Indonesian Journal of Global Health Research
Volume 7 Number 1, February 2025
e-ISSN 2715-1972; p-ISSN 2714-9749
http://jurnal.globalhealthsciencegroup.com/index.php/IJGHR

EFFECTIVENESS OF CENTELLA ASIATICA (PEGAGAN) SPRAY GEL ON PERINEAL WOUND HEALING IN POSTPARTUM WOMEN

Nanda Lutfia Salsabila[1], Diyah Fatmasari[1], Sri Wahyuni[2]
[1]Politeknik Kesehatan Kemenkes Semarang, Jl. Tirto Agung, Pedalangan, Banyumanik, Semarang, Central Java 50268, Indonesia
[2]Politeknik Kesehatan Kemenkes Surakarta, Jl. Ksatria No. 2 Danguran, Klaten Selatan, Klaten, Central Java 57425, Indonesia
*nndlutfias99@gmail.com

ABSTRACT

Perineal wounds in postpartum mothers can potentially cause infections. The perineal area exposed to lochia and moisture creates an environment conducive to bacterial growth, thus hindering the wound healing process. Infections of perineal wounds can involve various types of bacteria that naturally colonize the skin and genital mucosa. The application of centella asiatica spray gel is one of the non-pharmacological methods for healing perineal wounds in postpartum mothers. This study aims to determine the effectiveness of applying centella asiatica spray gel 3 times a day with a concentration of 25% for 7 days on perineal wound healing and the growth of Staphylococcus aureus bacteria in postpartum mothers. This is a True Experimental study with a pretest–posttest control group design. Based on the inclusion criteria of second-degree perineal wounds with sutures were selected using random sampling, 17 participants to receive centella asiatica spray gel and 17 participants received standard dry-clean care. The level of wound healing was measured using the REEDA score. The growth of Staphylococcus aureus bacteria was measured using a colony counter. REEDA score data were analyzed using the Friedman and Mann-Whitney tests, while Staphylococcus aureus growth was analyzed using the Wilcoxon and Mann-Whitney tests. Based on the average decrease in REEDA scores by 1.06, the application of centella asiatica spray gel was effective for perineal wound healing (p=0.000). There was a significant difference in the average growth of S.aureus (p=0.040) in perineal wounds of postpartum mothers, with the intervention group showing an average difference of 6.34. The application of centella asiatica spray gel 3 times a day with a concentration of 25% for 7 days was effective for perineal wound healing and reducing Staphylococcus aureus growth in postpartum mothers.

Keywords: centella asiatica; staphylococcus aureus; spray gel; perineal wound; postpartum

How to cite (in APA style)
Salsabila, N. L., Fatmasari, D., & Wahyuni, S. (2024). Effectiveness of Centella Asiatica (Pegagan) Spray Gel on Perineal Wound Healing in Postpartum Women. Indonesian Journal of Global Health Research, 7(1), 69-78. https://doi.org/10.37287/ijghr.v7i1.3960.

INTRODUCTION

Perineal injury refers to tissue damage that occurs due to tearing in the birth canal, either from rupture or episiotomy, which typically happens during childbirth. Several factors can lead to perineal injury in postpartum mothers, including uncontrolled and unassisted precipitous labor, difficulty stopping the pushing pressure, and edema and fragility of the perineum. Other contributing factors from the fetal perspective include a large baby size, abnormal head position, breech birth, and shoulder dystocia (Wahyuningsih, 2018).

According to the World Health Organization (WHO) in 2017, there were approximately 2.7 million cases of perineal injuries among mothers giving birth worldwide, with around 50% of these incidents occurring in Asia. This number is expected to rise to 6.3 million cases by 2050 (World Health Organization, 2019). The World Health Organization (WHO) also reported that in Indonesia, 75% of the 1,951 mothers who gave birth vaginally experienced perineal injuries, with 57% of them undergoing perineal suturing. Of this percentage, 8% were due to episiotomy tears, while 29% were due to spontaneous tears (World Health Organization, 2015).

