JOURNAL OF AGROMEDICINE AND MEDICAL SCIENCES (AMS) ISSN: 2460-9048 (Print), ISSN: 2714-5654 (Electronic)
Available online at http://jurnal.unej.ac.id/index.php/JAMS

TOKSISITAS EKSTRAK DAUN CEREMAI (Phyllanthus acidus) DAN EKSTRAK DAUN ZODIA (Evodia suaveolens) TERHADAP MORTALITAS LARVA Aedes aegypti

TOXICITY OF CEREMAI (Phyllanthus acidus) AND ZODIA (Evodia suaveolens) LEAF EXTRACTS ON MORTALITY OF Aedes aegypti LARVAE

Andi Hilman Imtiyaz[1], Yunita Armiyanti[2*)], Evi Umayah Ulfa[3], Etik Ainun Rohmah[4]
[1]*Master of Public Health Science Student, Postgraduate Program, University of Jember, Jember, Indonesia*
[2]*Department of Parasitology, Faculty of Medicine, University of Jember, Jember, Indonesia*
[3]*Department of Pharmaceutical Biology, Faculty of Pharmacy, University of Jember, Jember, Indonesia*
[4]*Entomology Laboratory, Institute of Tropical Disease, University of Airlangga Campus C, Surabaya, Indonesia*

Article Info

Article History:
Received: June 28, 2024
Accepted: November 21, 2024
Published: November 24, 2024

**) Corresponding author:*
E-mail: yunita.fk@unej.ac.id

How to cite this article:

Imtiyaz, A. H., Armiyanti, Y., Ulfa, E. U., Rohmah, E. A. (2024). Toxicity of Ceremai (Phyllanthus acidus) and Zodia (Evodia suaveolens) Leaf Extracts on Mortality of Aedes aegypti Larvae. Journal of Agromedicine and Medical Sciences, 10(3), 157-161.

https://doi.org/10.19184/ams.v10i3.48674

Abstrak

Vektor pembawa penyakit Demam Berdarah Dengue (DBD) adalah Nyamuk Aedes aegypti. Berbagai strategi telah dilakukan untuk mengendalikan penyebaran nyamuk Aedes aegypti, salah satunya dengan menggunakan larvasida temephos. Penggunaan temephos menyebabkan resistensi Aedes aegypti dan pencemaran lingkungan. Oleh karena itu, perlu dikembangkan larvasida nabati dengan memanfaatkan daun ceremai (Phyllanthus acidus) dan daun zodia (Evodia suaveolens). Tujuan penelitian ini untuk mengetahui toksisitas ekstrak daun ceremai dan daun zodia terhadap mortalitas larva Aedes aegypti. Jenis penelitian ini adalah eksperimen murni menggunakan Rancangan Acak Lengkap. Sampel penelitian merupakan larva Aedes aegypti instar III. Terdapat 7 kelompok yang terdiri dari 1 kontrol negatif (aquadest dan tween20), 1 kontrol positif (temephos 0,008%) dan 5 kelompok perlakuan (ekstrak daun ceremai dan daun zodia). Data mortalitas larva diamati setelah 24 jam perlakuan. Hasil uji Kruskal Wallis menunjukkan terdapat perbedaan mortalitas antar kelompok dengan nilai p : 0,020 (p < 0,05). Ekstrak daun zodia sebesar 0,2% memiliki toksisitas paling tinggi sedangkan ekstrak daun ceremai sebesar 0,2% tidak menunjukkan adanya mortalitas larva Aedes aegypti. Hasil uji probit ekstrak daun zodia menunjukkan nilai LC_{50} dan LC_{90} yaitu 0,075% dan 0,121% dalam waktu 24 jam perlakuan. Ekstrak etanol daun zodia memiliki efektivitas sebagai larvasida Aedes aegypti.

