Indonesian Journal of Chemistry and Environment
Vol. 9, No. 1, June 2026, pp. 10~17
e-ISSN: 2599-3186

Antioxidant Activity and Toxicity of the Ethyl Acetate and Dichloromethane Fractions of the Ethanol Extract of Sikkam Leaves (*Bischofia javanica* Blume)

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Article Info

Article history:

Received Apr 30th, 2026
Accepted Jun 29th, 2026
Published Jul 1st, 2026

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ABSTRACT

Sikkam (*Bischofia javanica* Blume) is traditionally used to treat sore throat, infected wounds, boils, and diabetes, but scientific evidence remains limited. This study aimed to determine the antioxidant activity and toxicity of the ethyl acetate and dichloromethane fractions of sikkam leaf ethanol extract obtained by maceration. Antioxidant activity was assessed using the DPPH method, and toxicity was evaluated using the BSLT method with *Artemia salina* larvae. The IC_{50} values of the ethyl acetate and dichloromethane fractions were 4.13 μg/mL and 26.19 μg/mL (both very strong), respectively, while the LC_{50} values were 1152.99 μg/mL (non-toxic) and 686.61 μg/mL (moderate), respectively. Both fractions demonstrated very strong antioxidant activity, with the ethyl acetate fraction exhibiting greater potential and being non-toxic, whereas the dichloromethane fraction showed moderate toxicity.

Keyword: Sikkam (*Bischofia javanica* Blum), fractionation, antioxidants, toxicity.

1. INTRODUCTION

The use of medicinal plants as a source of natural active ingredients continues to expand in line with the increasing demand for safer and more effective alternative therapies (Harefa, 2020). One of the plants which has great potential in the health field is sikkam (*Bischofia javanica* Blume), a species widely distributed in tropical Asia, including Indonesia (Sitohang, 2020). Traditionally, sikkam leaves have long been used to treat various ailments such as sore throat, infected wounds, boils, and diabetes (Julianti et al., 2024)

Several scientific studies have demonstrated various biological activities of sikkam leaves. oleh Lee et al., (2021) reported that the methanol extract of *Bischofia javanica* leaves showed significant antioxidant and anti-inflammatory activities through the regulation of Nrf2 and TAK1 gene expression, thereby suppressing the expression of proinflammatory cytokines such as IL-1β, TNF-α, and NO in RAW264.7 macrophages. Rumahorbo et al., (2021) showed that the ethanol extract of sikkam leaves can increase insulin expression and reduce the degree of insulitis in the pancreas of diabetic rats, with efficacy comparable to glibenclamide. Furthermore, Rumahorbo et al., (2023) developed a sikkam leaf nanoherbal preparation with a diameter of ±188 nm that has very strong antioxidant activity with an IC_{50} value of 28.24 μg/mL, while also demonstrating better physiological effects on blood, liver, and kidney parameters compared to regular extracts. Other research, Ilyas et al., (2022) reported that ethanol extract of sikkam leaves at a dose of 900 mg/kg BW improved sperm quality and reduced apoptosis in hyperglycemic rats through antioxidant activity and testicular histology repair. Tan et al., (2025) identified the main components of ethanol extract of sikkam leaves

as flavonols (kaempferol), phenolics (gallic acid), and sterols (β-sitosterol), with high antioxidant activity in DPPH and ABTS tests, as well as antibacterial activity against Staphylococcus aureus. Saragih, (2025) reported that the crude ethanol extract of air-dried sikkam leaves obtained by maceration showed very high antioxidant activity with an IC_{50} value of 10.87 μg/mL and was non-toxic with an LC_{50} of 3268.81 μg/mL.

Although these studies have provided a strong scientific foundation, most remain limited to the use of crude extracts and have not specifically examined certain solvent fractions, particularly ethyl acetate and dichloromethane fractions. In fact, liquid-liquid fractionation based on differences in solvent polarity can separate compound classes more selectively, allowing the contribution of each compound class to specific biological activities to be identified more clearly (Rachmatiah et al., 2022). Ethyl acetate is a semi-polar solvent known to be effective in extracting phenolic and flavonoid compounds, which belong to compound classes known for their high ability to neutralize free radicals and significantly contribute to antioxidant activity (Maharani et al., 2021). In contrast, dichloromethane is a less polar solvent that tends to dissolve triterpenoid, steroid, and phytosterol compounds—compound classes that have been scientifically proven to have potential as anti-inflammatory and cytotoxic agents, including anticancer activity (Fitriyanti et al., 2024). Separation based on polarity thus becomes important to further understand the relationship between chemical composition and the biological activity of each fraction.

