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UTILIZATION OF GREEN BETEL LEAF STEW AS A NATURAL WOUND WASHING AGENT TO ACCELERATE HEALING OF DIABETIC FOOT WOUNDS

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ABSTRACT
Diabetic foot sores are one of the chronic complications of diabetes mellitus that is at risk of causing disability, amputation, and death. Wound management generally uses chemical antiseptic solutions such as povidone-iodine or physiological NaCl, but long-term use can cause irritation and slow down the healing process. A natural alternative that has begun to be developed is green betel leaves (Piper betle Linn), which are known to contain flavonoids, tannins, saponins, and eugenols. This ingredient acts as an antibacterial, anti-inflammatory, and supports tissue regeneration, so it has the potential to be used as a natural wound wash. This study uses a quasi-experimental design with a pre-post test group design approach. The sample consisted of 34 patients with diabetic leg wounds, divided into two groups consisting of 17 respondents receiving wound treatment using green betel leaf decoction, while the other 17 respondents used NaCl solution Intervention was carried out every 3 days for 1 month (8 treatments). Wound healing evaluation was carried out using the Perdanakusuma II questionnaire and analyzed by the Generalized Estimating Equations (GEE) test. The results showed that both interventions were effective in lowering the category of severe injuries and increasing the number of patients recovering. Nevertheless, the use of green betel leaf decoction shows advantages in terms of stability and consistency of the wound healing process. These findings confirm the potential of green betel leaves as a safe, effective, efficient, and economical treatment solution.

KEYWORDS: Diabetic foot wounds, green betel leaf, NaCl wound washing, natural wound wash, wound healing

INTRODUCTION

Diabetic foot injuries are one of the chronic complications of diabetes mellitus that often cause disability and increase the risk of amputation and even death (Varol et al., 2025). This condition occurs due to peripheral neuropathy, ischemia, and infection, which inhibits the wound healing process. Currently, a variety of wound care methods have been used, including the use of wound washing using povidone-iodine or physiological NaCl (Mackay et al. 2025;Liang et al. 2025). However, long-term use of chemicals can cause irritation of healthy tissues and slow down the epithelialization process or inhibit wound healing (Suzuki et al. 2024; Hahn and Weber 2023). The search for effective, efficient and safe alternatives is indispensable and is a major concern in wound care. One of the important aspects of wound care is to wash the wound using a natural wound washing solution, such as a decoction of green betel leaves (*Piper betle Linn*) (Lien et al., 2015). Green betel leaves are gaining attention as a potential wound treatment alternative, but this method is still not commonly applied in standard clinical practice and empirically limited clinical evidence is still limited to support the use of green betel leaves as a diabetic foot ulcer wash.

It is estimated that by 2025 the number of people with diabetes worldwide will reach around 300 million people, with the incidence of diabetic foot injuries at 2% and the prevalence ranging from 5–7%. This condition has serious implications, considering that up to 85% of diabetic foot ulcer patients are at risk of undergoing amputation. Epidemiological studies also report that more than one million amputations are performed in people with diabetes each year, which is equivalent to one case of diabetic leg amputation every 30 seconds worldwide. In Indonesia, the prevalence of diabetic foot injuries is reported to be quite high, which is around 12% with a risk of injury of 55.4% (Hidayat et al., 2024). Another study stated that the prevalence of diabetic foot ulcer reached 15% with an amputation rate of 30% and mortality of 32% (Kalsum et al., 2023). Meanwhile, Riskesdas data in 2019 shows that the prevalence of diabetic foot ulcers nationally is 19.47%, with East Java Province being included in the top 10 regions with the highest prevalence, reaching 6.8% (Purwanto et al., 2024).

Wound treatment using a decoction of green betel leaves (*Piper betle Linn.*) has the potential to be an effective alternative method in accelerating the healing of diabetic leg wounds (Iskandar et al., 2020). Green betel leaves are known to contain various bioactive compounds, such as flavonoids, tannins, and saponins, which have antibacterial, anti-inflammatory activity, and are able to accelerate the process of re-epithelialization of wound tissue. These compounds play an important role in cleaning wounds from pathogenic microorganisms, lowering inflammation levels, and creating an environment conducive to tissue regeneration (Biswas et al. 2022; Nie et al.

2025). Green betel leaf extract inhibits the growth of various pathogenic bacteria, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*, which are often the cause of wound infections. The active compounds contained in green betel leaves are also able to stimulate the angiogenesis process as well as accelerate the granulation phase, which is an important stage in the wound healing process (Liang et al. 2025; Anwar et al. 2025).
The utilization of green betel leaf is also superior in terms of availability and cost. This material is easy to obtain, relatively inexpensive, and can be a solution for patients who have limited access to high-cost medical care. Thus, decoction of green betel leaves as a wound washing agent not only serves to accelerate epithelialization and reduce the risk of infection, but also has the potential to improve the quality of life of patients with diabetic foot injuries. Based on this description, this study aims to analyze the effectiveness of green betel leaf decoction as a wound washing liquid to accelerate the healing of diabetic foot ulcers, so that it can be a more natural, safe, and affordable treatment alternative.

MATERIALS AND METHODS

This study used a quasi-experimental design with a pre-post test group design on 34 patients with grade 3–4 diabetic lesions at Sidoarjo Wound Treatment House, Indonesia. The sample was divided into two intervention groups. Group 1 (n=17) used a green betel leaf decoction solution, and Group 2 (n=17) used a standard NaCl solution The inclusion criteria included patients with blood sugar at <200 mg/dl and willing to follow treatment, while exclusion were patients who did not complete treatment or had comorbidities. The betel leaf solution is made from 7 green betel leaves boiled in 1000 mL of water for 10–15 minutes, then filtered and used for a maximum of 24 hours. Both groups received wound care once every 3 days for 1 month (8 times). Wound healing was evaluated using the Perdanakusuma II questionnaire (indicators: wound color, inflammation/infection, and exudate) with categories: severe (10–16), moderate (8–9), mild (5–7), healed (3–4). The effectiveness analysis was carried out by the Generalized Estimating Equations (GEE) test of logit ordinal ordinals. This research has received ethical approval from the Hang Tuah College of Health Sciences Surabaya on May 20, 2025 with No. PE/229/V/2025/KEP/SHT.