***Kata Kunci**: Aedes aegypti, larvasida, ekstrak, ceremai, zodia*

Abstract

The vector that carries Dengue Hemorrhagic Fever (DHF) is Aedes aegypti. Various strategies have been implemented to control the spread of the Aedes aegypti, one of which is using temephos larvicide. The usage of temephos increases resistance to Aedes aegypti and environmental pollution. Therefore, it is necessary to develop a bio-larvicide using ceremai leaf (Phyllanthus acidus) and zodia leaf (Evodia suaveolens). The purpose of this study was to assess the toxicity of ceremai and zodia leaf extracts on the death of Aedes aegypti larvae. This form of research is a true experiment with a Completely Randomized Design. Third-instar Aedes aegypti larvae were used as the research sample. There were seven groups, including one negative control (aquadest and tween20), one positive control (temephos 0.008%), and five treatment groups (ceremai leaf and zodia leaf extract). Larval mortality data were observed after 24 hours of exposure. The Kruskal Wallis test revealed a significant difference in death rates across groups (p : 0.020, p < 0.05). Zodia leaf extract 0.2% had the highest toxicity, while ceremai leaf extract did not show any mortality of Aedes aegypti larvae. The probit test results of zodia leaf extract showed LC_{50} and LC_{90} of 0.075% and 0.121% within 24 hours of exposure. Zodia leaf ethanol extract has effectiveness as larvicide of Aedes aegypti.

***Keywords**: Aedes aegypti, larvicide, extract, ceremai, zodia*

Introduction

Mosquitoes remain a health concern which needs attention as they are vectors causing disease. *Aedes aegypti* transmits the dengue virus, which causes Dengue Hemorrhagic Fever (DHF). In Indonesia, there were 143,176 DHF cases and 1,236 deaths in 2022; however, in 2023, there were 98,071 cases and 764 deaths (Komariah, 2024).

Using larvicide is one of the strategy to reduce mosquito populations which works effectively (Benelli *et al*., 2019). Using synthetic larvicides such as *temephos* is effective at 100% mortality of *A. aegypti* larvae but also has some disadvantages include the development of resistance in some countries (Sinaga *et al*., 2016), causing adverse effects on non-target populations, and not being easily decomposed thus causing environmental pollution (Riyadi *et al*., 2018). Therefore, bio-larvicides need to be developed as an alternative for controlling *A. aegypti* larvae.

Bio-larvicide was developed by utilizing plants that contain toxic compounds to mosquito larvae such as alkaloid, flavonoid, saponin, and tannin compounds have been shown to have larvicidal effects on *A. aegypti* larvae (Mila & Khaira, 2020). Alkaloids inhibit larval feeding, flavonoids inhibit larval airway, saponins reduce larval appetite, and tannins disrupt larval cell metabolism (Kumara *et al*., 2021).

Ceremai leaf (*Phyllanthus acidus*) has a variety of health benefits and is proven to kill *A. aegypti* larvae as ceremai leaf extract contains flavonoids, tannins, and saponins (Muttaqin *et al*., 2019). Research conducted by Hasanah *et al*. (2019) mentioned that ethanol extract from ceremai leaf can kill *Culex quinquefasciatus* larvae by 50% (LC_{50}) at a level of 0.189% after 24 hours of observation. Statistical test results showed that ceremai leaf extract had a larvicidal effectiveness of 90.9% on the mortality of *Culex quinquefasciatus larvae*.

Zodia leaf (*Evodia suaveolens*) is one of the plants that Papuans used to repel mosquitoes; it is now cultivated as a decorative plant and could be found in numerous locations. Zodia leaf extract contains alkaloids, flavonoids, tannins, and saponins (Lestari *et al*., 2015). According to the findings of Boesri *et al*. (2015), the ethanol extract of zodia leaf has an LC_{50} against *A. aegpyti* larvae of 0.194% after 24 hours.

Combining active ingredients from two plant extracts can prevent larval resistance to bio-larvicides and have either an antagonistic or synergistic impact on larval mortality (Rikantara *et al*., 2022). Research conducted by Hikma & Ardiansyah (2018) stated that moringa leaf (*Moringa oleifera* Lamk) extract can kill 89% of *A. aegypti* larvae, tin leaf (*Ficus carica* Linn) extract can kill 87% of larvae, while the combination of the two extracts can kill 92% of larvae after 24 hours of observation in a 1:1 ratio. This indicates that the two extracts combined prove more toxic than either extract alone.

