions in target organisms through enzyme inhibition and cellular membrane damage (Rahman *et al.*, 2021; Ecevit *et al.*, 2022; Nisa *et al.*, 2024; De Rossi *et al.*, 2025; Elbouzidi *et al.*, 2025). It also advocates integrating ethnobotanical knowledge into developing modern, locally based larvicidal solutions. The practical implications of this study are substantial, particularly for Integrated Vector Management (IVM) programs.

Areca catechu extract, locally accessible and easily processed, represents a promising alternative to conventional insecticides—cost-effective, effective, safe, and community-empowering. The potential for ethanol- or water-based formulations in liquid or solid forms presents opportunities for environmentally friendly household larvicide products. Implementing these study findings could be advantageous in regions endemic to dengue and malaria, particularly rural areas with limited access to synthetic larvicides. Moreover, the ecological impact of plant-based larvicides is anticipated to be less detrimental to non-target organisms and aquatic ecosystems than organophosphate compounds such as temephos. So, the urgency of transitioning to ecologically based vector control strategies is critical, aligning with the Sustainable Development Goals (SDGs), notably Target 3.3 (combating communicable diseases) and Target 3.9 (reducing exposure to hazardous chemicals).

However, this study presented several limitations that warrant consideration. Firstly, the laboratory-based design did not fully replicate the natural environmental conditions of larval habitats, such as temperature variations, pH, predators, or other environmental contaminants. Secondly, the 24-hour exposure duration might be inadequate to capture sub-lethal and long-term toxic effects, such as disruptions in larval development or adult mosquito reproduction. Thirdly, although the sample size was statistically sufficient, its generalizability across larval populations from different geographic regions remains limited. Future studies are recommended to include semi-field and field trials to assess the stability and efficacy of the extract under more complex environmental conditions. Toxicological assessments on non-target organisms such as fish, plankton, and amphibians are also necessary to evaluate ecological risks. Additionally, studies on extract formulation and encapsulation techniques are essential to enhance the stability of active compounds and facilitate practical application. Evaluating the extract's efficacy against other mosquito species, such as *Culex quinquefasciatus*, may also help establish a broader spectrum of activity.

CONCLUSION

Areca catechu extract demonstrates potent, dose-dependent larvicidal activity against Aedes aegypti and Anopheles spp. The extract at 10,000 ppm within 24 hours achieved 100% mortality in Aedes aegypti and

https://doi.org/10.33086/jhs.v18.i03.7309

98% in Anopheles spp. Furthermore, Aedes aegypti indicates a higher susceptibility to the Areca catechu seed extract. This paper validates the bioactive potential of phytochemical constituents such as arecoline, saponins, and tannins in vector control. In addition, the comparative approach across multiple vector species represents a novel contribution, addressing a key gap in the current literature. Despite methodological constraints—including the absence of field validation and limited species range—the study establishes a foundational basis for developing sustainable, plant-derived larvicidal agents. Future investigations should focus on semi-field evaluations, formulation stability, and scalability for public health implementation. The findings offer practical relevance for integrating phytochemical-based strategies into community-level vector control programs, particularly in dengue and malaria-endemic regions, thereby supporting eco-friendly and sustainable disease prevention frameworks.

REFERENCES

Aziz, K., Badruttamam, M.I. and Rikadyanti, R. (2023) "Testing the Effectiveness of Red Betel Leaf Extract as an Insecticide on Aedes aegypti Mosquito Larvae | JIFMI : Jurnal Ilmiah Fitomedika Indonesia." Available at: https://ojs.stikesylpp.ac.id/index.php/JIFMI/article/view/591 (Accessed: May 15, 2025).

Bharathithasan, M., Ravindran, D.R., Rajendran, D., Chun, S.K., Abbas, S.A., Sugathan, S., Yahaya, Z.S., Said, A.R., Oh, W.-D., Kotra, V., Mathews, A., Mohd Amin, M.F., Ishak, I.H. and Ravi, R. (2021) "Analysis of chemical compositions and larvicidal activity of nut extracts from Areca catechu Linn against Aedes (Diptera: Culicidae)," *PLoS ONE*, 16(11), p. e0260281. Available at: https://doi.org/10.1371/journal.pone.0260281.

De Rossi, L., Rocchetti, G., Lucini, L. and Rebecchi, A. (2025) "Antimicrobial Potential of Polyphenols: Mechanisms of Action and Microbial Responses—A Narrative Review," *Antioxidants*, 14(2), p. 200. Available at: https://doi.org/10.3390/antiox14020200.

Ecevit, K., Barros, A.A., Silva, J.M. and Reis, R.L. (2022) "Preventing Microbial Infections with Natural Phenolic Compounds," *Future Pharmacology*, 2(4), pp. 460–498. Available at: https://doi.org/10.3390/futurepharmacol2040030.

Elbouzidi, A., Haddou, M., Baraich, A., Taibi, M., El Hachlafi, N., Pareek, A., Mesnard, F. and Addi, M. (2025) "Biochemical insights into specialized plant metabolites: Advancing cosmeceutical applications for skin benefits," *Journal of Agriculture and Food Research*, 19, p. 101651. Available at: https://doi.org/10.1016/j.jafr.2025.101651.

Hossain, S., Urbi, Z., Karuniawati, H., Mohiuddin, R.B., Moh Qrimida, A., Allzrag, A.M.M., Ming, L.C., Pagano, E. and Capasso, R. (2021) "Andrographis paniculata (Burm. f.) Wall. ex Nees: An Updated Review of Phytochemistry, Antimicrobial Pharmacology, and Clinical Safety and Efficacy," *Life*, 11(4), p. 348. Available at: https://doi.org/10.3390/life11040348.

