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Bioactivity of Songga Wood (*Strychnos ligustrina*) methanol extract: Antioxidant and Anti-inflammatory against Interleukin-8 (IL-8) levels *in Vivo*

(Bioaktivitas ekstrak metanol Kayu Songga (Strychnos ligustrina): antioksidan dan Antiinflamasi terhadap kadar Interleukin-8 (Il-8) secara in Vivo)

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ABSTRACT

Background: Songga wood (*Strychnos ligustrina*) from the genus Loganiaceae is a plant that is empirically used as a traditional medicine by people in several regions in Indonesia. This plant serves as a medicine for fever, malaria, as an antidote, and for treating wounds, boils, acne and scabies. **Objectives:** This study aims to determine the antioxidant and anti-inflammatory activity of methanol extract of songga wood with Interleukin-8 (IL-8) parameter. **Material and Methods:** Songga wood was macerated with methanol for 3x24 hours until a thick extract was obtained. Antioxidant activity test was conducted using the DPPH method and anti-inflammatory test was performed using ELISA with IL-8 parameter. Test animals were divided into six groups:the normal group, negative control (Na-CMC), positive control (diclofenac sodium) and treatment with three dose variations, 50, 100, and 200 mg/KgBB. **Results:** The results showed that the antioxidant activity value of Songga wood was IC_{50} 84.51 µg/ml. Furthermore, anti-inflammatory activity showed IL-8 levels at doses of 50 mg/kgBB extract (494.8 pg/ml), 100 mg/kgBB (216.2 pg/ml) and 200 mg/kgBB (118.7 pg/ml). **Conclusions:** This study concluded that methanol extract of songga wood has strong antioxidant activity and anti-inflammatory activity. The most effective dose to reduce IL-8 levels was 200 mg/kgBB, which was not significantly different from the positive control ($p>0.05$).

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INTRODUCTION

Free radicals are anatom or molecule with unpaired electrons in its outer shell, making it unstable and highly reactive in seeking partners electrons by attacking and binding electrons around it. When non-radical molecules meet free radicals, a new radical molecule is formed. Free radicals also play a role in the degeneration process which causes a gradual decrease in the tissue's ability to replace or repair itself to maintain its normal function. Compounds that play a role in counteracting free radicals are called antioxidants. Antioxidants donate single electrons or hydrogen atoms to stabilize free radicals (Satriyani, 2021). Excess free radicals in the body can trigger inflammation (Abdulkhaleq et al., 2018).

When inflammation occurs, one of the main mediators of the inflammatory response produced by monocytes, macrophages and endothelial cells is Interleukin-8 (IL-8). IL-8 plays an important role in the activation of leukocytes, bringing neutrophils and other immune cells to the site of infection and regulating migration. Itsconcentration increases immediately within one to three hours after infection (Memory et al., 2019). Anti-inflammatory compounds are needed to reduce IL-8 levels in the body when inflammation occurs.

The body's inflammatory response is characterized by various mediators, including pro-inflammatory cytokines such as IL-1, Tumour Necrosis Factor (TNF), Interferon (INF)-c, IL-6, IL-8, IL-12, and IL-18, in addition to anti-inflammatory cytokines such as IL-1Ra, IL-35Ra, IL-37, and IL-38. These mediators trigger various complex processes, including enzyme activation, mediator release, cell migration, fluid extravasation, increased protein denaturation, and membrane changes. Pro-inflammatory cytokines contribute to symptoms such as edema, swelling, redness, pain, and impaired function in the affected area, typical of inflammation (Fratiwi et al., 2022). Interleukin-8 is produced by a wide variety of cells, including monocytes, neutrophils, T cells, fibroblasts, endothelial cells, and epithelial cells, after exposure to antigens or inflammatory stimulants. IL-8 secretion will lead to the activation and migration of neutrophils from the peripheral blood to the site of infection, which plays a role in killing or inhibiting pathogens. IL-8 signaling is usually tightly regulated with minimal IL-8 expression in normal tissues and can increase due to inflammatory signals, reactive oxygen species, death receptors, and steroid hormones (Rosita et al., 2021).