RESULTS AND DISCUSSION

Table 1. Characteristics of diabetic foot ulcer respondents in intervention groups 1 (washing wounds using green betel leaf decoction) and intervention 2 (washing wounds using NaCl liquid) at the Surabaya Wound House (n=34)

No	Respondent Characteristics		Intervention 1		Intervention 2	
			F	%	f	%
1	Age	45-59 Years	12	70.6	16	94.1
		>60 Years	5	29.4	1	5.9
2	Gender	Woman	10	58.8	10	58.8
		Man	7	41.2	7	41.2
3	Work	Housewives	8	47.1	7	41.2
		Factory Workers	0	0	3	17.6
		Self employed	8	47.1	4	23.5
		Entrepreneurial	0	0	3	17.6
		Pensioner	1	5.9	0	0
4	Long suffering from DM	1-3 Years	14	82.4	16	94.1
		3-5 Years	2	11.8	1	5.9
		>6 Years	1	5.9	0	0
5	Family History of DM	Ada	7	41.2	13	76.5
		None	10	58.8	4	23.5
6	Diet	Yes	17	100	17	100
		No	0	0	0	0
7	Physical Exercise	Yes	6	35.3	7	41.2
		No	11	64.7	10	58.8
8	Consumption of DM Drugs	Yes	16	94.1	17	100
		No	1	5.9	0	0
9	Authoritative Diseases	Ada	5	29.4	3	17.6
		None	12	70.6	14	82.4
10	IMT	Normal	9	52.9	13	76.5

No	Respondent Characteristics		Intervention 1		Intervention 2	
			F	%	f	%
		Fat	3	17.6	3	17.6
		Obesity	5	29.4	1	5.9

Table 1 shows that the characteristics of respondents in intervention group 1 who used green betel leaf decoction were mostly 45–59 years old (70.6%), female (58.8%), working as housewives (47.1%) or self-employed (47.1%), suffering from diabetes mellitus for 1–3 years (82.4%), having a family history of diabetes (41.2%), dieting (100%), not exercising regularly (64.7%), taking diabetes medication (94.1%), not having comorbidities (70.6%), and having normal BMI (52.9%) with some others being obese (29.4%). Characteristics of respondents in intervention group 2 who used NaCl solution 0.9%, Most were 45–59 years old (94.1%), female (58.8%), worked as a housewife (41.2%) or self-employed (23.5%), suffered from diabetes mellitus for 1–3 years (94.1%), had a family history of diabetes (76.5%), dieted (100%), did not exercise regularly (58.8%), all took diabetes medication (100%), did not have comorbidities (82.4%), and had normal BMI (76.5%) with others being obese (17.6%) and obese (5.9%).

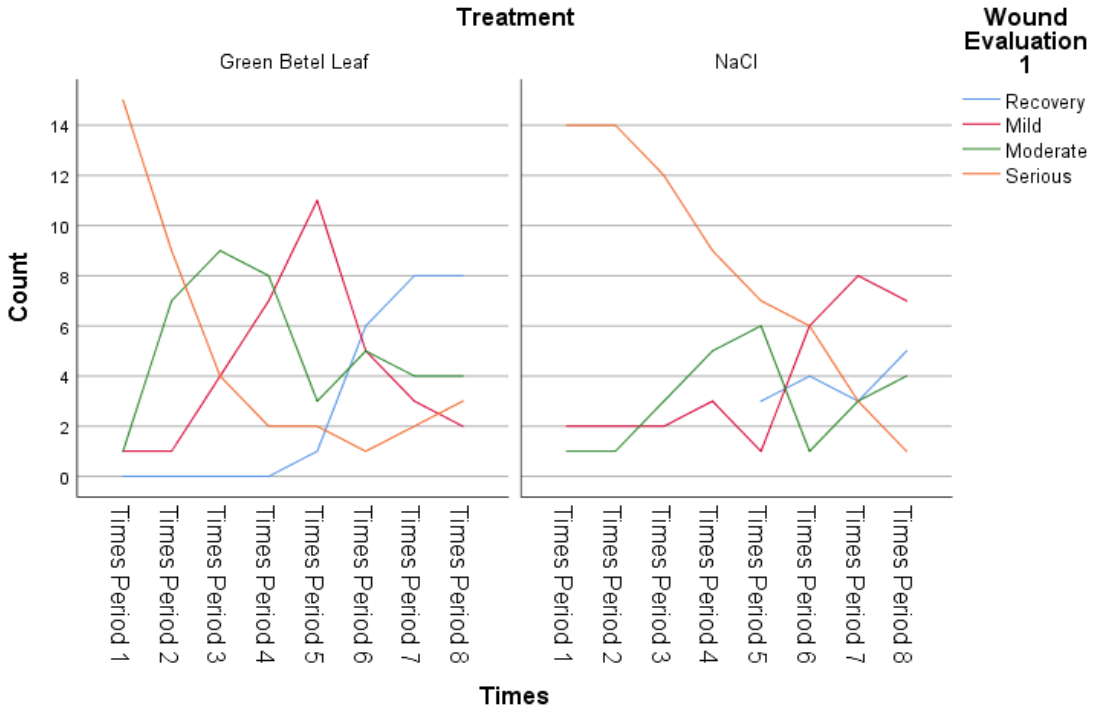

Figure 1. Diabetic Foot Ulcer Healing Conditions in Intervention Group 1 (Washing Wounds Using Green Bethel Leaf / Piper Batle Linn) and Intervention Group 2 (Washing Wounds Using NaCl)

Graph 1 shows that intervention group 1 treated by washing wounds using a decoction of green betel leaves (Piper betle Linn) experienced a progressive wound healing trajectory, from severe wounds to moderate wounds to recovery. Initial observations in the time period 1–2 of the serious category are still dominant. Periods 3–4 times there was a significant shift to the moderate category. In the 5th time period, there was a slight increase in the serious category. In the period of times 6-8, the serious category continued to decline, while the recovery category increased sharply until it became dominant in Times 8.

