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RESEARCH PAPER

Safety and termiticidal efficacy of *Gliricidia sepium* leaf extract: dermal irritation and toxicity againts *Coptotermes curvignathus*

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Abstract: The overuse of synthetic insecticides in agriculture and household pest control raises concerns regarding health risks, environmental toxicity, and insect resistance. In Indonesia, about 15% of agricultural and plantation land is affected by pest infestations, with *Coptotermes curvignathus* recognized as one of the most destructive species due to its wood-boring activity. This study aimed to develop an eco-friendly insecticide using *Gliricidia sepium* leaf extract, which contains bioactive compounds such as steroids, tannins, and saponins with insecticidal potential. Four formulations were prepared with extract concentrations of 0 g (F0), 0.15 g (F1), 0.3 g (F2), and 0.45 g (F3) in 100 mL solvent. Physicochemical evaluations included pH measurement, stability observation, and homogeneity testing, while safety was assessed through dermal irritation tests on rabbits using the Draize method. Efficacy against termites was evaluated using probit analysis (IBM SPSS v22). Results showed that all formulations were physically stable, homogenous, and exhibited suitable pH values. Irritation testing revealed no erythema or edema, with primary irritation indices below 0.5, classifying the formulations as non-irritating even at low pH values. Insecticidal testing demonstrated complete termite mortality, with the F3 formulation showing the most rapid and potent effect. These findings indicate that *G. sepium* extract-based formulations are safe, effective, and environmentally friendly, supporting their potential as botanical insecticides to replace synthetic alternatives in sustainable pest management systems.

Keywords: Gliricidia sepium, botanical insecticide, termite control, toxicity test, irritation test

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INTRODUCTION

The need to protect agriculture and residential properties from pest damage has become increasingly urgent in recent years. Insect pests not only threaten food security by reducing crop yield but also damage household structures, causing economic loss and jeopardizing infrastructure integrity [1]. According to the Indonesian Ministry of Agriculture, approximately 15% of agricultural land is affected by pest infestations annually [2][3]. This issue is not limited to farms alone data from the Ministry of Public Works and Housing (PUPR) indicate that pests, especially termites, also cause significant damage to residential buildings and public infrastructure [2][4]. Among the various pest species, termites, particularly *Coptotermes curvignathus*, are notorious for their destructive nature. These pests attack wooden structures, furniture, and even crops, making them a major threat in both rural and urban environments [5][6]. Consequently, many communities have resorted to the widespread use of chemical insecticides to eradicate termite infestations. While synthetic insecticides have proven effective in reducing pest populations, their overuse has led to new challenges, including resistance, pest resurgence, pesticide residues, secondary pest outbreaks, and environmental contamination [7].

The negative consequences of synthetic pesticides are well-documented. The World Health Organization (WHO) reports that more than 3 million agricultural workers suffer from pesticide poisoning each year, and approximately 18,000 die annually due to exposure to toxic chemicals. These alarming figures underscore the pressing need for safe, eco-friendly alternatives that can be used in pest management without compromising public health or environmental quality[8][9].

One such solution is the utilization of plant-based insecticides, which are generally biodegradable, less toxic to humans, and compatible with integrated pest management systems [10]. This approach aligns with Indonesia's rich biodiversity and the principle of sustainable resource use. Indonesia is home to a vast range of indigenous flora, many of which remain underutilized despite their potential for pharmacological or agricultural applications [7]. One notable plant in this regard is Gamal (*Gliricidia sepium*), a common shrub widely found in rural communities, often used as a live fence or shade plant. An illustration of Gliricidia sepium leaves is presented in the figure 1 below.