Globally, postpartum women who experience infection are around 0.1% - 23.6% and those who experience wound dehiscence are 0.21% - 24.6% (Jones et al., 2019). The incidence of infection experienced by postpartum women due to perineal wounds reached 1.1% (Woodd et al., 2019). The incidence of postpartum infection in Indonesia is 2.7% with 0.7% of cases developing into acute infection (Darulis et al., 2021). The prevalence of perineal wound in Indonesia in the age group of 25-30 years reached 24%, while in the age group of 32-39 years reached 62%. In a total of 20 million women giving birth in Indonesia, around 85% experience birth canal injuries. Of this percentage, 35% experience perineal wounds, 25% experience cervical tears, 22% experience vaginal injuries, and 3% experience urethral rupture (Rahmatia et al., 2022). According to Lampung Province Health Profile data, the incidence of infection in postpartum women was 48 cases and infectious complications were 67 cases (Dinkes Prov. Lampung, 2022).

The impact of perineal wounds on mothers, if not properly treated, can potentially lead to infection of the wound. This is due to the condition of the perineum, which is exposed to lochea and humidity, creating an environment that favours bacterial growth, delaying the wound healing process. Perineal wound infections can involve various types of bacteria that naturally colonise the skin and genital mucosa. These bacteria can include a number of pathogenic species, including Staphylococcus aureus, Streptococcus pyogenes and Escherichia coli. While under normal conditions these bacteria can be part of the body's normal flora, when a wound forms, this balance can be disrupted, and bacteria can take advantage of the favourable environment to multiply (Wong & Ramli, 2021).

Delayed healing is often indicated by symptomatic changes in vital signs related to bleeding and infection, evidenced by symptoms such as redness, fever, and pain. Typically, sutured perineal wounds heal within 7 to 10 days, with sutures dissolving over a span of ten to fifteen days. However, complications such as infection may prolong the healing process, usually becoming apparent around three to five days post-procedure (Mutia et al., 2021). Wound healing is a complex process that encompasses several stages, including inflammation, proliferation, and remodeling (Grubbs H, 2023).

Initially, the inflammatory phase of wound healing commences on the third to fourth day post-procedure, characterized by vasodilation of blood vessels to enhance blood flow to the wound site. During this phase, neutrophils and macrophages migrate to the wound area to remove cellular debris, bacteria, and other foreign substances (Grubbs H, 2023). The proliferative phase follows, spanning from the fourth day to the third week. This phase involves the synthesis of substances that form the wound's edge covering and the development of granulation tissue. This tissue, composed of epithelial cells, fibroblasts integrating collagen, and newly formed blood vessels, covers the wound surface and ensures an adequate supply of blood and nutrients. Finally, the maturation phase begins at the third week and can continue for up to a year. During this phase, the collagen produced in the proliferative phase undergoes remodeling to enhance the strength and elasticity of the tissue (Primadina et al., 2019).

Among the plants that can be utilized for medicinal purposes in wound healing is Centella asiatica (Pegagan). The active compounds found in Centella asiatica that aid in the wound healing process include triterpenoids, flavonoids, saponins, and tannins. Triterpenoid compounds, such as asiaticoside, asiatic acid, madecassoside, and madecassic acid, are the primary compounds in Pegagan leaves responsible for its beneficial effects on wound healing (Sh Ahmed et al., 2019). Flavonoids, known for their anti-inflammatory properties, contribute to wound healing by protecting cells from damage, inhibiting bacterial growth, and reducing inflammation (Zulkefli et al., 2023). Triterpenoid saponins in Centella asiatica accelerate wound healing by inhibiting inflammation, enhancing angiogenesis, inducing collagen synthesis, and promoting vasodilation (Diniz et al., 2023).