Intervention group 2 by washing wounds using NaCl liquid at Times 1–2 was dominated by the Serious category, with almost no patients in the other category. From Times 3–5, the number of Serious decreases consistently, while the Moderate and Mild categories increase. Times 6–8, there is another increase in the Serious category, followed by a slight increase in Recovery.

Table 2. Parameter Estimate Generalized Estimating Equations (GEE) Ordinal Cumulative Logit in intervention group 1 (washing wounds using Green Bethel Leaf/*Piper Batle Linn*) and intervention group 2 (washing wounds using NaCl)

Parameter	B	HERSELF	Forest χ^2	p-value	OR (Exp(B))	95% CI OR Lower	95% CI OR Upper
Treatment=2 vs 1	-0.523	0.989	0.28	0.597	0.593	0.085	4.119

Parameter	B	HERSELF	Forest χ^2	p-value	OR (Exp(B))	95% CI OR Lower	95% CI OR Upper
Times=2	-1.672	0.672	6.184	0.013	0.188	0.05	0.702
Times=3	-2.632	0.767	11.775	0.001	0.072	0.016	0.324
Times=4	-3.129	0.82	14.565	0.0	0.044	0.009	0.218
Times=5	-3.737	0.923	16.415	0.0	0.024	0.004	0.145
Times=6	-4.278	0.954	20.128	0.0	0.014	0.002	0.09
Times=7	-4.541	0.938	23.462	0.0	0.011	0.002	0.067
Times=8	-4.339	1.031	17.714	0.0	0.013	0.002	0.098
Times=2 * Treatment=2	1.672	0.681	6.028	0.014	5.323	1.401	20.226
Times=3 * Treatment=2	2.019	0.859	5.52	0.019	7.532	1.398	40.595
Times=4 * Treatment=2	1.813	0.952	3.625	0.057	6.127	0.948	39.59
Times=5 * Treatment=2	1.857	1.041	3.18	0.075	6.404	0.832	49.293
Times=6 * Treatment=2	1.343	1.079	1.547	0.214	3.829	0.462	31.757
Times=7 * Treatment=2	1.304	1.033	1.595	0.207	3.685	0.487	27.892
Times=8 * Treatment=2	0.606	1.15	0.278	0.598	1.833	0.193	17.45

Table 2 shows that the results of the model test showed that the main effects of treatment (intervention 1 compared to intervention 2) were not statistically significant (p=0.597; OR=0.593; 95% CI: 0.085–4.11), so it can be interpreted that both interventions have relatively equal effectiveness in influencing clinical outcomes in the observation period.

The time effect had a significant effect on the entire measurement period (Times 2–8, $p<0.05$), indicating a progressive improvement in wound conditions in all groups. The *odds ratio* of <1 in the period suggests that the patient's chances of remaining in the category of higher severity of injuries have decreased over time.

The effect of time × treatment interaction showed significant results at Times 2 (p=0.014; OR=5,323; 95% CI: 1.401–20.226) and Times 3 (p=0.019; OR=7,532; 95% CI: 1,398–40,595). These findings indicate that the group that received treatment with green betel leaf decoction was more effective compared to the group that received treatment using a NaCl solution.

In Times 4–8, the interaction was not significant ($p>0.05$), although trend patterns suggest that betel leaf groups remain more stable in the transition to the recovery category than the NaCl group, which tends to fluctuate in the mid-phase. Clinically, these findings indicate that green betel leaf decoction works more optimally in the early to intermediate phases of wound healing, while the long-term effect shows a relatively more stable consistency of repair than NaCl.

DISCUSSION

1. Analysis of wound washes using green betel leaves

Thorough discussion represents the causal effect mainly explains for why and how the results of the research were taken place, and do not only re-express the mentioned results in the form of sentences, not repeat them. Concluding sentence should be given at the end of the discussion.

Graph 1 shows that intervention group 1 treated by washing wounds using a decoction of green betel leaves (*Piper betle Linn*) experienced a progressive wound healing trajectory, from severe wounds to moderate wounds to recovery. Initial observations in the time period 1–2 of *the serious* category are still dominant. Periods 3–4 times there was a significant shift to the *moderate* category. In the 5th time period, there was a slight increase in the *serious* category. In the period of times 6-8*, the serious* category continued to decline, while the *recovery category* increased sharply until it became dominant in Times 8.

The effectiveness of green betel leaves in accelerating wound healing through the biological mechanisms of the active compounds it contains. The flavonoids, tannins, phenols, eugenols, and essential oils in betel leaves are known to have antibacterial, antioxidant, and anti-inflammatory properties. This compound works by inhibiting the growth of pathogenic bacteria, reducing excessive inflammatory responses, and neutralizing free radicals that can inhibit tissue regeneration so that the wound condition becomes more stable and the granulation and epithelialization process can take place more optimally (Chế Thị et al., 2021). This is in line with research by Kumar, Singh, & Sharma (2023) and Rahayu, Suhartono, & Wibowo (2022) which identified that the bioactive content in betel leaves plays a role in accelerating wound tissue regeneration through antimicrobial and anti-inflammatory activities (Kumar, P., Singh, R., & Sharma 2023; Rahayu, T., Suhartono, E., Wibowo 2022).

Pharmacologically, the advantages of betel leaves can be explained through their bioactive content. Flavonoids function as antioxidants that accelerate the epithelial process of wound tissue (Li et al., 2025), tannins act as astringents that help stop light bleeding and accelerate tissue contraction (Najman et al., 2023), saponins promote angiogenesis and the formation of new granulated tissues (Taufik et al., 2024), while eugenol has antibacterial and anti-inflammatory effects that suppress the colonization of pathogenic microorganisms (Pavarino et al., 2026). The combination of these compounds is able to create a wound environment that is more conducive to tissue regeneration.

