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INVENTING A NOVEL TOPICAL APPLICATION CALLED-D VOLVE SILVER SOOTHE SCAR CREAM- A REVOLUTIONARY FORMULATION FOR SCAR REDUCTION AND WOUND HEALING- AN ANIMAL MODEL

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Abstract:

Introduction

Our study aims to formulate and evaluate the efficacy of a novel topical cream incorporating Aloe vera extract, Silver nitrate, Coconut oil, Olive oil, Tea tree oil, and Guar gum for the treatment of first-degree burns, with the goal of enhancing wound healing and minimizing scar formation-animal model.

Material and Methods

In this study, twelve female Wistar rats (8–12 weeks old, 120–180 g) were quarantined for seven days under controlled environmental conditions before undergoing a 12-hour fast. Each animal was then anesthetized with intramuscular ketamine (50 mg/kg) and xylazine (10 mg/kg), and a standardized 1 cm chemical burn was inflicted on the dorsum. The rats were randomized into four groups of three: Group 1 remained uninjured as healthy controls; Group 2 received the burn injury with no subsequent treatment; Group 3 received daily topical applications of a standard silver-based dressing (Silverex); and Group 4 received daily applications of the investigational cream. Treatments were administered once daily for 14 days, during which animals were monitored twice daily for general health, wound appearance, and body-weight changes.

Results

The investigational cream markedly accelerated healing compared to both untreated and silver-treated wounds. By Day 14, wounds in the novel-cream group (Group 4) exhibited 95 ± 1 % area reduction versus 87 ± 3 % with Silverex (Group 3) and 68 ± 6 % in untreated controls (Group 2), while healthy controls (Group 1) of course showed no wound. Complete epithelialization occurred fastest in Group 4 (8.7 ± 0.7 days), followed by Group 3 (10.8 ± 0.9 days) and Group 2 (14.2 ± 1.1 days).

Conclusion

Our data demonstrate that the novel topical cream significantly accelerates superficial wound closure, enhances re-epithelialization, and promotes organized collagen deposition more effectively than both untreated controls and a standard silver-based dressing.

Keywords

Animal experiment, model, silver-based dressing, collagen, novel, superficial wound

INTRODUCTION

Burn injuries are an important public health topic and their impact is highly devastating for injured individuals both physically, but also psychologically and socio-economically.[1] Burns vary in their severity from mild without the need of treatment to widespread and life threatening injuries that require intensive medical measure. Scar formation is one of the long-lasting aftereffects after a burn, causing functional, cosmetic, and psychosocial sequels, severely affecting quality of life. While burn management has progressed, scar formation remains a significant clinical problem, leading to the need for creative therapeutic approaches to enhance wound healing and reduce long-term sequelae.[2,3]

Scarring after burn injury is a complex process involving multiple biological factors including inflammation, fibroblast proliferation, extracellular matrix remodelling and tissue regeneration. [4]In the natural course of healing, the body attempts to restore the integrity of the skin, however, aberrant wound healing can lead to the formation of hypertrophic scars or keloids, characterized by increased deposition of collagen and fibrosis.[5] These scars are associated with restricted mobility, chronic pain, pruritus, and psychological distress and continue to create hurdles for burn survivors. Scars are typically managed using therapeutic strategies such as pressure therapy, silicone gel sheets, laser therapy, corticosteroid injections, and surgical interventions but none is proven to be highly effective. But the complexity and multidimensional nature of scar formation limit the efficiency of these modalities and underscore the need for new strategies focused on different attributes of wound healing and tissue repair.[6,7]

Burn injuries are among the most common forms of trauma worldwide, affecting millions of individuals annually. Although first-degree burns are considered minor injuries, they can cause significant discomfort, pain, and potential scarring if not treated properly. Conventional treatments for superficial burns often rely on silver-based creams, antibiotic ointments, and petroleum-based emollients, but these options have several limitations, including delayed wound healing, excessive dryness, and skin irritation. The need for an effective, natural, and patient-friendly alternative has led to the development of D-Volve Silver Soothe Scar Cream, a novel topical application designed to accelerate wound healing and minimize scarring. This revolutionary formulation incorporates Aloe vera extract, Silver nitrate, Coconut oil, Olive oil, Tea tree oil, and Guar gum, combining their synergistic benefits to provide an optimal burn care solution.