Asiatic acid and madecassic acid are triterpenoid compounds derived from Centella asiatica leaves that exhibit significant antibacterial activity against Staphylococcus aureus. Previous research indicates that asiatic acid demonstrates notable antibacterial activity against Staphylococcus aureus, with minimum inhibitory concentrations ranging from 32-52 μg/mL (Liu et al., 2015). Furthermore, studies have shown that madecassic acid significantly impacts Staphylococcus aureus by inhibiting bacterial growth and biofilm formation (Wei, C., Cui, P., & Liu, 2023). Research on the use of Centella asiatica, formulated with 25% concentrated extract of its leaves, revealed that this formulation effectively accelerated drying time, scab development, and reduced wound diameter (Nurmalasari et al., 2017). Additionally, it was found that a 25% concentration of Centella asiatica leaf extract enhanced the healing of infected wounds more effectively than 50% and 75% concentrations, with a p-value 0.008 < 0,05 (Amaliya et al., 2013).

The use of Centella asiatica herb as a wound healing agent can be enhanced by incorporating it into a spray gel formulation. This approach minimizes the risk of contamination or infection, provides a longer drug contact time compared to other dosage forms, and offers a cooling sensation due to gel evaporation (Radhakrishnan, A., Kuppusamy, G., & Karri, 2018). Based on this context, the researchers are interested in demonstrating the efficacy of Centella asiatica leaves in spray gel form as a viable alternative to aid in the healing process of perineal wounds in postpartum women. This research aims to determine the effectiveness of applying centella asiatica spray gel 3 times a day with a concentration of 25% for 7 days on perineal wound healing and the growth of Staphylococcus aureus bacteria in postpartum mothers.

METHOD

This research is true experiment with pre and post test with control group design. The sample in this research was postpartum women who experienced second degree perineal laceration with suturing as many as 34 respondents. Sampling was done by random sampling method. This study divided the respondents into two groups, namely the intervention group of 17 postpartum women who experienced given spray gel of Centella asiatica, while as many as 17 postpartum women were only given dry clean treatment. The treatment that will be given to respondents is by giving a 25% concentration of Centella asiatica spray gel in the amount of 15 ml used 3 times a day, in the morning, afternoon, and evening after bathing or after washing for 7 days.

Before being given to the intervention group, the Centella asiatica spray gel has gone through laboratory tests. The results of the physical characteristics test obtained a thick spray gel dosage form with a brownish colour, has a strong aroma of Centella asiatica leaves, the gel is homogeneous, and a a measured pH of 4.61. Wound assessments using the REEDA scoring system were conducted on the first, third, fifth, and seventh days following treatment initiation. Additionally, on the third and seventh days, swab samples were collected from the perineal wounds to quantify the growth of Staphylococcus aureus bacteria. Swab samples were meticulously gathered using sterile cotton sticks and subsequently transferred into properly labeled sterile buffer tubes containing 10 ml of sterile NaCl to maintain sample integrity and prevent contamination. These samples were promptly transported in a cooled container with ice packs to ensure preservation during transit to the laboratory. Upon receipt, the samples underwent culture processes, and bacterial colonies were enumerated using a colony counter.

Statistical analysis of the data involved employing Friedman and Mann Whitney tests for evaluating changes in REEDA scores, while Wilcoxon and Mann Whitney tests were utilized to analyze the growth of Staphylococcus aureus bacteria. Ethics clearance for this research was obtained from the Ethics Commission of Poltekkes Kemenkes Semarang, registered under No. 0391/EA/KEPK/2024. The study was conducted from March to May 2024 in the Way Urang Health Centre working area.

RESULTS

Tabel 1.
Perineal Wound Healing Based on REEDA Score in Intervention Group and Control Group

Variable	Intervention Group (n = 17)	Control Group (n = 17)	*p-value*
	Mean ± SD	Mean ± SD	
Pre test (Day 1)	11,59±1,04	11,94±1,34	0,474[a]
Post test 1 (Day 3)	6,41±1,32	8,53±1,66	0,001[a]
Post test 2 (Day 5)	3,47±0,94	5,82±1,51	0,000[a]
Post test 3 (Day 7)	1,06±0,74	3,00±0,93	0,000[a]
p	0,000[b]	0,000[b]	

[a]Mann Whitney Test [b]Friedman Test

According to the Friedman test results in table 1, the value of $p < 0.05$ means that there is a difference in the average healing of perineal wounds on the first, third, fifth, and seventh day of observation using the REEDA score. Furthermore, based on the Mann Whitney test results after treatment on the third, fifth, and seventh days, the p value <0.05 means that there is a significant difference in the average wound healing using the REEDA score in the group given Centella asiatica spray gel (intervention) with the dry clean care group (control). The decrease in perineal wound healing based on REEDA score is presented in the following chart.

