

Effectiveness Of Lime Leaves (*Citrus aurantifolia*) as an Antibacterial For Cut Wound Infections Caused By *Staphylococcus aureus* In Male Wistar Rats

Marshall Jeremia Nadapdap¹, Linda Chiuman^{2*}, Qori Fadillah³

¹ Department of Biomedical Science, Faculty of Medicine, Dentistry and Health Science, Universitas Prima Indonesia, Medan

² Center of Excellence for Phytodegenerative and Lifestyle Medicine, Faculty of Medicine, Dentistry and Health Science, Universitas Prima Indonesia, Medan

³ Department Microbiology, Faculty of Medicine, Dentistry and Health Science, Universitas Prima Indonesia, Medan

*E-mail : : lindachiuman@unprimdn.ac.id

ABSTRACT

Skin infections caused by *Staphylococcus aureus* are a health problem that often hinders the wound healing process due to the bacteria's ability to form biofilms and resistance to antibiotics. The increasing cases of resistance require the development of alternative therapies based on natural ingredients. Lime peel (*Citrus aurantifolia*) contains flavonoids, saponins, tannins, alkaloids, and glycosides that have the potential to be antibacterial agents and wound-healing agents. This study aims to evaluate the antibacterial activity of an ethanol extract from lime peel against *S. aureus* and its effectiveness in accelerating the healing of infected wounds in vivo. Phytochemical screening showed positive results for flavonoids, saponins, tannins, alkaloids, and glycosides. Characterization tests showed a water content of 8.64%, a total ash content of 5.62%, and an ethanol-soluble extract content of 18.14%, in accordance with the Indonesian Herbal Pharmacopoeia standards. Antibacterial activity showed an increase in the diameter of the inhibition zone from 8.07 ± 0.05 mm at a concentration of 20% to 22.47 ± 0.05 mm at 100%, approaching the positive control ciprofloxacin (28.32 ± 0.12 mm). Statistical analysis using the Kruskal–Wallis test showed significant differences between groups ($p < 0.05$) with homogeneous data. Histopathologically, the extract group showed a lower number of fibroblasts (28.22 ± 0.72) and blood vessels (5.00 ± 4.80) compared to the negative control, as well as an increase in collagen density at a score of 2, indicating an optimal healing process. It was concluded that the ethanol extract of lime peel has antibacterial activity and accelerates the healing of wounds infected with *S. aureus* by increasing collagen formation and regulating the inflammatory response.

Keywords: *Citrus aurantifolia*, flavonoids, antibacterial, wound healing, *Staphylococcus aureus*.

INTRODUCTION

As the body's main barrier of defense, the skin is regularly subjected to trauma or injury, which can lead to infection. These infections typically develop as side effects from physical wounds, surgical treatments, or insect bites that damage the skin's outer layers or mucosa. They can form inside or near muscles, subcutaneous tissues, and hair follicles. Nonetheless, the body's chemical defense systems, the skin's natural microbiota, and its acidic pH all play important roles in halting the colonization of harmful microbes (Carvalho et al., 2021).

A wound occurs when a tissue's continuity or development is disrupted by an injury or surgery; physical or physiological contact can also result in skin tissue damage. An incision wound is one that results from being sliced by a sharp object, as one that happens during surgery or another procedure. Large blood arteries are frequently damaged by this kind of wound if the incision is sufficiently deep (about ± 2 cm) and subcutaneous (Kaban et al., 2020).

Wound skin infections represent a considerable health issue, frequently attributed to the bacterium *Staphylococcus aureus*. This bacterium is recognized as a principal etiological agent of skin and soft tissue infections, and its capacity to form biofilms and exhibit resistance to numerous antibiotics poses a significant therapeutic challenge. Given the escalating global antibiotic resistance, there is an urgent necessity for the exploration of safer and more effective alternative therapies (Panjaitan et al., 2022).