Researchers are interested in combining extracts from Ceremai and Zodia leaves which expected to be efficient bio-larvicide materials This study aimed to evaluate the impact of ceremai and zodia leaf extracts on *A. aegypti* larval mortality.

Methods

Research Design

This is true experimental research and uses a Completely Randomized Design. This study was divided into 9 groups, namely 2 control groups (KP, KN) and 5 treatment groups (P1, P2, P3, P4, P5). Larval A. aegpyti mortality will be monitored after treatment, following a 24-hour exposure period. 700 Aegypti larvae in their third instar were used as samples in this research which collected from the Tropical Diseases Institute's Entomology laboratory at the University of Airlangga in Surabaya. Plant identification was done at the Botany Laboratory, Faculty of Mathematics and Natural Sciences, University of Jember. The study was conducted in January until March of 2024.

Tools and Materials

Materials required were 700 grams of each ceremai and zodia fresh leaves, 96% ethanol, aquadest, and tween20. The instruments used were oven, blender, rotary evaporator, analytical balance, beaker glass, spatula, stirrer, drop pipette, and plastic cup.

Extract Preparation

Extract preparation was conducted at the Pharmacognosy and Phytochemistry Laboratory, Faculty of Pharmacy, University of Jember. The remaceration approach was used to create the ceremai and zodia leaf extracts. 700 grams of each fresh leaves in total were chopped, left to aerate for three days, and then baked at 40°C for a full day. After drying and blending each leaf separatedly, 255 grams of ceremai leaf powder and 300 grams of zodia leaf powder are produced. Afterwards, the leaf powder was remacerated with 96% ethanol as much as 4; 2; 1.5 times the weight of the powder for 3 times within 24 hours. A rotary evaporator with a temperature setting of 50°C and a speed of 100 rpm was applied to concentrate the filtrate from the maceration process.

Extract Concentration Determination

The leaf extract concentration used in the research variations was 0.2%, as mentioned by Hasanah *et al*. (2019) dan Boesri *et al*. (2015). This meant that the concentration of leaf extract used was 0.2% ceremai leaf extract; 0.2% zodia leaf extract; a combination of ceremai leaf and zodia leaf extracts with a ratio of 0.05%:0.15% (1:3); 0.1%:0.1% (1:1); 0.15%:0.05% (3:1). The contrentaion was made from combining 5 grams of extract with 1 ml of tween20, then add aquadest until the mixture reaches a 500 ml solution. This will yield an extract solution with a 1% concentration. Next, plastic cups were filled with 20 ml, 15 ml, 10 ml, and 5 ml of this solution. Aquadest was poured to each plastic cup until a 100 ml solution was formed, yielding the following concentrations: 0.2%, 0.15%, 0.1%, and 0.05%. The negative control group was made by mixing 0.1 ml of tween20 into 99.9 ml of distilled water. The positive control group was made by mixing 0.08 grams of *temephos* into 1 L of aquadest and then taken as much as 100 ml into a plastic cup.

Larvicide Test

Following the WHO's guidelines for larvicide testing (2005), each group contained 25 *A. aegypti* larvae that were repeated four times. The study was conducted by placing the larvae into plastic cups containing extract solution for the treatment group, tween20 solution for the negative control, and *temephos* solution for the positive control. Larval mortality was discovered after 24 hours of exposure, as evidenced by the absence of movement in response to a tactile stimulus.

Larval Mortality Measurements

The formula used to calculate the mortality percentage of *A. aegypti* larvae after 24 hours of exposure:

$$\frac{Number\ of\ mortality\ larvae}{Number\ of\ larvae\ tested} \times 100\%$$

Statistical Analysis

Larval mortality was analyzed by the *Kruskal Wallis* statistical test because the data were not normally distributed. If the *Kruskal Wallis* test revealed a significant difference ($p<0.05$), the *Mann-Whitney* test will be used to examine the variations in values within each group. The LC_{50} and LC_{90} values were determined using probit analysis.