Antioxidants and anti-inflammatories are closely related where antioxidant compounds inhibit oxidation by capturing free radicals, while anti-inflammatory compounds stabilize cell membranes when inflammation occurs (Armadany et al., 2020). Antioxidant and anti-inflammatory compounds can be found in plants, one of which is songga wood which is used as a medicinal plant in West Nusa Tenggara as a medicine for fever, malaria, antidote, boils, acne and scabies. In the Bima Sumbawa area, soaking or boiling the wood of this plant is used as an antidiabetic, antimalarial, anti-inflammatory,

antirheumatic, anticancer, and antihypertensive (Taek, 2023). This plant has also been studied to contain several secondary metabolites, namely flavonoids, tannins, triterpenoids, and alkaloid compounds, namely brucine and strychnine. Brucine and strychnine are the primary chemical compounds found in the seeds, leaves, and bark of the songga wood plant. Based on the results of pharmacological tests, brucine has anti-inflammatory, analgesic, and antitumor effects (Nurwanti et al., 2023). The investigation of the biological activities of songga wood has not been widely reported, so further research needs to be carried out, particularly regarding its antioxidant activity using the DPPH method and anti-inflammatory effects measured by IL8 parameters.

MATERIAL AND METHODS

Materials

Songga wood (*Strychnos ligustrina*) was obtained from Dompu, NTB. methanol, distilled water, DPPH (Aldrich®), quercetin (sigma®), Na-CMC 0.5% (Food Grade®), sodium diclofenac (Novell®), filter paper, aluminum foil, carrageenan 1%, aqua pro injection (Otsuka®), standard feed, drinking water, EDTA tube, 3 ml eppendorf tube (onemed®), injection syringe (onemed®).

Methods

Determination of sample

Samples were determined to ensure that the samples used in this study were songga wood (*Strychnos ligustrina*). Determination was conducted at the Faculty of Teacher Training and Education Biology Laboratory, Faculty of Teacher Training and Science, Halu Oleo University with No.717/UN29.18.1/PG/2023. This research has received approval from the ethics commission of Halu Oleo University with No. 3545a/UN29.20.1.2/PG/2023.

Extraction

A total of 3328 grams of songga wood simplisia obtained from West Nusa Tenggara, Indonesia, was extracted with methanol for 3 x 24 hours in a closed container. The filtrate obtained was concentrated with an evaporator until a thick extract was obtained (Ilyas Y et al., 2023; Jabbar et al., 2022)

Antioxidant Testing

Preparation of stock solution of methanol extract of songga wood

The stock solution was made using 100 mg of methanol extract of songga wood which was put into a measuring flask containing 1000 ml of methanol p.a., shaken until homogeneous. 6 concentration series were made using methanol solvent p.a. with concentrations of 20, 40, 60, 80, 100 and 120 ppm. The same thing was done in making the quercetin comparator solution

Antioxidant activity test by DPPH method

Antioxidant activity of methanol extract of songga wood (*Strychnos ligustrina*) by DPPH method was carried out with concentration series of 20, 40, 60, 80, 100, and 120 ppm with methanol p.a solvent 1 ml of methanol extract from songga wood was pipetted into each sample, followed by the addition of 1 ml of DPPH solution. The mixturethen incubated at room temperature and in a dark room to prevent light-induced reactions, then measured by UV-Vis spectrophotometer with a wavelength of 517 nm. The same treatment was also carried out in the preparation of quercetin as a standard control (Aiyuba et al., 2023).

Inhibition percentage

The results of absorbance measurements obtained from the UV-Vis Spectrophotometer were used to calculate antioxidant activity. Radical scavenging activity is expressed as a percentage of inhibition which can be calculated using the following formula (Jabbar, et al., 2022)

$$\% \text{ DPPH radical inhibition} = \frac{(absorbance\ \ control - abs.sample)}{absorbance\ control} \times 100\%$$

After obtaining the quenching percentage of the test solution and quercetin concentrations, the equation y = bx + a was determined by linear regression calculations where x is the concentration (ppm) and y is the percentage of DPPH inhibition (%). Antioxidant activity is expressed as Inhibition concentration 50% (IC50), namely if the sample concentration that can quench DPPH radicals is 50%. The IC50 value is obtained from the x value after replacing y with 50 (Aiyuba et al., 2023).

Anti-inflammatory activity Test

Grouping of test animals:

In this study, the test animals were divided into 6 groups: normal, positive, negative controls, and treatment groups (extract doses of 50, 100, and 200mg/KgBW). The grouping of test animals was carried out randomly by following the Federer formula. The number of test animals used was 30.

