Original Research Report

LARVICIDAL EFFECT OF BREADFRUIT (*Artocarpus altilis*) FLOWER EXTRACT AGAINST *Aedes aegypti*

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ABSTRACT

Dengue hemorrhagic fever remains a major problem in Indonesia. The mosquito that spreads this disease is the *Aedes aegypti* species. The use of larvicides is a viable method to inhibit the growth of larvae into adult mosquitoes. The flowers of breadfruits (*Artocarpus atilis*) have long been used as a natural mosquito killer. The objectives of this study were to determine the lethal dose 50 (LC50) of breadfruit flower extract and to analyze its potential as a larvicide against stage 2–3 instar *Aedes aegypti* larvae. In this true experimental research, each of four treatment groups was administered with breadfruit flower extracts at concentrations of 25, 50, 75, and 90 ppm, respectively. The positive control group was treated with temephos (Abate), while the negative control group received no treatment. Larval mortality was recorded at 1 hour, 2 hours, 3 hours, 4 hours post-intervention. The observed larval deaths were compared among the groups. Quantitative data encompassing the larval mortality in each group were analyzed using the repetitive analysis of variance (ANOVA) and the probit test with minimum p value <0.05. The results indicated that the LC50 value of breadfruit flower extract was 52.67–54.12 ppm. The doses of 50 ppm, 75 ppm and 90 ppm were effective in killing *Aedes aegypti* larvae. In conclusion, breadfruit flower extract of 50 ppm and higher can effectively kill *Aedes aegypti* larvae.

Keywords: Larvicide; *Atrocarpus*; dengue

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Highlights:

1. This study attempted an experiment on the novel invention of a naturally sourced larvacide, specifically breadfruit (*Artocarpus atilis*) flower extract, against *Aedes aegepti*.
2. The findings of this study suggest that breadfruit flower extract can serve as an effective larvacide, as evident by an increased mortality rate of *Aedes aegepti* larvae.

INTRODUCTION

Technological innovations continue to evolve as time progresses. One of these advancements has an impact on the development of anti-mosquito drugs around the world. Most mosquito repellents available on the market are in the form of mosquito coils. However, people remain largely unaware of the dangers associated with the smoke emitted by these coils, which can cause various health problems such as acute respiratory infection, poisoning, lung cancer, and asthma attacks. As a result, there is a necessity for mosquito repellent products that have minimal side effects and are both practical and safe for use by the public (Glover 2015).

Apart from the health risks associated with mosquito repellents, there is also the issue of resistance to repellent substances, such as those used in fogging. This resistance causes mosquitoes to avoid the effect of insecticides, absorb toxins at a reduced rate, and undergo genetic modification. The World Health Organization has recorded a 30-fold increase in cases of mosquito repellent resistance throughout the past 50 years. This results from the increasing strength of insecticide resistance over time (Muangmoon et al. 2018). Innovations in mosquito prevention are crucial to enhance their effectiveness, efficiency, and safety for public use, particularly through the use of materials derived from natural sources. The breadfruit plant has been used for generations as a mosquito repellant. Preliminary research has indicated that breadfruit leaves have the potential as an herbal insecticide (de Melo et al. 2018, Moniharapon et al. 2023).

Breadfruit, scientifically known as *Artocarpus altilis*, is a plant with numerous benefits. The plant can grow throughout Indonesia, more precisely in tropical areas, and is popular among the local people (Tian et al. 2016). All parts of this plant are nutritious and beneficial for health. Breadfruit flowers contain active compounds, such as flavonoids, saponins, and tannins. These compounds are useful as a mosquito-killing insecticide. In more detail, these compounds may act as respiratory inhibitors in mosquitoes by deactivating the cholinesterase enzyme, which regulates the functioning of the nervous system. The disruption of the cholinesterase enzyme in mosquitoes leads to increased respiratory muscle stimulation, resulting in convulsions, paralysis, and potential mortality. However, the use of breadfruit flowers in an extract form has not been widely studied (Haryani et al. 2020). This study aimed to analyze the larvicidal effect of breadfruit flower extract against *Aedes aegypti*. The effect was assessed by determining the lethal dose 50 (LD50) of the extract in a comparison between negative and positive controls, as indicated by the mortality rate of *Aedes aegypti* mosquito larvae.