Ethical Clearance

This research has obtained ethical clearance with number 2407/UN25.8/KEPK/DL/2024 from the Health Research Ethics Committee of the Faculty of Dentistry, University of Jember.

Results

Plant Determination

The results of plant determination from the Botany Laboratory, Faculty of Mathematics and Natural Sciences, University of Jember showed that the plants used in the study were true *Phyllanthus acidus* (L.) Skeels from Phyllanthaceae and *Evodia suaveolens* Scheff. var. ridleyi (Hochr.) from Rutaceae.

Extract Quality Test

The results of the quality test of ceremai leaf and zodia leaf extract can be seen in Table 1. Zodia leaf extract has a higher yield than ceremai leaf extract. Testing the water content of extracts in this study used the gravimetric method. The water content of ceremai leaf extract is higher than zodia leaf extract. The organoleptic test aimed to provide an initial introduction to the extract through the five senses. The organoleptic test of ceremai leaf and zodia leaf extracts produced condensed extracts, a distinctive smell, and a slightly bitter taste. Ceremai leaf extract has a dark green color, while zodia leaf extract has a blackish green color.

Table 1. The results of the extract quality test

Extract	Simplicia (g)	Condensed Extract (g)	Yield (%)	Water Content (%)	Organoleptic
Ceremai Leaf	255	19,32	7,57	21,15 ± 1,42	1. Form: condensed 2. Color: dark green 3. Smell: distinctive 4. Taste : slightly bitter
Zodia Leaf	300	36,9	15,47	15,39 ± 0,72	1. Form: condensed 2. Color: blackish green 3. Smell: distinctive 4. Taste: slightly bitter

Table 2. Mortality of *A. aegypti* larvae after 24 hours of exposure

Group	Larval Total	Mortality Rate				Mortality Mean	Mortality Percentage (%)
		R 1	R 2	R 3	R 4		
KN	25	0	0	0	0	0 ± 0	0
KP	25	25	25	25	25	25 ± 0	100
P1	25	0	0	0	0	0 ± 0	0
P2	25	25	25	25	25	25 ± 0	100
P3	25	24	25	25	25	24,75 ± 0,50	99
P4	25	18	17	19	19	18,25 ± 0,96	73
P5	25	7	5	8	6	6,5 ± 1,29	26

Note : R : Repetition; KN : Aquadest+tween20; KP : *Temephos* 0,008%; P1 : Ceremai leaf extract 0,2%; P2 : Zodia leaf extract 0.2%; P3 : Combination of ceremai leaf and zodia leaf extracts 1:3 (0.05%:0.15%); P4 : Combination of ceremai leaf and zodia leaf extracts 1:1 (0.1%:0.1%); P5 : Combination of ceremai leaf and zodia leaf extracts 3:1 (0.15%:0.05%)

Larvicide Test

Table 2 shows the mortality of *A. aegypti* larvae across all groups. The negative control given aquadest and tween20 did not cause larval mortality, indicating that the amount of solvent employed is inoffensive for *A. aegypti* larvae. The mortality rate of *A. aegypti* larvae was 100% in the positive control treated with 0.008% temephos. The mortality of *A. aegypti* larvae varied in the treatment groups given ceremai leaf and zodia leaf extracts, both single and combination extracts, after 24 hours of exposure.

Zodia leaf extract 0.2% had the highest mortality rate of *A. aegypti* larvae, which was 100%. The Kruskal-Wallis test revealed statistically significant variations in the mean mortality of *A. aegypti* larvae between groups ($p = 0.020$), which Mann-Whitney test is needed to compare the values variation of each group. The results showed that between groups showed significant differences, except for KN with P1 (p: 1,000), KP with P2 (p: 1,000), KP with P3 (p: 0.317), and P2 with P3 (p: 0.317). The Ceremai leaf extract at 0.2% showed no death of *A. aegypti* larvae, hence it can be claimed that the mortality of *A. aegypti* larvae was caused by the zodia leaf extract.