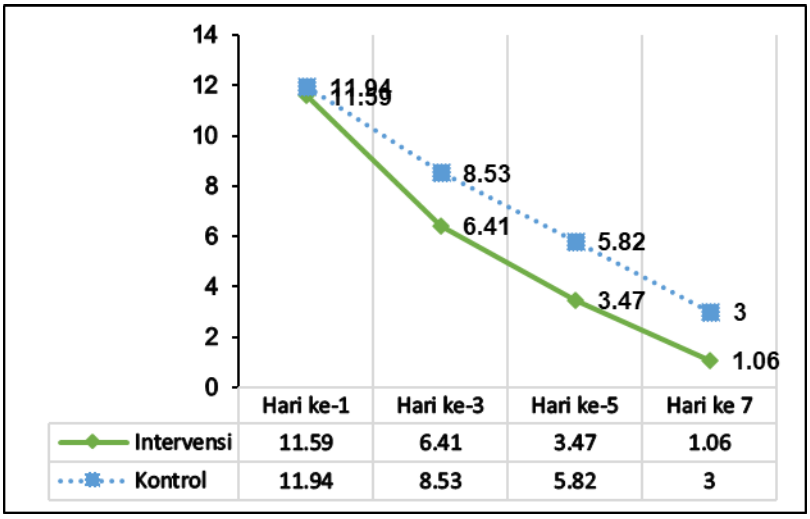

Figure 1. Mean of Perineal Wound Healing Based on REEDA Score

Based on Figure 1, it is known that on the first day of observation before treatment, there was no decrease in the mean rate of perineal wound healing in the intervention group with a mean value of 11.59 and the control group with a mean value of 11.94. Meanwhile, after the treatment on the third, fifth, and seventh days, the results showed a significant decrease in the mean level of perineal wound healing based on the REEDA score in the group given Centella asiatica leaf spray gel (intervention) with the dry clean care group (control). There was a difference in the results of the post test on the 7th day of observation, which is the mean REEDA score in the group given gotu kola leaf spray gel (intervention) is 1.06 while the mean REEDA score in the group given dry clean treatment (control) is 3.00.

Table 2.
Perineal Wound Healing Based on Staphylococcus Aureus Bacteria Decrease

Variable	Intervention Group (n = 17)	Control Group (n = 17)	*p-value*
	Mean ± SD	Mean ± SD	
Measurement Results on Day 3 (Pre test)	6,85±9,24	6,42±8,74	0,945[a]
Measurement Results on Day 7 (Post test)	1,63±2,03	6,86±6,42	0,002[a]
Δ mean	6,34±8,77	0,81±8,47	0,040[a]
p	0,017[b]	0,813[b]	

[a]Mann Whiney Test [b]Wilcoxon Test

According to the Wilcoxon test results which presented in table 2, it is known that the intervention group that were given Centella asiatica spray gel had a p value (0.017) <0.05. This is indicating that perineal wound healing has a significant difference in the decrease of Staphylococcus Aureus bacteria before and after the application of gotu kola leaf spray gel. Meanwhile, the p value (0.813) > 0.05 in the perineal wound healing of the control group given dry clean treatment. This shows that there is no significant difference in the reduction of Staphylococcus Aureus bacteria in the measurement results of day 3 (pretest) and day 7 (posttest).

