

THE EFFECTIVENESS OF *ZIZIPHUS MAURITIANA* LEAF EXTRACT LOTION COMBINED WITH *CENTELLA ASIATICA* ON HEALING BURN WOUNDS IN RATS

*Efektivitas Lotion Ekstrak Daun Ziziphus mauritiana yang Dikombinasikan
Centella asiatica terhadap Penyembuhan Luka Bakar pada Tikus*

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ABSTRAK

Luka bakar merupakan cedera umum yang memerlukan penanganan cepat dan efektif guna mencegah komplikasi serta mempercepat penyembuhan. Ekstrak daun *Ziziphus mauritiana* dan *Centella asiatica* dipercaya dapat mempercepat penyembuhan luka. Penelitian ini bertujuan mengevaluasi efektivitas losion berbasis ekstrak daun *Ziziphus mauritiana* dan *Centella asiatica* terhadap penyembuhan luka bakar. Desain penelitian menggunakan eksperimen post-test dengan kelompok kontrol positif pada model tikus, masing-masing terdiri dari 10 ekor. Luka bakar derajat dua dibuat di area punggung tikus, dengan menempelkan pelat logam panas (2 cm, dipanaskan 5 menit) selama 5 detik hingga muncul kemerahan dan bula, dilanjutkan dengan pemberian losion ekstrak kombinasi pada kelompok intervensi dan losion komersial pada kelompok kontrol. Analisis data menggunakan independent t-test. Hasil menunjukkan proses penyembuhan lebih cepat secara signifikan pada kelompok intervensi (mean=74,5; SD=15,11) dibanding kontrol (mean=44,46; SD=28,98) dengan p=0,009. Pengamatan morfologis menunjukkan granulasi jaringan lebih tebal dan penutupan luka lebih cepat pada kelompok intervensi. Losion kombinasi *Ziziphus mauritiana* dan *Centella asiatica* terbukti efektif mempercepat penyembuhan luka bakar pada tikus. Hasil ini mendukung pengembangan intervensi keperawatan holistik berbasis terapi alami dalam kerangka model Orem untuk meningkatkan perawatan diri pasien. Penelitian lanjutan pada manusia disarankan untuk mengonfirmasi efektivitas klinisnya.

Kata kunci: luka bakar, pegagan, penyembuhan luka, *Ziziphus mauritiana*

ABSTRACT

Burns are common injuries that require quick and effective treatment to prevent complications and promote healing. *Ziziphus mauritiana* and *Centella asiatica* leaf extracts are believed to accelerate wound healing. This study aims to evaluate the effectiveness of *Ziziphus mauritiana* and *Centella asiatica* leaf extract-based lotions on burn wound healing. The research design used a post-test experiment with a positive control group on a rat model, each consisting of 10 rats. Second-degree burns were made in the area of the rat's back by attaching a hot metal plate (2 cm, heated for 5 minutes) for 5 seconds until redness and ulcers appeared, followed by administration of the combined extract lotion in the intervention group and commercial lotion in the control group. Data were analyzed using an independent t-test. Results showed that the healing process was significantly faster in the intervention group (mean=74.5; SD=15.11) compared to the control group (mean=44.46; SD=28.98) with p=0.009. Morphological observations showed thicker tissue granulation and faster wound closure in the intervention group. The combination of *Ziziphus mauritiana* and *Centella asiatica* lotion proved effective in accelerating burn wound healing in rats. These results support the development of holistic nursing interventions based on natural therapies within the

framework of the Orem model to improve patient self-care. Further studies in human subjects are needed to validate its clinical efficacy.

Keywords: burns, *Centella asiatica*, wound healing, *Ziziphus mauritiana*

INTRODUCTION

Burns are injuries when skin, tissue, or muscle cells are damaged by hot liquids, hot solids, radioactive waves, electricity, and chemicals [1]. Burns are the fourth most common type of accident after traffic accidents, falls, and being trapped in complex situations, and burns account for 5-12% of global accidents [2]. Data from the Ministry of Health's Basic Health Research in 2018 stated that 0.7% of the Indonesian population had experienced burn injuries, indicating the national prevalence of burns among the general population.. Burns rank sixth in unintentional injuries after falls at 40.9%, motorcycles at 40.6%, sharp or blunt objects at 7.3%, other land transportation at 7.1%, and falls at 2.5% [3].