Induction of Inflammation

A total of 0.1 ml of 1% carrageenan solution was induced on the right hind paw of rats subcutaneously, resulting in edema. This method was selected because carrageenan is effective in causing oedema without leaving lasting marks or causing significant tissue damage, making it ideal for assessing the efficacy of anti-inflammatory drugs. Its sensitivity in detecting anti-inflammatory effects is greater compared to other irritants (Suryandari et al., 2015).

Measurement of Rat Paw Edema

The data obtained is in the form of rat paw volume, then used to calculate the volume of edema. The volume of edema is the difference between the rat's paw before and after inflammation. The equation for calculating the volume of edema is:

$$Vu = Vt-Vo$$

Description:

Vu: rat paw edema volume at each time t

Vt: rat paw volume after being induced with 1% carrageenan at time t

Vo: initial volume of rat paw before being induced with 1% carrageenan

Interleukin-8 Level Test

After the rats were induced with 1% carrageenan and experienced edema after 1 hour, the rats were treated with the administration of methanol extract of songga wood (doses of 50, 100, and 200 mg/kgBW), Na-CMC 0.5% as a negative control and diclofenac sodium as a positive control, then blood samples were taken at the second hour to assess the levels of inflammatory mediator IL-8. Blood was taken from the heart of the rats. Blood samples obtained were put into a tube containing EDTA anticoagulant, and then IL-8 levels were measured by Elisa (Elabscience®) with 450 nm waves.

Data analysis

Data analysis was performed using Excel and SPSS software. Data analysis was performed using the One-Way ANOVA method for Interleukin-8 parameters and linear regression for determining IC_{50} of Songga Wood.

RESULTS AND DISCUSSION

Antioxidant Activity of DPPH Method

The DPPH method is one of the antioxidant testing methods in plants. The DPPH method is a simple, fast and easy method for determining the radical scavenging activity of several compounds. In addition, this method has been proven to be accurate and practical (Sadono, 2011). The working principle of the DPPH method is based on the ability of DPPH to accept hydrogen atoms donated by antioxidants. The color of DPPH will change from purple to yellow with the addition of antioxidants, namely when the single electron in DPPH pairs with hydrogen from the antioxidant (Haryoto et al., 2019).

Antioxidant activity testing was carried out quantitatively using the DPPH method, where methanol extract of songga wood was used as a sample and quercetin as a standard solution. Quercetin was used as a comparator because it is a class of flavonoids that show several biological activities with a strong ability to capture free radicals. capture free radicals (Hasanah et.al 2023; Gusnidar et.al 2009).

Antioxidant testing is expressed by the IC_{50} (inhibition concentration) parameter. The magnitude of antioxidant activity is indicated by the IC_{50} value, namely the concentration of sample solution needed to inhibit 50% of free radicals. The smaller the IC_{50} value of a compound, the greater the ability of the compound to ward off free radicals. The antioxidant strength level is stated as very strong if the IC_{50} value is <50 µg/ml, strong if the IC_{50} value is 51-100 µg/ml, moderate if the IC_{50} value is 101-150 µg/ml, weak if the IC50 value is 151-200 µg/ml and very weak or inactive if the IC_{50}> 200 µg/ml (Aiyuba et al., 2023). Measuring the absorbance of methanol extract of songga wood using the DPPH method using a UV-Vis spectrophotometer begins with determining the maximum DPPH wavelength and operating time. Determination of the maximum wavelength aims to provide maximum absorbance during measurement. The results of determining the maximum wavelength of the DPPH solution are 517 nm. Determination of operating time aims to determine the optimum incubation time of the sample with the DPPH solution to react, which is indicated by stable absorbance (Puspitasari & Ningsih, 2016). The results of the determination of operating time obtained stable absorption starting from the 40th minute. The results of the DPPH method antioxidant activity test can be seen in (Table 1).

Table 1. Results of the DPPH method antioxidant activity test

Sample	IC50±SD (µg/ml)	Category
Songga wood	84.5±1.21	Strong
Quercetin	5.8±1.03	Very strong

Based on Table 1, the results of the antioxidant activity measurement obtained the IC_{50} value of the methanol extract of songga wood of 84.51 µg/ml and the IC_{50} value of quercetin of 5.8 µg/ml. Based on these results, quercetin was declared very strong with an IC_{50} value of <50 µg/ml and the methanol extract of songga wood was declared strong with an IC_{50} value of 51-100 µg/ml (Aiyuba et al., 2023; Molyneux., 2004).