Based on the results of the Mann Whitney test, the observation of the growth of Staphylococcus Aureus bacteria on day 3 showed that there was no significant difference in the intervention group given Centella asiatica leaf spray gel with the control group of dry clean treatment with p value (0.945) > 0.05. Meanwhile, the observation of the growth of Staphylococcus Aureus bacteria on the 7th day showed that there was a significant difference in the intervention group given Centella asiatica leaf spray gel with the control group of dry clean treatment with a p value (0.002) <0.05. The results of the analysis of the average difference in the growth of Staphylococcus Aureus bacteria obtained a p value (0.040) <0.05, meaning that there was a difference in the average difference between the intervention group and the control group.

The intervention group with Centella asiatica spray gel exhibited a decrease in the average growth of Staphylococcus aureus bacteria. Meanwhile, the control group with dry clean treatment demonstrated an increase in the average growth of Staphylococcus aureus bacteria. On the third day of observation, the average growth of Staphylococcus aureus bacteria in the group receiving the gotu kola leaf spray gel was 6.85 x 10^3 CFU/ml, which was higher than the control group's average of 6.42 x 10^3 CFU/ml. However, by the seventh day, the intervention group showed a significantly lower average bacterial growth of 1.63 x 10^3 CFU/ml, compared to the control group's average of 6.86 x 10^3 CFU/ml.

DISCUSSION

The decrease in the average REEDA score is due to the active compounds contained in Centella asiatica that support the wound healing process involving triterpenoids, flavonoids, saponins, and tannins. Triterpenoid compounds including asiaticoside, asiatic acid, madecassoside, and madecassic acid are the main compounds of Centella asiatica leaves that are responsible for the positive effects in wound (Sh Ahmed et al., 2019). Centella asiatica's mechanisms in accelerating the wound healing process include inhibiting inflammation, inducing collagen synthesis, enhancing angiogenesis and inducing vasodilation. The wound healing activity of Centella asiatica is also related to growth factors such as endothelial growth factor, fibroblast growth factor, and vascular endothelial growth factor (Diniz et al., 2023).

The results of this study are supported by previous research by Amalia that pegagan leaf extract with a concentration of 25% has the effect of accelerating the healing of infected wounds in wistar strain white rats better than with a concentration of 50% and 75% with a p value (0.008) <0.05 (Amaliya et al., 2013). This research also in line with previous research by Harsa (2020) found that pegagan leaf extract (Centella asiatica) can accelerate the healing process of incision wounds in male white rats (Rattus norvegicus) wistar strain compared to the administration of 0.9% Nacl and povidone iodine (Harsa, 2020). Wound healing in the proliferation stage occurs from day 3 to day 14 after trauma. The main goal of the proliferation phase is to create a balance between scar tissue formation and tissue regeneration. There are three main processes that occur in the proliferation phase, namely angiogenesis, fibroblast, and re-epithelialisation (Grubbs H, 2023).

Active compounds in Centella asiatica leaves that stimulate the proliferation phase are triterpenoid compounds including asiaticoside, asiatic acid, madecassoside, and madecassic acid. Triterpenoids in Centella asiatica leaves can increase collagen, accelerate cell proliferation, and regulate the balance of MMP (Matrix Metalloproteinase) and TIMP (Tissue Inhibitor of Metalloproteinase) enzymes (Bandopadhyay et al., 2023). Wound healing is significantly aided by collagen, especially type I and type III collagen found in skin tissue. Based on the results of previous studies on RT-PCR, asiaticoside and madecassoside significantly increased the mRNA levels of type I and type III collagen in fibroblasts. In addition, ELISA detected an increased amount of type I and type III procollagen (Wu et al., 2012). This is supported by previous research that Asiaticoside derived from the ethanol extract of Centella asiatica, showed no toxicity to human skin fibroblast cells and human skin keratinocyte cells. By in vitro, Asiaticoside showed significant effect on human dermal fibroblasts and human dermal keratinocytes in the scratch test (Azis et al., 2017).