MATERIALS AND METHODS

This study employed a true experimental research design. The research samples used *Aedes aegypti* mosquito larvae as experimental animals, grouped into six different groups: positive control, negative control, treatment 1, treatment 2, treatment 3, and treatment 4. The positive control group consisted of larvae administered with temephos (Abate, PT. BASF, Indonesia). The negative control group comprised larvae that were not given any treatment. Treatment groups 1, 2, 3, and 4 received breadfruit flower extract at concentrations of 25 ppm, 50 ppm, 75 ppm, and 90 ppm, respectively (Gladys & Bukola 2019). This research was carried out from February until April 2024 at the Faculty of Medicine and Health Sciences, Universitas Warmadewa, Denpasar, Indonesia.

Plant identification was conducted prior to the extraction of breadfruit flowers. While breadfruit trees could reach a height of up to 30 m, they typically measured around 12 m in rural regions. Breadfruit trees could be clonally propagated, often resulting in shorter trees with less branching. Distinctive characteristics used for the plant identification were as follows: breadfruit trees growing up to 8 m in height, featuring big, straight stems, and were accompanied by low, extended plank roots or buttresses. The breadfruit trees exhibited huge leaves arranged in an alternating pattern, horizontal branches, and a loose canopy. The leaves measured 20–40 x 20–60 cm and had extensive pinnation. Their texture was strong and leathery, with a lustrous dark green upper surface and a dull, rough, and hairy underside. Large, cone-shaped supporting leaves enveloped the buds. All parts of the plant released white sap or latex upon injury to the tree. The identification of breadfruit flowers was performed by finding the inflorescences, located close to the end of the twigs around the leaf axils. Male flowers were characterized by elongated, dangling spikes resembling clubs, a light green color that would turn yellow upon ripening. The pollen was yellow and readily dispersed by the wind. The female compound flowers, which were round or slightly cylindrical, measured 5–7 × 8–10 cm and exhibited a green color. The formation of complex female flowers, measuring between 10 and 30 cm in diameter, led to the production of compound fruit (Jones et al. 2013).

The materials used during the extraction of breadfruit flowers comprised 500 g of breadfruit flower powder, 5 L of 96% ethanol, 75 mL of breadfruit flower extract, 900 mL of 70% alcohol, 9 fiber sticks, 3 glass bottles of 50 mL capacity, 6 latex gloves, 5 ovitraps, 3 sheets of litmus paper, and a filter paper of 2 m. The tools used for the extraction of breadfruit flowers consisted of a blender, a sifter, two glass bottles covered with aluminum foil, four pipettes, a small funnel, a beaker, a spatula spoon, and two buckets. The research variables employed in the tests included independent variables (i.e., different concentrations of breadfruit flower extract) and dependent variables (i.e., larval mortality and LC50) (Pineda-Cortel et al. 2019).

Prior to breadfruit flower extract preparation, the sample materials were collected from a garden in Tangkas Village, Klungkung, Indonesia. The breadfruit flowers were harvested before 10:00 a.m. to avoid sun exposure, then immediately washed, cleaned, and air dried at room temperature to preserve the effectiveness of the breadfruit flower contents. Once dry, the breadfruit flowers were ground using a blender to produce the final result in powder form (de Melo et al. 2018).

