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Comparative Effect of Topical Sucralfate Cream on Wound Size in Sprague–Dawley Rats with Second-Degree Burns

Vrenda Alia*, Triasari Oktavriana, Prasetyadi Mawardi, Muhammad Eko Irawanto, Arie Kusumawardani
Universitas Sebelas Maret, Indonesia
Email: dr.vrendaalia@gmail.com*

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Burn wound size, second-degree burn, silver sulfadiazine, sucralfate

ABSTRACT

Background: Second-degree burns cause significant tissue damage and require optimal management to prevent complications and delayed healing. Silver sulfadiazine (SSD) is widely used as a standard topical therapy for burn wounds. Topical sucralfate has cytoprotective properties and has been suggested to enhance wound healing, making it a promising adjunct therapy in burn management. Objective: This study aimed to compare the reduction in second-degree burn wound size following treatment with 10% sucralfate cream, 7% sucralfate cream, and silver sulfadiazine in a rat model. **Methods**: This experimental study used a post-test-only control group design involving 48 Sprague–Dawley rats with standardized second-degree burn injuries. The animals were randomly allocated into four groups: a negative control group with no treatment (NC), a positive control group treated with silver sulfadiazine (PC), a treatment group receiving 7% sucralfate cream (T1), and a treatment group receiving 10% sucralfate cream (T2). Wound size was measured on days 1, 3, 7, and 14 using digital photographic analysis. **Results**: A statistically significant difference in wound size reduction was observed among the groups on day 14 ($p < 0.001$). The 10% sucralfate group (T2) showed the greatest wound reduction, with a mean wound diameter of 44.62 ± 21.43 mm, which was comparable to the silver sulfadiazine group (48.89 ± 10.41 mm). Both groups demonstrated significantly smaller wound sizes compared to the 7% sucralfate group (281.35 ± 99.33 mm) and the negative control group (936.48 ± 159.71 mm). **Conclusion**: The 10% sucralfate group showed a smaller second-degree burn wound size compared with the 7% sucralfate group and was comparable to the silver sulfadiazine group.

INTRODUCTION

Burns are among the most common forms of physical trauma and represent a significant global health burden. Globally, burn injuries account for approximately 180,000 deaths annually, with the highest incidence occurring in low- and middle-income countries (Jeschke et al., 2020). Pathophysiologically, second-degree (partial-thickness) burns involve damage to the epidermis and part of the dermis, triggering a complex inflammatory response. If not properly managed, this condition may lead to impaired wound healing, secondary infections, and hypertrophic scar formation, which can compromise both function and aesthetic outcomes (World Health Organization [WHO], 2023).

Currently, 1% silver sulfadiazine (SSD) remains a standard topical treatment for burn management due to its broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria as well as fungi. However, several clinical limitations have been reported. SSD has been shown to exert cytotoxic effects on proliferating keratinocytes and fibroblasts,

which may delay re-epithelialization and wound closure. In addition, prolonged use of SSD has been associated with potential systemic adverse effects, including leukopenia, agranulocytosis, and argyria (Hadrup et al., 2018; Mimura et al., 2020). These limitations highlight the need for alternative topical therapies that are not only effective in preventing infection but also capable of promoting optimal wound healing with a better safety profile (Mamun et al., 2024; Pfalzgraff et al., 2018; Pinto et al., 2020).

Sucralfate, an aluminum salt–based mucoprotective agent commonly used in peptic ulcer therapy, has attracted attention as a topical wound-healing agent. Its mechanism of action involves the formation of sucrose octasulfate complexes with proteins in damaged tissue, creating a protective barrier against further injury. Moreover, sucralfate can bind and enhance the bioavailability of endogenous growth factors such as epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF) (Lumintang et al., 2021). This interaction promotes cellular proliferation, angiogenesis, and granulation tissue formation, which are essential processes in wound healing (Kudaravalli & Pendyala, 2024).

Although the potential of sucralfate in wound healing has been reported, comparative studies evaluating different concentrations of topical sucralfate on macroscopic clinical outcomes remain limited. This study aimed to analyze and compare the effectiveness of 10% and 7% sucralfate cream versus standard therapy with silver sulfadiazine in accelerating wound size reduction (wound contraction) in a second-degree burn rat model. This research is expected to provide scientific evidence regarding the optimal dosage of sucralfate as a safe and effective alternative topical therapy.

METHOD

Study Design and Ethics

This study was a true experimental laboratory study with a post-test-only control group design. Ethical approval was obtained from the Health Research Ethics Committee (KEPK) of the Faculty of Medicine, Sebelas Maret University (No: 1.670/VII/HREC/2025). The study was conducted at the Center for Food and Nutrition Studies Laboratory, Gadjah Mada University, where the experimental animals were housed and treated, from July to December 2025.

Experimental Animals

The subjects were 48 male white rats of the Sprague Dawley strain, aged 9 weeks, weighing 180–200 grams. Subject selection was performed using random sampling. Inclusion criteria included healthy, active rats with no anatomical abnormalities. The rats were acclimatized for 7 days prior to treatment in individual cages under standard room temperature (25±2°C), a 12-hour light-dark cycle, and provided with food and water ad libitum.