Rat Paw Edema Examination

Edema is the accumulation of fluid in the lower layers of the skin which is one of the signs of inflammation. In this study, measurements were made of the volume of the rat's feet before inflammation, during inflammation and after treatment to determine the decrease in edema volume after being given an agent suspected of having anti-inflammatory activity. The edema volume in rats was assessed by measuring the initial volume of the rats' feet with a mercury plethysmometer, followed by the induction of inflammation using 1% carrageenan to quantify the increase in foot volume, which could then be compared to the reduction after the administration of anti-inflammatory agents (Fratiwi et al., 2022). The inflammation testresults, the data obtained from the measurement of the edema volumein the rat's feet, are illustrated in Figure 1.

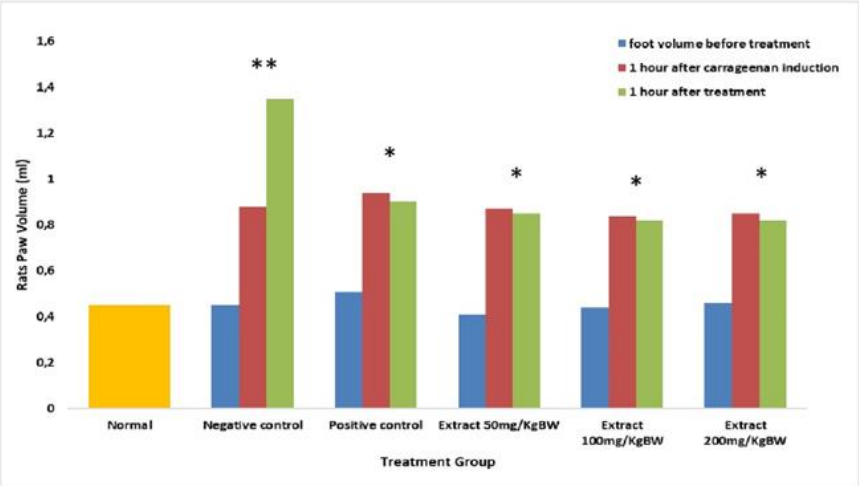

Figure 1. Volume of edema before and after treatment
(*not significantly different, P>0.05), **significantly different, P<0.05)

The results of this study indicate that the induction of inflammation using 1% carrageenan in vivo on the feet of mice has been proven to trigger inflammation. The inflammation that forms is characterized by signs of acute inflammation on the feet of mice, namely redness, edema and the inability of mice to walk normally. The results of the research are in line with research conducted by Walidah, 2014, where the induction of 1% carrageenan intraplantar in the legs of mice can trigger local swelling in the legs of mice accompanied by redness due to the accumulation of inflammatory mediators. Along with the inflammation that occurs due to carrageenan injection, there is also the release of pro-inflammatory cytokines such as TNF-α, IL-1β, IL-6, IL-8, and IL-12 (Huang et al., 2013).

Based on the data in Figure 1, it is known that there is a difference in the volume of edema in each treatment group. The negative control group showed a very high percentage of edema formed and continued to increase. This is because the test animals given 0.5% Na-CMC could not inhibit the formation of edema and the response to edema relied only on the immune response of the mice (Wenas et al., 2020). When compared to the positive control group, the treatment of songga wood methanol extract at doses of 50, 100 and 200 mg/KgBW showed that the volume of edema formed was not much different. Therefore, it can be concluded that songga wood methanol extract has anti-inflammatory activity in inhibiting the formation of edema in the soles of the feet of mice.

The results of phytochemical screening on songga wood are known to contain flavonoids, phenols, and tannins (Sadono, 2011). This plant also contains alkaloid groups such as striknin, brucine, and loganin (Hadi & Bremner, 2001).

The decrease in IL-8 levels from methanol extract of songga wood is due to its secondary metabolite content. Secondary metabolites that are thought to be responsible for providing anti-inflammatory effects are flavonoids and alkaloids. Flavonoids and alkaloids are known for their antioxidant properties that can prevent damage due to oxidative stress, namely inflammation.