Figure 1 the morphological characteristics of Gliricidia sepium leaves

Gliricidia sepium has been traditionally used by local populations as a natural pest repellent. Its leaves are known to contain bioactive compounds such as steroids, tannins, and saponins, which have demonstrated toxic effects on insects, including disruption of their digestive and nervous systems [7]. The accessibility of gamal in community settings, combined with its pesticidal properties, makes it an ideal candidate for development into a botanical insecticide. The insecticidal activity of Gliricidia sepium leaf extract is largely attributed to its bioactive phytochemical constituents, particularly steroids, tannins, and saponins. Each of these secondary metabolites contributes to pest control mechanisms through distinct biochemical and physiological effects on target insects such as Coptotermes curvignathus.

Steroids present in G. sepium play a crucial role in disrupting the hormonal balance of insects. These compounds can interfere with the normal functioning of ecdysteroids hormones responsible for insect molting and development thereby impeding growth and reproduction [11]. By mimicking or antagonizing insect hormones, plant-derived steroids can induce lethal developmental abnormalities or sterility in termites. Tannins, a group of polyphenolic compounds, exhibit insecticidal properties primarily through their ability to bind proteins and digestive enzymes in the insect gut. In termites, tannins can inhibit nutrient absorption and impair digestive efficiency, leading to starvation and death [12]. Moreover, tannins also act as antifeedants, deterring termites from consuming treated substrates by producing astringent or bitter sensations. Saponins contribute significantly to the toxicity profile of the extract. These glycosides possess surfactant-like properties that can disrupt cellular membranes, leading to increased permeability, ion imbalance, and ultimately cell lysis. In insects, saponins can cause gut membrane damage, impair respiration, and interfere with nervous system function. Their presence in higher concentrations has been correlated with faster mortality rates in termites.

Collectively, the synergistic action of these phytochemicals enhances the potency of G. sepium leaf extract as a botanical insecticide, making it a promising and eco-friendly alternative for termite control. such as steroids, tannins, and saponins presented in the figure 2,3 and 4 below.

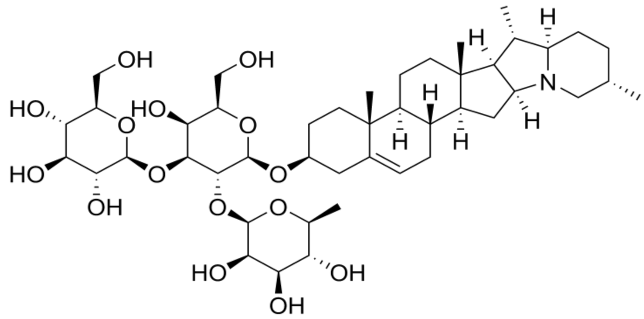

Figure 2. Saponin

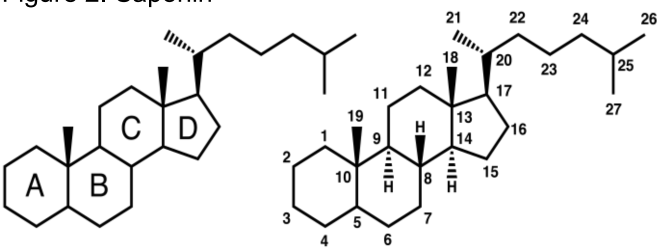

Figure 3. Steroid

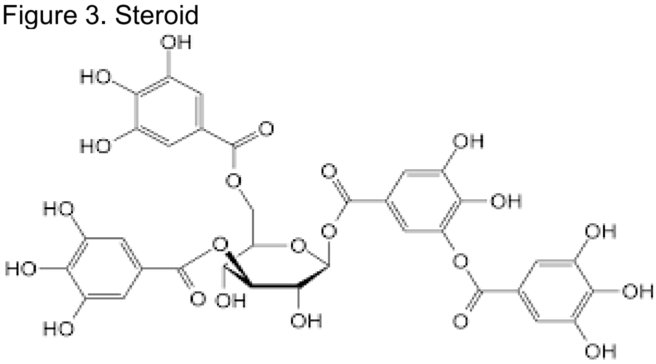

Figure 4. Tanin

Previous studies, including one conducted by the authors, have provided preliminary evidence of the insecticidal activity of *G. sepium* leaf extract against *C. curvignathus*. That study, however, focused solely on toxicity evaluation, without addressing safety parameters such as dermal irritation or product stability [7][13]. It also utilized various solvents (ethanol and methanol) to assess extraction efficiency but did not proceed to full formulation or consumer safety assessment. Thus, the findings, while promising, remain incomplete in terms of product readiness.