Burns often cause discomfort in the form of pain and a hot sensation and leave wounds that require further treatment. In line with what Farahani et al. (2023) said, short-term complications of burns can include pain, wounds, disability, and limited mobility, while hypertrophic scars are one of the long-term consequences. According to Donaldson et al.[2], burns cause damage to the skin, which is the body's natural protective barrier, and can lead to infection, poor wound healing, contractures, and disability. As many as 69% of burn incidents occur in domestic areas or home environments, especially those involving children and adults at home [4]. These burns often occur due to cooking activities, the use of liquid fuels, and electrical accidents. Most reported cases are first- and second-degree burns requiring immediate treatment.

According to Himawan [4], most first-hand treatments carried out by the community use objects around them, such as toothpaste, ice water, margarine, oil, or soy sauce, and only 14% carry out proper treatment. This is done to reduce discomfort from burns. However, if misused, the product can cause damage or worsen the injury. Although toothpaste provides a cooling sensation, it also contains several chemicals that can cause irritation and allergies. It is also important not to apply anything to the burn area, such as margarine or coconut oil, because it tends to trap heat and worsen the situation. Although applying ice to the burn area can provide an incredible sensation and relieve pain temporarily, it is dangerous because it can cause frostbite, which worsens the condition of the affected tissue [4].

Tropical and subtropical areas such as Indonesia have diverse plant species with therapeutic or medicinal potential and have traditionally been widely used by the community. Therapeutic use is entirely based on local practices, beliefs, and traditions [5]. Traditional medicine is part of the cultural system of society that has potential benefits in the development of public health. The use of traditional self-care medicine is increasing [6],[7]. *Ziziphus mauritiana* leaves and *Centella asiatica* are two herbal plants that have long been used in traditional medicine. The leaves of the *Ziziphus mauritiana* plant contain tannins, saponins, glycosides, and phenols. Tannins are part of secondary metabolites that can precipitate microbial proteins so that these proteins cannot be utilized anymore [6].

Ziziphus mauritiana leaves treat typhus, fever, asthma, and wounds [8]. The constituents contained in *Centella asiatica* are triterpenoids, saponins known as centelloids, essential oils, flavonoids, tannins, phytosterols, amino acids, and sugars [9]. Flavonoids, phenolic compounds, alkaloids, and organic acids can prevent the formation of the cyclooxygenase enzyme, which increases pain and inflammation [10]. Both plants are known as anti-inflammatory, antioxidant, and tissue regeneration stimulants, antimicrobial, or antifungal, which positively affect wound healing by preventing pathogen development, increasing cell proliferation, increasing collagen production,

increasing wound contraction, increasing epithelialization, vascularization, and normal regeneration, and preventing fibrosis [11].

According to research by Farahani et al. [1], oral administration of *Centella asiatica* extract administered as 200 mg capsules taken twice daily was found to reduce pain in patients with burns. In the wound healing process, the reduction in wound size is faster, and the level of damage to the underlying tissue and the amount of necrotic tissue are less. The amount of granulation tissue in the treatment group is significantly better compared to the control group. The *Ziziphus mauritiana* leaf extract has the highest efficacy for healing burns in rabbits, with an extract concentration of 15% better than the control group using bay leaf extract [1][12]. Hovaneţ et al. [11], in their study, found that *Zizyphus jujube mill* extract ointment had healing activity comparable to Cicatrizin (a product marketed in the pharmaceutical market) in Wistar rats and had a moderate anti-inflammatory effect compared to the control group, but statistically comparable to indomethacin in the inflammation test in rats induced by kaolin intraplantar[11]. The healing and anti-inflammatory properties of the ointment tested were associated with the content of phenolic acids and flavonoids. The public believes the use of herbal medicine to be safer than using chemical drugs. The use of chemical drugs that are often used for burns in the form of creams containing neomycin, silver sulfadiazine, and povidone-iodine; these components help kill germs and accelerate the wound healing process but have side effects such as irritation and allergic reactions and if given for an extended period causes resistance and the use of silver which is the standard for burn therapy has a toxic effect on keratinocytes and slows down wound healing [13]. Farahani et al. [1] stated that herbal medicine is cheaper than modern medicine, has fewer side effects, and is more compatible.