Skin abscesses, which are collections of pus that develop as a result of the immune system's reaction to a bacterial infection, are a common type of infection. This abscess typically manifests as a painful, large, red lump on the skin, frequently accompanied by fever and other systemic signs. When *Staphylococcus aureus* enters the tissue through a wound or other skin damage, the process of abscess formation starts (Dewi et al., 2023). This bacteria then causes a severe inflammatory response by infecting the subcutaneous tissue. Immune cells like neutrophils will attempt to combat *S. aureus* when it infects tissue (Zebua et al., 2024). At the infection site, neutrophils will assemble and release pro-inflammatory chemicals and enzymes that kill germs. But the surrounding tissue may also sustain harm as a result of this reaction. *S. aureus* has the ability to build a fibrin capsule to shield itself from the host's immune system attack. In addition to preventing the spread of infection, this capsule provides the perfect conditions for bacteria to grow unhindered (Kaban, Ginting, et al., 2024). Diabetes mellitus, obesity, immunosuppressive medication use, and other illnesses that compromise the immune system are among the factors that can raise the risk of skin abscesses. This virus can also spread through direct contact with polluted settings or infected people. In order to extract pus from inside the abscess, an incision and drainage operation are typically used to treat skin abscesses (Zhao et al., 2020). Furthermore, systemic antibiotics are frequently required to stop additional problems, particularly if the infection has spread to other tissues or if the patient has underlying medical difficulties (Nasri et al., 2025).

One nation with a wealth of natural resources is Indonesia. Many of these plants are regarded as herbal remedies because our predecessors utilized them to cure a variety of illnesses. Lime is a common herbal plant used in Indonesian traditional medicine because it contains alkaloids, flavonoids, essential oils, and saponins that can be used to cure wounds. Researchers are interested in testing the efficacy of lime leaf ethanol extract as a wound healer in mice infected with *Staphylococcus aureus* because of its high secondary metabolite concentration.

METHODS

Instrument, Reagents, and Medium

The instruments used in this study were glass jars, rotary evaporators, test tubes, test tube shelves, micropipets, yellow tips, blue tips, digital balance, vortex, mortar, Erlenmeyer, diameter, steel barrier, tweezers, aluminum foil, petri dishes, bunsen, incubator and calipers. Materials used in this study were 96% ethanol, sterile distilled water, 500 mg ciprofloxacin, sterile PZ, *Staphylococcus aureus* bacteria stock, Standard Mc. Farland 0.5, and nutrient agar.

Lime peel extract preparation and phytochemical analysis

4.5 liters of 96% ethanol were macerated with 500 grams of powdered lime peel. For three days, 500 grams of powder were macerated by immersing them fully in 1.5 liters of 96% ethanol. After that, aluminum foil was used to line the beaker. It was filtered with filter paper after soaking for three days. A vacuum evaporator was used to mix and concentrate the resultant filtrates until a thick extract was produced. Glycosides, alkaloids, flavonoids, tannins, and saponins were all subjected to phytochemical study. Macroscopic and microscopic

inspections, water and total ash content measurements, acid-insoluble ash content measurements, water-soluble extract measurements, ethanol-soluble extract measurements, and drying loss measurements were all part of the simplex's quality testing and characterization (Permadi et al., 2024).

Animals

32 healthy adult male Wistar rats, ages 2-3 months, weighing 180-200 grams on average, were used in this investigation. Every sample was allowed to acclimate for seven days. After acclimatization, the animals were weighed and given normal laboratory food and water. All of the study's animals received humane treatment in compliance with global standards.

Antibacterial Activity Test for Lime Peel Extract

By weighing 0.2 g, 0.4 g, 0.6 g, 0.8 g, and 1 g of lime peel extract, respectively, and dissolving each in 1 ml of sterile distilled water, the test solutions were made at concentrations of 20%, 40%, 60%, 80%, and 100% w/v. Five milliliters of NA were added to a sterile petri dish and left to set. After that, three fertilizer cylinders were set up, with three replicates for each treatment, and the spacing between them was changed. Next, 20 milliliters of NA medium were added to the bacterial solution. After pouring the slurry onto a Petri dish, a steel cylinder was positioned within as a second layer, and the fluid was left to harden. The steel cylinders were aseptically extracted from the Petri dishes, forming wells, following compaction. Test solutions containing 50–100 µl of different lime peel extracts at varying dosages, negative controls, and positive controls were each placed into a separate well. The petri dishes were then incubated for twenty-four hours at 37 degrees Celsius. Following incubation, the inhibitory zones were examined, and a caliper was used to quantify their diameters (Julaeha et al., 2024; Nasri et al., 2024).