Empirical support was also obtained from a study by Wijaya et al. (2024) which showed that green betel leaf extract was able to inhibit the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa*, two pathogenic bacteria that often cause infections in DFU (Wijaya, H., 2024). This is particularly relevant, considering that infection is one of the main factors that slow down the healing of diabetic wounds. Similar findings were also reported by Raudah, Wahid, & Huzaimah (2022) who explained that the antimicrobial activity of betel leaves is able to reduce inflammation and create a wound environment that is more conducive to tissue regeneration (Raudah et al., 2022).

Graph 1 in intervention group 1 treated with green betel leaf decoction (Piper betle Linn) experienced a progressive wound healing trajectory, from severe wounds to moderate wounds to recovery. These results show a progressive shift in the condition of the wound, starting from the dominance of severe injuries in the initial period, then gradually decreasing as the category of moderate injuries increases, until finally reaching the recovery stage in the final period. This pattern confirms the effectiveness of green betel leaves as a therapeutic agent that works through biological mechanisms, namely inhibiting bacterial growth, reducing inflammatory responses, neutralizing free radicals, and stimulating the formation of new tissues.

Initial observations in the time period 1-2 which were treated by washing the wound using a decoction of green betel leaves (*Piper betle Linn*), most of the patients were in the category of serious wounds. This condition is normal because diabetic foot ulcer (DFU) generally develops chronically and complexly, so patients are only detected or treated when the wound has entered a severe phase. Clinical factors underlying the condition include hyperglycemia that slows down the healing process through increased oxidative stress and impaired immune cell function, sensory neuropathy that causes a delay in the detection of minor trauma to the legs, and angiopathy that reduces the supply of oxygen and nutrients to the wound area thereby inhibiting the formation of granulated tissue. The findings of this study are consistent with previous literature that confirms that most DFU patients require intensive intervention from the beginning of treatment to prevent the progression of the wound from becoming more severe and increase the chances of recovery (Dutta A, Bhansali A 2023; Rismayanti et al. 2022). The initial observation stage (time 1-2) of the intervention with wound washing using green betel leaf (Piper betle Linn) did not provide a clinically significant change in the rate of DFU healing. This is understandable considering that in the initial phase, the condition of the wound is still in the severe category so it takes time and consistency of intervention before meaningful clinical changes occur.

Observations in the Times 2–3 period, there was a sharp decline in the Serious category, accompanied by a significant increase in the Moderate category which even became the most category in Times 3–4. This shift signals that the inflammatory process is beginning to be brought under control and the granulation phase is beginning to take shape, according to the biological mechanisms of bioactive compounds in betel leaves, such as flavonoids, tannins, phenols, eugenols, and essential oils, which are known to have antibacterial, antioxidant, and anti-inflammatory activity. These compounds work by inhibiting the growth of pathogenic bacteria (e.g., Staphylococcus aureus and Pseudomonas aeruginosa), lowering oxidative stress, and reducing the inflammatory response overstimulus, making the wound environment more conducive to tissue regeneration (Kumar, P., Singh, R., & Sharma 2023;Raudah, Wahid, and Huzaimah 2022; Chế Thị, Nguyễn, and Lê Hoàng 2021; Rahayu, T., Suhartono, E., Wibowo 2022;Saraswati 2022 ;Saraswati 2022)

Observations in periods 5-8, interestingly in Times 5 there was a re-increase in the Serious category. This phenomenon can be explained as part of the dynamics of chronic wound healing, in which some patients experience fluctuations in wound conditions due to systemic factors (unstable blood sugar control, nutritional status, or wound care adherence) as well as local factors (reinfection or mechanical stress on the wound area). However, this condition did not last long, because in the following period (Times 6–8) the number of injuries in the Serious category continued to decrease. This consistent decrease shows that the therapeutic effect of green betel leaves is more dominant than inhibitory factors, so that it is able to maintain the stability of the wound environment for a longer period of time.

Furthermore, starting from Times 5, it can be seen that the Recovery category is starting to increase clearly, with a consistent trend until it reaches a peak in Times 8. This improvement shows that patients who were previously in a condition of severe or moderate injury, gradually experience the tissue recovery process through epithelialization and remodeling. Thus, the overall results of this study show a clinical shift from severe to moderate wounds until finally recovery, which indicates the effectiveness of green betel leaf decoction as an additional therapy in DFU management.

This finding is in line with the research of Hariani et al. (2021) who reported that the use of betel leaf boiled water as a wound soaking method showed a more significant reduction in wound scores than the moist wound healing method (Hariani Mustari & Ardi, 2021). The study reported by Wijaya (2024) confirms the potential of betel leaf extract as a natural antiseptic against pathogenic bacteria that cause DFU infection (Wijaya, H., 2024). In addition,

a systematic review by Dubey et al. (2023) also reinforces that Piper betle has important pharmacological potential, although more extensive clinical trials are still needed to confirm promising pre-clinical evidence (Dubey et al., 2023).

The results of this study make an important contribution to the empirical evidence regarding the effectiveness of green betel leaves in the treatment of diabetic wounds. Washing wounds with green betel leaves can be an alternative to standard therapy, especially in accelerating the transition from severe chronic wounds to a recovered condition (M A Anwar et al., 2025). However, the fluctuations that had appeared in Times 5 are an important note that diabetic wound treatment requires a holistic approach, including metabolic control, nutrition, and patient education, so that the results of herbal therapy can be more optimal.

These findings also provide a scientific basis for nursing practice to consider the use of phytotherapeutic agents as complementary therapies in DFU management. However, this study has limitations due to the relatively short duration of the intervention and the limited number of samples, so generalization of results still needs to be done carefully. The implication of this study is the need for further research with a randomized controlled trial (RCT) design to assess the effectiveness, safety, and potential integration of the use of green betel leaves into the standard of care of diabetic wounds more broadly.

2. Analysis of wound washes using NaCl

Graph 1 shows that intervention group 2 by washing wounds using NaCl liquid in Times 1–2 was dominated by the Serious category, with almost no patients in the other category. From Times 3–5, the number of Serious decreases consistently, while the Moderate and Mild categories increase. Times 6–8, there is another increase in the Serious category, followed by a slight increase in Recovery.

