BIODIVERSITAS
Volume 24, Number 8, August 2023
Pages: 4584-4589

ISSN: 1412-033X
E-ISSN: 2085-4722
DOI: 10.13057/biodiv/d240862

Antibacterial activity of *Blumea balsamifera* leaf extracts from Aceh, Indonesia

MASYUDI[1,♥], ANITA NOVIYANTI[2], MUHAMMAD RIDHWAN[2], SALFAUQI NURMAN[3], JAILANI[2], ARMI[2], T. M. RAFSANJANI[1], SAID USMAN[4], MUHAMMAD HANAFIAH[5], MARLINA[6]

[1]Department of Public Health, Faculty of Public Health, Universitas Serambi Mekkah. Jl. Unmuha, Batoh, Lueng Bata, Banda Aceh 23245, Aceh, Indonesia. ♥email: masyudi@serambimekkah.ac.id

[2]Department of Biologi, Universitas Serambi Mekkah. Jl. Unmuha, Batoh, Lueng Bata, Banda Aceh 23245, Aceh, Indonesia

[3]Department of Ship Engineering, Politeknik Pelayaran Malahayati. Jl. Laksamana Malahayati No.Km.19, Durung, Mesjid Raya, Aceh Besar 23381, Aceh, Indonesia

[4]Faculty of Medicine, Universitas Syiah Kuala. Jl. Teuku Nyak Arief No.441, Kopelma Darussalam, Syiah Kuala, Banda Aceh 23111, Aceh, Indonesia

[5]Laboratory of Parasitology, Faculty of Veterinary Medicine, Universitas Syiah Kuala. Jl. Teuku Nyak Arief No.441, Kopelma Darussalam, Syiah Kuala, Banda Aceh 23111, Aceh, Indonesia

[6]Faculty of Nursing, Universitas Syiah Kuala. Jl. Teuku Nyak Arief No.441, Kopelma Darussalam, Syiah Kuala, Banda Aceh 23111, Aceh, Indonesia

Manuscript received: 20 May 2023. Revision accepted: 31 August 2023.

Abstract. *Masyudi, Noviyanti A, Ridhwan M, Nurman S, Jailani, Armi, Rafsanjani TM, Usman S, Hanafiah M, Marlina. 2023. Antibacterial activity of* Blumea balsamifera *leaf extracts from Aceh, Indonesia. Biodiversitas 24: 4584-4589. Blumea balsamifera* L. has long been used as traditional medicine by communities in Aceh, Indonesia and from various parts of the world. For generations, this plant has been believed to have properties to cure various diseases. The results of the GCMS analysis of *B. balsamifera* leaf from Aceh-Indonesia in the previous study contain various compounds for wound healing, including borneol, jasmoline, camphor, and caryophyllene. The present study aimed to analyze the antibacterial activity of *B. balsamifera* leaves from Aceh. The sample was taken from the village of Gunongpulo, South Aceh-Indonesia, and the extraction process was carried out using three different types of solvents: ethanol, ethyl acetate, and n-hexane. Three variations of the extract obtained were then tested for antibacterial against *Staphylococcus aureus* and *Pseudomonas aeruginosa* by analyzing the inhibitory of each extract. The results showed that the inhibition zone formed on *S. aureus* against ethanol extract was 2.4 mm, ethyl extract was 9.2 mm, and n-hexane extract was 2.3 mm. In comparison, the inhibition zone formed on *P. aeruginosa* against ethanol extract was 0 mm, ethyl extract was 9 mm, and n-hexane extract was 4.9 mm. Conclusion: *B. balsamifera* leaf extract from Aceh contains antibacterial, with the highest inhibition against *S. aureus* at 9.2 mm and Pseudomonas at 9.0 mm. It is recommended that in the process of extracting *B. balsamifera* leaves by maceration, the best solvent used is ethyl acetate.

Keywords: Antibacterial, *Blumea balsamifera*, *capa*, inhibition, solvent

INTRODUCTION

The people of Aceh and Indonesia, in general, have long used traditional medicines, including green plants, as medicine for a long time and then preserved them for generations (De Boer and Cotingting 2014). Plants used by the community do not contain synthetic chemicals and are relatively safer for daily use. Treating wounds using synthetic chemical drugs has side effects that may inhibit wound healing (Gonzalez et al. 2016), responsible for some effects such as allergic reactions and skin irritation. It is necessary to re-examine so that other safer alternatives are found (Imamah 2017). The World Health Organization (WHO), in the book Traditional Medicine Strategy 2014-2023, issued in December 2013, states that using medicines with natural ingredients, including herbal medicines, is useful for maintaining health in the community for the prevention or treatment of disease (WHO 2013).