Preparation and creation of wounds on test animals

The test animals' fur was shaved smooth on their backs the day before the incision was done. A scalpel was used to make two millimeters deep and two centimeters long wounds on the mouse's back. A 0.1 mL subcutaneous (sc) injection of ketamine was used to put the mice to sleep. The rat's back was treated with 70% alcohol prior to therapy. Each location received a 0.2 mL suspension of *Staphylococcus aureus* germs. One gram of lime leaf ethanol extract preparation was applied twice daily, in the morning and evening, to rabbit skin infected with *Staphylococcus aureus* germs. The skin was then wrapped with sterile gauze and adhesive tape (Falcone et al., 2021; Palette, 2023).

Testing the effectiveness of healing infected wounds

Depending on the treatment group, each rabbit with a back injury had a cut wound therapy infected with 0.2 ml of *Staphylococcus aureus*. In order to determine whether the wound was impacted by the bacterial infection, *Staphylococcus aureus* was administered. Rabbits with cuts infected with *Staphylococcus aureus* were treated twice daily, in the morning and the evening, from day 0 to day 12. The area that was cut had a *Staphylococcus aureus* infection. In order for a wound to be deemed healed, it had to be visually closed or its length had reached zero (Basov et al., 2021; Ulfa et al., 2020).

Histopathology Test Observation

According to the journal histological preparations are made using a skin sample that has been fixed with 10% formalin, dehydrated, and then cleaned three times with 10% formalin, 70% alcohol, 96% alcohol, three times with absolute alcohol, three times with xylol, and twice with liquid paraffin in a 23-hour period. Following a half-hour cooling period, the sample is blocked with liquid paraffin and then sliced using a microtome. Staining is done first using the HE method, which involves soaking in xylol I, II, and III for five minutes each, before mounting. Lastly, it soaks for five minutes in pure alcohol I and II. It is soaked in distilled water for one minute before to being immersed in the HE solution for fifteen minutes. The

sample is steeped in distilled water once more for one minute, followed by five to seven minutes in 10% acid alcohol, and then twice for one minute and fifteen minutes. Eosin is then used to stain it. After that, the stained slides were submerged four times for three minutes each in 96% alcohol. After that, they spent five minutes being washed in xylol I and xylol II. This study looked at the density of collagen fibers, the number of blood vessels, and the number of fibroblasts (Kaban, Nasri, et al., 2024; Nuralifah et al., 2022).

Data Analysis

To test the effectiveness of lime leaf ethanol extract on the healing of cuts infected with *Staphylococcus aureus* in rabbits, all data were statistically analyzed using ANOVA (Analysis of Variance).

RESULTS

The results of the phytochemical screening test showed that lime peel contained flavonoids, saponins, tannins, and alkaloids.

Table I shows the results of the phytochemical screening test on the ethanol extract of lime leaves.

Table 1. Secondary Metabolites of Ethanol Extract of Lime Leaves

NO	Compound Components	Identification Results
1.	Sapoin	Positive
2.	Tannin	Positive
3.	Flavonoid	Positive
4.	Alkaloid	Positive
5.	Glycoside	Positive

An essential first step in evaluating the quality of raw materials for traditional medicines is the characterization of crude medications. Before the crude medicine is used in the extraction procedure or preparation formulation, this test is carried out to guarantee its consistency, purity, and stability. Moisture content, water-soluble extractives, ethanol-soluble extractives, total ash content, and acid-insoluble ash content are among the characteristics that have been established. The result of characterization results of lime leaf simplex can be seen in table 2.

Table 2. Characterization Results Of Lime Leaf Simplex

NO	Parameter	Hasil
1.	Moisture content	8.64%
2.	Water-soluble extractive value	26.67%
3.	Ethanol-soluble extractive value	18.14%
4.	Total ash content	5.62%
5.	Acid-insoluble ash content	0.35%

The results of the effectiveness test of lime peel extract against the bacteria that causes skin wound infections, namely *Staphylococcus aureus*, are presented in Figure 1 and Table 3.