Kasman, K., Ishak, H., Alam, G., Amiruddin, R., Hastutiek, P., Arsin, A.A., Nasir, S., Ridha, M.R. and Wahid, I. (2025) "Resistance status of Aedes mosquitoes as dengue vectors and the potential of plant larvicides from Indonesia for biological control: A narrative review." Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC12059870/ (Accessed: May 15, 2025).

Kuka, T.T., Bakoma, B., Kuka, F.C. and Adjei-Mensah, B. (2023) "*In ovo* effect of Soursop (*Annona muricata* L.) leaf extract on hatching and post-hatch performance of Noiler chickens," *Veterinary and Animal Science*, 21, p. 100311. Available at: https://doi.org/10.1016/j.vas.2023.100311.

Lu, K., Song, Y. and Zeng, R. (2021) "The role of cytochrome P450-mediated detoxification in insect adaptation to xenobiotics," *Current Opinion in Insect Science*, 43, pp. 103–107. Available at: https://doi.org/10.1016/j.cois.2020.11.004.

Martianasari, R. and Hamid, P.H. (2019) "Larvicidal, adulticidal, and oviposition-deterrent activity of Piper betle L. essential oil to Aedes aegypti," *Veterinary World*, 12(3), pp. 367–371. Available at: https://doi.org/10.14202/vetworld.2019.367-371.

Nawarathne, M.P. and Dharmarathne, C. (2024) "Control of dengue larvae of Aedes aegypti and Aedes albopictus using the larvicidal bioactive compounds in different plant extracts and plant extract-mediated nanoparticles," *Tropical Medicine and Health*, 52, p. 95. Available at: https://doi.org/10.1186/s41182-024-00654-9.

Nisa, R.U., Nisa, A.U., Tantray, A.Y., Shah, A.H., Jan, A.T., Shah, A.A. and Wani, I.A. (2024) "Plant phenolics with promising therapeutic applications against skin disorders: A mechanistic review," *Journal of Agriculture and Food Research*, 16, p. 101090. Available at: https://doi.org/10.1016/j.jafr.2024.101090.

Noya, A., Rahardjo, D. and Prakasita, V.C. (2022) "Pengaruh Konsentrasi Ekstrak Biji dan Kulit Buah Pinang (Areca catechu L.) Terhadap Mortalitas Larva Nyamuk Aedes aegypti," *EduMatSains : Jurnal Pendidikan, Matematika dan Sains*, 6(2), pp. 267–280. Available at: https://doi.org/10.33541/edumatsains.v6i2.3429.

de Oliveira, A.C., da Silva, F.M.A., de Sá, I.S., Leocadio, B.R.C., Lima, S.C., Lima da Costa, M.L., Roque, R.A. and Nunomura, R. de C.S. (2025) "Bioassay-Guided Isolation of Piplartine from Piper purusanum Yunck (Piperaceae) and Evaluation of Its Toxicity Against Aedes aegypti Linnaeus, 1762, Anopheles darlingi Root, 1926 (Culicidae), and Non-Target Animals," *Plants*, 14(5), p. 774. Available at: https://doi.org/10.3390/plants14050774.

Onen, H., Luzala, M.M., Kigozi, S., Sikumbili, R.M., Muanga, C.-J.K., Zola, E.N., Wendji, S.N., Buya, A.B., Balciunaitiene, A., Viškelis, J., Kaddumukasa, M.A. and Memvanga, P.B. (2023) "Mosquito-Borne Diseases and Their Control Strategies: An Overview Focused on Green Synthesized Plant-Based Metallic Nanoparticles," *Insects*, 14(3), p. 221. Available at: https://doi.org/10.3390/insects14030221.

Rahman, F.A., Naday, Q.A. and Utami, T.W. (2021) "The Effect Of Soursop (Annona Muricata L.) Essential Oils On Viability Cells: An In-Vitro Study," *Odonto : Dental Journal*, 8(1), pp. 28–33. Available at: https://doi.org/10.30659/odj.8.1.28-33.

Rahman, Md.M., Rahaman, Md.S., Islam, Md.R., Rahman, F., Mithi, F.M., Alqahtani, T., Almikhlafi, M.A., Alghamdi, S.Q., Alruwaili, A.S., Hossain, Md.S., Ahmed, M., Das, R., Emran, T.B. and Uddin, Md.S. (2021) "Role of Phenolic Compounds in Human Disease: Current Knowledge and Future Prospects," *Molecules*, 27(1), p. 233. Available at: https://doi.org/10.3390/molecules27010233.

Sembiring, F.K. and Hasan, R.S.B. (2020) "The Effectiveness Test of Betel Leaf Extract Toward The Development Of Aedes Aegypti Sp Larvae," *Biospecies*, 13(1), pp. 1–7. Available at: https://doi.org/10.22437/biospecies.v13i1.8386.

Sun, H., Yu, W., Li, H., Hu, X. and Wang, X. (2024) "Bioactive Components of Areca Nut: An Overview of Their Positive Impacts Targeting Different Organs," *Nutrients*, 16(5), p. 695. Available at: https://doi.org/10.3390/nu16050695.

Syahputra, B.S. and Ginting, T.Y. (2024) "The Effect of Soursop and Betel Leaf Extracts as Organic Pesticides in Pest Control of Spodoptera exigua (Lepidoptera: Noctuidiae) on Onion (Alium ascalonicum L.) Cultivation," *Jurnal Pembelajaran dan Biologi Nukleus*, 10(1), pp. 254–265. Available at: https://doi.org/10.36987/jpbn.v10i1.5393.

WHO (2022) *World malaria report 2021*. Available at: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2021 (Accessed: May 15, 2025).