Blumea balsamifera L. or *capa* (Acehnese) has long been known in the community as a traditional medicine, usually used to treat diarrhea, cure itching, and heal wounds (Masyudi et al. 2022). This plant grows in people's yards and the forest; this plant is easy to grow and does not require special care. The use of plants as medicinal plants is most commonly found in Aceh and other parts of Indonesia, especially in rural or remote areas and remote areas. The healing effect of using this plant to treat the results is quite satisfactory (Yuan et al. 2016).

The results of a previous study by the author on people's habits in using traditional medicinal plants were found in the interior of South Aceh. Traditional midwives use *B. balsamifera* leaves mixed with turmeric, then squeezed and drunk as one of the ingredients postpartum mothers give to heal internal wounds (Masyudi and Usman 2019). Other research states that people for generations have used the juice of *B. balsamifera* leaves by affixing them to the injured skin area, and it is believed to be able to heal wounds (Nuryadin 2017).

Staphylococcus aureus and *P. aeruginosa* bacteria are often found in infected wounds. The presence of these bacteria causes infection and prolongs wound healing. *S. aureus* is a gram-positive in the form of cocci arranged in groups that are described as grape-like. These organisms can grow in salt up to 10% on medium, and colonies are

often gold. *Staphylococcus aureus* can grow aerobically or anaerobically at 18° and 40°C (Tong et al. 2015).

Staphylococcus aureus can be found in normal human flora on the skin and the environment. In healthy skin, *S. aureus* usually does not cause infection, but in wounds, if it enters the bloodstream or internal tissues, it causes various infections (Balasubramanian et al. 2017; van Belkum and Schrenzel 2014). *Pseudomonas aeruginosa* is a rod-shaped bacterium with a size of 0.6 × 2 micrometers. These bacteria are gram-negative and appear in a single form, in pairs, sometimes in short chains, and can move (motile) due to a single flagellum. These bacteria live and thrive in the absence of oxygen. *Pseudomonas aeruginosa* isolates form three kinds of colonies (Soekiman 2016). In areas of the skin that do not have normal defenses, such as being wounded, *P. aeruginosa* becomes pathogenic, such as mucous membranes and skin or other parts injured by direct tissue (Singh et al. 2018). Pathogenicity may also occur with a urinary or intravenous catheter if neutropenia occurs, as in cancer chemotherapy (Gito and Rochmawati 2018; Asif et al. 2017). These bacteria easily adhere, forming colonies on mucous membranes or skin, invading locally, and causing systemic disease. *Pseudomonas aeruginosa* is resistant to many antimicrobial drugs, so this bacterium becomes dominant and important when normal flora is more sensitive (Tong et al. 2015).

For this reason, in this study, researchers will look at the antibacterial activity of *B. balsamifera* leaf extract from Aceh by looking at the inhibition zones for the two bacteria. This study aims to examine the antibacterial activity of *B. balsamifera* leaf from Aceh extracted by n-hexane, ethyl acetate, and ethanol as solvents against *S. aureus* and *P. aeruginosa*.

MATERIALS AND METHODS

Study location

Leaves of the *B. balsamifera* plant were collected from the Gunongpulo village, Kluet Utara Sub-district, South Aceh District, Indonesia (Figure 1) with coordinates 03°07'13.7"N and 97°20'28.2" E. The sampling location was the same as in our earlier paper regarding the bioactive chemicals found in *B. balsamifera* leaf extracts from South Aceh, Indonesia (Masyudi et al. 2022).

Materials

The main ingredients used were *B. balsamifera* leaves; solvents were ethanol, ethyl acetate, and n-hexane; the test bacteria were *S. aureus* and *P. aeruginosa*, 10% DMSO solution + 0.5% Tween 80, Aquades, Ethanol Solvent, Positive control (1% gentamicin), and negative control gel with carbopol 940 base. Meanwhile, the tools used included analytical balances, Erlenmeyer, test tubes, petri dishes, spiritus/Bunsen lamps, autoclaves, incubators, Rotary evaporator, loop needle, tweezers, caliper, stirring rod, empty discs of antibiotics (blank disc brand OXOID d=6mm), MHA media, cotton swabs, and pipettes.

Plant identification

The plants were determined to be members of the genus *Blumea* and the species *Blumea balsamifera* L., by taxonomist from the Biology Laboratory, Faculty of Mathematics and Natural Sciences, Syiah Kuala University, Banda Aceh, Indonesia. This decision was necessary to verify that the plants utilized as research samples accurately represented their species.

Preparation of *Blumea balsamifera* leaf extract

Blumea balsamifera leaf was taken as the mature leaves, with the criteria that they have grown perfectly with the age of over 4 months, the leaves are old but not yet from yellowed, the leaves are close to the twigs and not including the shoots, clean from dirt and dust, grows wild in the forest and the yards of people's houses (Viena et al. 2018).