The breadfruit flowers were harvested periodically until 500 g of breadfruit flower powder was obtained. The sample extraction proceeded with maceration, wherein breadfruit flower powder was dissolved in 5L of 96% ethanol for 3 x 24 hours. Maceration was carried out four times using 100 mL of 96% ethanol solvent for each repetition, accompanied by occasional stirring. The liquid resulting from the maceration was stored in a container. Afterwards, thickening was performed using a rotary evaporator at a temperature of 50 °C to produce an extract with a thick consistency, which was subsequently weighed and dissolved in distilled water. The diluted breadfruit flower extract was prepared in different concentrations of 25, 50, 75, and 90 ppm with the help of a pipette. The solution was stirred using a spatula or by gently shaking the beaker glass in a circular motion. The process of shaking was performed carefully to prevent the solution from foaming, as it could destroy the produced aroma otherwise. Each mixture concentration consisted of different formulations. The concentrations of 25, 50, 75, and 90 ppm were achieved using varying amounts of breadfruit flower extract at 25, 50, 75, and 90 mg, respectively, disolved in 1,000 mL of distilled water.

Mosquito eggs were collected using ovitraps in Denpasar, Gianyar, and Karangasem, Indonesia. After the eggs were trapped inside the ovitraps, they were collected using filter paper. The ovitraps were colored to effectively attract *Aedes* sp. mosquitoes for egg-laying purposes. A total of 50 larvae were used in one test (Muangmoon et al. 2018). The larvae acquired on the filter paper were placed in a plastic container filled with well water and were let to grow into stage 3–4 instar larvae. These larvae were picked using a drop pipette, then transferred to a tray and provided with larval food. A plastic container filled with 100 mL of water was prepared for each group. Afterwards, the concentrations of breadfruit flower extract, namely 25, 50, 75, and 90 ppm, were determined for administration to the assigned groups (Kurniawan et al. 2020). The extract was taken using a measuring pipette and then put in containers. Before administration, the extract was homogenized or mixed with each water mixture according to the dosage. A total of 10 larvae per group was transferred using a pipette into each container to determine the LC50 value. The time of larval death was recorded after an hour, two hours, three hours, and four hours. The dead larvae were later observed under a light microscope at 10X magnification. After 1 x 24 hours, the dead larvae were removed and discarded (Moniharapon et al. 2023a).

Quantitative data were collected, including the number of larval deaths in each group, and thereafter analyzed by the repetitive analysis of variance (ANOVA) wit level of significance $p<0.05$. The data were presented using frequency distribution tables accompanied by a narrative explanation. The LC50 values for each group were analyzed and compared using probit analysis with the help of IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, N.Y., USA) (Halmi et al. 2018).

RESULTS

Table 1 shows the results of administering breadfruit flower extract at different concentrations of 25, 50, 75, and 90 ppm. The administration of the extract indicated that concentrations of 75 and 90 ppm resulted in the highest rate of larval mortality.

Table 1. The number of observed larvae.

Dose (ppm)	Larvae (n)	Larval mortality (n)
25	10	0
50	10	9
75	10	10
90	10	10

An observation at one hour after the intervention showed that a dose of 90 ppm killed the mosquito larvae more effectively compared to the concentrations of 25 and 50 ppm. The increasing of larvae mortality was due to dose dependent effect. Breadfruit extract had been able to effectively exterminate the larvae started at a dose of 50 ppm. It indicated that even a lower dose had been able to provide significant inhibitory effect.

Table 2. The percent of mortality larvae by dose concentration

Percent Mortality (%)	95% confidence limits		
	Estimate lethal doses (ppm)	Lower bounds	Upper bounds
10	37.88	30.68	42.48
15	40.71	34.40	44.90
20	42.95	37.30	46.88
25	44.88	39.75	48.61
30	46.62	41.90	50.21
35	48.22	43.85	51.74
40	49.74	45.66	53.24
45	51.22	47.36	54.73
50	52.67*	48.98*	56.26*
55	54.12*	50.54*	57.84*
60	55.59	52.08	59.49
65	57.11	53.62	61.26
70	58.72	55.19	63.17
75	60.45	56.82	65.29
80	62.38	58.59	67.71
85	64.63	60.59	70.58
90	67.46	63.03	74.27
99	79.52	73.01	90.44

Legend: The lethal dose 50 (LD50) is indicated by an asterisk (*).