The mechanism of action of flavonoids as an anti-inflammatory can be through several pathways with inhibition of cyclooxygenase (COX) and lipooxygenase activity, inhibition of leukocytes, inhibition of neutrophil degradation, and inhibition of histamine. Alkaloids suppress histamine release by mast cells and reduce the secretion of pro-inflammatory cytokines (Rahayu et al., 2022). Flavonoids with anti-inflammatory properties can interact with molecules involved in the inflammatory pathway and reduce the activity of pro-inflammatory cytokines (Wenas et al., 2020).

Results of IL-8 level examination

Enzymed-Linked Immunosorbent Assay (ELISA) is one method to determine the protein, immunity and immune response by determining the presence of antigens or antibodies in the sample. The basic principle of ELISA is to react antigens with antibodies labeled with enzymes and then add a substrate to hydrolyze it into a colored precipitate that can be detected using an ELISA reader (Santoso, et.al 2020). Examination of IL-8 levels using the ELISA Kit Rat IL-8. Based on the ELISA test, the average results of IL-8 level measurements were obtained in each treatment group (Figure 2).

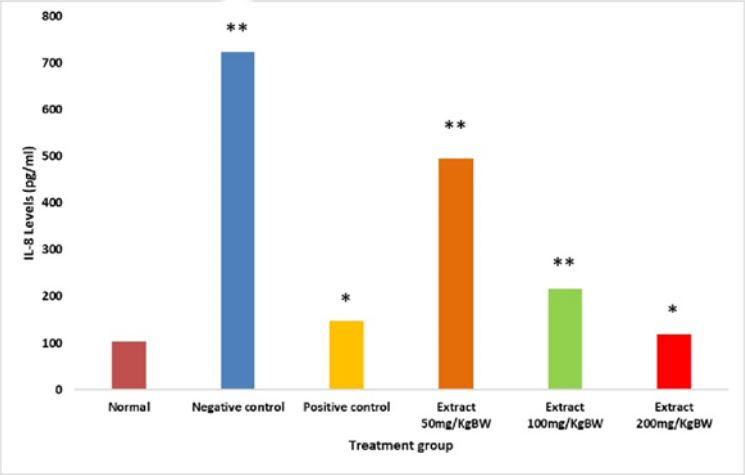

Figure 2. IL-8 levels in the treatment and normal group
(*not significantly different, P>0.05), ** significantly different, P<0.05)

Based on Figure 2, it can be seen that each treatment group has different mean IL-8 levels. The highest mean IL-8 level of 724.3 pg/ml was found in the negative control group of 0.5% Na-CMC, which proves that Na-CMC does not have anti-inflammatory activity to reduce the production of pro-inflammatory cytokine IL-8 (Fratiwi et al., 2022). The positive control group using diclofenac sodium had an average

IL-8 level of 147.9 pg/ml. In the Songga wood methanol extract group with dose variations of 50, 100, and 200 mg/kgBB, the mean IL-8 levels were 494.8 pg/ml, 216.2 pg/ml, and 118.7 pg/m, respectively. The average IL-8 level obtained in the 200 mg/kgBB songga wood methanol extract group was not significantly different from the positive control of diclofenac sodium ($p>0.05$).

Based on the results of the One Way ANOVA test, the p-value = 0.000 <0.05 was obtained, so it can be concluded that there is an effect of methanol extract of songga wood on IL-8 in male Wistar rats induced by 1% carrageenin intraplantar. Furthermore, the post hoc LSD test was conducted to determine significant differences in each group.

The decrease in IL-8 levels from the methanol extract of songga wood is due to its secondary metabolite content. Secondary metabolites that are thought to be responsible for providing anti-inflammatory effects are flavonoids and alkaloids. Flavonoids and alkaloids are known for their antioxidant properties that can prevent damage due to oxidative stress, namely inflammation. The anti-inflammatory action mechanism of flavonoids can be through several pathways, y inhibiting cyclooxygenase (COX) and lipoxygenase activity, inhibiting leukocytes, inhibiting neutrophil degradation, and inhibiting histamine. Alkaloids suppress histamine release by mast cells and reduce the secretion of pro-inflammatory cytokines (Rahayu et al., 2022).

Based on the results obtained, songga wood has antioxidant and anti-inflammatory activities. Both are interrelated, where antioxidants neutralize potential damage caused by free radicals, and anti-inflammation suppresses inflammation caused by excessive oxidative stress.