Before the extraction process, the *B. balsamifera* leaves are cleaned using running water to remove dirt and dust attached to the leaves. This is important so that the results of identifying the chemical content of *B. balsamifera* leaves become more accurate. *Blumea balsamifera* leaves that have been washed and then air-dried for 2 weeks without direct sunlight. The process of extraction is shown in Figure 2.

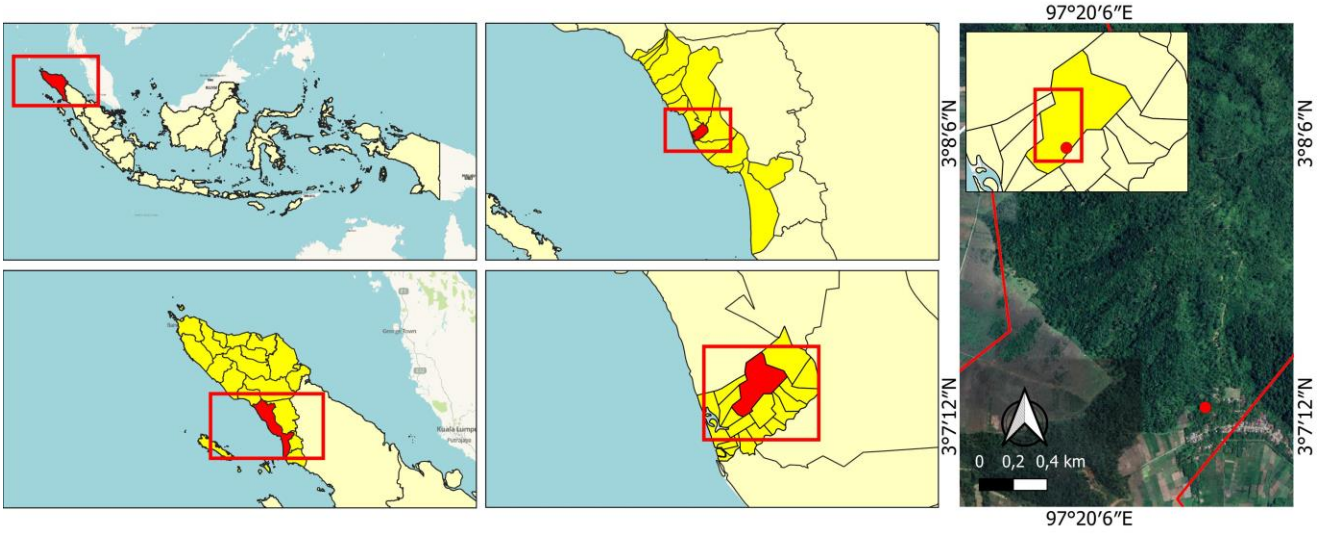

Figure 1. Location sampling in Gunongpulo village, Kluet Utara Sub-district, South Aceh District, Indonesia

Figure 2 shows the stages of the *B. balsamifera* leaf extraction process by the maceration method using three different types of solvents. Figure 2A shows that *B. balsamifera* is in the yard of a community house in Gunong Pulo village, South Aceh-Indonesia; the selected plants are over 4 months old, not yellowing, and not damaged. Figure 2B The process of drying *B. balsamifera* leaves is not exposed to direct sunlight; drying is at room temperature until the *B. balsamifera* leaves are completely dry and protected from bacteria. Figure 2C shows dry *B. balsamifera* leaves mashed using a dry blender; this dry powder is soaked using 3 different solvents, as shown in Figure 2D. After soaking for 24 hours, the solvent is separated from the *B. balsamifera* leaf pulp using filter paper. Then, the *B. balsamifera* leaf extract is separated from the solvent using Rotary Evaporate, as shown in Figure 2E, and the extract obtained is as shown in Figure 2F.

Samples are then tested for water content so that the samples are not easy for bacteria to grow; the moisture content of a good sample is below 5%. After the water content test, the dried *B. balsamifera* leaves are mashed using a blender to obtain *B. balsamifera* leaf powder. In this study, 20 kg of *B. balsamifera* leaves that had been selected after drying became 2.4 kg, and then the extraction process was carried out by the maceration method.

After placing 200 grams of *B. balsamifera* powder in three distinct containers, it was submerged in 1,000 mL of ethanol, n-hexane, and ethyl acetate and stirred once every 24 hours. After 24 hours, the mixture was filtered using filter paper to extract the filtrate. The residue is given another soaking in the solvent, which continues until the solvent loses its color (Asmilia et al. 2020; Seriana et al. 2021; Ernilasari et al. 2021). The filtrate obtained was dried by vacuum evaporation (Rotary evaporator) at a temperature of 50°C to obtain a thick extract of *B. balsamifera* leaf of each solvent as much as 180 g.