Table 3. Characterization Results Of Lime Leaf Simplex

NO	Sampel	Result ± SD
1.	Lime Leaf Ethanol Extract 20%	8.07 ± 0.05
2.	Lime Leaf Ethanol Extract 40%	9.37 ± 0.06
3.	Lime Leaf Ethanol Extract 60%	11.80 ± 0.06
4.	Lime Leaf Ethanol Extract 80%	15.72 ± 0.10

5.	Lime Leaf Ethanol Extract 100%	22.47 ± 0.05
6.	Positive Control	28.32 ± 0.12
7.	Negative Control	0.00 ± 0.00

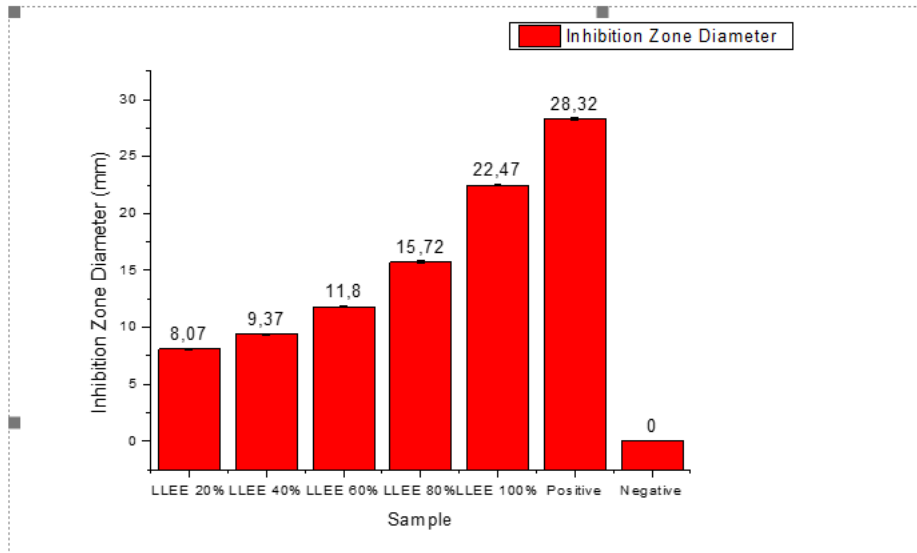
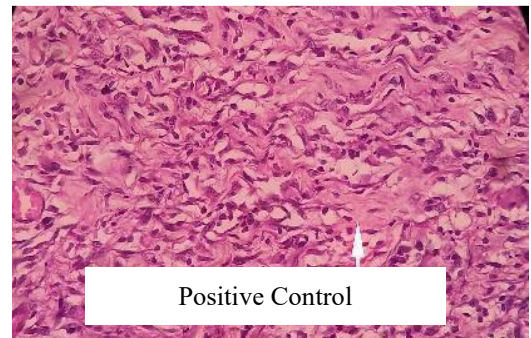
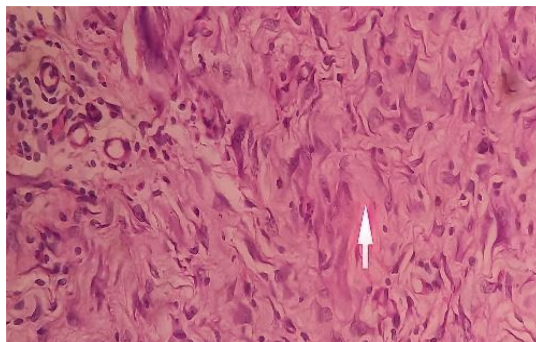


Figure 1. Sample Inhibition Zone Value Diagram

The density of collagen fibers formed during the wound healing process was calculated after HE staining and observed using an Olympus BX51 microscope and an Olympus DP 20 camera at 10 x 10 magnification over three fields of view. A pink collagen image was obtained, which was then calculated using a scoring method. The results of the collagen density can be seen in Figure 2 and Table 4.

Table 4. Collagen Fiber Density Scoring Results

No	Sample	Skor			
		1	2	3	4
1.	Lime Leaf Ethanol Extract	1	8	0	0
2.	Positive Control	0	1	8	0
3.	Negative Control	0	0	0	9



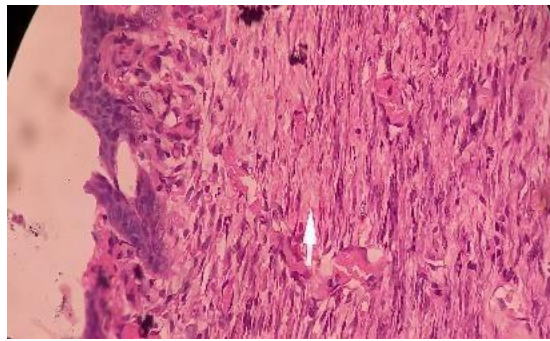
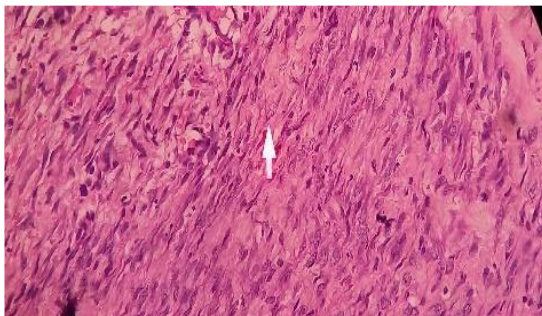