CONCLUSION

Methanol extract of songga wood exhibits strong antioxidant activity with an IC_{50} value of 84.51 µg/ml and shows the potential as an anti-inflammatory agent, with a most effective dose of 200 mg/kgBW for reducing IL-8 levels, which is not significantly different from the positive control ($P>0.05$). This research can be a reference as an antioxidant and anti-inflammatory agent derived from natural sources

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CONFLICT OF INTEREST

The authors declare no conflict of interest

REFERENCES

Abdulkhaleq, L. A., Assi, M. A., Abdullah, R., Zamri-Saad, M., Taufiq-Yap, Y. H., & Hezmee, M. N. M. (2018). The Crucial Roles of Inflammatory Mediators In Inflammation: A Review. Veterinary World, 11(5), 627–635. Https://Doi.Org/10.14202/Vetworld.2018.627-635

Aiyuba, D. S., Rakhmatullah, A. N., & Restapaty, R. (2023). Antioxidant Activity Test of Methanol Extract of Ramania Leaf (Bouea macrophylla Griffith.) Using DPPH Method. Jurnal Surya Medika, 9(1), 81–87. https://doi.org/10.33084/jsm.v9i1.5150

Armadany, F. I., Wahyuni, W., Ardianti, M., & Mallarangeng, A. N. T. A. (2020). Test of Anti-inflammatory Potential of Ethanol Extract of Bamboos Leaf (Polygonum pulchrum Blume) with Red Blood Cell Membrane Stabilisation Method In Vitro. Majalah Farmasetika., 4. https://doi.org/10.24198/mfarmasetika.v4i0.25873

Fratiwi, N., Saranani, S., Agastia, G., & Isrul, M. (2022). Anti-inflammatory Activity of Ethanol Extract of Kirinyuh Leaf (Chromolaena odorata L.) and its Effect on Interleukin 6 (IL-6) Levels in Wistar Male Rats. Jurnal Pharmacia Mandala Waluya, 1(2), 54–67. https://doi.org/10.54883/28296850.v1i2.24

Gusnidar, T, Herawati, R, Kartassmita, R, E, & Adriyana, I, K, (2009), 'Sintesis Kuersetin Terklorinasi dan Aktivitas Perlindungan Terhadap Tukak Lambung', Majalah Farmasi Indonesia 20 (4) hal. 163-169

Hadi, S., & Bremner, J. B. (2001). Initial Studies on Alkaloids from Lombok Medicinal Plants. Molecules, 6, 117–129. http://www.mdpi.org

Haryoto, H., Frista, A., Achmad Yani Tromol Pos, J., Kartasura, P., (2019). Antioxidant Activity of Ethanol Extract, Polar, Semipolar and Non Polar Fractions of Mangrove Kacangan (Rhizophora apiculata) Leaves by DPPH and FRAP Methods. J. Sains Kes, 2(2). https://doi.org/10.25026/jsk.v2i2.129

Hasanah, N., Dahlia, A. A., & Handayani, V. (2023). Uji Aktivitas Antioksidan Ekstrak Daun Kedondong Laut (Nothopanax fructicosum (L.) Miq) Dengan Metode Peredaman Radikal Bebas DPPH. Makassar Natural Product Journal, 1(2), 10–17.

Huang, N., Wang, F., Wang, Y., Hou, J., Li, J., & Deng, X. (2013). Ulinastatin improves survival of septic mice by suppressing inflammatory response and lymphocyte apoptosis. Journal of Surgical Research, 182(2), 296–302. https://doi.org/10.1016/j.jss.2012.10.043

Ilyas Y., M., Sahidin, I., Jabbar, A., Yodha, A. W. M., Diantini, A., Pradipta, I. S., Amalia, R., Febrianti, R. M., Hadisaputri, Y. E., Ghozali, M., & Julaeha, E. (2023). Effect of Immunomodulating Extract and Some Isolates from Etlingera rubroloba A.D. Poulsen Fruits on Diabetic Patients with Tuberculosis. Molecules, 28(5), Article 5. https://doi.org/10.3390/molecules28052401

Jabbar, A., Sahidin, Monstavevi, S., Malaka, M., Malik, F., & Ilyas, M. Y. (2022). Antioxidant and Anti-Inflammatory Activity of Ethanol Extract Stem of Etlingera rubroloba A.D. Poulsen. Pakistan Journal of Biological Sciences, 25(10), 885–891. https://doi.org/10.3923/pjbs.2022.885.891

Jabbar, A., Wahyuni, W., Leorita, M., Yusuf, M. I., Salsabila, H., & Sahidin, I. (2022). Antihyperuricemia Activity of Wualae Fruit (Etlingera elatior Jack R. M. Smith) Ethanol Extract

In Vivo. Jurnal Farmasi Sains dan Praktis, 104–111. https://doi.org/10.31603/pharmacy.v1i1.6083

Memory, E., Aman, A. K., & Hanafie, A. (2019). Relationship between Interleukin-8 and Procalcitonin levels in severe sepsis patients at the Haji Adam Malik Central General Hospital, Medan. The Journal of Medical School (JMS), 52(2), 56–60.