In addition to the selection of fractionation solvents, the drying method for plant material before extraction also plays a crucial role in maintaining the stability of bioactive compounds. Drying at high temperatures, such as oven drying, although time-efficient, may degrade thermolabile compounds like flavonoids and phenolics, thereby significantly reducing their effectiveness (Taylor, 2022). Therefore, this study uses the air-drying method at room temperature, which is considered more appropriate for preserving the chemical integrity and biological activity of the compounds present in sikkam leaves (Jurčević Šangut et al., 2024)

For this reason, this study aims to determine the antioxidant activity and toxicity of the ethyl acetate and dichloromethane fractions from the ethanol extract of sikkam leaves (Bischofia javanica Blume). Antioxidant activity was assessed using the DPPH (2,2-diphenyl-1-picrylhydrazyl) method, and toxicity was evaluated through the Brine Shrimp Lethality Test (BSLT) method using Artemia salina larvae.

2. RESEARCH METHOD

Tools, Materials, and Instruments

The equipment used in this research includes a blender, a set of maceration tools, desiccator, separatory funnel, analytical balance, magnetic stirrer, Schott Duran glass bottles, a set of simple distillation apparatus, thermometer, vial bottles, burette, and aquarium.

The materials used in this research are sikkam leaves (Bischofia javanica Blume) and the chemicals used are technical ethanol 96%, methanol p.a 95%, n-hexane, ethyl acetate, dichloromethane, Artemia salina eggs (O.S.I Red Top Marine Shrimp Eggs (Artemia Cysts)), seawater, DMSO, vitamin C, and DPPH.

The instrument used in this research is the Ultraviolet-Visible (UV-Vis) Spectrophotometer 2600i Shimadzu.

Ethyl Acetate and Dichloromethane Fractionation of Ethanol Extract of Sikkam Leaves

Fractionation was performed on the ethanol extract of sikkam leaves. The ethanol extract was prepared using the maceration method. The sikkam leaves were blended until smooth, sieved, weighed 50 g, and placed into a Schott Duran bottle. Ethanol totaling 250 mL was added to the sikkam leaves and stirred for 2–3 minutes. Maceration was performed for 3 × 24 hours. After filtration, the obtained macerate was centrifuged, after which the filtrate was evaporated using

rotary evaporation to separate the extract from the solvent. The viscous extract obtained before fractionation was stored in a desiccator.

The thick extract was divided into two equal parts. Each part was placed into a 100 mL separatory funnel. The initial fractionation was performed using n-hexane solvent, 3 × 50 mL, to remove residual chlorophyll in the extract. The ethanol-water residue obtained from the n-hexane fractionation was then fractionated using ethyl acetate solvent. Fractionation with ethyl acetate was performed 3 × 50 mL in a separatory funnel. The mixture was shaken for 2–3 minutes and allowed to separate into two layers, consisting of the ethyl acetate fraction and the ethanol-water fraction. The two layers were then separated. The ethyl acetate fraction obtained was subsequently distilled using vacuum-assisted rotary evaporation to remove the solvent. The remaining solvent was removed by further evaporation to obtain the dry extract of the ethyl acetate fraction of sikkam leaves.

The same procedure was applied to the second thick extract using dichloromethane as a solvent. The ethanol-water residue obtained from n-hexane fractionation was further fractionated using dichloromethane as a solvent, 3 × 50 mL, using a separatory funnel. The mixture was shaken for 2–3 minutes and allowed to stand until two layers formed, consisting of the dichloromethane layer and the ethanol-water layer. Both layers were then separated. The obtained dichloromethane fraction was subsequently distilled using vacuum-assisted rotary evaporation to remove the solvent. The remaining solvent was removed by further evaporation to obtain a dry extract of the dichloromethane fraction of sikkam leaves.