Burn Induction Procedure and Intervention

Before induction, the rats were anesthetized using an intraperitoneal injection of ketamine (80 mg/kgBW) and xylazine (10 mg/kgBW). The hair on the rats' backs was shaved over an area of 4x4 cm and cleaned with 70% alcohol. Second-degree burn induction was performed using a modified Hot Plate method, by applying a round aluminum metal plate (25 mm diameter) that had been heated to a temperature of 100°C. The plate was applied to the dorsal area of the rats for 10 seconds without additional pressure to produce a deep partial-thickness second-degree burn. The experimental animals were randomly grouped into four groups (n=12) receiving topical intervention twice daily for 14 days: the Negative Control (NC) group, which did not receive any therapeutic intervention; the Positive Control (PC) group with the application of 1% Silver Sulfadiazine cream; and Treatment 1 (T1) and Treatment 2 (T2) groups, which received 7% and 10% Sucralfate cream, respectively, applied topically twice daily at a dose of 0.5 g per application for a total duration of 14 days.

Wound Size Measurement

The primary parameter assessed was the burn wound diameter (in millimeters). Measurements were taken serially on day 1 (D1), day 3 (D3), day 7 (D7), and day 14 (D14) post-induction. Wound documentation was performed using a digital camera positioned perpendicularly at a fixed distance (25 cm) from the wound surface, including a measuring ruler for scale calibration. Digital image data were then analyzed using ImageJ software (National Institutes of Health, USA) to calculate the wound diameter precisely.

Statistical Analysis

Data were processed using IBM SPSS Statistics software version 29. Data normality was tested using the Shapiro-Wilk test. Given that the data were normally distributed but the variances between groups were not homogeneous (Levene test $p<0.05$), the analysis of mean wound size comparison between groups was performed using the Welch ANOVA test followed by the Dunnett T3 Post Hoc test to determine specific differences between group pairs. The level of statistical significance was set at $p < 0.05$.

RESULT AND DISCUSSION

Macroscopic observation of the progression of second-degree burn wound healing showed distinct clinical characteristic differences between treatment groups over the 14-day observation period. On the first day post-induction, all experimental animals exhibited burns with similar characteristics, appearing as pale white eschar surrounded by an area of erythema, with no signs of infection. Over time, the Negative Control (NC) group showed the slowest healing process, characterized by the persistence of thick, wet crusts and a relatively static wound size until the end of the study. Conversely, the treated groups, particularly the 10% Sucralfate Cream (T2) and Silver Sulfadiazine (PC) groups, demonstrated progressive healing acceleration. In both these groups, the wound area appeared drier, wound edges merged more rapidly (wound contraction), and significant re-epithelialization occurred by day 14.

Quantitative analysis of burn wound diameter was performed to confirm these clinical observations. The Welch ANOVA statistical test showed a statistically significant difference in the mean wound size among the four treatment groups at all measurement time points ($p<0.001$), except on day 1 where the wound size was relatively uniform as baseline data. The T2 group (10% Sucralfate) consistently showed the sharpest trend in wound size reduction compared to the other groups. On day 14, the T2 group reached the smallest wound size with a mean of 44.62 ± 21.43 mm, followed by the PC group (SSD) at 48.89 ± 10.41 mm. Meanwhile, the T1 group (7% Sucralfate) lagged with a mean of 281.35 ± 99.33 mm, and the CN group had the largest wound size at 936.48 ± 159.71 mm.

To evaluate specific effectiveness between groups, a Post Hoc analysis using the Dunnett T3 test was conducted. The results of this further test revealed that on day 14, the administration of 10% Sucralfate cream (T2) resulted in a wound size significantly smaller compared to the NC group ($p<0.001$) and the 7% Sucralfate group (T1) ($p<0.001$). An interesting finding was observed in the comparison between the 10% Sucralfate group (T2) and the standard therapy group, Silver Sulfadiazine (PC), where no statistically significant difference was found ($p>0.999$). This indicates that the effectiveness of 10% Sucralfate cream in reducing second-degree burn wound size is equivalent to the effectiveness of SSD as the current standard therapy. Complete data regarding the dynamics of wound size changes and statistical test results are presented in Table 1 and Table 2.