Bacterial growth is also related to the stages of wound healing, namely the inflammatory phase, which begins immediately after trauma and lasts until day 5. The main goal of this phase is to remove dead tissue and prevent colonisation and infection by pathogenic microbial agents. Once haemostasis is complete, neutrophils and acute inflammatory cells will invade the area of inflammation and destroy all bacteria and debris. Lymphocytes, macrophages along with neutrophils are the first cells to reach the wound area playing an important role in initiating the inflammatory response by resisting infection, clearing cellular matrix debris and foreign objects (Primadina et al., 2019).

The role of flavonoids as antibacterial in Centella asiatica has an inhibitory effect on a number of bacterial species, including Gram-positive and Gram-negative ones. Flavonoids can inhibit the growth of various pathogenic bacteria by damaging the bacterial cell wall or cell membrane, flavonoids are able to interact with bacterial DNA, preventing replication and transcription necessary for bacterial growth and spread, flavonoids have a strong ability to inhibit active oxygen species, help reduce oxidative stress in the wound area, and prevent biofilm formation (Zulkefli et al., 2023). The mechanism of action of tannins as antibacterials is to inhibit the enzymes reverse transcriptase and DNA topoisomerase so that bacterial cells cannot form. with its ability to activate microbial cell adhesins, activate enzymes, and interfere with protein transport in the inner layer of the cell (Widiatami et al., 2022).

This research is in line with Kurniawan (2021), namely the formation of an inhibition zone indicates that endophytic bacterial isolates from Centella asiatica leaves have antibacterial properties against S. aureus. Isolate I2, which has similarities with Bacillus based on colony morphology, cell morphology, and biochemical activities that produce secondary metabolites such as triterpenoids, saponins, and alkaloids, showed the strongest antibacterial activity against S. Aureus (Kurniawan et al., 2021). This is aligned with the research of Wei (2023) that madecassic acid showed a significant antibacterial effect on Staphylococcus aureus by inhibiting bacterial growth and biofilm formation (Wei, C., Cui, P., & Liu, 2023). Increased bacterial growth due to a compromised innate immune system may inhibit the body's ability to fight infection and clear bacteria from the wound, causing a failure in the transition of macrophages from M1 (pro-inflammatory) to M2 (anti-inflammatory and tissue repair) phenotype, prolonging the inflammatory phase (MacLeod & Mansbridge, 2016).

Common conditions that compromise the immune system or reduce the effectiveness of antibiotic drugs may favour the development of wound biofilms. Biofilms can inhibit wound healing even when wound conditions appear to be improving. Biofilms provide physical protection from external threats such as the immune system, antibiotics and other antimicrobial agents. Biofilms stimulate a chronic inflammatory response in an attempt to remove the biofilm from the wound. The response results in neutrophils and macrophages surrounding the biofilm. These inflammatory cells secrete high levels of reactive oxygen species (ROS) and proteases (matrix metalloproteinase (MMP) and elastase). Proteases help break down the bonds between biofilm and tissue, releasing the biofilm from the wound. However, ROS and proteases spread to the surrounding area, thus interfering with the overall wound healing process (Sen et al., 2021).

CONCLUSION

Based on the results of the research, the intervention group given spray gel of Centella asiatica leaves was more significant than the control group with dry clean treatment, because the giving of Centella asiatica leaves spray gel is proven to be effective in healing perineal wounds and reducing Staphylococcus aureus bacteria in postpartum women. Therefore, the development of the use of Centella asiatica leaves spray gel as an alternative treatment for perineal wounds needs to be done in order to provide comprehensive midwifery care in the health services of postpartum women.

REFERENCES

Amaliya, S., Soematri, B., & Utami, Y. W. (2013). Efek Ekstrak Daun Pegagan (Centella asiatica) dalam Mempercepat Penyembuhan Luka Terkontaminasi Pada Tikus Putih (Rattus novergicus) Galur Wistar. *Jurnal Ilmu Keperawatan*, *1*(1), 19–25.