Antioxidant Activity Test Using the DPPH Method

The stock solution of the ethyl acetate fraction was prepared at a concentration of 10 μg/mL, while the dichloromethane fraction was prepared at a concentration of 100 μg/mL, using 95% pro analysi (p.a.) methanol as the solvent. This stock solution was then diluted into several series of concentrations, resulting in concentrations of 0, 2, 3, 4, 5, 6, 7, 8, 9, and 10 μg/mL for the ethyl acetate fraction and concentrations of 0, 10, 20, 30, 40, 50, 60, and 70 μg/mL for the dichloromethane fraction.

The DPPH solution as the test reagent was prepared by dissolving 0.0019 g of DPPH powder in pro analysi (p.a.) methanol to a volume of 50 mL, resulting in a concentration of 40 μg/mL. As a reference (positive control), vitamin C was used, prepared as a stock solution at 10 μg/mL and serially diluted to concentrations of 0, 1, 2, 3, 4, 5, and 10 μg/mL.

At the testing stage, 2 mL of sample solution from each concentration was mixed with 2 mL of DPPH solution in a tightly sealed vial wrapped in aluminum foil to prevent light-induced degradation. The mixture was then homogenized on a shaker for 30 minutes to ensure complete reaction between the sample and DPPH radicals. After incubation, the absorbance of each sample was measured using a UV-Vis spectrophotometer. The absorbance values obtained for each concentration were used to calculate the percentage of free radical inhibition, which was then used to determine the IC_{50} value, the concentration of the sample required to inhibit 50% of DPPH free radicals.

$$IC_{50\%} = \frac{A_0 - A_1}{A_0} \times 100$$

Toxicity Test Using Brine Shrimp Lethality Test (BSLT) Method

The stock solutions of ethyl acetate and dichloromethane fractions of sikkam leaves were each prepared at a concentration of 2000 μg/mL by first dissolving 0.5 g of each fraction in 2 mL of DMSO (dimethyl sulfoxide). After the fraction was completely dissolved, the solution was then diluted with seawater to a volume of 250 mL. From this stock solution, a series of working solutions was prepared at concentrations of 0, 100, 200, 300, 400, 500, 1000, and 1500 μg/mL. The 0 μg/mL concentration was used as a negative control: a container containing only seawater and larvae,

without the addition of extract, to ensure that larval death is attributable solely to the extract rather than environmental factors.

Hatching of Artemia salina Leach eggs as test animals. The eggs were hatched in an aquarium containing seawater, which was divided into two compartments using a perforated partition, namely a dark side and a light side. The eggs were placed on the tightly closed dark side to stimulate hatching. The successfully hatched larvae moved phototactically, naturally migrating toward the lighter side in response to light from a lamp. This phototactic mechanism also serves as a natural selection to separate active, healthy larvae from unhatched egg shells. The aquarium temperature was maintained at 25–30°C for 24 hours until the larvae were ready for testing.

Testing was conducted in 9 treatment containers, each containing 10 active Artemia salina larvae, 2.5 mL of seawater, and 2.5 mL of serial extract solution at the predetermined concentration. One additional container was prepared as a negative control without the addition of extract. All containers were then incubated for 24 hours. After the incubation period, the number of larvae that died in each container was counted and recorded. The mortality data obtained were further analyzed using probit analysis to determine the LC_{50} value, defined as the extract concentration that causes death in 50% of the test larval population.

3. RESULTS AND ANALYSIS

3.1. Fractionation of Sikkam Leaf Extract

Fractionation is a liquid-liquid separation that can produce compound classes that are more specific and homogeneous compared to the total extract, making them easier to characterize, purer, and requiring smaller doses in biological activity testing. The fractionation process employed ethyl acetate and dichloromethane solvents based on differences in their polarity. The results of the fractionation of sikkam leaf extract are shown in **Table 1.**

Table 1. Yield of Ethyl Acetate and Dichloromethane Fractionation of Sikkam Leaf Extract

Fractionation	Sample Mass (g)	Fraction Mass (g)	Yield (%)	Color
ethyl acetate	50	4,2598	8,5196	Chocolate
dichloromethane	50	3,5561	7,1122	Greenish chocolate