Figure 2. Histop: Negative Control **1 Fiber Density**

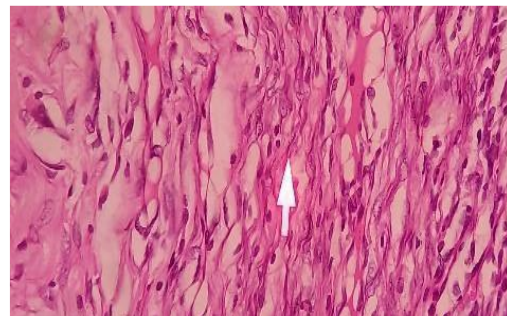
Examination of the number of fibroblasts and histopathological description of the number of fibroblasts can be seen in figure 3 and table 5.

Table 5. Average Number of Fibroblasts

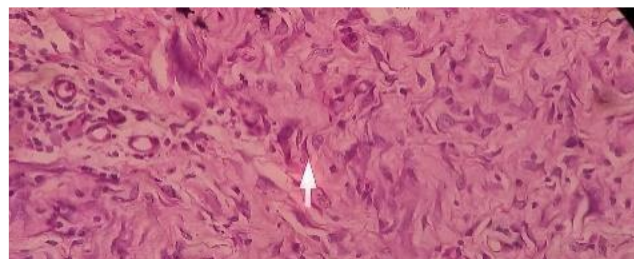
NO	Sampel	Result ± SD
1.	Lime Leaf Ethanol Extract	28.22 ± 0.72
2.	Positive Control	18.22 ± 0.53
3.	Negative Control	96.67 ± 1.45



Lime Leaf Ethanol Extract



Positive Control



Negative Control

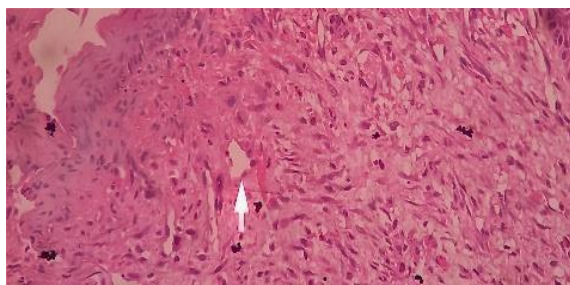
Figure 3. Histopathological picture of fibroblast cells.

The number of blood vessels and histopathology results of blood vessels can be seen in the table 6 and figure 4.

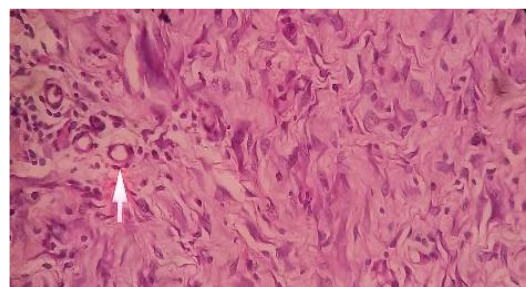
Table 6. Average Number of Fibroblasts

NO	Sampel	Result ± SD
----	--------	-------------

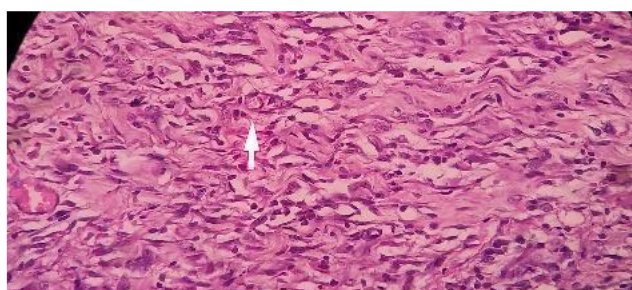
1.	Lime Leaf Ethanol Extract	5,00 ± 4,80
2.	Positive Control	3,00 ± 1,80
3.	Negative Control	10,67 ± 1,00