The water and ash content test of *B. balsamifera* extracts

The water content of *B. balsamifera* leaf extract was first tested for water content with the condition that the water content was not more than 10%. In addition, measurements of the ash content of the extract were also carried out with the condition that it must be below 10%. The extract's water content is measured as follows: *B. balsamifera* leaf extract was weighed as much as 3 grams and then put into a porcelain cup. Furthermore, the porcelain cup filled with ingredients was put into the oven. Samples were dried at 105°C for 3 hours, and the cup was cooled in the desiccator; after it cooled down, the extracts were weighed, and the water content was calculated using the following formula:

Water content = (B-C)/(B-A) x 100%

Where:
A = weight of the cup
B = weight of extracts before drying + cup
C = weight of extracts after drying + cup

Antibacterial tests

Antibacterial activity tests were conducted at the Microbiology Laboratory, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Banda Aceh, Indonesia. The stages of antibacterial testing are as Figure 3.

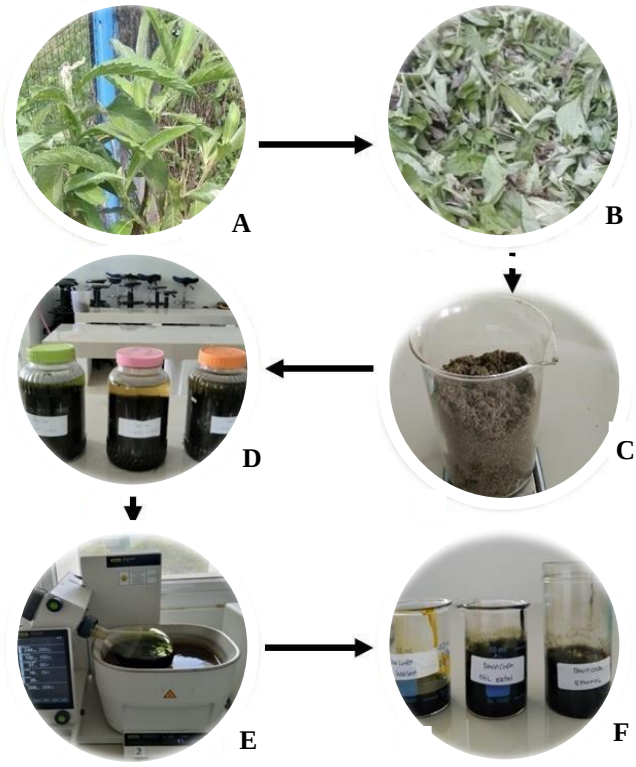

Figure 2. Preparation of *Blumea balsamifera* leaf extract

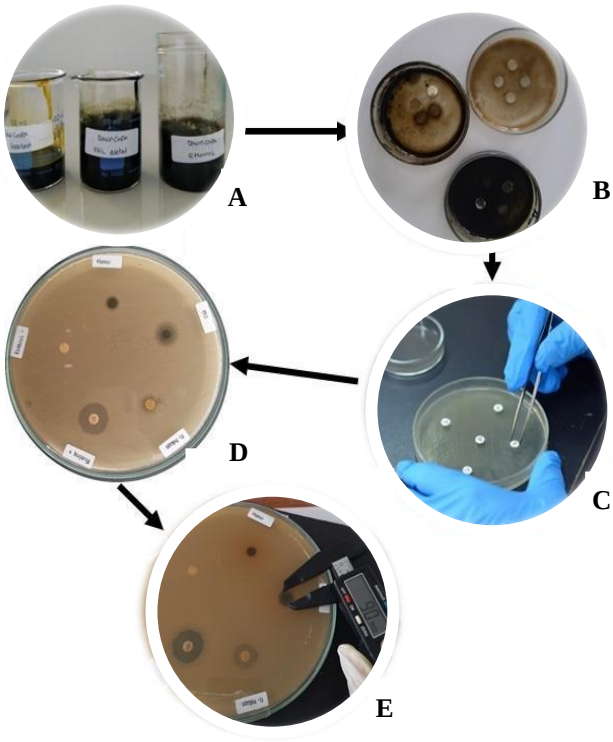

Figure 3. Process of antibacterial test

Figure 3 describes the antibacterial test process using Mueller Hinton Agar (MHA) media. Figure 3A shows *B. balsamifera* leaf extract obtained through the maceration method extraction process using three different types of solvents, i.e.: ethanol, ethyl acetate, and n-hexane. Blank disc OXOID brand antibiotic with a diameter of 6 mm was dipped in *B. balsamifera* leaf extract from 3 different solvents and waited for 20 minutes for the extract to seep into the disc (Figure 3B). Furthermore, the disc is placed into a petri dish filled with agar media with isolate *S. aureus* and *P. aeruginosa* (Figure 3C). After incubation for 24 hours, a clear zone is visible around the disc, which is not overgrown with bacteria (Figure 3D). Then, the area of the clear zone on each disc was measured to determine the inhibition of bacterial growth (Figure 3E).