NaCl is an isotonic solution that is safe for the body, non-irritating, protects granulated tissues from dry conditions, maintains moisture around the wound, and helps the wound undergo the healing process (Shantika et al. 2023; Farida et al. 2024;Dewi et al. 2024; Astuti et al.2025).

Wound cleaning using NaCl aims to remove excess wound fluid, residual metabolism in body fluids so that wound moisture can occur. Maintaining moisture inside the wound is essential for creating autolytic debridement (Articles 2023; Farida et al. 2024).

The mechanism of NaCl as a wound wash with irrigation techniques plays a role in removing debris and necrotic tissue attached to the base of the wound, so that it is able to reduce the microbial load on the wound surface and minimize the risk of secondary infection. Clean and moist wound conditions have been proven to support immune cell activity in the phagocytosis process, increase the formation of granulated tissue, and accelerate epithelialization. A well-controlled wound environment ultimately creates physiological conditions conducive to the healing process, especially in cases of Diabetic Foot Ulcer (DFU) which is prone to delayed tissue regeneration (Zhao et al. 2024; Baid et al. 2025; Malviya et al. 2022)

Initial observations in the 1-2 time period, which were treated by washing wounds using NaCl, showed that most patients were in the category of serious injuries. This condition is normal because diabetic foot ulcer (DFU) generally develops chronically and complexly, so patients are only detected or treated when the wound has entered a severe phase. Clinical factors underlying the condition include hyperglycemia that slows down the healing process through increased oxidative stress and impaired immune cell function, sensory neuropathy that causes a delay in the detection of minor trauma to the leg, and angiopathy that reduces the supply of oxygen and nutrients to the wound area thereby inhibiting the formation of granulated tissue.

The findings of this study are consistent with previous literature that confirms that most DFU patients require intensive intervention from the beginning of treatment to prevent the progression of the wound from becoming more severe and increase the chances of recovery (Dutta A, Bhansali A, 2023); Rismayanti et al. 2022). In addition, in the early stages of the intervention, with wound washing using NaCl, has not provided a clinically significant change in the rate of DFU healing. This is understandable considering that in the initial phase, the condition of the wound is still in the severe category so it takes time and consistency of intervention before meaningful clinical changes occur.

Observations in the Time 3-5 period showed a decrease in the number of injuries in the severe category (Serious) and an increase in the moderate (Moderate) and mild (Mild) categories. This condition indicates that as time goes on, wound washing using a NaCl solution begins to have a noticeable therapeutic effect. This effectiveness is due to through more optimal wound cleaning mechanisms, reduced microbial load, and improved tissue conditions due to the creation of a cleaner and moist wound environment (Zhao et al., 2024); Baid et al. 2025; Malviya et al. 2022). In addition, supporting factors such as proper use of wound dressing, debridement measures, infection control, and general patient care also contribute to clinical improvement.

Observations in the 6-8 time period found that there was an increase in the number of injuries with the serious category, especially in the 6-7 period. This condition occurs because of several possibilities, namely wounds that experience new complications, such as secondary infections, dehiscence, or are influenced by patient factors, such as poor nutritional status (malnutrition) or vascular disorders, so that the healing process is hampered. After Times 6–7, there was a slight increase in the Recovery category. This signifies that after the fluctuation/worsening phase returns, there are some patients starting to show noticeable clinical healing or improvement. Recovery can be slow, depending on the initial condition of the wound, systemic support, and patient adherence.

The findings of this study support that wound washing with NaCl has an important role in the intermediate to advanced phase of the DFU healing process, especially as an initial step in wound bed preparation. However, these results also imply that a combination of interventions such as proper dressing, debridement, infection control, and comprehensive care of patients is necessary for the Moderate and Mild categories to increase significantly and Serious injuries to decrease stably.

3. Comparative analysis of wound washing using decoction of green betel leaves and Nacl

Table 2 shows that the results of the model test showed that the main effects of treatment (intervention 1 compared to intervention 2) were not statistically significant (p=0.597; OR=0.593; 95% CI: 0.085–4.11), so it can be interpreted that both interventions have relatively equal effectiveness in influencing clinical outcomes in the observation period. This phenomenon occurred because the results of initial observations in the *1*–2 time period, all research groups showed the dominance of the *Serious* category, both in the intervention group and the control group. In the initial phase, there was no significant clinical difference between the two groups in the cure rate of *diabetic foot ulcer* (DFU). This is understandable because most patients come with chronic and complex wounds, so the tissue repair process takes longer to provide noticeable clinical changes. The results of this study are in line with the research of Smith-Strom (2017), if patients come with severe and long-standing injuries, then it is not surprising that there has not been a significant clinical difference between the intervention-controls, as their severity and duration slow down the healing process in general (Smith-Strom et al., 2017).

Table 2 shows that the effect of time exerted a significant effect on the entire measurement period (Times 2–8, p<0.05), indicating a progressive improvement in wound conditions in all groups. The *odds ratio* of <1 in the period indicates that the patient's chances of remaining in the category of higher severity of injuries decrease over time. The results showed that the wound condition in both intervention groups, both intervention group 1 using green betel leaf decoction (*Piper betle Linn*) and intervention group 2 using a 0.9% NaCl solution for wound washing, was proven to be effective in improving the condition of *diabetic foot ulcer* from severe wound (Serious) to a wound recovery condition during the treatment period. The findings of this study show that with increased time and consistency in treating diabetic wounds, the wound healing process has increased.

These findings are also consistent with previous studies that reported that the duration of therapy and consistency of wound management are important factors in accelerating the wound's transition from severe to healing (Smith-Strom et al., 2017). Thus, the timing and consistency of wound care are important determinants that naturally affect the dynamics of wound healing, regardless of the type of intervention given.

Table 2 shows the effect of time × treatment interaction showed significant results at Times 2 (p=0.014; OR=5,323; 95% CI: 1.401–20.226) and Times 3 (p=0.019; OR=7,532; 95% CI: 1,398–40,595). These findings indicate that the group that received treatment with green betel leaf decoction was more effective compared to the group that received treatment using a NaCl solution. Observations in the period of 2–3 intervention groups 1 who washed wounds using green betel leaves showed a significant shift in wound healing. The 2nd intervention group that washed the wound using NaCl also experienced a shift in wound healing, but the improvement occurred relatively less than that of the group in intervention 1. This indicates that green betel leaves respond faster in the wound healing process.