Fractionation of 50 g of concentrated sikkam leaf extract produced an ethyl acetate fraction yield of 8.5196% and a dichloromethane fraction yield of 7.1122%. The consistently higher yield of the ethyl acetate fraction in both repetitions indicates that ethyl acetate is more effective for extracting compounds from sikkam leaf extract compared with dichloromethane

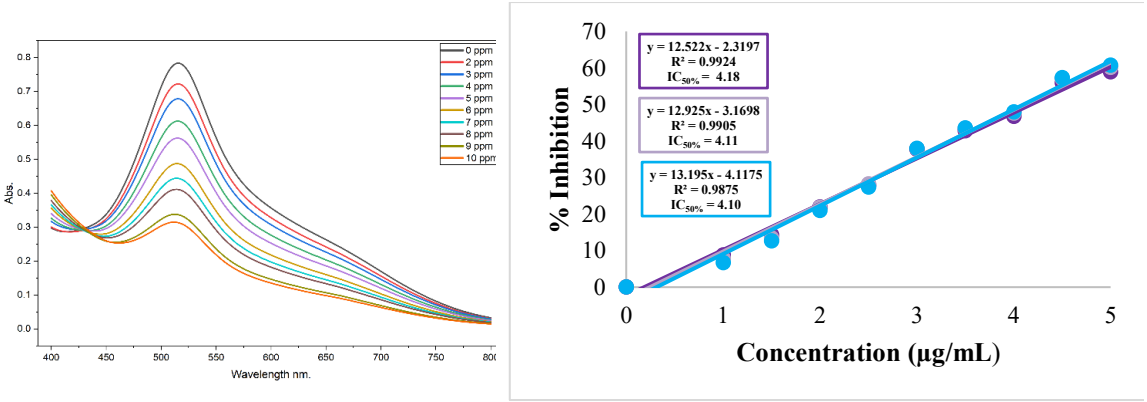
This difference in yield can be explained by the principle of like dissolves like. Ethyl acetate, as a semipolar solvent ($\varepsilon = 6.02$; polarity index = 4.4), can extract compounds over a wider range of polarity, including flavonoids, phenolics, and tannins that dominate the phytochemical composition of plants in the Phyllanthaceae family (Ningsih et al., 2020). In contrast, dichloromethane, which is nonpolar to weakly semipolar ($\varepsilon = 9.08$), is more selective in extracting nonpolar compounds such as terpenoids, steroids, and chlorophyll, present in lower quantities in leaf tissues, resulting in a lower yield. Organoleptically, the ethyl acetate fraction is brown, reflecting the presence of oxidized phenolic compounds and condensed tannins, whereas the dichloromethane fraction is brownish-green due to the co-extraction of lipophilic chlorophyll pigments.

These findings are consistent with the results of the study (Manurung et al., 2020) which reported that the ethyl acetate fraction of sikkam stem bark also yielded a higher recovery (21.4%) compared with the n-hexane fraction (3.9%), reinforcing the conclusion that the dominant compounds in the sikkam plant *(Bischofia javanica*) are semi-polar. Nevertheless, the yield of the ethyl acetate fraction from sikkam leaves in this study was lower than that reported in the study. This difference is not contradictory, but can be explained by the different plant parts used, as the stem