In experimental research, animals such as rats are often used. Because rats are physiologically and genetically related to humans, they are suitable for modeling human diseases and their responses to therapy. The research results on rats can be applied to human health because about 95% of mouse genes are similar to human genes [14]. Compared to other animal models, rats also have relatively low costs for care and maintenance [15]. This study combines *Ziziphus mauritiana* and *Centella asiatica* leaf extracts formulated into a topical lotion. The extracts were obtained via maceration: 200 grams of dried *Ziziphus mauritiana* leaves in 1,500 mL of 96% ethanol (yield: 8.8%) and 200 grams of *C. asiatica* leaves in 1,500 mL of 70% ethanol (yield: 11.02%). The resulting thick extracts are used for their potential to reduce inflammation, lower infection risk, and promote tissue regeneration in burn wound healing. Many studies have explored the content and efficacy of *Ziziphus mauritiana* and *Centella asiatica*. However, only a few have examined their efficacy when combined with a lotion to heal burns in rats and the specific effects of each wound healing process, such as the inflammatory, proliferation, and recovery phases. This is very important to understand the effects of therapy on the burn healing process. The novelty of this research lies in the use of a combination of *Ziziphus mauritiana* and *Centella asiatica* extracts formulated into a lotion for burn wound healing, which has not been extensively explored before. The objective of this research is to evaluate the effectiveness of the combined herbal lotion in accelerating the healing process of second-degree burns in rats.

Frontline burn care is the domain of nurses, who will provide better patient care if they are informed about complementary therapies, such as herbal lotions. In addition, when nurses have gained enough information about these therapies to increase their sense of efficacy, they can convey this knowledge to their patients and use herbal lotions in wound care at home. Research on rats can provide valuable preliminary information in determining these parameters. In addition, this research also has the potential for the development of more effective and affordable herbal-based burn care products. Our research will contribute to the scientific evidence on burn care, focusing on herbal-based

therapies. The results of this study can be used for further clinical research and the development of guidelines for nurses in using herbal lotions in holistic burn care.

METHODS

This research used an experimental study with a post-test research design using a positive control group. This research was conducted in June - July 2024 in the Biomedical laboratory of STIKes Kuningan. The study was conducted to evaluate the effect of a lotion containing *Ziziphus mauritiana* leaf extract, combined with *Centella asiatica* leaves. This study used male white rats (*Rattus Novergicus*), aged 2-3 months, with a body weight of 100-150 g, which were adapted to the room for seven days before the intervention. The number of samples used was 20, with each group comprising ten. The sample size was taken based on the ethical principle in animal research, namely 'Reduction,' where the number of animals is minimized without reducing the validity of the research results. Therefore, the researcher selectively selected samples and conducted strict control during the intervention to minimize data variability.

Before conducting the research, research materials were prepared. *Centella asiatica* leaves were obtained from Cisantana Village, Kuningan Regency, while *Ziziphus mauritiana* from Sukoharjo Regency. Dark green and fresh leaves were selected, washed, and dried. The drying process was carried out in several stages. First, the leaves were dried in indirect sunlight for five days. The second stage of drying was carried out in an oven at 50 °C for 24 hours for *Ziziphus mauritiana* leaves and at 45°C for 6 hours for *Centella asiatica* leaves. Both leaves were ground into simplicia powder and extracted using the maceration technique with a ratio of 1:7.5, namely 200 grams of *Ziziphus mauritiana* leaves simplicia powder was soaked in 1,500 ml of Ethanol 96%. In a separate place, 200 grams of *Centella asiatica* leaves simplicia powder was soaked in 1,500 ml of Ethanol 70% for 3 x 24 hours; every 6 hours, stirring was carried out. Every 24 hours, filtering is carried out using a coffee filter and a flannel cloth. Furthermore, the extract was evaporated using a Rotary Evaporator and then thickened in a water bath at 50 °C for 20 days. The final result is a thick extract, with an extract yield of 8.8% for *Ziziphus mauritiana* leaves and 11.02% for *Centella asiatica* leaves, meeting the standards of the Indonesian Herbal Pharmacopoeia 2017[16].