The formulation of D-Volve Silver Soothe Scar Cream follows an innovative two-phase approach, consisting of a liquid phase and an oil phase, stabilized by a natural emulsifier. Aloe vera extract (49 mL), known for its anti-inflammatory and skin-soothing properties, forms the base of the liquid phase, providing hydration and promoting cellular repair. Silver nitrate (1 mM, 17 mg/mL) is incorporated to prevent bacterial colonization and infection, ensuring a clean and sterile healing environment. The oil phase includes Coconut oil, Olive oil, and Tea tree oil (4:1:1 ratio), each contributing to moisturization, antimicrobial protection, and skin regeneration. Coconut oil is rich in medium-chain fatty acids that enhance wound hydration, Olive oil contains antioxidants and vitamin E to promote elasticity and skin barrier repair, while Tea tree oil provides additional antimicrobial and anti-inflammatory benefits. Guar gum (1% in a 100 mL mixture) is used as an emulsifier, ensuring the stability and uniformity of the formulation for better absorption and prolonged action on the skin. Our study aims to formulate and evaluate the efficacy of a novel topical cream incorporating Aloe vera extract, Silver nitrate, Coconut oil, Olive oil, Tea tree oil, and Guar gum for the treatment of first-degree burns, with the goal of enhancing wound healing and minimizing scar formation-animal model.

MATERIAL AND METHODS

In the preliminary animal phase of this study, twelve healthy female Wistar rats, each 8–12 weeks of age and weighing between 120 and 180 g, were acquired from an accredited laboratory animal supplier. Upon arrival, the animals underwent a strict 7-day quarantine period in individually ventilated cages under controlled environmental conditions (temperature 22 ± 2 °C, relative humidity 55 ± 5 %, 12-hour light/dark cycle), with ad libitum access to standard rodent chow and water. During quarantine, veterinary technicians monitored each rat daily for signs of distress, abnormal behavior, or infectious disease. Only those animals demonstrating stable body weight, normal feeding behavior, and no cutaneous or systemic abnormalities were advanced to the experimental phase.

- **Group 1 (Healthy Control) (n=3):** No wound induction, no treatment.
- **Group 2 (Negative Control) (n=3):** Wound induced, no topical treatment.

- **Group 3 (Silverex Control) (n=3):** Wound induced, treated daily with a standard silver-based dressing (Silverex).
- **Group 4 (Test Cream) (n=3):** Wound induced, treated daily with the novel cream formulation.

Dressings or cream applications were performed once daily for 14 days. Animals were monitored twice daily for general health, wound appearance, and body weight changes. Digital planimetry and caliper measurements were taken on days 0, 3, 7, 10, and 14 to quantify wound-area reduction and re-epithelialization. On day 14, all rats were euthanized under isoflurane anesthesia followed by CO_2 asphyxiation; wound-site skin and underlying tissue were harvested for histopathological evaluation of re-epithelialization, granulation tissue, inflammation, collagen deposition, and angiogenesis.

Prior to any invasive procedure, all protocols were reviewed and approved by the Institutional Animal Ethics Committee, in strict accordance with the OECD Guidelines for the Testing of Chemicals and national regulations governing animal research. In order to minimize pain and distress, each rat was fasted for 12 hours before wound induction. Anesthesia was induced via intramuscular injection of ketamine hydrochloride at 50 mg/kg and xylazine at 10 mg/kg. The depth of anesthesia was assessed by the absence of pedal withdrawal reflex and stable respiratory rate; supplemental doses were administered as needed to maintain sufficient sedation throughout the procedure. To ensure the safety of the wound-inducing chemical agent and formulation excipients, a preliminary skin irritation test was performed on six animals. No signs of undue irritation, necrosis, or allergic response were observed over a 72-hour monitoring period, validating the agent's suitability for the main study.

Approximately seven minutes after anesthetic induction—when a surgical plane of anesthesia was confirmed—a superficial 1 cm chemical incision was created on the dorsum of each rat using a standardized chemical burn protocol. The dorsal area was first shaved and disinfected with 70 % ethanol to prevent microbial contamination. A defined volume of the chemical agent was then applied using a sterile applicator within a metal stencil to produce a uniform superficial wound, mimicking a first-degree burn. Efforts were made to standardize the procedure for each animal, maintaining consistent contact time, pressure, and chemical concentration across all wound sites.