In light of these gaps, the present study aims to conduct a comprehensive evaluation of *G. sepium* leaf extract formulated as a botanical insecticide. Specifically, the research investigates (1) the toxicity of different extract concentrations against termites, (2) the stability and homogeneity of the formulations, and (3) the potential for dermal irritation, ensuring the product is both effective and safe for use by the general population.

The novelty of this study lies in the dual evaluation of insecticidal efficacy and safety, an approach rarely addressed in prior research. Furthermore, the research is supported by a comparative review of previous studies summarized in Table 1, which shows that earlier investigations primarily focused on specific insects or toxicity but lacked integrated assessments involving physical stability and human safety. These include studies on tomato leafminer (*Tuta absoluta*), onion leaf caterpillars, *Aedes aegypti* mosquitoes, whiteflies, and previous termite experiments with *G. Sepium*[14][15].

Table 1. Previous Research on Natural Insecticides

Citation	Title	Test Organism
[15]	Comparative toxicity of new insecticide generations against tomato leafminer *Tuta absoluta* and their biochemical effects on tomato plants	*Tuta absoluta*
[4]	Antimicrobial activity of flavonoids. *International Journal of Antimicrobial Agents*	Onion leaf caterpillars
[13]	Botanical Aerosol Insecticide and Its Effect on *Aedes aegypti* Mortality. *Jurnal Kedokteran Meditek*	*Aedes aegypti*
[7]	Effect of *Gamal* leaves (*Gliricidia sepium*) extract against termite (*Coptotermes curvignathus*)	*C. curvignathus*
[14]	Effects of high temperature on insecticide tolerance in whitefly *Bemisia tabaci*. *Pesticide Biochemistry and Physiology*	*Bemisia tabaci*

The findings of this study are expected to contribute to the development of an environmentally safe, community-friendly insecticide, based on local botanical resources. Moreover, it promotes the utilization of native Indonesian biodiversity, aligning with national goals of conservation and sustainable use of biological resources [16]. The gamal plant, with its abundance and proven pesticidal potential, is thus positioned as a strategic solution for modern pest control challenges that is grounded in science and responsive to the practical needs of society.

The novelty of this study lies in its dual evaluation of both **safety and efficacy** of *Gliricidia sepium* extract, an approach rarely integrated in earlier works. Previous studies on *G. sepium* primarily focused on toxicity or extraction efficiency [7,13], but lacked combined assessments involving dermal irritation, physicochemical stability, and formulation quality. By bridging these gaps, this research provides new insights into the readiness of *G. sepium* extract for practical application as a botanical termiticide.

MATERIALS AND METHODS

Plant Material and Extract Preparation

Fresh leaves of *Gliricidia sepium* were collected from local sources in Indonesia, washed thoroughly with distilled water to remove dirt and debris, and then air-dried at room temperature in a shaded area to prevent degradation of active compounds. Once dried, the leaves were ground into a fine powder using a mechanical grinder. The extraction process was performed using ethanol via maceration for 72 hours. After maceration, the solution was filtered, and the solvent was evaporated under reduced pressure using a rotary evaporator to obtain a semi-solid extract.

Insecticide Formulation

The insecticide formulations were prepared by incorporating the *G. sepium* extract into a standardized base composed of emulsifiers, water, and stabilizing agents. Four formulations were designed based on different concentrations of the extract:

- F0 (Control): 0g of extract
- F1: 0.15g of extract
- F2: 0.3g of extract
- F3: 0.45g of extract

The extract was prepared at concentrations of 0.15%, 0.30%, and 0.45% w/v (equivalent to 0.15 g, 0.30 g, and 0.45 g of crude extract dissolved in 100 mL of distilled water). These units (% w/v) were used consistently throughout the study in tables, figures, and statistical analysesEach formulation was mixed until uniform and stored in sealed containers at room temperature for further testing.