The lotion was formulated by combining *Ziziphus mauritiana* extract (5%) and *Centella asiatica* extract (5%) into a cream base. The cream base consisted of stearic acid (15%), cetyl alcohol (2%), liquid paraffin (5%), glycerin (10%), triethanolamine (1%), methylparaben (0.2%), propylparaben (0.1%), and distilled water (q.s. to 100%). All ingredients were mixed using the standard emulsification method: oil and water phases were heated separately to 70°C, then emulsified while stirring until a homogeneous lotion was formed and cooled to room temperature. After the lotion was prepared, the test animals were treated by creating standardized burn wounds. The burn wound was made by shaving the rat on its back 3-5 cm, then disinfecting it using an alcohol swab, then anesthetizing it using 0.1 gram of Topsy ointment, and leaving it for 2 minutes. Create a burn wound by heating a plate with a diameter of 2 cm for 5 minutes, then attach the plate to the rat's back for 5 seconds until a 2nd-degree burn is formed, which is characterized by the presence of a reddish color and bullae. Measure the area of the burn using a ruler.

The intervention group was given treatment by applying *Ziziphus mauritiana* leaves extract lotion with a combination of 0.1 gram of *Centella asiatica* leaves to 10 rats in the burn area, which had been made as soon as possible, with a dose of once a day. In comparison, the control group was given treatment by applying 0.1 grams of bioplacenton ointment to 10 rats in the area of burns that had been made as soon as possible, once a day.

The wounds were observed daily to determine whether there was an infection by observing signs of infection such as redness, swelling, pus, and wound healing status. The general conditions of the rats were observed, including food intake, drinking water, and movement. Observations were made at five time points after treatment. The wound healing rate at different periods was calculated for each group using the following formula[17]:

$$\text{Wound healing rate} = \frac{(\text{initial wound area} - \text{unhealed wound area})}{\text{Initial wound area}} \times 100\%.$$

The average time required for wound healing of rats in each group was recorded. Data were analyzed using the SPSS application for univariate analysis using central tendency and bivariate analysis with an independent sample T-test. This study has received approval from the Health Research Ethics Committee at Universitas Bhakti Husada Indonesia with reference number 04/EP/UBHI/VI/2024.

RESULTS

Extracts of *Ziziphus mauritiana* leaves and *Centella asiatica* leaves were subjected to phytochemical tests to determine the active compounds contained therein, as explained in Table 1.







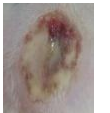



Table 1. Phytochemical Screening Results on *Ziziphus mauritiana* Leaves Extract and *Centella asiatica* Leaves Extract.

No	Active Compounds	Test Method	Results
1	Flavanoids	Magnesium + concentrated HCl + amyl alcohol	Orange
2	Alkaloids	a. Mayer b. Bouchardat c. Dragendrof	a. White/yellow b. Dark Chocolate c. Brick red
3	Tannin	FeCl ₂	Black Blue
4	Triterpenoid/ Steroid	Lieberman Buchard	Blue Green, Red/purple
5	Saponins	Heated	Foam 1-10 cm

According to Table 1, the results of the phytochemical examination of the extracts showed that flavonoids (+) were seen from the color change to yellow or orange. Alkaloids (+) can be seen in forming a red or orange precipitate in solution. Tannins (+) can be seen from the formation of a black or brown precipitate. Triterpenoid/steroid (+) can be seen from the color change of the solution. Positive saponins (+) can be seen by forming a yellow or brown precipitate. Based on these results, it can be concluded that all active compounds tested are present in the samples analyzed. These results indicate a variety of phytochemical compounds in the samples, which may contribute to the wound healing process.

The results of the organoleptic test were obtained in the form of a brownish-green preparation with a distinctive smell of *Ziziphus mauritiana* leaves and a liquid form. The sample test results showed a homogeneous composition characterized by the absence of coarse grains in the preparation applied to the glass. The results of the spreadability test of the lotion of *Ziziphus mauritiana* leaves extract combined with *Centella asiatica* leaves are 8.5. These results indicate that the lotion has good spreadability. It is easy to apply to the skin, with a spread of 5–7 cm. The pH of the lotion formulated with *Ziziphus mauritiana* leaves extract and *Centella asiatica* leaves extract was 7.24. This shows that the lotion preparation has met the standard. Quality requirements for lotion standard pH according to SNI 16-4399-1996 range from 4.5 to 8.0 [18]. In this sense, the irritation test displayed no erythema or edema. This stability test shows that the lotion intermixture of *Ziziphus mauritiana* leaves extract with *Centella asiatica* leaves within specific periods could be a stable formula. The shape, smell, color, and homogeneity are all unchanged, and the pH value is within a given scope of 4.5-8.0

Table 2. Mean Difference in The Percentage of Burn Wound Healing and Morphological Description of Wound Development The Intervention and Control Group