Lime Leaf Ethanol Extract



Positive Control



Negative Control

Figure 4. Histopathological Image of Blood Vessel Count.**DISCUSSION**

Flavonoids, saponins, tannins, and alkaloids are all found in lime peel, according to phytochemical studies. Because of their anti-inflammatory properties, lime flavonoids have an impact on wound healing and healing time (Anggraeny et al., 2024). The ethanol extract of lime peel (*Citrus aurantifolia*) contains flavonoids, saponins, tannins, alkaloids, and glycosides, according to the results of the phytochemical screening (Jafari & Shahsavar, 2021). These substances are known to possess antibacterial and wound-healing pharmacological properties. By decreasing the synthesis of pro-inflammatory mediators like TNF- α and IL-6 and by promoting collagen synthesis and fibroblast proliferation during the wound proliferation phase, flavonoids have anti-inflammatory and antioxidant properties (Shukla & Gupta, 2008). While tannins act as astringents that aid in wound closure and inhibit microbial growth in the wound region, saponins stimulate angiogenesis and re-epithelialization. Additionally, alkaloid concentration contributes to granulation acceleration and increased cell migration. These results are in line with studies conducted by (Kumar & More, 2019) (Johnson et al., 2020), which found that the combination of these phytochemical substances promotes skin tissue regeneration through local immunomodulatory and synergistic antioxidant mechanisms. With a moisture content of 8.64%, total ash content of 5.62%, acid-insoluble ash content of 0.35%, water-soluble extract content of 26.67%, and ethanol-soluble extract content of 18.14%, the crude drug's characterisation revealed good quality results. The crude medication satisfies the requirements for stability and purity for use as an ingredient in traditional medicine since these values fall within the bounds established by the Indonesian Herbal Pharmacopeia, Second Edition. While the relatively high levels of ethanol and water-soluble solids content indicate a decent number of polar and semipolar

metabolites, such as flavonoids and glycosides, which are important to the extract's biological action, the low water content suggests a low danger of microbial development. In the test for antibacterial activity against *Staphylococcus aureus*, the diameter of the inhibitory zone increased with increasing extract concentration: 8.07 ± 0.05 mm (20%), 9.37 ± 0.06 mm (40%), 11.80 ± 0.06 mm (60%), 15.72 ± 0.10 mm (80%), and 22.47 ± 0.05 mm (100%). This number is significantly higher than the negative control (0 mm) and is comparable to the inhibitory power of the positive control ciprofloxacin, which is 28.32 ± 0.12 mm. The Kruskal-Wallis statistical test analysis revealed a significant difference between the groups ($p < 0.05$), suggesting that antibacterial activity was considerably impacted by increasing extract concentration. Additionally, the data exhibits high group homogeneity of variance, indicating that treatment differences rather than random data spread are responsible for the observed mean differences. These outcomes corroborate those of Mahmoud et al. (2021), who found that citrus flavonoids can stop *S. aureus* from growing by preventing the formation of biofilms and altering the permeability of bacterial cell membranes. The group treated with lime peel ethanol extract had more fibroblasts (28.22 ± 0.72 cells/field of view) than the positive control (18.22 ± 0.53) and less than the negative control (96.67 ± 1.45), according to histopathological analysis of wound tissue. According to physiological principles, collagen remodeling has taken place when the quantity of fibroblasts in the late stage of wound healing declines. The angiogenesis phase had moved toward tissue maturation, as seen by the extract group's decreased blood vessel count (5.00 ± 4.80) in comparison to the negative control (10.67 ± 1.00). The extract therapy had a significant impact on the tissue regeneration process, as evidenced by the significant differences between groups ($p < 0.05$) in the Kruskal-Wallis test on the parameters of fibroblast and blood vessel count. The group that received the extract demonstrated dominance in the collagen fiber density observation data, scoring a score of 2, followed by the positive control at a score of 3, and the negative control at a score of 4. This suggests that, in comparison to untreated wound tissue, wound tissue treated with lime extract experiences a more regular healing process. A good remodeling phase is consistent with the more mature and well-organized collagen that is generated. According to the Kruskal-Wallis test, this difference in collagen scores is likewise significant ($p < 0.05$), suggesting that extract administration has a genuine biological impact on enhancing the quality of wound healing. Angiogenesis is altered and the amount of fibroblasts is controlled. This process is thought to be connected to the antibacterial and antioxidant properties of tannins, flavonoids, and saponins, which lower oxidative stress in the wound region, stop harmful bacteria from growing, and speed up tissue regeneration. These results are in line with studies by Rahman et al. (2023) and Jafari et al. (2020), which found that phenolic compounds in the Citrus genus have potent wound-healing properties by speeding up epithelial closure and decreasing neutrophil infiltration.