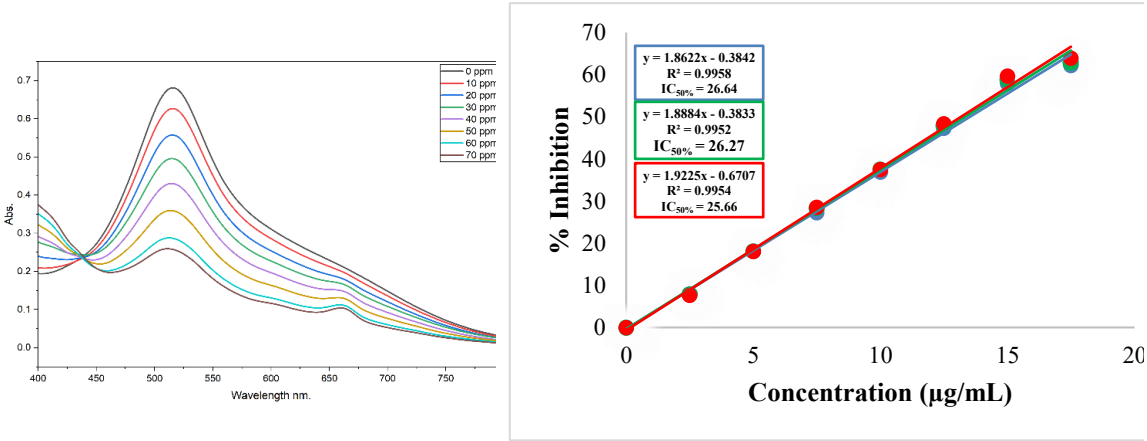
bark generally contains higher concentrations of secondary metabolites compared with leaves, as it functions as a mechanical and chemical protector against pathogens. In addition, differences in growing environmental conditions, harvest time, and drying of plant material also contributes to variations in secondary metabolite levels in plant materials.

3.2. Antioxidant Activity

The IC_{50} values of both fractions the ethyl acetate fraction and dichloromethane fraction of sikkam leaf extract, were determined using linear regression equation-based analysis derived from the calibration curve of the relationship between percentage inhibition and sample concentration. The results of the antioxidant activity of these two fractions are presented in **Figure 1.**



Ethyl Acetate Fraction



Dichloromethane Fraction

Figure 1. UV-Vis Spectrum of Antioxidant Activity and the Curve of the Relationship Between Percentage Inhibition and Concentration.

The test results showed that the ethyl acetate fraction demonstrated higher antioxidant activity compared with the dichloromethane fraction, with IC_{50} values of 4.1311 µg/mL and 26.1923 µg/mL, respectively. Based on the classification, both IC_{50} values fall into the very strong antioxidant category (IC_{50} < 50 µg/mL), with the ethyl acetate fraction demonstrating greater potential.

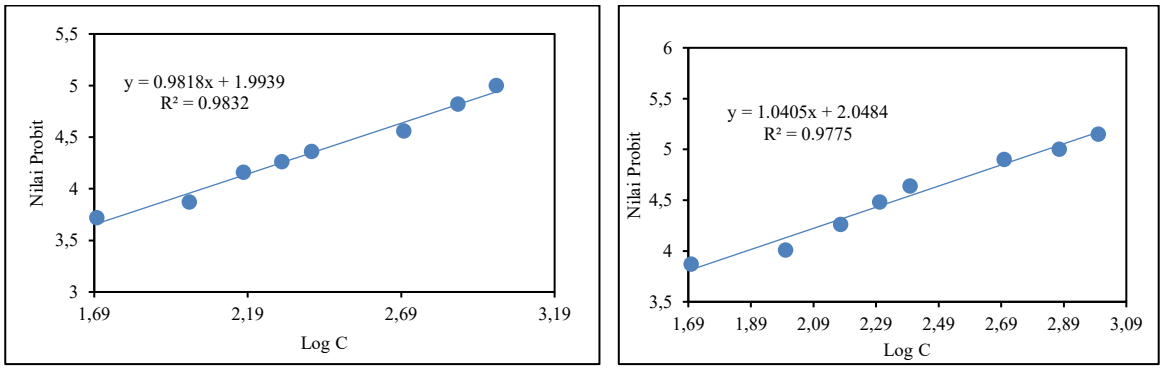
The difference in antioxidant activity between these two fractions is suspected to be closely related to the difference in solvent polarity used during fractionation. Ethyl acetate is semipolar, thereby tending to attract phenolic and flavonoid compounds, which are known to have hydroxyl (–OH) groups attached to an aromatic ring. The (–OH) groups in these compounds act as hydrogen atom donors to the DPPH radical, and their stability is enhanced by electron resonance in the

aromatic ring, resulting in higher radical-scavenging ability, whereas dichloromethane, being more nonpolar, tends to attract lipophilic compounds such as terpenoids and steroids, which generally do not have free phenolic (–OH) groups, making their antioxidant activity relatively lower (Putri et al., 2023) This aligns with the principle of like dissolves like in extraction chemistry, where the composition of compounds extracted in each fraction is strongly influenced by the polarity of the solvent used (Obenu, 2019)