Group	Value	D3	D6	D9	D12	D14
Intervention	Mean	6.44	11.15	33.39	54.41	74.50
	Median	0	14.00	30.00	52.50	75.75
	SD	10.94	26.93	21.55	14.43	15.11
	Min - Max	0.00-33.30	-50.00-46.7	0.00-73.30	33.30-73.30	50.00-100
						
Control	Mean	1.18	-21.72	3.08	21.97	44.46
	Median	0	0	20	27.75	48.35
	SD	3.37	63.36	43.71	30.99	28.98
	Min - Max	0-11.80	-160-50	-100-43.80	-40-62.50	-10-81.30
						

Based on Table 2, the intervention group began to show early effects on the third day, with a mean of 6.44 (SD 10.94), higher than the control group's mean of 1.18 (SD 3.37). On the sixth day, the intervention group's mean increased significantly to 11.15, while the control group's mean decreased to -21.72. On the tenth day, the intervention group's mean increased substantially to 33.39, while the control group's mean only slightly increased to 3.08. Overall, from Days 6–14, the intervention group showed consistent and significant improvement compared to the control group. The intervention group had a mean of 74.50 and a median of 75.75, while the control group had only 44.46 with a median of 48.35.

Figure 1 shows that by day 3, the intervention group began forming granulation tissue with reduced wound size, while the control group showed minimal granulation and visible exudate. By day 6, the intervention group exhibited clearer granulation and early re-epithelialization, whereas the control group remained in early granulation with signs of inflammation. On day 9, re-epithelialization progressed further in the intervention group, with the wound nearly closed. By day 14, the wound was almost fully covered by new epithelium, appearing clean and flat. In contrast, the control group's wound remained partially open with scarring. These findings suggest that the lotion containing *Ziziphus mauritiana* and *Centella asiatica* extracts is more effective than bioplacenton in accelerating wound healing.

Table 3. Distribution Of Mean Burn Wound Healing In Intervention And Control Groups

Group	Mean	SD	SE	p-value	N
Intervention	74.50	15.11	4.77	0.009	10
Control	44.46	28.98	9.16		10

Based on Table 3, the intervention group showed a faster and more consistent wound healing process compared to the control group. This can be seen from the mean and standard deviation values: intervention group (mean=75.5: SD=15.11) and control group (mean=44.46: SD=28.98), with a p-value of 0.009.

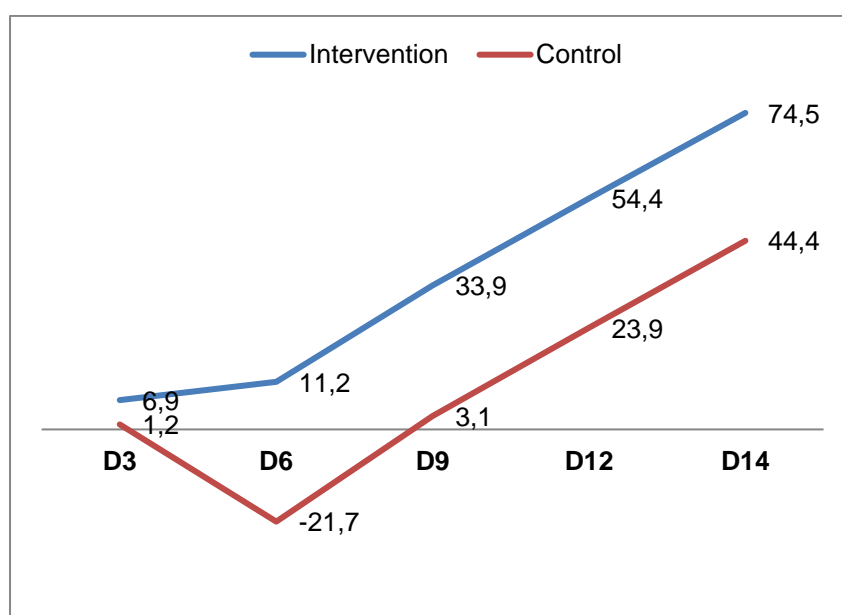


Figure 1. Percentage of Burn Wound Healing in The Intervention and Control Group

Based on Figure 1, the intervention group experienced a consistent increase in scores from day 3 to day 14, reaching 74.5 on day 14. In contrast, the control group experienced fluctuations, with a significant decrease on day six and only reaching 44.4 on day 14. This confirms that the intervention had a more significant and stable effect than the control group.