Evaluation of Physical Properties

All formulations were evaluated for physical characteristics, including color, consistency, pH, and homogeneity. pH was measured using a digital pH meter. Homogeneity was visually assessed by spreading a sample of each formulation on a glass slide and observing for any clumping or separation. Stability was assessed over a 14-day observation period by monitoring changes in color, phase separation, or sedimentation.

Irritation Test

Dermal irritation tests were conducted on healthy rabbits in compliance with ethical guidelines. A small area on the rabbit's back was shaved, and each formulation was applied topically. The test area was observed for signs of erythema (redness) and edema (swelling) at intervals of 24, 48, and 72 hours. The results were recorded based on the Draize scoring system for skin irritation.

Toxicity Test and LC50 Determination

The toxicity of each formulation was tested on *Coptotermes curvignathus* by exposing a group of termites to filter paper treated with the respective formulations. Each test group contained the same number of termites under identical environmental conditions. Termite mortality was recorded after 24 hours of exposure. The data were analyzed using probit analysis via IBM SPSS Version 22 software to calculate the LC50 (lethal concentration that kills 50% of the test population), which serves as an indicator of insecticidal potency. Only worker caste termites were used for the bioassay. Each replicate consisted of 20 termites placed in a 9 cm diameter Petri dish (arena size = 63.6 cm²). Filter paper discs (Whatman No. 1, 5 cm diameter, area = 19.6 cm²) were treated with 1 mL of each formulation and air-dried for 30 minutes before exposure, resulting in a loading rate of approximately X mg/cm² extract.
Three replicates (n = 3) were conducted per treatment. Termites were maintained at 27 ± 1 °C, 75 ± 5% relative humidity, under a 12:12 h light:dark photoperiod. Mortality was recorded at 6 h, 12 h, and 24 h post-exposure, and dead termites were identified by lack of movement upon probing. All experiments were conducted in triplicate (n = 3). Data are expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way ANOVA followed by Tukey's post-hoc test ($p < 0.05$) to compare differences among formulations.

RESULTS AND DISCUSSION

Physicochemical Properties

All four formulations were observed to be physically stable throughout the 14-day testing period. There were no signs of color change, phase separation, or sedimentation, indicating that the formulations maintained their integrity [17]. The pH values of the formulations remained stable around pH 5, a slightly acidic range that is suitable for topical and agricultural applications. Homogeneity assessments showed that all formulations had uniform texture and consistency, with no visible separation of components. These results suggest that the presence of *G. sepium* extract, even at higher concentrations, did not compromise the physical quality of the formulation. The stable pH and consistent appearance indicate that the product would be practical for real-world use in field conditions.

Toxicity

The termite mortality data revealed a clear dose-dependent response. The control group (F0) exhibited no significant mortality. Formulations F1 and F2 showed moderate termite deaths, while F3 (0.45g extract) produced the highest mortality rate. The probit analysis of the mortality data yielded an LC50 value significantly lower than the F3 dose, suggesting that even smaller doses may be effective under optimized conditions.

The data of toxicity of isecticides against termites can be described and show in the table 2 below

Table 2. Toxicity Against Termite

Formulation	Extract Concentration (% w/v)	Average Time to Death of Termites (second, Mean ± SD)	Solvent
F0 (Control –)	0.00	0.0 ± 0.0	Ethanol
F1	0.15	170.3 ± 12.5	Ethanol
F2	0.30	129.7 ± 9.8	Ethanol
F3	0.45	100.5 ± 7.6	Ethanol
Control (+)	–	27.4 ± 2.1	Commercial Insecticide