Molyneux, P. (2004). The use of the stable radical Diphenylpicrylhydrazyl (DPPH) for estimating antioxidant activity. Songklanakarin J. Sci. Technol., 26(2), 211–219.

Nurwanti, S. W., Sarnoko, A., & Atika, W. (2023). Identification of Alkaloid Compounds from Ethanol Extract of *Strychnos ligustrina* Bark Using Liquid Chromatography-Mass Spectrometry (LC-MS). Journal Borneo Science Technology and Health Journal Artikel, 3(2). https://doi.org/10.57174/jborn.v3i2.82

Puspitasari, E., & Ningsih, E. Y. (2016). Antioxidant Capacity of Salak Fruit Extract (Salacca Zalacca (Gaertn.) Voss) Granulated Sugar Variant Using DPPH Radical Capture Method. Pharmacy, 13(1).

Rahayu, A. A. D., Prihantini, A. I., Krisnawati, & Nugraheni, Y. M. M. A. (2022). Chemical components of different parts of *Strychnos ligustrina*, a medicinal plant from Indonesia. IOP Conference Series: Earth and Environmental Science, 959(1), 012061. https://doi.org/10.1088/1755-1315/959/1/012061.

Rosita, F., Fatiharani Dewi, P., Eko Irawanto, M., & Sidharta, R. (2021). Astaxantin Topikal Sebagai Terapi Adjuvan terhadap Kadar Serum Interleukin 8 pada Akne Vulgaris. Jurnal Health Sains, 2(9), 1197–1208. https://doi.org/10.46799/jhs.v2i9.269

Sadono, A. (2011). Antioxidant Activity and Composition Analysis of Phenolic Compounds from Sea Bidara Tree (*Strychnos ligustrina*). IPB.

Santoso, U., Medriana, U., & Mauritz, P.M. (2020). Antibacterial and antifungal activity of yellow rootstock extract (Fibraurea chloroleuca Miers) against Escherichia coli, Staphylococcus aureus and Candida albicans. Jurnal Kesehatan Bakti Tunas Husada, 20(2), 194-208.

Satriyani, D. P. P. (2021). Review Artikel: Antioxidants of Moringa Leaf Extract (Moringa Oleifera Lam.). Jurnal Farmasi Malahayati, 4(1).

Setiani, L. A., Moerfiah, M., & Yulianita Yulianita. (2020). Anti-inflammatory Activity Test of African Leaf Infusa (Vernonia amygdalina) on Carrageenan-Induced White Rats. Jurnal Farmasi Indonesia, 17(1). http://journals.ums.ac.id/index.php/pharmacon

Suryandari, S. S., De Queljoe, E., & Datu, O. S. (2021). Anti-Inflammatory Activity Test of Ethanol Extract Of Sesewanua Leaves (Clerodendrum Squamatum Vahl.) Towards White Rats (Rattus Norvegicus L.) Induced by Carrageenan. Pharmacon, 10(3).

Taek, M. M. (2023). Kayu Ular: Snake Wood: Ethnomedicine, Phytochemistry, Activity and Toxicity of Timorese Traditional Antimalarial Medicine (Issue 1). Rena Cipta Mandiri.

Walidah, C. (2014). Test of Anti-inflammatory Effect of Ethyl Acetate Extract of Mastigophora Diclados Liverwort In Vivo. Uin Syarif Hidayatullah .

Wenas, D. M., Aliya, L. S., & Janah, N. U. (2020). Anti-inflammatory Activity of Ethanol Extract of Arabica Coffee Leaves (Coffea Arabica L.) on Rat Edema. Spices and Medicinal Plants Research Bulletin 31(2), 75. https://doi.org/10.21082/bullittro.v31n2.2020.75-84