Azis, H. A., Taher, M., Ahmed, A. S., Sulaiman, W. M. A. W., Susanti, D., Chowdhury, S. R., & Zakaria, Z. A. (2017). In vitro and In vivo wound healing studies of methanolic fraction of Centella asiatica extract. *South African Journal of Botany*, *108*, 163–174.

https://doi.org/10.1016/j.sajb.2016.10.022

Bandopadhyay, S., Mandal, S., Ghorai, M., Jha, N. K., Kumar, M., Radha, Ghosh, A., Proćków, J., Pérez de la Lastra, J. M., & Dey, A. (2023). Therapeutic properties and pharmacological activities of asiaticoside and madecassoside: A review. *Journal of Cellular and Molecular Medicine*, *27*(5), 593–608. https://doi.org/10.1111/jcmm.17635

Darulis, N. O., Kundaryanti, R., & Novelia, S. (2021). The Effect of Betel Leaf Water Decoction on Perineal Wound Healing among Post Partum Women. *Nursing and Health Sciences Journal (NHSJ)*, *1*(2), 130–135. https://doi.org/10.53713/nhs.v1i2.64

Diniz, L. R. L., Calado, L. L., Duarte, A. B. S., & de Sousa, D. P. (2023). Centella asiatica and Its Metabolite Asiatic Acid: Wound Healing Effects and Therapeutic Potential. *Metabolites*, *13*(2). https://doi.org/10.3390/metabo13020276

Dinkes Provinsi Lampung. (2023). *Profil Dinas Kesehatan Provinsi Lampung Tahun 2022*. Bandar Lampung: Dinkes Provinsi Lampung

Grubbs H, M. B. (2023). *Wound Physiology*. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK518964/

Harsa, I. M. S. (2020). Efek Pemberian Ekstrak Daun Pegagan (Centella Asiatica) terhadap Penyembuhan Luka Sayat pada Tikus Putih Jantan (Rattus Norvegicus) Galur Wistar. *Jurnal Ilmiah Kedokteran Wijaya Kusuma*, *2071*(1), 21–27.

Jones, K., Webb, S., Manresa, M., Hodgetts-Morton, V., & Morris, R. K. (2019). The incidence of wound infection and dehiscence following childbirth-related perineal trauma: A systematic review of the evidence. *European Journal of Obstetrics and Gynecology and Reproductive Biology*, *240*, 1–8. https://doi.org/10.1016/j.ejogrb.2019.05.038

Kurniawan, S. E., Mahyarudin, M., & Rialita, A. (2021). Aktivitas antibakteri isolat bakteri endofit daun pegagan (Centella asiatica) terhadap Staphylococcus aureus. *Bioma : Jurnal Ilmiah Biologi*, *10*(1), 14–29. https://doi.org/10.26877/bioma.v10i1.7140

Liu, W. H., Liu, T. C., & Mong, M. C. (2015). Antibacterial effects and action modes of asiatic acid. *BioMedicine (Taiwan)*, *5*(3), 22–29. https://doi.org/10.7603/s40681-015-0016-7

MacLeod, A. S., & Mansbridge, J. N. (2016). The Innate Immune System in Acute and Chronic Wounds. *Advances in Wound Care*, *5*(2), 65–78. https://doi.org/10.1089/wound.2014.0608

Mutia, W. O. N., Usman, A. N., Jaqin, N., Prihantono, Rahman, L., & Ahmad, M. (2021). Potency of complemeter therapy to the healing process of perineal wound; turmeric (Curcuma longa Linn) Infusa. *Gaceta Sanitaria*, *35*, S322–S326. https://doi.org/10.1016/j.gaceta.2021.10.045

Nurmalasari, N., Kartadarma, E., & Gadri, A. (2017). Formulasi Sediaan Spray Gel Anti Luka Mengandung Ekstrak Daun Pegagan (Centella asiatica (L.) Urb) dan Uji Aktivitas Anti Luka terhadap Tikus Wistar. *SPeSIA (Seminar Penelitian Sivitas Akademika Unisba)*, *3*(2), 526–533. http://karyailmiah.unisba.ac.id/index.php/farmasi/article/view/8068

Primadina, N., Basori, A., & Perdanakusuma, D. S. (2019). Proses Penyembuhan Luka

Ditinjau Dari Aspek Mekanisme Seluler dan Molekuler. *Qanun Medika*, *3*(1), 31–43.