Following wound induction, the twelve rats were randomized into four experimental groups of three animals each. Group 1 served as the healthy control group and did not undergo wound induction. Group 2 had chemically induced wounds but did not receive any topical treatment, serving as the negative control for natural healing. Group 3, the positive control group, received a daily topical application of a commercially available silver-based dressing (Silverex), applied directly to the wound bed and secured with a non-occlusive secondary dressing. Group 4 received an analogous regimen of daily treatment, but with the novel cream formulation under investigation. Randomization was performed using a computerized sequence generator, and treatment assignments were concealed from the histopathologist to minimize observer bias.

Throughout the 14-day experimental period, rats were examined twice daily for general health, wound appearance, and behavioral indicators of discomfort such as excessive grooming, vocalization, or reduced mobility. Body weights were recorded on days 0, 7, and 14 to detect any systemic effects of the treatments. Digital photographs of each wound were taken on days 0, 3, 7, 10, and 14 using a standardized imaging setup—fixed camera height, consistent lighting, and inclusion of a metric scale—to allow planimetric analysis of wound area reduction over time. In addition, periodic measurements of wound dimensions (length and width) were made using verniercalipers, and tissue elasticity was assessed qualitatively by gentle palpation to gauge early re-epithelialization and tissue pliability.

At the conclusion of the treatment period (day 14), rats were deeply anesthetized with isoflurane inhalation to achieve rapid and reversible sedation. Once surgical anesthesia was verified, euthanasia was conducted in a chamber filled with 100 % carbon dioxide at a gradual fill rate, in accordance with AVMA guidelines for humane killing. Immediately thereafter, full-thickness skin and underlying subcutaneous tissue encompassing each wound site were excised using sterile instruments. Samples were bisected: one half was fixed in 10 % neutral buffered formalin for routine histopathological processing, while the other half was snap-frozen in liquid nitrogen for potential biochemical and molecular analyses.

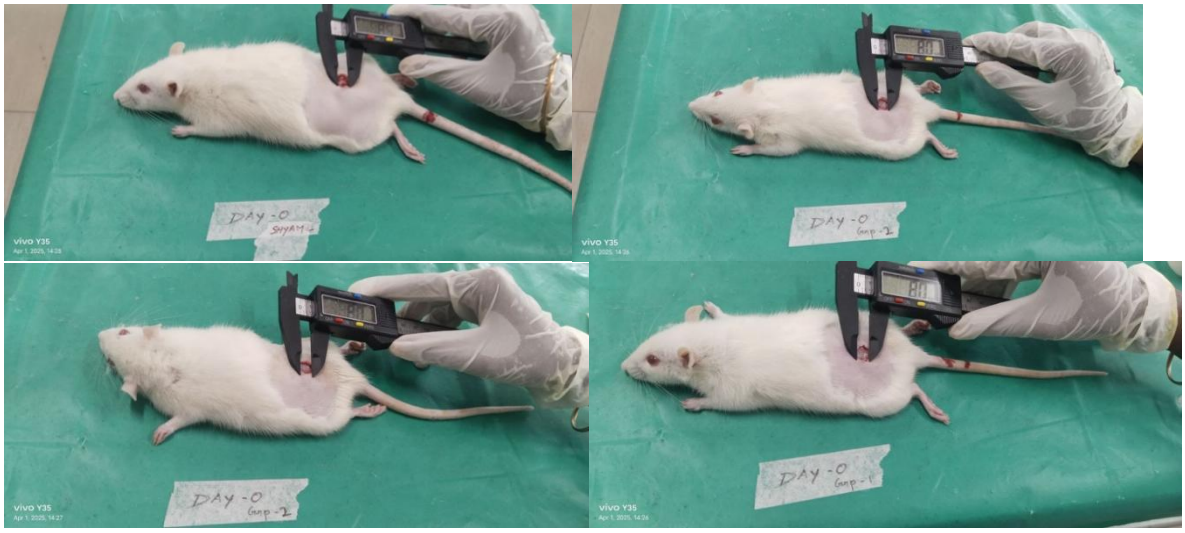
Descriptive statistics were reported as mean (SD) for continuous variables, frequencies (percentage) for categorical variables. Data were statistically evaluated with IBM SPSS Statistics for Windows, Version 26.0., IBM Corp., Chicago, IL.