These results affirm the insecticidal potential of *G. sepium* extract, likely due to the synergistic action of its bioactive components. The effectiveness against *C. curvignathus*, a notoriously resistant pest, suggests that this plant-based formulation can serve as a viable alternative to synthetic insecticides [18][19]. The results of this study indicate that higher concentrations of *Gliricidia sepium* (gamal) leaf extract significantly accelerate the mortality rate of the test insects, particularly *Coptotermes curvignathus* termites. This pattern suggests a dose-dependent toxicological response, where increased levels of bioactive compounds such as flavonoids, tannins, and saponins lead to more rapid physiological disruption in the termites. At higher concentrations, these secondary metabolites may interfere more effectively with the insects' digestive or nervous systems, ultimately causing quicker death [19][2]. The enhanced efficacy observed at elevated extract levels supports the hypothesis that the pesticidal properties of *G. sepium* are concentration-sensitive and reinforces its potential as a botanical alternative to synthetic termiticides.Furthermore, the absence of irritation coupled with high insecticidal activity makes this product particularly promising for sustainable pest control strategies. Formula incticides can be described from table 3 below.

Table 3. Formula incticides

Ingredients	F0	F1	F2	F3
***Gliricidia sepium* leaf extract**	0	0,15	0,30	0,45
Ethanol (95%)	2	2	2	2
Glycerol	1	1	1	1
Tween 80 (Polysorbate 80)	1	1	1	1
Distilled water	Add up to 100 ml	Add up to 100 ml	Add up to 100 ml	Add up to 100 ml

The insecticide formulations (F0–F3) were designed to evaluate the effect of increasing concentrations of *Gliricidia sepium* leaf extract on termite control efficacy, while maintaining consistent proportions of supporting ingredients. All formulations contained 2% ethanol (as solvent), 1% glycerol (as humectant and stabilizer), and 1% Tween 80 (as emulsifying agent), with distilled water added to reach a final volume of 100 mL. The only variable across the formulations was the concentration of *G. sepium* extract, which was set at 0% for the control (F0), 0.15% for F1, 0.30% for F2, and 0.45% for F3.

This gradient design allows for a comparative analysis of bioactivity, where any observed increase in insecticidal performance can be attributed directly to the rising concentration of the active botanical component. The inclusion of a negative control (F0) ensures that baseline effects from the solvent and excipients are accounted for. Overall, this formulation strategy is appropriate for determining the dose-response relationship of *G. sepium* extract against termite populations. Organoleptic test can be describe from the table 4 below.

Table 4. Organoleptic Test

	F0	F1	F2	F3
Color	Clear	Slightly cloudy clear	Dark yellow	Dark yellow
Aroma	The smell of etanol	The smell of extract	The smell of extract	The smell of extract
Nature	sticky	sticky	sticky	sticky

The organoleptic evaluation of the four insecticide formulations (F0–F3) revealed notable differences in color and aroma corresponding to the increasing concentration of *Gliricidia sepium* leaf extract, while the texture remained consistent across all samples. In terms of **color**, the control formulation (F0), which contained no plant extract, appeared clear, while F1 exhibited a slightly cloudy appearance. Formulations F2 and F3, which contained higher extract concentrations (0.30% and 0.45%, respectively), displayed a distinct dark yellow coloration. This color change indicates the presence and increasing intensity of plant-derived pigments and compounds within the formulation. Regarding **aroma**, F0 primarily exhibited the characteristic smell of ethanol, due to the absence of the extract. In contrast, F1 through F3 produced a noticeable plant-based odor associated with the *G. sepium* extract, suggesting the presence of volatile bioactive constituents that may contribute to the insecticidal properties.

The texture of all formulations was described as sticky, which is likely attributable to the inclusion of glycerol and the emulsifier (Tween 80), both of which contribute to the viscosity and adhesion properties of the formulation. The consistent stickiness across all variants suggests that the extract concentration does not significantly affect the physical consistency of the product. These organoleptic characteristics not only confirm the successful incorporation of the extract into the formulation but also provide preliminary indicators of product stability and user acceptability. Homogeneity test can be described from the table 5 below.