Research conducted by Saragih, (2025) reported antioxidant activity using the DPPH method on crude ethanol extracts of sikkam leaves from air-dried maceration, air-dried soxhletation, sun-dried maceration, and sun-dried soxhletation, yielding values of 10.87, 24.71, 22.32, and 24.31 µg/mL, respectively. Manurung et al., (2020) reported IC_{50} values for sikkam stem bark extracts, including crude extract of 20.94 µg/mL, ethanol fraction 36.29 µg/mL, ethyl acetate fraction 83.28 µg/mL, and n-hexane fraction 39.13 µg/mL. Meanwhile, research by Jambak dkk., (2019) on ethanol extract and n-hexane fraction of sikkam stem bark showed very strong antioxidant activity with IC_{50} values of 12.248 µg/mL and 39.622 µg/mL, respectively.

3.3. Toxicity

The results of the toxicity tests of the ethyl acetate fraction and dichloromethane fraction of Sikkam leaf extract (Bischofia javanica Blume) are fully presented in Figure 2. Probit analysis results showed that the ethyl acetate fraction had an LC_{50} value of 1152.99 µg/mL, while the dichloromethane fraction obtained an LC_{50} value of 686.61 µg/mL, indicating that the dichloromethane fraction is classified as toxic, whereas the ethyl acetate fraction is classified as non-toxic. Although both are derived from the same plant source, the difference in toxicity values is likely due to differences in the polarity of the solvents used during fractionation, resulting in distinct active compound profiles in each fraction. Dichloromethane solvent tends to attract semi-polar to non-polar compounds that are potentially more toxic, whereas ethyl acetate extracts compounds with different polarity ranges, resulting in lower cytotoxic activity (Yunita & Sari, 2022). This is consistent with the principle that the variation in concentration and type of active compounds in each fraction strongly determines the level of toxicity to test organisms.



Ethyl Acetate Fraction Dichloromethane Fraction

Figure 2. Curve of the Relationship between Percentage of Log C and Probit Values

Both dichloromethane and ethyl acetate fractions may contain phenolic compounds such as flavonoids, saponins, and tannins that may induce larval death through various toxic mechanisms. Phenolic compounds can cause larval death in three ways: by inhibiting larval feeding, acting as stomach poisons, and inhibiting taste receptors in the larval mouth, preventing larvae from recognizing their food, experiencing nutrient deficiencies, and eventually dying (Rachmatiah et al., 2022). Saponins are known to disrupt digestive enzyme function and nutrient absorption pathways,

while tannins inhibit digestion by inactivating digestive enzymes or forming complexes with dietary proteins (Yana et al., 2023).

Research by Hairani et al.,(2024) reported that the dichloromethane extract contains flavonoids, phenolics, and triterpenoids with an LC_{50} value of 303.68 μg/mL. When compared to the crude ethanol extract of sikkam leaves reported by Saragih (2025), the LC_{50} values of all crude extracts were above 1000 μg/mL, specifically 3268.81, 2418.29, 2063.76, and 1875.33 μg/mL for air-dried maceration, air-dried Soxhlet extraction, sun-dried maceration, and sun-dried Soxhlet extraction treatments, respectively, and are therefore categorized as non-toxic. This indicates that the fractionation process with dichloromethane solvent can effectively separate and concentrate cytotoxic bioactive compounds that are insufficiently extracted in the crude ethanol extract, whereas the ethyl acetate fraction and crude ethanol extract tend to be safe and non-toxic. Thus, sikkam leaves have significant potential to be developed as a medicinal plant with a good safety profile.

4. CONCLUSION

Based on the research results, it can be concluded that the antioxidant activity (IC_{50}) of the ethyl acetate and dichloromethane fractions of sikkam leaf extract are 4.1311 μg/mL (very strong) and 26.1923 μg/mL (very strong), respectively, and the toxicity (LC_{50}) of the ethyl acetate and dichloromethane fractions of sikkam leaf extract are 1152.99 μg/mL (non-toxic) and 686.61 μg/mL (moderate), respectively.