The media used is Mueller-Hinton Agar media. The media that has been sterilized is poured as much as 75 mL per petri dish with a diameter of 15 cm. The test method was carried out by the disc diffusion method. Ethanol, ethyl, and n-hexane extracts were made into a solution by adding 10% DMSO + 0.5% Tween 80 solutions; ethyl and n-hexane extracts were insoluble in distilled water, while ethanol was soluble in ethanol as a solvent. Therefore, all extracts were dissolved with DMSO 10% + 0.5% Tween 80 solvent so that this antibacterial test was homogeneous (Walil and Roslim 2021). All extracts were made with a concentration of 100% because this test was carried out to determine which solvent had the widest zone of inhibition in the extract of *B. balsamifera* leaves.

Empty antibiotic discs (*blank disc brand* OXOID d=6mm) were immersed in each extract and allowed to stand for 20 minutes to absorb the extract into the disc (Morales et al. 2003). Then, the MHA media were swabbed with a cotton swab dipped with *S. aureus* and *P. aeruginosa* isolates. Discs dripped with extract, positive control, and negative are placed on the surface of the media swabbed with the test bacteria to be incubated and observed.

RESULTS AND DISCUSSION

Test the water content and ash content of extracts

The results extract water content test of *B. balsamifera* leaves obtained at 4.2%, while the ash content is 5.5%. Water level and ash level extract following the requirements water level that is not more than 10%. The test result of the water level and ash level extract *B. balsamifera* can be seen in Table 1. This table shows the water and ash content of the extract *B. balsamifera* filled the press standard requirements and can be used for antibacterial tests. The extract with a water content exceeding 10% can easily grow microorganisms and fungi, affecting the study results.

Antibacterial test

Antibacterial test results from ethanol, ethyl, and n-hexane extracts of *B. balsamifera* leaves can be seen in Table 2. where not all extracts produced inhibition zones on Mueller Hinton Agar, which had been grown with *S. aureus* and *P. aeruginosa*. The average inhibition zone that forms a large diameter is found in the test bacteria *S. aureus* and *P. aeruginosa*, extracts that can inhibit the large inhibitory zone against the two test bacteria, namely ethyl acetate extract.

Table 1. Results of the water and ash content test of *Blumea balsamifera* leaf extract

Test	***B. balsamifera* ethanolic extract (%)**	***B. balsamifera* ethyl extract (%)**	***B. balsamifera* n-hexane extract (%)**
Water content	4.20	4.15	4.20
Ash content	5.50	5.45	5.50

Table 2. Table of antimicrobial test results for *Blumea balsamifera* leaf

Bacteria test	Sample	Inhibitory zone diameter (mm)
S. aureus	*B. balsamifera* ethanolic extract	2.40
	B. balsamifera ethyl extract	9.20
	B. balsamifera n-hexane Extract	2.30
	Positive control	14.00
	Negative control	0.00
P. aeruginosa	*B. balsamifera* ethanol	0.00
	B. balsamifera ethyl	9.00
	B. balsamifera N-hexane extract	4.90
	Positive control	11.50
	Negative control	0.00

Note: Positive control: Gentamicin disc 10 µg, Negative control: Gel base carbopol 940

The inhibition zone formed on *S. aureus* against ethanol extract was 2.4 mm, ethyl acetate extract was 9.2 mm, n-hexane extract was 2.3 mm, positive control was 14 mm, and the negative control was 0 mm, as in Figure 4. The inhibition zone formed on *P. aeruginosa* against ethanol extract was 0 mm, ethyl extract was 9 mm, n-hexane extract was 4.9 mm, and positive control was 11.5 mm. The negative control showed negative results with an inhibition zone diameter of 0 mm, as in the following Figure 5.

According to the earlier study that was carried out by Katno et al. (2009) with *B. balsamifera* plant samples from Tawangmangu Karanganyar, Central Java, a dose of 92 mg/kg body weight of *B. balsamifera* leaves extracted using water as a solvent can reduce edema by up to 6.4%. The presence of severe edema or inflammation is a factor that slows the wound-healing process. The leaves of *B. balsamifera* reduce edema, which speeds up the healing process. Many researchers (Fan et al. 2015; Gito and Rochmawati 2018) found that extracts of *B. balsamifera* leaves taken from China and extracted with ethanol solvent were able to prevent the development of the microorganisms *Escherichia coli* and *S. aureus*, but differences in test results using different concentrations. Meanwhile, the results of this study varied using the type of solvent.

The results of the GCMS analysis of *B. balsamifera* leaves from Aceh are known to contain various compounds that play a role in wound healing, including borneol, jasmoline, camphor, and caryophyllene (Masyudi et al. 2022); these compounds are known important in wound healing (Fan et al. 2015; Pang et al. 2014). This study showed that Aceh's *B. Balsamifera* leaf extract contains antibacterial properties of up to 9.2 mm with strong inhibition. In line with another study by Pang et al. (2017) explained that *B. balsamifera* leaf extract had a better effect on wound healing on the skin of white rats (Pang et al. 2017; Lee et al. 2012).