DISCUSSION

The normal wound healing process consists of several overlapping phases, namely, homeostasis, inflammation, proliferation, and remodeling [19]. In the hemostasis phase, platelet clots form, forming a fibrin matrix that functions as a place for cell infiltration. While in the inflammation phase, there is a process of hypervascularization in the wound area, and leukocyte migration occurs as the body's defense to fight infection and clean the wound area; this facilitates the proliferation phase, where new tissue and granulation are formed. Finally, in the remodeling phase, the tissue maturation process occurs with collagen tissue reorganization until the wound-healing process occurs [20]. In this study, the intervention group showed a faster wound healing process with a faster and more controlled inflammation phase and a more consistent and faster proliferation phase. This indicates better readiness for the remodeling phase. In the control group, the inflammation phase lasted longer, and signs of infection were found early in the wound healing process.

Based on the results of phytochemical tests, it was proven that *Ziziphus mauritiana* leaf extract combined with *Centella asiatica* contains flavonoids, alkaloids, tannins, triterpenoids, steroids, and saponins. These bioactive compounds support wound healing through antioxidant, anti-inflammatory, and antimicrobial mechanisms. Flavonoids and tannins assist in counteracting free radicals and inhibiting microbial growth, saponins promote collagen formation, while triterpenoids and steroids reduce inflammation and stimulate tissue regeneration [21]. These phytochemical effects were corroborated by in vivo findings. On day 14, the mean wound healing percentage in the intervention group was significantly higher ($74.50\% \pm 15.11$) compared to the control group ($44.46\% \pm 28.98$), with a statistically significant difference ($p = 0.009$). This result confirms the therapeutic potential of the lotion formulation, suggesting that the synergistic action of the two extracts effectively accelerates the wound healing process in second-degree burns.

The antioxidant properties of flavonoids can reduce oxidative stress that can damage cells and tissues around the wound, thereby increasing cell regeneration [22]. Excessive inflammation can slow down wound healing. Flavonoids inhibit the production of pro-inflammatory cytokines such as TNF- α and IL-6, which reduce inflammation in the wound area and support an environment conducive to wound healing [23]. Flavonoids are also known to modulate the activity of enzymes that play a role in the degradation of the extracellular matrix and tissue remodeling; this helps regulate scar tissue formation and repair tissue structure in the wound area [24]. Research conducted by Su et al. [26] showed that extracted tannins accelerate wound healing in animal models by reducing inflammation and increasing epithelial cell proliferation. Tannins also have an astringent effect that causes tissue shrinkage, so wound closure occurs faster [27].

Meanwhile, saponin compounds support wound healing by stimulating the formation of collagen and antiseptics that kill germs that usually arise in wounds, preventing severe infections [24]. According to research by Ghaderi et al. [28], terpenoids have anti-inflammatory properties and accelerate wound healing by increasing fibroblast proliferation and collagen production. The antioxidant and antibacterial properties of the bioactive compounds contained in *Ziziphus mauritiana* leaves extract are very safe to give and do not cause toxic reactions and resistance like the use of chemical drugs, so it is very safe to give to humans [29]. The healing effects observed in this study are linked to flavonoids, tannins, triterpenoids, and saponins in *Ziziphus mauritiana* and *Centella asiatica*, which act as antioxidants, anti-inflammatories, and collagen modulators. These compounds accelerate wound closure, reduce inflammation, and enhance tissue regeneration, as evidenced by the significant wound size reduction in the intervention group.

Although *Ziziphus mauritiana* and *Centella asiatica* have been shown to have a positive impact on wound healing, there is a risk of hypersensitivity reactions, although they are scarce [30]. Active compounds such as saponins, flavonoids, and tannins found in these plants can trigger allergic reactions, including contact dermatitis, itching, or redness [30]. In addition, the bioactive compounds of *Centella asiatica* are sensitive to environmental conditions. Studies show that these compounds are stable at acidic to neutral pH (pH 5.8-7.0), but undergo significant degradation under alkaline conditions (pH 8.2). In addition, storage at high temperatures or exposure to light can accelerate the degradation of these active compounds, resulting in a decrease in the therapeutic effectiveness of the lotion. Therefore, the formulation and storage of lotions should consider these factors to maintain their stability and effectiveness [31][32].