Table 1. Dynamics of mean burn wound size changes (mm) over 14 days of observation

Treatment group	Day 1 (Mean ± SD)	Day 3 (Mean ± SD)	Day 7 (Mean ± SD)	Day 14 (Mean ± SD)
Negative control	898.80 ± 16.15	833.28 ± 178.78	896.01 ± 168.87	936.48 ± 159.71
Positive control	657.79 ± 61.76	482.08 ± 209.23	347.67 ± 73.45	48.89 ± 10.41
7% Sucralfate	773.85 ± 95.86	538.72 ± 65.58	512.87 ± 126.70	281.35 ± 99.33
10% Sucralfate	729.46 ± 174.76	370.89 ± 209.66	216.64 ± 120.14	44.62 ± 21.43
p-value (Welch ANOVA)	<0.001*	<0.001*	<0.001*	<0.001*

Table 2. Post hoc analysis (Dunnett T3) of wound size differences between groups on day 14

Compared Group Pairs	Mean Difference	Standard Error	p-value	Interpretation
NC vs 10% Sucralfate	891.85	46.52	<0.001*	Significant
7% Sucralfate vs 10% Sucralfate	236.73	29.34	<0.001*	Significant
PC vs 10% Sucralfate	4.26	6.94	>0.999	Not Significant (Equivalent)
NC vs PC	887.59	46.21	<0.001*	Significant

The results of this study provide empirical evidence that the topical administration of 10% sucralfate cream is effective in accelerating the healing of second-degree burns in Sprague Dawley rats, characterized by a significant reduction in wound diameter by day 14. The main finding of this study indicates that the 10% sucralfate group achieved the most optimal wound reduction, far superior to 7% sucralfate and the negative control, and equivalent to SSD. This aligns with a study by Banati et al. (2018) stating that topical sucralfate was able to accelerate epithelialization in a rat burn model compared to placebo. The effectiveness of sucralfate is also supported by research by Beheshti et al. (2019) on second-degree burn patients, where sucralfate significantly reduced healing time and pain intensity compared to standard therapy.

The mechanism of accelerated wound contraction in the sucralfate group can be explained through the unique pharmacodynamic effects of this agent. When applied to exudative wounds, sucralfate dissociates into aluminum ions and sucrose octasulfate, which polymerize to form a physical protective layer or "mechanical barrier" (Masuelli et al., 2010). This layer binds strongly to necrotic tissue proteins at the wound base, protecting new granulation tissue from physical irritation and secondary infection (Tsakayannis et al., 2018). Additionally, this layer creates a moist wound healing microenvironment conducive to keratinocyte migration, as explained by Winter (2019), that wound moisture accelerates re-epithelialization up to 50% faster compared to dry conditions.

In addition to its cytoprotective effect, accelerated healing in the 10% sucralfate group is closely related to the ability to modulate growth factors. Sucralfate has a high affinity for binding and stabilizing endogenous growth factors such as Epidermal Growth Factor (EGF) and Basic Fibroblast Growth Factor (bFGF) at the wound site, preventing their degradation by proteolytic enzymes (Volkin et al., 2017). The accumulation of these growth factors triggers intracellular signaling cascades that stimulate fibroblast proliferation, collagen synthesis, and neoangiogenesis, manifesting as accelerated wound contraction (Burch & McMillan, 2018). Masuelli et al. (2020) also found that sucralfate increases the expression of Vascular Endothelial Growth Factor (VEGF), which is crucial for new blood vessel formation in granulation tissue.

The superiority of 10% sucralfate compared to the 7% concentration indicates a dose-dependent effect. A higher concentration provides a more adequate amount of active molecules to coat the wound surface and maximize growth factor bioavailability, resulting in a more efficient wound closure process (Rehman & Zulfiqar, 2020). This is consistent with findings by Gupta and Kumar (2021), who reported that high-concentration sucralfate formulations yielded better chronic wound healing results compared to low concentrations.

The comparison between 10% sucralfate and SSD showed statistically equivalent results at the end of observation. This is an important clinical finding, considering SSD is often associated with cytotoxic effects on keratinocytes and fibroblasts that can delay re-epithelialization, as well as the risk of systemic silver absorption (Hussain & Ferguson, 2019; Mimura et al., 2020). Research by Aziz et al. (2022) emphasized that although SSD is effective as an antimicrobial, its cytotoxic effects often slow the proliferation phase compared to cytoprotective agents like sucralfate. With wound closure capability comparable to SSD but a better safety profile working locally without damaging cell viability, 10% sucralfate offers a promising alternative (Solanki & Greenwood, 2021).

In the negative control group without therapy, wound healing proceeded slowly and inadequately. This confirms that without pharmacological intervention, burns are prone to undergoing a prolonged inflammatory phase that hinders healing (Eming et al., 2019). Sucralfate intervention prevents this delay, reducing the risk of pathological scar complications such as hypertrophic scars or keloids, which often occur due to delayed wound healing (Finnerty et al., 2020; WHO, 2023).

CONCLUSION

Based on the data analysis and discussion, it can be concluded that topical administration of 10% sucralfate cream was effective in accelerating the reduction of second-degree burn wound size in the Sprague–Dawley rat model. The wound-healing efficacy of 10% sucralfate was superior to that of 7% sucralfate and the no-treatment group and was comparable to the standard therapy, silver sulfadiazine (SSD). These findings support the potential of 10% sucralfate as an effective and safe alternative therapeutic option for the management of second-degree burns, particularly in promoting faster wound closure without the cytotoxic side effects commonly associated with conventional topical antimicrobial agents.

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