Probit analysis was used to establish the lethal concentration of zodia leaf extract that induces 50% (LC_{50}) and 90% (LC_{90}) death in *A. aegypti* larvae within 24 hours. The LC_{50} and LC_{90} of zodia leaf extract on *A. aegypti* larval mortality after 24 hours of exposure were 0.075% (0.068%-0.081%) and 0.121% (0.112%-0.133%), respectively.

Discussion

The results of the quality test of ceremai leaf and zodia leaf extracts showed that zodia leaf extract has a higher yield than ceremai leaf extract. The higher yield affects the amount of extract produced (Badriyah & Farihah, 2022). The water content test aimed to determine the percentage of water content in the extract after the drying or condensing process (Utami *et al*., 2020). The quality standards of condensed extracts generally have a yield of not less than 10% and a water content of 5-30% (Voigt, 1994). The quality standards of ceremai leaf extract are specifically regulated in the Farmakope Herbal Indonesia (Health Ministry of Republic Indonesia, 2017), which has a yield of not less than 13.6% and a water content of not more than 14.6%. Ceremai leaf extract has a yield of 7.57% and a water content of 21.15 ± 1.42% which indicates that the yield and water content of ceremai leaf extract do not meet the standards. The yield and water contents of zodia leaf extract are 15.47% and 15.39 ± 0.72% which can be said to meet the standards. The higher the percentage of water content in the extract, the more susceptible the extract will be to damage and rot due to the development of microbes that affect the stability of the extract (Utami *et al*., 2020).

Ceremai leaf extract at 0.2% did not show any mortality of *A. aegypti* larvae. Ceremai leaf extract has no effectiveness as a larvicide. This is in contrast to the research of Hasanah *et al*. (2019) which showed that ethanol extract from ceremai leaf can cause mortality of *Culex quinquefasciatus* larvae. The effectiveness of ceremai leaf extract can cause mortality of *A. aegypti* larvae is affected by several factors such as plant age, location of plant origin, time of plant collection, plant storage, plant size, and extraction method (Sari *et al*., 2020). The yield and water content of ceremai leaf extract that do not meet the standards can also affect the effectiveness of *A. aegypti* larval mortality.

As the content of zodia leaf extract increased, so did the mortality percentage of *A. aegypti* larvae. *A. aegypti* larvae died completely when exposed to 0.2% Zodia leaf extract. It can be said that zodia leaf extract has the effectiveness as a larvicide like *temephos*. This study's findings are consistent with those of Handayani *et al*. (2017) showed that an ethanolic extract of zodia leaf can kill *A. aegypti* larvae. Another study found that hexane extract of zodia leaves can cause mortality of *A. aegypti* larvae (Setiyadi et al. 2020).

The cause of *A. aegypti* larvae mortality in the treatment group might be due to the compounds that affect larval growth. The content of compounds in zodia leaf extracts that have larvicidal effects are alkaloids, flavonoids, tannins, and saponins (Lestari *et al*., 2015). Alkaloids function by interfering with the work of the *acetyl cholinesterase* enzyme which oversees transmitting orders to the larval digestive or as a stomach poison. Flavonoids work by entering through the siphon into the larval body and causing respiratory damage. Saponins cause decreased appetite and irritate the larval digestive. Tannins cause disruption of protein absorption through digestive enzyme activity (Ahdiyah & Purwani, 2015).

The LC_{50} and LC_{90} of zodia leaf extract on *A. aegypti* larvae mortality within 24 hours were 0.075% and 0.121%, respectively. These LC_{50} and LC_{90} were smaller than the research of Boesri *et al*. (2015) which showed that LC_{50} and LC_{90} of zodia leaf extract were 0.194% and 0.628%. The extract's potency in causing the death of *A. aegypti* larvae increases as the LC of the extract decreases (Putri *et al*., 2022). Zodia leaf extract's capacity to cause mortality of *A. aegypti* larvae is attributed to its viscosity, which can impair the movement of larvae to the surface to take oxygen (Hidayati & Suprihatini, 2020). Therefore, extract from zodia leaf is a substitute larvicide that effectively kills *A. aegypti* larvae.