The phytochemical content of *B. balsamifera* leaves was identified as containing flavonoids, alkaloids, steroids, tannins, and glycosides (Balangcod et al. 2012; Kinho et al. 2011; Pang et al. 2014). *B. balsamifera* originating from Tawangmangu, Bogor, and Malang comprised of tannins, flavonoids, L-campor, borneol, caryophyllene, -camphene, and humulene (Isnawati et al. 2016). *B. balsamifera* leaf extracts from China and Bangladesh have been shown to contain active compounds that function as antibacterial (Isnawati et al. 2016), anti-oxidant (Huang et al. 2006), anti-inflammatory (Yan et al. 2015; Pang et al. 2014) and anti-obesity (Kubota et al. 2009). *B. balsamifera* has long been used by the community for various types of diseases, such as wound healing. Traditionally, people use *B. balsamifera* leaves by squeezing and affixing them to the injured skin area. It is believed to prevent bacterial infection, so the wound heals faster and does not become chronic, such as the emergence of pus (Masyudi and Usman 2019; Nuryadin et al. 2017; BPS Aceh Selatan 2016).

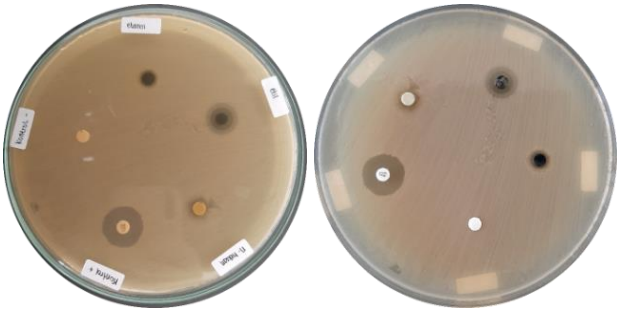

Figure 4. Diameter of the inhibition zone on the *Staphylococcus aureus*

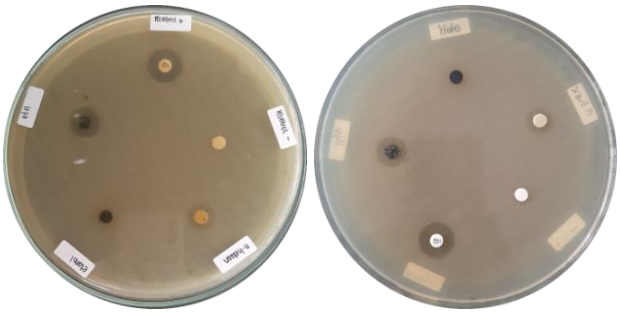

Figure 5. Diameter of the inhibition zone on the *Pseudomonas aeruginosa*

An inhibition test was carried out using the diffusion method to observe how much the active substance could kill certain bacteria. Inhibition tests can be done by *Kirby Bauer* (Matuschek et al. 2013). In this study, the test bacteria used were *S. aureus* and *P. aeruginosa*. These two bacteria are most commonly found in wounds. *S. aureus* was a flora of normal humans located in the skin, membranes, slime, and environment. *S. aureus* on healthy skin usually does not cause infection, but in the wound, if it enters blood flow or internal tissues, these bacteria can cause various infections (Balasubramanian et al. 2017; Tong et al. 2015; Van Belkum and Schrenzel 2014).

Antibacterial is one factor that accelerates wound healing; B. balsamifera leaves extracted from Aceh have an inhibitory power of up to 9.2 mm on the two test bacteria used. This explains that *B. balsamifera* from Aceh has the potential to be developed as a source of active compounds for wound treatment.

In conclusion, *B. balsamifera* leaves from Aceh have the potential as a wound medicine because they are proven to contain antibacterial. From the antibacterial test results of 3 types of *B. balsamifera* leaf extract against the test bacteria *S. aureus* and *P. aeruginosa*, it was found that the ethyl acetate extract of *B. balsamifera* leaves had the most extensive inhibition, namely 9.2 mm for *S. aureus* and 9 mm for *P. aeruginosa*. So, it is recommended to use Ethyl-acetate solvent for the *B. balsamifera* leaf extraction process.

ACKNOWLEDGEMENTS

The author, thanks to the MIPA Laboratory at Universitas Serambi Mekkah, Indonesia and the Microbiology Laboratory at the Faculty of Mathematics and Natural Sciences, Universitas Syiah Kuala, Indonesia, are acknowledged with gratitude by the authors. This study was made possible thanks to the financial support of the Indonesian Ministry of Research, Technology, and Higher Education.

REFERENCES

Asif M, Jafari SF, Iqbal Z, Revadigar V, Oon CE, Majid AS, Majid AM. 2017. Ethnobotanical and phytopharmacological attributes of Mesua ferrea: A mini review. J Appl Pharm Sci 7 (4): 242-251. DOI: 10.7324/JAPS.2017.70435.