Probit analysis was employed to estimate the fatal concentration for 50% mortality. A dosage of 52.67 ppm of breadfruit extract was able to eliminate 50% of the total detected larvae. Increasing the extract dose to 79.52 ppm was found to be able to eliminate 99% of the larvae (Table 2).

Table 3. Differences in larval mortality rates among the groups.

Groups (doses)	n	Mean	SD	95% CI of the mean		Min	Max
				Lower bounds	Upper bounds		
25	10	0.00	0.00	0.00	0.00	0.00	0.00
50	10	4.37	3.11	1.77	6.97	0.00	9.00
75	10	9.62	0.74	9.00	10.24	8.00	10.00
90	10	10.00	0.00	10.00	10.00	10.00	10.00

The ANOVA test was employed to analyze the comparison between doses, revealing a significant difference in the mean mortality of larvae among the groups. A dose of 25 ppm exhibited little impact on larval mortality. An enhanced effect was noted at a 50 ppm dose, with a mean larval mortality of 4.37. Table 3 indicates that the optimal concentrations for larval mortality were 75 ppm and 90 ppm. These data indicated that a higher dose correlated with an increased mortality rate.

Table 4. Multiple comparisons of larval mortality rates between groups.

Groups (doses)	Comparison groups (doses)	p	95% CI	
			Lower bounds	Upper bounds
25	50	0.000	-6.01	-2.73
	75	0.000	-11.26	-7.98
	90	0.000	-11.63	-8.36
50	25	0.000	2.73	6.01
	75	0.000	-6.88	-3.61
	90	0.000	-7.26	-3.98
75	25	0.000	7.98	11.26
	50	0.000	3.61	6.88
	90	0.643	-2.01	1.26
90	25	0.000	8.36	11.63
	50	0.000	3.98	7.26
	75	0.643	-1.26	2.01

Legend: CI=confidence interval.

The multiple comparison results between groups are presented in Table 4. The mortality rates of the larvae showed a significant difference between 25 ppm and the concentrations of 50 ppm, 75 ppm, and 90 ppm. However, there was no significant difference between 75 ppm and 90 ppm.

DISCUSSION

The probit analysis conducted in this study revealed that the LD50 of breadfruit (*Artocarpus altilis*) flower extract was 52.67 ppm. Most breadfruit methanol extracts contain terpenes, phenols, and fatty acids that have been linked to biological activity against insects. Exposure to breadfruit extract was found to dramatically reduce hemolymph serotonin levels (de Melo et al. 2018). It has also been demonstrated that a combined extract of breadfruit leaves and flowers is superior to single extracts in terms of killing *Aedes aegypti* larvae. Breadfruit extract, known for its ability to impede the growth of mosquito larvae, is commonly derived from specific breadfruit varieties and utilized as a larvicide in mosquito control efforts (Hafid et al. 2016).

It is important to note that the precise mechanism of breadfruit extract against mosquito larvae may change depending on the formulation. Compounds in breadfruit extract may obstruct the larvae's capacity to correctly assimilate nutrition (Hidayati et al. 2020). This disturbance may inhibit their growth or even lead to their death. Certain extracts contain compounds that are poisonous to mosquito larvae. These poisonous compounds can potentially harm the physiological development of mosquitoes or prevent them from maturing into adults. Because of its biological characteristics, such as its antibacterial or antifungal actions, breadfruit extract may be disadvantageous to the growth of mosquito larvae. In certain instances, the extract may attract larvae to locations where they are more likely to be attacked or exposed to hazardous environments while also impeding their growth (Aladesanmi et al. 2022, Tuwemu et al. 2024).