Table 5. Homogenty Test

Homogenity	F0	F1	F2	F3
textures	soft	soft	soft	soft
grain	No coarse grains	No coarse grains	No coarse grains	No coarse grains
absorbing speed	Quick	Quick	Quick	Quick
color	Clear	Clear	Clear	Clear

The homogeneity assessment of all formulations (F0–F3) indicated that the physical characteristics of the insecticide remained consistent and stable across varying extract concentrations. All samples exhibited a soft texture, free from any coarse or undissolved particles, suggesting that the components were well-mixed and uniformly dispersed within the solution. In terms of absorption speed, each formulation demonstrated rapid absorption, which implies good penetration potential when applied to targeted surfaces or substrates an important trait for contact-based insecticidal activity. Interestingly, despite the increasing levels of plant extract from F1 to F3, there were no observed changes in absorption rate, indicating that the extract concentration did not hinder fluid uptake.

Additionally, the color of all formulations under the homogeneity test remained clear, in contrast to the organoleptic color observations where F2 and F3 appeared dark yellow. This discrepancy may be due to differences in observation context color under homogeneity evaluation typically refers to the uniformity and absence of phase separation or sedimentation, rather than visual intensity alone. Overall, the data confirm that the insecticide formulations maintained good homogeneity and stability, regardless of extract concentration, supporting the feasibility of Gliricidia sepium extract incorporation without compromising formulation integrity The physical assessment of the insecticide formulations (F0–F3), including homogeneity, organoleptic properties, and pH, demonstrated consistent formulation quality with progressive changes attributable to increasing concentrations of Gliricidia sepium leaf extract. All formulations displayed soft textures, were free from coarse grains, and showed rapid absorption, indicating good physical homogeneity and applicability. No signs of phase separation or sedimentation were observed, and the solutions remained clear under homogeneity conditions, confirming formulation stability and uniform dispersion of ingredients.

The organoleptic evaluation revealed progressive changes in color and aroma with rising extract concentrations. While F0 was clear and ethanol-scented, F1 was slightly cloudy, and both F2 and F3 appeared dark yellow and emitted a strong herbal odor associated with the plant extract [20][21]. Despite these sensory changes, the formulations remained physically stable and visually homogeneous. The pH test results showed a clear decreasing trend in acidity with increased extract concentration: pH 5 for F0 and F1, pH 4 for F2, and pH 3 for F3. This acidification is likely due to the presence of phenolic and organic acid compounds within the G. sepium extract. While slightly acidic pH values may enhance insecticidal activity, they must also be considered in terms of producsafety, material compatibility, and potential irritancy during field application. In summary, the data indicate that the incorporation of *G. sepium* extract affects certain physical and chemical parameters particularly aroma, color, and Ph without compromising homogeneity, absorption rate, or formulation stability. These findings support the suitability of the extract for insecticidal use in liquid formulations, while also highlighting the need for pH adjustment depending on the intended application environment [7][22]. The graph below illustrates the physical properties of the insecticide formulations, including pH, stability, and homogeneity as the figure 5.

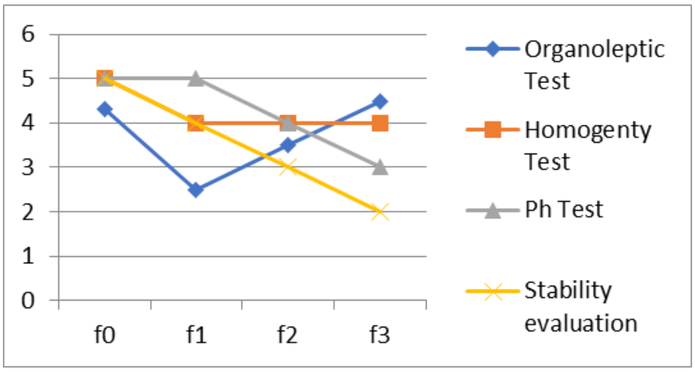

Figure 5. The graph below illustrates the physical properties.