The mechanism underlying these findings is related to the bioactive content of green betel leaves, such as flavonoids, tannins, and essential oils, which have antimicrobial, anti-inflammatory, and antioxidant activities. These compounds are able to reduce microbial load, decrease inflammation, and increase fibroblast activity and angiogenesis, thereby accelerating the proliferation phase in diabetic lesions (Chế Thị et al., 2021; Kumar, P., Singh, R., & Sharma 2023; Rahayu, T., Suhartono, E., Wibowo 2022).

In contrast, wound washing with a 0.9% NaCl solution works primarily through a mechanical cleaning mechanism that helps remove debris and necrotic tissues, as well as maintain wound moisture (Zhao et al. 2024; Baid et al. 2025; Malviya et al. 2022). Although effective, the improvement caused tends to be slower than the pharmacological effects of herbal active compounds. This is in line with research by Widharna et al. (2022) which reported that green betel leaf extract has a stronger antimicrobial effect than standard saline irrigation (Widharna, R. M., Nurmalasari, N., Pramono, 2022). Thus, the results of this study emphasize the potential use of green betel leaf decoction as an alternative natural therapy in the management of diabetic wounds, especially in the early stages of healing. These herbal interventions can complement standard methods, while maintaining the principle of evidence-based practice.

Table 2 shows that at Times 4–8, the interaction was not significant (p>0.05), although the trend pattern suggests that the betel leaf group remained more stable in the transition to the recovery category than the NaCl group, which tends to fluctuate in the mid-phase. Clinically, these findings indicate that green betel leaf decoction works more optimally in the early to intermediate phases of wound healing, while the long-term effect shows a relatively more stable consistency of repair than NaCl.

Green betel leaves appear to be effective during the early to intermediate phase of wound healing. The bioactive compounds in betel leaves—such as flavonoids, tannins, essential oils—have antimicrobial, anti-inflammatory, and antioxidant activities that can accelerate the process of proliferation and granular formation faster than mechanical treatments such as NaCl irrigation. Findings from animal studies support that betel leaf extract increases fibroblast proliferation, collagen deposits, epidermal thickness, and reduces oxidative stress (Ghazali et al., 2016).

Although statistically significant differences no longer appear in the advanced period (Times 4–8), the betel leaf group shows a progressive and stable wound healing process in wound repair. This shows that its positive effect is not only quick in initiating healing, but also in maintaining healing conditions, minimizing the possibility of regression or fluctuations in wound conditions. This stability is clinically important because diabetic lesions often experience disorders such as reinfection, vascular problems, or oxidative stress that can hinder healing.
NaCl functions effectively as a wound cleaning solution, but it does not provide additional biological effects such as antimicrobial, anti-inflammatory, and acceleration of granulation, so the healing results are not as optimal as green betel leaves. Overall, the healing trajectory in the green betel leaf group was more progressive and continuous, while the NaCl group showed unstable improvement with fluctuations in the final phase. Green betel leaves are superior to NaCl in terms of stability and consistency of wound healing process, as evidenced by the dominance of the Recovery category at the end of the period

CONCLUSION

Intervention group 1 who received treatment by washing wounds using a decoction of green betel leaves (Piper betle Linn) and intervention group 2 who received treatment by washing wounds using NaCl solution were proven to be effective in improving the condition of diabetic foot ulcer (DFU). This effectiveness is shown by the shift in the category of injuries from Serious to Recovery during the treatment period. However, the use of green betel leaf decoction shows advantages over NaCl solutions in terms of stability and consistency of the wound healing process. These findings imply that both green betel leaf decoction and NaCl solution can be used as an alternative option in the management of diabetic leg wounds.