Prior research conducted by Muangmoon et al. (2018) identified the presence of octadecadienoic acid in breadfruits through analysis using gas chromatography-mass spectrometry (GC-MS). Octadecadienoic acid can function as an anti-inflammatory, an antiatherogenic agent, and an inducer of apoptosis in mosquito larvae. A mixed Artocarpus sample was found to exhibit the highest insecticidal activity among single Artocarpus varieties. Haemolymph serotonin levels were dramatically decreased after exposure to the breadfruit extract. The LC50 value for the administration of breadfruit flower extract was determined to be 2.18±0.09 mg/mL according to the larvicidal activity after 48 hours.

Extracts derived from *Artocarpus blancoi* have exhibited larvicidal and ovicidal properties against *Aedes aegypti*. However, the ovicidal and larvicidal properties depend on the extract dosage. Qualitative phytochemical screening has revealed modest levels of glycosides and sterols, along with trace amounts of triterpenes, flavonoids, saponins, and tannins. Across Oceania, the local communities burn the dried male inflorescences of breadfruits (*Artocarpus altilis*, Moraceae) to keep away flying insects, especially mosquitoes. Fatty acids in male breadfruit blossoms may have anti-mosquito properties. The extract administration on the fourth instar of *Culex quinquefasciatus* larvae has demonstrated the presence of the methyl esters of oleic, linoleic, linolenic, palmitic, and stearic acids. When insects are exposed to linoleic acid, the insect become convulsion due to blockage spiracle and decrease of oxygen supply. Linolenic acid considerably enhances acetylcholinesterase activity (Udonkang et al. 2018, Widyawaruyanti et al. 2020, Tumewu et al. 2024).

This study revealed that male breadfruit flower extract may act as a larvacide, with a LC50 of 52 ppm. In comparison with the negative control group, the administration of breadfruit flower extract resulted in significantly different results. The findings of this study align with prior research conducted by Hidayati et al. (2023), Yang et al. (2022), and Chaurasia & Pandey (2024), which employed different doses of breadfruit extract. The administration of male breadfruit powder has exhibited a biolarvacidal effect against *Anopheles sp*. Extracts derived from other parts of the plant, such as stems, barks, and leaves, have also raised the mortality rate of *Anopheles sp*.

The one-way ANOVA test indicated that breadfruit flower extract was effective in killing mosquito larvae. The findings of this study confirmed other studies, including those carried out by Senthil-Nathan (2020), Wang et al. (2016), and Hari & Mathew (2018). The combined use of breadfruit leaves and flowers has been found to be superior to extracts derived from individual parts of the plant in terms of exterminating *Aedes aegypti* larvae. The proposed mechanism of this phenomenon is that the extract can block the spiracle pore in the exchange of oxygen (O_2) and carbon dioxyde (CO_2). The extract can also induce apoptosis in vital organs by accumulating in the midgut or cell vacuole to prevent energy production.

Strength and limitations

This research suggests the potential of breadfruit flower extract as an effective larvacide against *Aedes aegypti* larvae. However, this study is limited by the lack of evidence regarding the mechanism of action of breadfruit flower extract in killing *Aedes aegypti* larvae.

CONCLUSION

Breadfruit flower extract has the potential as an effective larvicide against *Aedes aegypti*. It is noteworthy, however, that its effectiveness as a larvicide depends on various factors, including concentration, environmental conditions, and the specific mosquito species being targeted. The lethal dose of the extract required to kill half of the mosquito larvae may be most effective against stage 2–3 instar larvae. Further research is necessary to analyze the active compounds in breadfruit flower extract that directly affect larval mortality.

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Conflict of interest

None.

Ethical consideration

This study received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, Universitas Warmadewa, Denpasar, Indonesia, under reference No. 358/Unwar/FKIK/EC-KEPK/IX/2023 dated 20/9/2023.

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Author contribution

NWW contributed to the conception and design, analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, statistical expertise, provision of administrative, technical, or logistic support, and collection and assembly of the data. PIB contributed to the conception and design, analysis and interpretation of the data, critical revision of the article for important intellectual content, final approval of the article, statistical expertise, and collection and assembly of the data. NKMJ contributed to the conception and design, drafting of the article, and collection and assembly of the data.

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