ACKNOWLEDGEMENTS

We sincerely thank the Integrated Research Laboratory of Ganesha University of Education for their assistance in UV-Vis spectrophotometry analysis.

REFERENCES

Fitriyanti, D., Tutik, T., & Ulfa, A. M. (2024). *Uji Toksisitas Bslt (Brine Shrimp Lethality Test) Terhadap Larva Udang Ekstrak Metanol Kulit Bawang Merah (Allium Cepa L.) Dengan Metode Ekstraksi Sokletasi Dan Refluks*. JFM (Jurnal Farmasi Malahayati), 7(1), 95–104. https://doi.org/10.33024/jfm.v7i1.8386

Hairani, R., Ruga, R., & Jonathan. (2024). *Skrining Fitokimia Dan Uji Toksisitas Ekstrak Diklorometana Rimpang Temu Kunci (Boesenbergia rotunda)*. Jurnal Atomik, 9(2), 62–68. https://jurnal.kimia.fmipa.unmul.ac.id/index.php/JA

Harefa, D. (2020). *Pemanfaatan Hasil Tanaman Sebagai Tanaman Obat Keluarga (TOGA)*. Madani : Indonesian Journal of Civil Society, 2(2), 28–36. https://doi.org/10.35970/madani.v2i2.233

Ilyas, S., Hutahaean, S., Sinaga, R. S. H., & Situmorang, P. C. (2022). *Effect of sikkam (Bischofia javanica Blume) ethanolic extract on the quality and quantity of hyperglycemic rat sperm*. Journal of Pharmacy and Pharmacognosy Research, 10(2), 270–278. https://doi.org/10.56499/jppres21.1204_10.2.270

Julianti, E., Barus, K., Ritonga, A. H., & Herlina, H. (2024). Uji Aktivitas Antiinflamasi Ekstrak Etanol Daun Sikkam (Bischofia Javanica Blume) Dan Precipitated Calcium Carbonate (Pcc) Terhadap Mencit (Mus Musculus). 8(3), 192–207.

Jurčević Šangut, I., Pavličević, L., & Šamec, D. (2024). I*nfluence of Air Drying, Freeze Drying and Oven Drying on the Biflavone Content in Yellow Ginkgo (Ginkgo biloba L.) Leaves*. Applied Sciences (Switzerland), 14(6). https://doi.org/10.3390/app14062330

Lee, S., Ha, J., Park, J., Kang, E., Jeon, S. H., Han, S. B., Ningsih, S., Paik, J. H., & Cho, S. (2021). *Antioxidant and anti-inflammatory effects of bischofia javanica (Blume) leaf methanol extracts through the regulation of Nrf2 and TAK1*. Antioxidants, 10(8). https://doi.org/10.3390/antiox10081295

Maharani, A. I., Riskierdi, F., Febriani, Kurnia, I. K. A., Rahman, N. A., Ilahi, N. F., & Farma, S. A. (2021). *Peran Antioksidan Alami Berbahan Dasar Pangan Lokal dalam Mencegah Efek Radikal Bebas*. Prosiding Seminar Nasional Bio, 17(2), 171–178. https://journal.unhas.ac.id/index.php/bioma

Manurung, D. P., Sundaryono, A., & Amir, H. (2020). P*enentuan Potensi Ekstrak Kulit Batang*

Tumbuhan Sikkam (Bischofia Javanica Blume) Sebagai Antioksidan Dengan Metode DPPH Dan Sitotoksik Dengan Metode BSLT. Alotrop, 4(1), 83–91. https://doi.org/10.33369/atp.v4i1.13715

Ningsih1, I. S., & , Moralita Chatri1 * , Linda Advinda1, V. (2020). *Senyawa Aktif Flavonoid yang Terdapat Pada Tumbuhan Idos*. Jurnal Penelitian Tanaman Industri, 8(2), 61. https://doi.org/10.21082/jlittri.v8n2.2002.61-66