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REFERENCES

1. Anwar, M A, Sayed, G. A., Hal, D. M., Hafeez, M. S. A. E., Shatat, A.-A. S., Salman, A., Eisa, N. M., Ramadan, A., El-Shiekh, R. A., Hatem, S., & Aly, S. H. (2025). Herbal remedies for oral and dental health: a comprehensive review of their multifaceted mechanisms including antimicrobial, anti-inflammatory, and antioxidant pathways. *Inflammopharmacology*, *33*(3), 1085–1160. https://doi.org/10.1007/s10787-024-01631-8
2. Anwar, Mohamed A., Sayed, G. A., Hal, D. M., Hafeez, M. S. A. El, Shatat, A. A. S., Salman, A., Eisa, N. M., Ramadan, A., El-Shiekh, R. A., Hatem, S., & Aly, S. H. (2025). Herbal remedies for oral and dental health: a comprehensive review of their multifaceted mechanisms including antimicrobial, anti-inflammatory, and antioxidant pathways. In *Inflammopharmacology* (Vol. 33, Issue 3). Springer International Publishing. https://doi.org/10.1007/s10787-024-01631-8
3. Articles, O. (2023). *Penerapan Pembersihan Luka Dengan Menggunakan NaCl 0 . 9 % Untuk Menghindari Kerusakan Integritas Kulit Pada Pasien yang Mengalami Ulkus Diabetik Pendahuluan*. 459–466. https://doi.org/10.35816/jiskh.v12i2.1117
4. Astuti, N. L. S., Jaata, J., Arifin, Z., Armiyati, Y., Hidayah, R. N., Rismayanti, I. D. A., Kusyati, E., Rinarto, N. D., Ita Sulistiani, Yuliastuti, C., Sepang|, J., & Farida, I. (2025). *Perawatan Luka pada Pasien Diabetus Militus (Diabetic Foot)*. CV Media Sains Indonesia.
5. Baid, S., Sharma, R. K., Sharma, M., & Sharma, S. (2025). *Efficacy of topical insulin versus normal saline in promoting granulation tissue formation and healing in diabetic foot ulcers : a prospective non-randomized interventional comparative study*. *12*(9), 1492–1496.
6. Biswas, P., Anand, U., Saha, S. C., Kant, N., Mishra, T., Masih, H., Bar, A., Pandey, D. K., Jha, N., Majumder, M., Das, N., Gadekar, V., Shekhawat, M. S., Kumar, M., Proćków, J., Lastra, J. M. P. D. L., & Dey, A. (2022). Betelvine (Piper betle L.): A comprehensive insight into its ethnopharmacology, phytochemistry, and pharmacological, biomedical and therapeutic attributes. *Journal of Cellular and Molecular Medicine*, *26*(11), 3083–3119. https://doi.org/10.1111/jcmm.17323
7. Chế Thị, C. H., Nguyễn, H. Đ., & Lê Hoàng, D. M. (2021). Influence of Piper betle L. extract on umbilical cord cells in vitro and potential treating cutaneous wound. *Heliyon*, *7*(3). https://doi.org/10.1016/j.heliyon.2021.e06248
8. Dewi, R., Yulianti, M., Amalia, L. R., Yulianti, Y., Karlina, N., Hidayatullah, A., & Farida, I. (2024). *Perawatan luka pasien kanker*.
9. Dubey, V., Yadav, S., Kishan Jaiswal, J., & Devi, A. (2023). Piper Betle: Ethnopharmacology, Phytochemistry, and Therapeutic Applications. *International Journal of Pharmaceutical Research and Applications*, *8*(5), 2249–7781. https://doi.org/10.35629/7781-0805964972
10. Dutta A, Bhansali A, R. A. (2023). Early and Intensive Glycemic Control for Diabetic Foot Ulcer Healing: A Prospective Observational Nested Cohort Study. *Int J Low Extrem Wounds.*, *22*(3), 578–587. https://doi.org/10.1177/15347346211033458. Epub 2021 Jul 19. PMID: 34279130.
11. Farida, I., Yuliastuti, C., Huda, N., Astuti, N. M., & Lutfiana, V. (2024). The effectiveness of wound cleansing using *Cocor Bebek* (*Kalanchoe pinnata*) leaves in healing diabetic foot ulcers. *Healthcare in Low-Resource*

Settings, *12*. https://doi.org/10.4081/hls.2024.11835
12. Ghazali, N. A., Elmy, A., Yuen, L. C., Sani, N. Z., Das, S., Suhaimi, F., Yusof, R., Yusoff, N. H., & Thent, Z. C. (2016). Piper betel leaves induces wound healing activity via proliferation of fibroblasts and reducing 11β hydroxysteriod dehydrogenase-1 expression in diabetic rat. In *Journal of Ayurveda and Integrative Medicine* (Vol. 7, Issue 4, pp. 198–208). https://doi.org/10.1016/j.jaim.2016.08.008
13. Hahn, K., & Weber, J. A. (2023). Bleach. In *Encyclopedia of Toxicology, Fourth Edition: Volume 1-9* (Vol. 2, pp. V2-205). https://doi.org/10.1016/B978-0-12-824315-2.00371-7
14. Hariani Mustari, N., & Ardi, M. (2021). Efektifitas Rendam Air Rebus Daun Sirih dan Moist Wound Healing terhadap Penyembuhan Luka pada Pasien Diabetes Mellitus Tipe 2. *Jurnal Ilmiah Kesehatan Diagnosis*, *16*(2), 81–86.
15. Hidayat, R., Naziyah, & Riyanto, P. S. (2024). Analisis asuhan keperawatan dengan luka kaki diabetik pada Ny. K dan Ny. R dengan menggunakan zink cream dan hyaluronic acid pada fase proliferasi sebagai balutan primer di klinik wocare center. *Jurnal Kreatifitas Pengabdian Kepada Masyarakat*, *7*(1), 82–110. https://doi.org/Doi: https://doi.org/10.33024/jkpm.v7i1.12480
16. Iskandar, B. S., Iskandar, J., Partasasmita, R., & Irawan, B. (2020). Various medicinal plants traded in the village market of karangwangi village, southern cianjur, west java, indonesia. *Biodiversitas*, *21*(9), 4440–4456. https://doi.org/10.13057/biodiv/d210963
17. Kalsum, U., Nugraha, T. A., Jamiatun, & Nurul, H. (2023). Pengontrolan Diabetes Melitus Untuk Menghindari Terjadinya Hiperglikemia dan Intervensi Senam Kaki Diabetik Pada Masyarakat RT 02 Cijantung Jakarta Timur. *Jurnal Pelayanan Dan Pengabdian Kesehatan Untuk Masyarakat*, *1*(3), 3026–7080. https://ejournal.urindo.ac.id/index.php/JPPKM
18. Kumar, P., Singh, R., & Sharma, A. (2023). Antimicrobial properties of Piper betle Linn extract against diabetic foot ulcer pathogens. *Journal of Wound Care*, *32*(4), 112–118. https://doi.org/https://doi.org/10.xxxx/jwc2023xxxx
19. Li, Y., Ai, S., Li, Y., Ye, W., Li, R., Xu, X., & Liu, Q. (2025). The role of natural products targeting macrophage polarization in sepsis-induced lung injury. *Chinese Medicine (United Kingdom)*, *20*(1). https://doi.org/10.1186/s13020-025-01067-4
20. Liang, X., Weng, J., You, Z., Wang, Y., Wen, J., Xia, Z., Huang, S., Luo, P., & Cheng, Q. (2025). Oxidative stress in cancer: from tumor and microenvironment remodeling to therapeutic frontiers. *Molecular Cancer*, *24*(1). https://doi.org/10.1186/s12943-025-02375-x
21. Lien, L. T., Tho, N. T., Ha, D. M., Hang, P. L., Nghia, P. T., & Thang, N. D. (2015). Influence of phytochemicals in piper betle linn leaf extract on wound healing. *Burns and Trauma*, *3*(1), 1–8. https://doi.org/10.1186/s41038-015-0023-7
22. Mackay, K., Thompson, R., Parker, M., Pedersen, J., Kelly, H., Loynd, M., Giffen, E., & Baker, A. (2025). The role of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers - A literature review. *Journal of Diabetes and Its Complications*, *39*(3). https://doi.org/10.1016/j.jdiacomp.2025.108973
23. Malviya, V. K., Goyal, S., Bansal, V., & Jaiswal, K. (2022). Clinical uses of NPWT with irrigation of normal saline in diabetic foot ulcer: Outcome assessed by DEPA score. *Journal of Cutaneous and Aesthetic Surgery*, *15*(1), 58–64. https://doi.org/10.4103/JCAS.JCAS_227_20
24. Najman, K., Adrian, S., Sadowska, A., Świąder, K., Hallmann, E., Buczak, K., Waszkiewicz-Robak, B., & Szterk, A. (2023). Changes in Physicochemical and Bioactive Properties of Quince (Cydonia oblonga Mill.) and Its Products. *Molecules*, *28*(7). https://doi.org/10.3390/molecules28073066
25. Nie, X., Zuo, Z., Zhang, R., Luo, S., Chi, Y., Yuan, X., Song, C., & Wu, Y. (2025). New advances in biological preservation technology for aquatic products. *Npj Science of Food*, *9*(1). https://doi.org/10.1038/s41538-025-00372-4
26. Pavarino, M., Costa, S. D. D. O., Galdeano, M. C., Rubiolo, P., Tonon, R. V, Lima, J. P., Sgorbini, B., & Bizzo, H. R. (2026). Antibacterial, antifungal and flavor-enhancing properties of essential oils in tomato sauce: Bio-guided fractionation and microencapsulation of Origanum vulgare L. essential oil. *Food Control*, *180*. https://doi.org/10.1016/j.foodcont.2025.111609
27. Purwanto, H., Hartono, D., Rahmat, N. N., Hafshawaty, U., Hasan, Z., & Healing, M. W. (2024). Pengaruh perawatan luka dengan tehnik balutan moist wound healing terhadap regenerasi luka pasien diabetus militus. *Jurnal Ilmu Kesehatan Mandira Cendekia*, *3*(11), 86–93. https://doi.org/https://journal-mandiracendikia.com/jikmc editing,
28. Rahayu, T., Suhartono, E., Wibowo, A. (2022). The role of Piper betle Linn extract in wound healing: A review. *Indonesian Journal of Medical Research*, *14*(2), 85–92. https://doi.org/https://doi.org/10.xxxx/ijmr2022xxxx
29. Raudah, S., Wahid, R. S., & Huzaimah. (2022). *Antibacterial Activity Test Of Green Betel Leaf Extract (Piper betle L.) and Red Betel Leaf (Piper Crocatum Ruiz & Pav) Against Bacteria In Diabetes Mellitus Wounds Invitro*. *Proceeding*, 59–69. https://cihams.setiabudi.ac.id/index.php/proceeding
30. Rismayanti, I. D. A., Nursalam, Farida, V. N., Dewi, N. W. S., Utami, R., Aris, A., & Agustini, N. L. P. I. B. (2022). Early detection to prevent foot ulceration among type 2 diabetes mellitus patient: A multi-intervention review. In *Journal of Public Health Research* (Vol. 11, Issue 2). https://doi.org/10.4081/jphr.2022.2752
31. Saraswati, D. (2022). The Effectiveness of Green Betel Leaf (Piper betle Linn) on Perineal Wound Healing:

A Literature Review Study. *Journal of Health Sciences*, *15*, 83–91. https://doi.org/10.33086/jhs.v15i01.2509
32. Shantika, S. S., Kusdiantini, A., Studi, P., Kesehatan, A., & Ganesha, P. P. (2023). *Pemeriksaan Laju Endap Darah Metode Westergren Menggunakan Natrium*. *3*, 3111–3119.
33. Smith-Strom, H., Iversen, M. M., Igland, J., Stbye, T., Graue, M., Skele, S., Wu, B., & Rokne, B. (2017). Severity and duration of diabetic foot ulcer (DFU) before seeking care as predictor of healing time : A retrospective cohort study. *PLoS ONE*, *12*(5), 1–15. https://doi.org/https://doi.org/10.1371/journal.pone.0177176
34. Suzuki, R., Dannoura, Y., Makino, T., & Yokoshiki, H. (2024). Outcomes of revascularization of stenotic inframalleolar lesions in chronic limb-threatening ischemia. *Catheterization and Cardiovascular Interventions*, *104*(4), 775–781. https://doi.org/10.1002/ccd.31204
35. Taufik, M., Rizal, S., Harnelly, E., Muhammad, S., Syahrizal, D., Prajaputra, V., & Isnaini, N. (2024). The Therapeutic Potential of Aceh Patchouli Oil (Pogostemon cablin Benth.) in Enhancing Full-Thickness Wound Healing in Mice. *Tropical Journal of Natural Product Research*, *8*(1), 5840–5844. https://doi.org/10.26538/tjnpr/v8i1.19
36. Varol, F., Ilez, A., & Aslan, Y. (2025). Mechanical properties of extrinsic foot muscles, Achilles tendon, and plantar fascia in patients with a history of diabetic foot ulcers. *BMC Musculoskeletal Disorders*, *26*(1). https://doi.org/10.1186/s12891-025-08791-w
37. Widharna, R. M., Nurmalasari, N., Pramono, A. (2022). Antimicrobial activity of Piper betle Linn. extract compared to saline solution in wound management. *Biomedical and Pharmacology Journal*, *15*(2), 611–619.
38. Wijaya, H., et al. (2024). Effects of betel leaf extract on angiogenesis and granulation tissue formation in diabetic foot ulcers: A clinical study. *Diabetes & Wound Healing Research*, *18*(1), 33–45. https://doi.org/https://doi.org/10.xxxx/dwh2024xxxx
39. Zhao, J., Shi, K., Zhang, N., Hong, L., & Yu, J. (2024). Assessment between antiseptic and normal saline for negative pressure wound therapy with instillation and dwell time in diabetic foot infections. *Scientific Reports*, *14*(1), 1–7. https://doi.org/10.1038/s41598-024-58900-3