Radhakrishnan, A., Kuppusamy, G., & Karri, V. V. S. R. (2018). Spray bandage strategy in topical drug delivery. *Journal of Drug Delivery Science and Technology*, *43*, 113–121.

Rahmatia, D. A., Wijayanti, K., & Ramlan, D. (2022). Kersen leaf extract gel (Muntingia calabura L.) to Improve the healing of perineal wounds in postpartum mothers. *Medisains*, *20*(3), 87. https://doi.org/10.30595/medisains.v20i3.15597

Sen, C. K., Roy, S., Mathew-Steiner, S. S., & Gordillo, G. M. (2021). Biofilm Management in Wound Care. *Plastic and Reconstructive Surgery*, *148*(2), 275E-288E. https://doi.org/10.1097/PRS.0000000000008142

Sh Ahmed, A., Taher, M., Mandal, U. K., Jaffri, J. M., Susanti, D., Mahmood, S., & Zakaria, Z. A. (2019). Pharmacological properties of Centella asiatica hydrogel in accelerating wound healing in rabbits. *BMC Complementary and Alternative Medicine*, *19*(1), 1–7. https://doi.org/10.1186/s12906-019-2625-2

Wahyuningsih, H. P. (2018). *Asuhan Kebidanan Nifas dan Menyusui*. Jakarta: Kementerian Kesehatan RI.

Wei, C., Cui, P., & Liu, X. (2023). Antibacterial Activity and Mechanism of Madecassic Acid against Staphylococcus aureus. *Molecules (Basel, Switzerland)*, *28*(4), 1895. https://doi.org/https://doi.org/10.3390/molecules28041895

Widiatami, T., Rasipin, R., & Fatmasari, D. (2022). Effectiveness of the Giving Starfruit Leaf Extract (Averrhoa Bilimbi L.) and Cinnamon (C. Burmanii) As an Alternative To Antibacterials for the Healing of Perineum Wounds in Rattus Norvegicus. *International Journal of Nursing and Midwifery Science (Ijnms)*, *5*(3), 176–184. https://doi.org/10.29082/ijnms/2021/vol5/iss3/369

Wong, J. X., & Ramli, S. (2021). Antimicrobial activity of different types of Centella asiatica extracts against foodborne pathogens and food spoilage microorganisms. *Lwt*, *142*(February), 111026. https://doi.org/10.1016/j.lwt.2021.111026

Woodd, S. L., Montoya, A., Barreix, M., Pi, L., Calvert, C., Rehman, A. M., Chou, D., & Campbell, O. M. R. (2019). Incidence of maternal peripartum infection: A systematic review and meta-analysis. *PLoS Medicine*, *16*(12). https://doi.org/10.1371/journal.pmed.1002984

World Health Organization. (2015). Health in 2015: from MDGs, Millennium Development Goals to SDGs, Sustainable Development Goals. In *World Health Organisation*. World Health Organization. http://who.int/gho/publications/mdgs-sdgs/en/

World Health Organization. (2019). Trends in maternal mortality: 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: World Health Organization; 2019. In *WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division*. World Health Organization.

Wu, F., Bian, D., Xia, Y., Gong, Z., Tan, Q., Chen, J., & Dai, Y. (2012). Identification of major active ingredients responsible for burn wound healing of Centella asiatica herbs. *Evidence-Based Complementary and Alternative Medicine*, *2012*. https://doi.org/10.1155/2012/848093

Zulkefli, N., Che Zahari, C. N. M., Sayuti, N. H., Kamarudin, A. A., Saad, N., Hamezah, H. S., Bunawan, H., Baharum, S. N., Mediani, A., Ahmed, Q. U., Ismail, A. F. H., & Sarian, M. N. (2023). Flavonoids as Potential Wound-Healing Molecules: Emphasis on Pathways Perspective. *International Journal of Molecular Sciences*, *24*(5). https://doi.org/10.3390/ijms24054607