CONCLUSION

Ethanol extract of lime leaves can inhibit the growth of *Staphylococcus aureus* bacteria and accelerate the healing of cuts in mice induced by *Staphylococcus aureus* bacteria.

ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to the Faculty of Medicine, Dentistry, and Health Sciences, Biomedical Study Program, Universitas Prima Indonesia, for providing research facilities, laboratory access, and administrative support throughout this study. The authors also extend their appreciation to the staff of the Pharmacognosy and Microbiology Laboratories for their valuable technical assistance during the antibacterial and histopathological analyses. Special thanks are given to all students and laboratory assistants who contributed to the completion of data collection and animal handling. This research was

conducted as part of the institutional initiative to develop natural-based therapeutic agents for infectious wound management.

REFERENCES

- Anggraeny, Y. N., Setiasih, S., Puspito, S., Widodo, S., Wardi, W., Prihandini, P. W., Antonius, A., Istiqomah, N., Haryanto, B., & Kurniawati, A. (2024). Profile of secondary metabolites of *Citrus hystrix* DC from several solvents and its potential as an antibacterial substance. *IOP Conference Series: Earth and Environmental Science*, 1292(1), 012018.
- Basov, A. A., Fedosov, S. R., Malyshko, V. V., Elkina, A. A., Lyasota, O. M., & Dzhimak, S. S. (2021). Evaluation of effectiveness of a new treatment method for healing infected wounds: An animal model. *Journal of Wound Care*, 30(4), 312–322.
- Carvalho, M. T., Araújo-Filho, H. G., Barreto, A. S., Quintans-Júnior, L. J., Quintans, J. S., & Barreto, R. S. (2021). Wound healing properties of flavonoids: A systematic review highlighting the mechanisms of action. *Phytomedicine*, 90, 153636.
- Dewi, N. P., Vedora, M. P., Vani, A. T., Abdullah, D., & Triansyah, I. (2023). Effect Of Aloin Extract On The Increase Of Fibroblas Cell Expression On Healing Of Wound Wounds Of Horse White Rats (*Rattus norvegicus*) By The Aging Process. *MSJ: Majority Science Journal*, 1(4), 171–179.
- Falcone, M., De Angelis, B., Pea, F., Scalise, A., Stefani, S., Tasinato, R., Zanetti, O., & Dalla Paola, L. (2021). Challenges in the management of chronic wound infections. *Journal of Global Antimicrobial Resistance*, 26, 140–147.
- Jafari, M., & Shahsavari, A. (2021). The effect of foliar application of melatonin on changes in secondary metabolite contents in two citrus species under drought stress conditions. *Frontiers in Plant Science*, 12, 692735.
- Johnson, B. Z., Stevenson, A. W., Prêle, C. M., Fear, M. W., & Wood, F. M. (2020). The role of IL-6 in skin fibrosis and cutaneous wound healing. *Biomedicines*, 8(5), 101.
- Julaeha, E., Puspita, W. R., Permadi, N., Harja, A., Nurjanah, S., Wahyudi, T., & Al-Anshori, J. (2024). Optimization of *Citrus aurantifolia* peel extract encapsulation in alginate-gelatin hydrogel microbeads for antibacterial wound dressing applications. *Carbohydrate Polymer Technologies and Applications*, 7, 100406.
- Kaban, V. E., Aritonang, J. O., Hasibuan, Y. C., & Meliala, D. I. P. (2020). Efektivitas Penyembuhan Luka Sayat Menggunakan Salep Ekstrak Etanol Daun Senggani (*Melastoma Malabathricum* L.) Pada Kelinci. *Jurnal Penelitian Farmasi & Herbal*, 2(2), 8–14.
- Kaban, V. E., Ginting, J. G., Nasri, N., Sagala, H. U. B., & Tarigan, S. A. B. (2024). Uji Efektivitas Gel Ekstrak Daun Jarak Pagar (*Jatropha Curcas* L.) sebagai Penyembuhan Luka Sayat. *INSOLOGI: Jurnal Sains Dan Teknologi*, 3(4), 432–441.
- Kaban, V. E., Nasri, N., Rani, Z., Suci, N., Sekali, E. S. K., & Sagala, H. U. B. (2024). The effect of turmeric parent extract gel (*Curcuma longa* Linn) on incision wound healing in male white rats (*Rattus norvegicus*). *Journal of Pharmaceutical and Sciences*, 616–627.
- Kumar, M., & More, D. (2019). Phytochemical analysis and bioactivity of selected medicinal plant of butterfly-pea (*Clitoria ternatea* L.) used by Kolam tribe Addjoing region of Telangana and Maharashtra states. *Pharma Innovation*, 8(1), 417–421.
- Nasri, N., Kaban, V. E., Lubis, M. F., Nugraha, S. E., Wahyudi, W., Tania, C. G., Suci, N., & Rani, Z. (2025). Exploring Antioxidant, Antibacterial, and Toxicity Prediction of Purslane Herb (*Portulaca oleracea* L.) from Several Extraction Solvents. *Palestinian Medical and Pharmaceutical Journal (Pal. Med. Pharm. J.)*, 9999(9999), None-None.
- Nasri, N., Satria, D., Kaban, V. E., Tania, C. G., Syahputra, H. D., & Rani, Z. (2024). Antibacterial Potential of Ethanolic Extract of Avocado Leaves (*Persea americana* mill.) against Clinical Isolate of *Klebsiella pneumoniae* and *Proteus mirabilis*. *Trends in Sciences*, 21(7), 7821–7821.