Asmilia N, Fahrimal Y, Abrar M, Rinidar R. 2020. Chemical compounds of malacca leaf (*Phyllanthus emblica*) after triple extraction with N-hexane, ethyl acetate, and ethanol. Sci World J 2020: 2739056. DOI: 10.1155/2020/2739056.

Balangcod TD, Vallejo VL, Patacsil M, Apostol O, Laruan LM, Manuel J, Cortez S, Gutierrez RM. 2012. Phytochemical screening and Antibacterial activity of selected medicinal plants of Bayabas, Sablan, Benguet Province, Cordillera Administrative Region, Luzon, Philippines. Indian J Tradit Knowledge 11 (4): 580-585.

Balasubramanian D, Harper L, Shopsin B, Torres VJ. 2017. *Staphylococcus aureus* pathogenesis in diverse host environments. Pathog Dis 75 (1): 1-13. DOI: 10.1093/femspd/ftx005.

De Boer HJ, Cotingting C. 2014. Medicinal plants for women's healthcare in southeast Asia: A meta-analysis of their traditional use, chemical constituents, and pharmacology. J Ethnopharmacol 151 (2): 747-767. DOI: 10.1016/j.jep.2013.11.030.

BPS Aceh Selatan. 2016. Aceh Selatan dalam Data. Tapak tuan: BPS Aceh Selatan. [Indonesian]

Ernilasari E, Walil K, Fitmawati F, Roslim DI, Zumaidar Z, Saudah S, Rayhannisa R. 2021. Antibacterial activity of leaves, flowers, and fruits extract of *Etlingera elatior* from Nagan Raya District, Indonesia against *Escherichia coli* and *Staphylococcus aureus*. Biodiversitas 22 (10). DOI: 10.13057/biodiv/d221039.

Fan ZW, Pang YX, Wang K, Yu FL, Wang D, Yang Q, Ma QS, Li XT, Zou J, Zhang WQ, Wu LF. 2015. *Blumea balsamifera* oil for the acceleration of healing of burn injuries. Molecules 1: 17166-17179. DOI: 10.3390/molecules200917166.

Gito G, Rochmawati E. 2018. Effectiveness of modern wound dressing on the growth of *Staphylococcus aureus* bacteria. J Keperawatan 9 (2): 88. DOI: 10.22219/jk.v9i2.5160.

Gonzalez AC, Costa TF, Andrade ZD, Medrado AR. 2016. Wound healing - A literature review. Anais Brasileiros de Dermatologia 91 (5): 614-620. DOI: 10.1590/abd1806-4841.20164741.

Huang YL, Zhao ZG, Wen YX. 2006. Determination of total flavonoid in different sections of *Blumea balsamifera*. Guihaia 26 (1): 453-455.

Imamah IN. 2017. Pengaruh hidrogel *Centalla asiatica* untuk penyembuhan luka insisi. Jurnal Ilmiah Sehat Bebaya 1 (2): 125-131. [Indonesian]

Isnawati A, Raini M, Alegantina S. 2016. Standarisasi simplisia dan ekstrak etanol daun sembung (*Blumea balsamifera* (L)) dari tiga tempat tumbuh. Media Litbang Kesehatan 16 (2): 1-6. [Indonesian]

Katno, Haryanti S, Triyono A. 2009. Uji daya hambat ekstrak etanol daun sembung (*Blumea balsamifera*) terhadap pertumbuhan mikroba *E. coli*, *S. aereus* dan *C. albicans*. Jurnal Tumbuhan Obat Indonesia 2 (1). [Indonesian]

Kinho J, Diah IDA, Supratman T, Harwiyaddin K, Yermias K, Syamsir S, MC. 2011. Tumbuhan Obat Tradisional Di Sulawesi Utara Jilid I Kemeterian Kehutanan dan Lingkungan Hidup, Jakarta. [Indonesian]

Kubota H, Kojima-Yuasa A, Morii R, Huang X, Norikura T, Rho SN, Matsui-Yuasa I. 2009. Anti-obesity effect of *Blumea balsamifera* extract in 3T3-L1 preadipocytes and adipocytes. Am J Chin Med 37 (5): 843-854. DOI: 10.1142/S0192415X09007326.

Lee DG, Mok SY, Choi C, Cho EJ, Kim HY, Lee S. 2012. Analysis of apigenin in *Blumea balsamifera* Linn DC. and its inhibitory activity against aldose reductase in rat lens. J Agric Chem Environ 1 (1): 28-33. DOI: 10.4236/jacen.2012.11005.