In the meantime the irritation test showed that there were no signs of erythema or irritation on the skin of the animal test (rabbits), indicating that all formulas were safe to use and did not cause irritating reactions. Result of iritation test describe in table 6 below.

Table 6. Iritation Test 3x24 Hours

Irritation Parameter	F0 (Control, 0%)	F1 (0.15% w/v)	F2 (0.30% w/v)	F3 (0.45% w/v)
Erythema (score, Mean ± SD)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Edema (score, Mean ± SD)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Result	No irritation	No irritation	No irritation	No irritation

The irritation test, conducted to evaluate the dermal safety of the Gliricidia sepium insecticide formulations (F0–F3), showed no signs of erythema or edema across all tested concentrations. Neither the control formulation (F0) nor the extract-containing variants (F1–F3) produced visible redness, swelling, or any adverse skin reactions during the observation period. These findings indicate that the formulations are non-irritating to the skin, even at the highest extract concentration (0.45%). The absence of irritation symptoms suggests that the secondary metabolites present in G. sepium extract, such as flavonoids, tannins, and saponins, are either present in low enough concentrations or are non-reactive with skin tissue under the tested conditions .

From a safety perspective, this result is significant, as it demonstrates that the insecticide is dermally safe for topical application or incidental contact, which is especially important for field workers and users handling the product directly. Moreover, the inclusion of ethanol, glycerol, and emulsifiers did not contribute to any irritant effects, supporting the biocompatibility of the overall formulation. Overall, the lack of irritation in all formulations enhances the practical applicability and user acceptability of the G. sepium-based insecticide as a natural alternative to conventional chemical agents.

No signs of erythema or edema were observed across all formulations (Table 6). The irritation index values were consistently below 0.5% (mean ± SD), indicating non-irritating classification. Statistical comparison showed no significant differences ($p > 0.05$) among treatment groups.

CONCLUSION

This study demonstrated that *Gliricidia sepium* leaf extract can be formulated into stable, pH-balanced, and homogeneous insecticides. The formulations were safe in dermal irritation tests and showed concentration-dependent toxicity, with F3 (0.45 g) being the most effective against *Coptotermes curvignathus*. These findings support *G. sepium* as a safe and eco-friendly alternative to synthetic insecticides, with strong potential for further development and broader application in sustainable pest management.

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REFERENCES

[1] Reddy KN, Paschapur A. Employing environmentally safer and novel synthetic insecticides in organic farming for eco-friendly.

[2] Muhsin LB, Pratiwi By. Perbandingan Efektivitas Ekstrak Daun Gamal (*Gliricidia Sepium*) Dengan Pelarut Etanol Dan Metanol Sebagai Insektisida Alami. Celebica Jurnal Kehutanan Indonesia. 2023 Dec 17;4(2):137-46.

[3] Nigusse AH, Belayneh A. Potential of *Gliricidia sepium* as a source of biofuel. Renewable and Sustainable Energy Reviews. 2017;76:963-70..

[4] Cushnie T, Lamb AJ. Antimicrobial activity of flavonoids International Journal of Antimicrobial Agents 26 (5): 343-56.

[5] Leekha S, Terrell CL, Edson RS. General principles of antimicrobial therapy. InMayo clinic proceedings 2011 Feb 1 (Vol. 86, No. 2, pp. 156-167). Elsevier.

[6] Gupta RC, Mukherjee IR, Malik JK, Doss RB, Dettbarn WD, Milatovic D. Insecticides. InBiomarkers in toxicology 2019 Jan 1 (pp. 455-475). Academic Press.

[7] Pratiwi BY, Muhsin LB. Effect of gamal leaves (*Gliricidia sepium*) extract against termite (*Coptotermes curvignathus*). Jurnal Pijar Mipa. 2023 Nov 30;18(6):970-5.