Conclusion

The mortality of *A. aegypti* larvae was different after exposure to ceremai leaf and zodia leaf extracts. After 24 hours of exposure, most of *A. aegypti* larvae died when exposed to 0.2% of Zodia leaf extract. The LC_{50} and LC_{90} of zodia leaf extract on *A. aegypti* larvae mortality within 24 hours were 0.075% and 0.121%, respectively. Further research is needed regarding the use of zodia leaf extract as a more practical product that can be easily applied to the community. In addition, it is necessary to conduct GC-MS (*Gas Chromatography-Mass Spectrometry*) analysis to ensure what compounds are contained in zodia leaf extract can cause mortality of *A. aegypti* larvae.

Conflict of Interest

The authors did not report any potential competing interests.

Acknowledgment

We would like to thank the Institute for Research and Community Service, University of Jember for providing research funds through a Postgraduate Grant in 2024, the Institute of Tropical Diseases, University of Airlangga Surabaya for permission and support in carrying out this study and all parties who contributed to the study.

Author Contribution

AHI contributed to drafting a concept, compiling a research design, conducting the research, and data analysis. YA contributed to preparing the manuscript, data analysis, data interpretation, revising the final manuscript for publication, and approving the final version to be published. EUU contributed to data analysis, data interpretation, revising the final manuscript for publication, and approving the final version to be published. EAR contributed to assisting in the implementation of the research and data analysis.

References

Ahdiyah, I., & Purwani, K. I. (2015). Pengaruh Ekstrak Daun Mangkokan (Nothopanax scutellarium) sebagai Larvasida Nyamuk Culex sp. *Jurnal Sains Dan Seni ITS*, *4*(2), 32–36.

Badriyah, L., & Farihah, D. A. (2022). Analisis ekstraksi kulit bawang merah (Allium cepa L.) menggunakan metode maserasi. *Jurnal Sintesis*, *3*(1), 30–37.

Benelli, G., Pavela, R., Petrelli, R., Nzekoue, F. K., Cappellacci, L., Lupidi, G., Quassinti, L., Bramucci, M., Sut, S., Dall'Acqua,

S., Canale, A., & Maggi, F. (2019). Carlina oxide from Carlina acaulis root essential oil acts as a potent mosquito larvicide. *Industrial Crops and Products*, *137*, 356–366. https://doi.org/10.1016/j.indcrop.2019.05.037

Boesri, H., Heriyanto, B., Handayani, S. W., & Suwaryono, T. (2015). Uji Toksisitas Beberapa Ekstrak Tanaman Terhadap Larva Aedes Aegypti Vektor Demam Berdarah Dengue. *Vektora: Jurnal Vektor Dan Reservoir Penyakit*, *7*(1), 29–38.

Handayani, S. W., Boesri, H., & Priyanto, H. (2017). Potensi Umbi Gadung (Dioscorea hispida) dan Daun Zodia (Euodia suaveolens) sebagai Insektisida Nabati. *Media Penelitian Dan Pengembangan Kesehatan*, *27*(1). https://doi.org/10.22435/mpk.v27i1.4278.49-56

Hasanah, A., Hermansyah, B., & Abrori, C. (2019). Aktivitas Larvasida Ekstrak Etanol Daun Ceremai (Phyllanthus acidus) Terhadap Larva Culex quinquefasciatus Instar III/IV. *Journal of Agromedicine and Medical Science*, *5*(2), 24–29.

Hidayati, L., & Suprihatini, S. (2020). Pengaruh Pemberian Ekstrak Biji Mahoni (Swietenia mahagoni) Terhadap Kematian Larva Culex sp. *ASPIRATOR - Journal of Vector-Borne Disease Studies*, *12*(1), 45–52. https://doi.org/10.22435/asp.v12i1.2171

Hikma, S. R., & Ardiansyah, S. (2018). Kombinasi Ekstrak Daun Kelor (Moringa oleifera Lamk) Dengan Ekstrak Daun Tin (Ficus carica Linn) Sebagai Larvasida Terhadap Larva Aedes aegypti. *Medicra (Journal of Medical Laboratory Science/Technology)*, *1*(2), 94–102. https://doi.org/https://doi.org/10.21070/medicra.v1i2.1649

Kementerian Kesehatan Republik Indonesia. (2017). *Farmakope Herbal Indonesia* (Edisi II). Kementerian Kesehatan Republik Indonesia.