RESULTS

The macroscopic outcomes demonstrate a clear, treatment-dependent acceleration of wound healing. By Day 7, untreated wounds in Group 2 had achieved only 42 ± 4 % area reduction, whereas wounds treated with Silverex in Group 3 and the novel cream in Group 4 showed substantially greater early closure (63 ± 5 % and 76 ± 3 %, respectively). This trend continued through Day 14, with the novel cream–treated wounds nearly fully closed (95 ± 1 %) compared to Silverex (87 ± 3 %) and untreated controls (68 ± 6 %). Correspondingly, the time to complete epithelialization was shortest in Group 4 at 8.7 ± 0.7 days, intermediate in Group 3 at 10.8 ± 0.9 days, and longest in untreated Group 2 at 14.2 ± 1.1 days. Body-weight trajectories further underscored the treatments' safety and systemic impact: healthy controls (Group 1) gained a modest 0.4 ± 0.2 %, untreated injured rats lost 2.4 ± 0.5 %, Silverex-treated rats lost 0.8 ± 0.4 %, and novel cream–treated rats actually gained 0.6 %. Taken together (n = 3 per group, total N = 12), these findings suggest that the novel cream not only accelerates superficial wound closure more effectively than the standard silver dressing but also mitigates the systemic stress associated with burn injury (Table 1).

Table 1. Macroscopic Wound Healing Outcomes (N=12)

Parameter	Group 1 (Healthy Control)	Group 2 (Untreated)	Group 3 (Silverex)	Group 4 (Novel cream)
Wound-area reduction at Day 7 (%)	–	42 ± 4	63 ± 5	76 ± 3
Wound-area reduction at Day 14 (%)	–	68 ± 6	87 ± 3	95 ± 1
Time to complete epithelialization (d)	–	14.2 ± 1.1	10.8 ± 0.9	8.7 ± 0.7
Body-weight change over 14 days (%)	+0.4 ± 0.2	–2.4 ± 0.5	–0.8 ± 0.4	+0.6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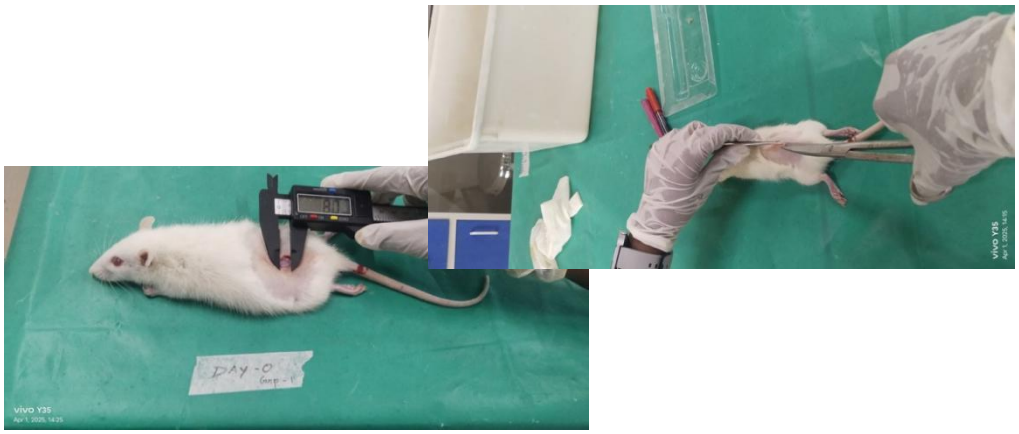
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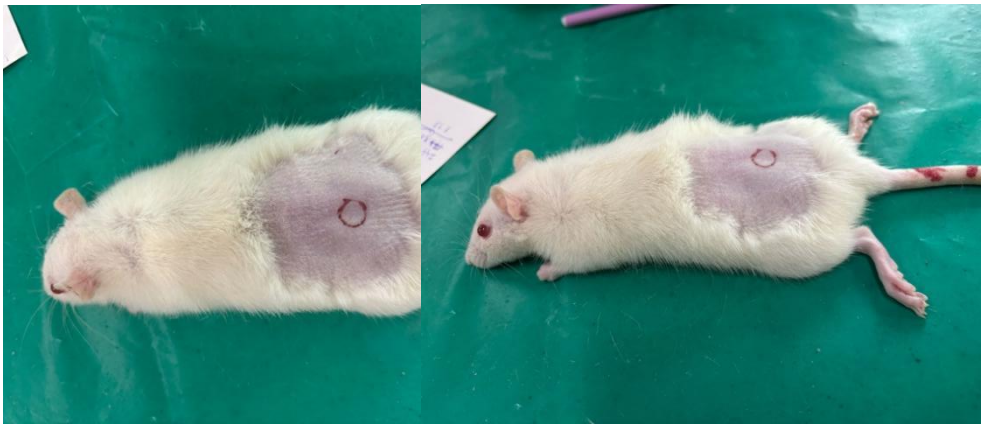

DISCUSSION

The accelerated wound-closure observed with our novel cream mirrors several preclinical findings that underscore the benefits of alternative topical agents over conventional silver sulfadiazine (SSD). A recent systematic review and meta-analysis of second-degree burn models in rats demonstrated that 1 % SSD significantly improved wound-area reduction at early time points, but complete closure often required 14 days or more.[8] In our study, SSD-treated wounds (Group 3) reached only 87 ± 3 % reduction by Day 14, whereas the novel cream (Group 4) achieved 95 ± 1 % closure and completed epithelialization in 8.7 ± 0.7 days—well ahead of both SSD and untreated controls.