From a theoretical perspective, the findings of this study align with Dorothea Orem's Self-Care Deficit Nursing Theory, which emphasizes that individuals have the capacity and responsibility to engage in self-care to maintain health and promote recovery. In his theory, Orem revealed three main components: self-care, self-care deficit, and the nursing system [33]. The results of this study can be applied to self-care that can be done independently to accelerate the wound healing process. According to research by Khademian et al. [34], using natural ingredients in self-care improves the healing process and reduces self-care deficits in patients with chronic conditions. Self-care has been shown to positively impact the quality of life, where patients are responsible for themselves, in control, and flexible in care related to their disease condition [35].

In Orem's theory, a self-care deficit occurs when an individual cannot meet their own care needs, thus requiring nursing intervention [36]. Orem divides the level of patient needs fulfillment into three categories: wholly compensatory, partly compensatory, and educational supportive [37]. In the process of independent wound care, patients need to be educated on how to perform wound care, starting from removing, bandaging, cleaning wounds, changing dressings, identifying wound conditions, and using assistive devices [37],[38]. Self-care can be optimized if the patient has good knowledge about the disease

and its treatment, and good skills and efficacy; this also helps improve their awareness and quality of life [39]. A study by Chen et al. [40] revealed that proper self-care can significantly reduce the burden of health care in hospitals. Environmental factors greatly support the wound healing process; this is in line with the nursing theory put forward by Nightingale, which states that good environmental conditions will improve the healing process of the disease; conversely, a lousy environment can inhibit the healing process of the disease, these environmental factors are cleanliness, clean air, clean water, light, and temperature control [41].

Applying Nightingale's theory, this study highlights the role of environmental factors in wound healing, supported by safe, natural ingredients. The herbal lotion with *Ziziphus mauritiana* and *Centella asiatica* aids skin regeneration, maintains moisture, and prevents infection. Its base enhances absorption, bioavailability, and protection, while the extracts' antibacterial and anti-inflammatory effects foster optimal healing conditions. This aligns with research conducted by Tottoli et al. [42], which stated that using natural ingredients and a clean environment has improved wound healing. A study by Xu et al. [43], showed that wound care using natural ingredients such as herbal extracts can improve the wound microenvironment. Wound environment management, including moisture control and natural antimicrobial agents, is critical in wound healing [44]. This supports the Nightingale approach, which emphasizes the role of the environment in the patient's recovery process. Using natural ingredients in wound care is an application of the integration of traditional and modern care, which is the basis of the holistic aspect of nursing. Holistic nursing not only appreciates but also supports the application of various natural therapies that are in harmony with the human body [45].

The holistic nursing paradigm emphasizes optimizing resources in the surrounding environment that can be used as therapy and have economic value. Holistic care is defined as care carried out holistically, emphasizing the physical aspects and the mind and soul, which in practice is associated with complementary or alternative modality therapies [46]. WHO supports the use of traditional and complementary therapies integrated into conventional medicine, such as ayurveda and yoga, the application of mindfulness techniques in the treatment of depressed patients, and the use of herbs in reducing antibiotic use as an effort to prevent drug resistance [47]. Research by Gethin G. et al. [48] shows that a holistic approach to wound care, including natural ingredients, significantly improves wound healing and patient satisfaction.

Implications and Limitations

Ziziphus mauritiana and *Centella asiatica* leaf extract lotion is recommended for nursing practice as a natural, cost-effective burn therapy. It promotes wound healing, prevents infection, and reduces scarring. However, the study has limitations, including a small sample size, untested extract dosage variations, and no evaluation of long-term side effects. Conducted on rats, the findings may not fully apply to humans. Further research, including clinical trials, is needed to assess the safety, efficacy, and mechanism of these extracts in human burn care.

CONCLUSION

Ziziphus mauritiana leaf extract combined with *Centella asiatica* has been proven to contain flavonoid, alkaloid, terpenoid, tannin, and saponin compounds, which are active in accelerating the wound healing process. This is evidenced by the acceleration of granulation, epithelialization, and reduction of inflammation in the intervention group compared to the control group.

The group of rats given *Ziziphus mauritiana* leaf extract lotion therapy combined with *Centella asiatica* showed a faster wound healing process compared to the control group given bioplacenton; this proves that the combination of these two extracts has the potential as an effective alternative therapy in the burn wound healing process. The

results of this study still need to be developed, including developing clinical trials in humans to confirm the effectiveness and safety of this combination of extracts in burn wound healing, including determining the optimal dose and potential side effects.

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