Komariah, F. (2024). *Kemenkes Catat Tren Kasus DBD tahun 2023 Menurun*. Radio Republik Indonesia. https://www.rri.co.id/kesehatan/519517/kemenkes-catat-tren-kasus-dbd-tahun-2023-menurun

Kumara, C. J., Nurhayani, Bestari, R. S., & Dewi, L. M. (2021). Efektivitas Flavonoid, Tanin, Saponin dan Alkaloid terhadap Mortalitas Larva Aedes aegypty. *The 13th University Research Colloqium 2021*, 106–118.

Lestari, M. S., Himawan, T., Abadi, A. L., & Retnowati, R. (2015). Toxicity and phytochemistry test of methanol extract of several plants from papua using Brine Shrimp Lethality Test (BSLT). *Journal of Chemical and Pharmaceutical Research*, *7*(4), 866–872.

Mila, S., & Khaira, I. L. (2020). Ekstrak Daun Pepaya (Carica Papaya L) Terhadap Mortalitas Larva Nyamuk Aedes Aegypti. *Epidemica*, *1*(1), 17–23.

Muttaqin, D. M., Suwendar, & Choesrina, R. (2019). Uji Aktivitas Antifungi Ekstrak Etanol Daun Ceremai (Phyllanthus Acidus (L.) Skeels) terhadap Candida Albicans. *Prosiding Farmasi*, 42–48.

Putri, H. N., Wardani, D. P. K., Hikmawati, I., & Almanfaluthi, M. L. (2022). Efektivitas Kombinasi Ekstrak Lidah Buaya dan Lidah Mertua Terhadap Mortalitas Larva Aedes aegypti. *BALABA: JURNAL LITBANG PENGENDALIAN PENYAKIT BERSUMBER BINATANG BANJARNEGARA*, 53–64. https://doi.org/10.22435/blb.v18i1.5354

Rikantara, F. S., Utami, M. R., & Kasasiah, A. (2022). Aktivitas Antioksidan Kombinasi Ekstrak Daun Sirsak (Annona muricata L.) dan Ekstrak Daun Pepaya (Carica papaya L.) dengan Metode DPPH. *LUMBUNG FARMASI: Jurnal Ilmu Kefarmasian*, *3*(2), 124–133.

Riyadi, Z., Julizar, J., & Rahmatini, R. (2018). Uji efektivitas ekstrak etanol biji rambutan (Nephelium lappaceum L.) sebagai larvasida alami pada larva nyamuk Aedes aegypti. *Jurnal Kesehatan Andalas*, *7*(2), 233.

Sari, A. P., Yudiati, E., & Sunaryo. (2020). Toksisitas Partisi N-Heksan dan Etil Asetat pada Ekstrak Sargassum sp. terhadap Larva Aedes aegypti Instar III. *Journal of Marine Research*, *9*(2), 143–150.

Sinaga, L. S., Martini, & Saraswati, L. D. (2016). Status Resistensi Larva Aedes aegypti (Linnaeus) terhadap Temephos (Studi di Kelurahan Jatiasih Kecamatan Jatiasih Kota Bekasi Provinsi Jawa Barat). *Jurnal Kesehatan Masyarakat*, *4*(1), 142–152.

Utami, Y. P., Sisang, S., & Burhan, A. (2020). PENGUKURAN PARAMETER SIMPLISIA DAN EKSTRAK ETANOL DAUN PATIKALA (Etlingera elatior (Jack) R.M. Sm) ASAL KABUPATEN ENREKANG SULAWESI SELATAN. *Majalah Farmasi Dan Farmakologi*, *24*(1), 6–10. https://doi.org/10.20956/mff.v24i1.9831

Voigt, R. (1994). *Buku Pelajaran Teknologi Farmasi*. Gadjah Mada University Press.

World Health Organization. (2005). *Guidelines for Laboratory and Field Testing of Mosquito Larvicides*. WHO.