Masyudi M, Hanafiah M, Rinidar R, Usman S, Marlina M. 2022. Phytochemical screening and GC-MS analysis of bioactive compounds of *Blumea balsamifera* leaf extracts from South Aceh, Indonesia. Biodiversitas 23 (3): 1346-1354. DOI: 10.13057/biodiv/d230319.

Masyudi, Usman S. 2019. Creating Synergy between Village Midwives and Traditional Midwives : To Reduce the Mortality Rate of Mothers and Babies : In the Central Kluet Sub-District Health Centre in South Aceh Creating Synergy between Village Midwives and Traditional Midwives : To. J Phys: Conf Ser 1232 (1): 012051. DOI: 10.1088/1742-6596/1232/1/012051.

Matuschek E, Brown DFJ, Kahlmeter G. 2013. Development of the EUCAST disk diffusion antimicrobial susceptibility testing method and its implementation in routine microbiology laboratories. Clin Microbiol Infect 20 (4): O255-O266. DOI: 10.1111/1469-0691.12373.

Morales G, Sierra P, Mancilla A, Paredes A, Loyola LA, Gallardo O, Borquez J. 2003. Secondary metabolites from four medicinal plants from northern Chile: Antimicrobial activity and biotoxicity against *Artemia salina*. Boletin de la Sociedad Chilena de Quimica 48 (2): 13-18. DOI: 10.4067/s0717-97072003000200002.

Nuryadin M, Herlina, Fithri, Annuria N. 2017. Formulasi dan uji penyembuhan luka gel sembung rambat. [Undergraduate Thesis]. Universitas Sriwijaya, Palembang. [Indonesian]

Organization WHO. 2013. WHO traditional med strategy: 2014-2023.

Pang Y, Wang D, Fan Z, Chen X, Yu F, Hu X, Wang K, Yuan L. 2014. *Blumea balsamifera*—A phytochemical and pharmacological review. Molecules 19 (7): 9453-9477. DOI: 10.3390/molecules19079453.

Pang Y, Wang D, Hu X. 2014. Experimental study effect of volatile oil from *Blumea balsamifera* (L.) DC. leaves on wound healing in mice. J Tradit Chin Med 34 (6): 716-724. DOI: 10.1016/S0254-6272(15)30087-X.

Pang Y, Zhang Y, Huang L, Xu L, Wang K, Wang D, Guan L, Zhang Y, Yu F, Chen Z, Xie X. 2017. Effects and mechanisms of total flavonoids from *Blumea balsamifera* (L.) DC. on skin wound in rats. Intl J Mol Sci 18 (12): 2766. DOI: 10.3390/ijms18122766.

Seriana I, Akmal M, Darusman D, Wahyuni S, Khairan K, Sugito S. 2021. Phytochemicals characterizations of neem (*Azadirachta indica* A . Juss) leaves ethanolic extract: an important medicinal plant as male. 14 (1): 343-350. DOI: 10.31788/ RJC.2021.1415899.

Singh A, Kumar A, Srivastava V. 2018. Extraction of bioactive compound from different medicinal plants and rhizospheric soil bacteria and their comparative study against human pathogens. J Pharmacognosy Phytochem 7 (6): 528-533.

Soekiman S. 2016. Infeksi Nosokomial di Rumah Sakit. Pertama. Edited by Mariyam. Surabaya. [Indonesian]

Tong SY, Davis JS, Eichenberger E, Holland TL, Fowler Jr VG. 2015. *Staphylococcus aureus* infections: Epidemiology, pathophysiology, clinical manifestations, and management. Clin Microbiol Rev 28 (3): 603-661. DOI: 10.1128/CMR.00134-14.

Van Belkum A, Schrenzel J. 2014. *Staphylococcus aureus*: The innocent culprit? Infect Genet Evol 21: 509. DOI: 10.1016/j.meegid.2013.09.001.

Viena V, Yunita I, Irhamni I, Saudah S, Ernilasari E. 2018. Biodiversitas tumbuhan obat oleh masyarakat gampong pulo seunong kecamatan tangse kabupaten pidie. Elkawnie: J Islamic Sci Technol 4 (1): 89-100. DOI: 10.22373/ekw.v4i1.3027. [Indonesian]

Walil K, Roslim DI. 2021. Antibacterial activity of leaves, flowers, and fruits extract of Etlingera elatior from Nagan Raya District, Indonesia against *Escherichia coli* and *Staphylococcus aureus*. Biodiversitas 22 (10): 4457-4464. DOI: 10.13057/biodiv/d221039.

Yan X, Xiang L, Jian-wei C. 2015. Anti-inflammatory, analgesic and hemostasis activities of different extracting fractions of *Blumea balsamifera* Residue. Nat Prod Res Dev 27 (6): 1086-1091. DOI: 10.16333/j.1001-6880.2015.06.027.

Yuan H, Ma Q, Ye L, Piao G. 2016. The traditional medicine and modern medicine from natural products. Molecules 21: 559. DOI: 10.3390/molecules21050559.