Obenu, N. M. (2019). *Ekstraksi dan Identifikasi Komposisi Metabolit Fraksi Diklorometana dan Aquades Ektrak Metanol Daun Sirsak (Annona muricata Linn)*. Jurnal Saintek Lahan Kering, 2(1), 17–19. https://doi.org/10.32938/slk.v2i1.717

Putri, N. P., Anggreni, C., Refina, N. P., Yanti, D., Ayu, K., Pratiwi, P., Nyoman, N., Udayani, W., & Farmasi, P. S. (2023). *Uji Aktivitas Antioksidan Gummy Candy Ekstrak Daun Sirih Cina (Peperomia pellucida L. Kunth) dengan Metode DPPH.* Indonesian Journal of Pharmaceutical Education (e-Journal), 3(3), 2775–3670. https://doi.org/10.37311/ijpe.v3i3.22117

Rachmatiah, T., Daud, J. J., & Artanti, N. (2022). *Aktivitas Antioksidan, Toksisitas, Kandungan Senyawa Fenol dan Flavonoid Total dari Daun Leilem (Clerodendrum minahassae Teijsm. & Binn)*. Sainstech Farma, 15(1), 35–43. https://doi.org/10.37277/sfj.v15i1.1103

Rumahorbo, C. G. P., Hutahaean, S., & Ilyas, S. (2021). *Insulin expression and insulitis degree of diabetic rats after giving sikkam leaves (Bischofia javanica Blume)*. Journal of Pharmacy and Pharmacognosy Research, 9(5), 598–608. https://doi.org/10.56499/jppres20.998_9.5.598

Rumahorbo, C. G. P., Ilyas, S., Hutahaean, S., Zuhra, C. F., & Situmorang, P. C. (2023). *The Improvement Of The Physiological Effects Of Nanoherbal Sikkam Leaves (Bischofia javanica)*. Rasayan Journal of Chemistry, 16(2), 766–772. https://doi.org/10.31788/RJC.2023.1628245

Saragih, N. A. B. (2025). *Uji Aktivitas Antioksidan Dan Toksisitas (Bischofia javanica Blume) Kering Udara Dan Matahari Yang Diisolasi Dengan Metode Maserasi Dan Sokletasi*. Universitas Pendidikan Ganesha.

Sitohang, P. A. M. (2020). *Studi Morfologi Dan Anatomi Tumbuhan Sikkam (Bischofia Javanica Blume) Di Desa Tigabolon Kecamatan Sidamanik Kabupaten Simalungun*. In thesis. http://dx.doi.org/10.1016/j.gde.2016.09.008%0Ahttp://dx.doi.org/10.1007/s00412-015-0543-8%0Ahttp://dx.doi.org/10.1038/nature08473%0Ahttp://dx.doi.org/10.1016/j.jmb.2009.01.007%0Ahttp://dx.doi.org/10.1016/j.jmb.2012.10.008%0Ahttp://dx.doi.org/10.1038/s4159

Tan, L., Liu, X., Chen, Q., Eissa, M. A., Pan, Z., & Azeem, F. (2025). *Chemical composition, antioxidant potential, and antibacterial mechanism of Bischofia javanica ethanol extract against Staphylococcus aureus*. Lwt, 222(December 2024), 117682. https://doi.org/10.1016/j.lwt.2025.117682

Taylor, B. R. (2022). *Air-drying depresses rates of leaf litter decomposition*. Soil Biology and Biochemistry, 30(3), 403–412. https://doi.org/10.1016/S0038-0717(97)00126-0

Yana, Y., Adhiksana, A., & Amborowati, C. (2023). *Identifikasi Senyawa Metabolit Sekunder Dan Uji Toksisitas Hasil Fraksinasi Ekstrak Kulit Buah Naga Merah (Hylocereus Polyrhizus)*. Jurnal Teknik Kimia Vokasional (Jimsi), 3(1), 15–21. https://doi.org/10.46964/jimsi.v3i1.364

Yunita, E., & Sari, D. R. A. P. (2022). *Aktivitas Antioksidan dan Toksisitas Fraksi Etil Asetat dan Fraksi N-Heksan Daun Pegagan (Centella Asiatica L.)*. Jurnal Mandala Pharmacon Indonesia, 8(1), 58–66. https://doi.org/10.35311/jmpi.v8i1.167