[8] Oberemok VV, Laikova KV, Gninenko YI, Zaitsev AS, Nyadar PM, Adeyemi TA. A short history of insecticides. Journal of Plant Protection Research. 2015;55(3).

[9] Kayhan FE, Kaymak G, Yön ND. Insecticide groups and their effects in aquatic environment. Marmara Fen Bilimleri Dergisi. 2013;25(4):167-83.

[10] Kerns DL, Tellez T. Evaluation of new insecticides for aphid control in green leaf lettuce.

[11] Sari MP, Susilowati RP. Insektisida Nabati dalam Bentuk Aerosol Terhadap Mortalitas Aedes aegypti. Jurnal Kedokteran Meditek. 2022 May 7;28(2):186-92.

[12] Guo L, Su M, Liang P, Li S, Chu D. Effects of high temperature on insecticide tolerance in whitefly Bemisia tabaci (Gennadius) Q biotype. Pesticide biochemistry and physiology. 2018 Sep 1;150:97-104.

[13] Seal DR, Sabines CM. Effectiveness of biological insecticides in

controlling the diamondback moth (Lepidoptera: Plutellidae) on cabbage.

[14] Kandil MA, Sammour EA, Abdel-Aziz NF, Agamy EA, El-Bakry AM, Abdelmaksoud NM. Comparative toxicity of new insecticides generations against tomato leafminer Tuta absoluta and their biochemical effects on tomato plants. Bulletin of the National Research Centre. 2020 Dec;44:1-3.

[15] Annam AC, Khasanah N. Keanekaragaman arthropoda pada pertanaman kubis (Brassica oleracea L.) yang diaplikasi insektisida kimia dan nabati. Agrotekbis: Jurnal Ilmu Pertanian (e-journal). 2017 Jun 30;5(3):308-14.

[16] Atanasova B, Spasov D, Spasova D, Ilievski M. Impact of insecticides on beneficial organisms. Journal of Agriculture and Plant Sciences. 2023;21(2):9-14.

[17] Venkataiah M, Anilkumar B, Chauhan S. Efficacy of newer insecticides against sucking insect pests of groundnut (Arachis hypogaea L.). Journal of Oilseeds Research. 2016;33(4):259-61.

[18] Trisnayanti NK, Dewantara IG, Prasetia IG. Uji iritasi gelling agent semi sintetik HPMC pada kelinci. Skripsi Fakultas Matematika dan Ilmu Pengetahuan Alam Universitas Udayana. 2015.

[19] Kandárová H, Hayden P, Klausner M, Kubilus J, Kearney P, Sheasgreen J. In vitro skin irritation testing: improving the sensitivity of the EpiDerm skin irritation test protocol. Alternatives to Laboratory Animals. 2009 Dec;37(6):671-89.

[20] Bos PM, Zwart A, Reuzel PG, Bragt PC. Evaluation of the sensory irritation test for the assessment of occupational health risk. Critical reviews in toxicology. 1992 Jan 1;21(6):423-50.

[21] Siegwart M, Graillot B, Blachere Lopez C, Besse S, Bardin M, Nicot PC, Lopez-Ferber M. Resistance to bio-insecticides or how to enhance their sustainability: a review. Frontiers in plant science. 2015 Jun 19;6:138200.

[22] Akbar M, Islamiyati R, Mustabi J, Indrawirawan I. Kandungan Tanin, VFA dan Amonia pada Sistem Rumen in Vitro Daun Maja (Aegle marmelos) dan Daun Gamal (*Gliricidia sepium*). Buletin Nutrisi dan Makanan Ternak. 2023 Apr 3;17(1):28-40.

[23] Zulianti B, Hamid IS, Yudhana A, Rahmahani J, Yunita MN, Wibawati PA. Ekstrak Daun Gamal (*Gliricidia sepium*) Meningkatkan Mortalitas Fasciola gigantica Secara In Vitro. Jurnal Medik Veteriner. 2021;4(2):193-8.