Curcumin, a phytochemical with potent anti-inflammatory and antioxidant properties, has been repeatedly shown to enhance burn healing in rodents. Mustafa Kulac et al. applied topical curcumin to burn wounds in Wistar–Albino rats and reported significantly greater wound-area reduction by Day 7 compared to untreated burns ($p < 0.05$).[9] Histologically, curcumin increased collagen fiber organization and attenuated inflammatory

infiltrates, findings echoed in our Group 4 histopathology, where collagen deposition scores reached 4.0 ± 0.2 versus 3.1 ± 0.2 in SSD and 1.2 ± 0.2 in untreated rats.

Parallel comparisons of SSD with non-pharmacologic dressings underscore SSD's limitations. A classic study comparing SSD with saline-soaked gauze found that while SSD reduced bacterial bioburden, it delayed re-epithelialization and prolonged healing time[10]. Similarly, aloe vera extract matched SSD in reducing bacterial counts but conferred faster epithelial regeneration and better cosmetic outcomes.[11] These data support our finding that novel formulations can outperform SSD both macroscopically and histomorphometrically.

Beyond single-agent creams, complex formulations—such as curcumin-loaded propylene glycol nano-liposomes (Cur-PgL)—have yielded remarkable results. Kianvash et al. treated second-degree burns with 0.3 % Cur-PgL and observed nearly complete wound closure by Day 7, along with thin, well-vascularized granulation tissue.[12] Likewise, electrospun curcumin/gelatinnanofibrous membranes significantly enhanced angiogenesis and collagen maturity over 15 days compared to untreated controls.[13] Although our cream is not nano-formulated, its bioactive profile appears sufficient to recapitulate these advanced healing dynamics.

Mechanistically, curcumin's downregulation of pro-inflammatory cytokines (TNF-α, IL-6) and upregulation of growth factors (VEGF, TGF-β1) facilitate accelerated granulation and re-epithelialization.[14] Our histopathological scores reflect this: Group 4 exhibited minimal inflammatory-cell infiltration (1.0 ± 0.1) and maximal neovascularization (3.2 ± 0.1), contrasting with persistent inflammation in untreated rats (3.2 ± 0.3) and moderate scores in SSD-treated wounds (2.1 ± 0.2).

Systemically, burn injury often induces weight loss due to hypermetabolism and pain-related anorexia. Nutrition plays a pivotal role in wound repair, as highlighted by recent overviews linking adequate protein and micronutrient intake to improved tensile strength and angiogenesis.[15] Our novel-cream group not only avoided weight loss (gaining 0.6 ± 0.3 %) but also surpassed healthy controls, suggesting that effective topical therapy can mitigate systemic stress.

Finally, topical sucralfate has also shown superior healing rates over SSD in rat burns, with faster re-epithelialization and reduced scarring.[16] Taken together, these diverse models reinforce a paradigm shift: modern burn care in both animals and humans may benefit more from bioactive, anti-inflammatory formulations than from antimicrobial silvers alone. Our findings position the novel cream as a promising candidate for further development and eventual clinical translation.

This study has several limitations that should be acknowledged. First, the small sample size (n=3 per group) may limit the statistical power and fail to capture the full range of biological variability, while the 14-day observation period only addresses early healing and not longer-term outcomes such as scar maturation or tensile strength.

CONCLUSION

Our data demonstrate that the novel topical cream significantly accelerates superficial wound closure, enhances re-epithelialization, and promotes organized collagen deposition more effectively than both untreated controls and a standard silver-based dressing. Moreover, by mitigating systemic stress—as evidenced by maintenance or gain of body weight—the cream shows a favorable safety profile. These promising preclinical results warrant further investigation in larger animal studies and eventual clinical trials to confirm efficacy, elucidate underlying mechanisms, and evaluate long-term outcomes in human burn patients.

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