- Nuralifah, N., Parawansah, P., & Trisetia, M. (2022). Histopatologi organ pankreas tikus DM tipe 2 yang diberi ekstrak etanol daun gedi merah (*Abelmoscus manihot* L. Medik). *Journal Syifa Sciences and Clinical Research (JSSCR)*, 4(1).
- Palette, S. N. (2023). Efek Ekstrak Daun Jarak Pagar (*Jatropha Curcas* L.) Terhadap Penyembuhan Luka Pada Mukosa Rongga Mulut (Ulser Traumatik) Tikus Putih Jantan Galur Wistar (*Rattus Norvegicus*)= Effects Of Daun Jarak Pagar Leaf Extract (*Jatropha Curcas* L.) On Wound Healing In Oral Mucosa (Traumatic Ulcer) Of Wistar Male White Rats (*Rattus norvegicus*) [PhD Thesis, Universitas Hasanuddin]. <http://repository.unhas.ac.id/id/eprint/34331/>
- Panjaitan, J., Girsang, E., & Chiuman, L. (2022). Effectiveness of temulawak (*Curcuma xanthorrhiza*) ointments as wound healing agents in wistar rats. *Jurnal Teknologi Laboratorium*, 11(2), 95–104.
- Permadi, N., Nurzaman, M., Doni, F., & Julaeha, E. (2024). Elucidation of the composition, antioxidant, and antimicrobial properties of essential oil and extract from *Citrus aurantifolia* (Christm.) Swingle peel. *Saudi Journal of Biological Sciences*, 31(6), 103987.
- Shukla, S., & Gupta, S. (2008). Apigenin-induced prostate cancer cell death is initiated by reactive oxygen species and p53 activation. *Free Radical Biology and Medicine*, 44(10), 1833–1845.
- Ulfa, A. M., Marcellia, S., & Rositasari, E. (2020). Efektivitas formulasi krim ekstrak kulit jeruk nipis (*Citrus aurantifolia-pericappium*) sebagai pengobatan luka sayat stadium II pada tikus putih (*Rattus novergicus*) galur wistar. *Jurnal Farmasi Malahayati*, 3(1), 42–52.
- Zebua, W. I., Chiuman, L., & Fachrial, E. (2024). Histopathological evaluation of green betel leaf extract ointment on incision wounds infected with *Staphylococcus aureus* in wistar rats. *Jurnal Teknologi Laboratorium*, 13(2), 71–82.
- Zhao, H., Huang, J., Li, Y., Lv, X., Zhou, H., Wang, H., Xu, Y., Wang, C., Wang, J., & Liu, Z. (2020). ROS-scavenging hydrogel to promote healing of bacteria infected diabetic wounds. *Biomaterials*, 258, 120286.