RESEARCH ARTICLE

Opuntia cochenillifera Cream Accelerates Incision and Burn Wound Healing in Streptozotocin-Induced Diabetic Mice by Enhancing Fibroblast

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Abstract

BACKGROUND: Diabetes mellitus (DM) often leads to chronic, slow-healing wounds due to impaired tissue regeneration and sustained inflammation, which can progress to diabetic ulcers. *Opuntia cochenillifera* has been reported to possess antioxidant and anti-inflammatory potential, making it a promising candidate for natural wound therapies. However, standardized topical formulations and *in vivo* evaluations are limited. This study was conducted to develop and assess the wound-healing effects of *Opuntia cochenillifera* cream in diabetic mice.

METHODS: Forty-eight male Balb/C mice were randomly assigned to different groups: healthy control (HC), negative control (C−), positive control (C+), and treatment (T) groups. DM was induced by a single intraperitoneal injection of 180 mg/kgBW streptozotocin. After confirming hyperglycemia, incisions and burn wounds were created and monitored for 7 and 14 days. Wound healing was assessed macroscopically (incision length, width, and burn diameter) and microscopically (fibroblast proliferation and re-epithelialization). The formulated *Opuntia cochenillifera* cream was evaluated for pH, homogeneity, adhesion, and spreadability using standard topical formulation tests.

RESULTS: The formulated cream exhibited good homogeneity, adhesion (4.97 s), spreadability (5.10 cm), and skin-compatible pH (6.44). Phytochemical analysis confirmed the presence of flavonoids, tannins, terpenoids and alkaloids. *In vivo*, *Opuntia cochenillifera* cream significantly accelerated wound closure and increased fibroblast proliferation compared to the C− group ($p<0.05$). Its effects were comparable to those of the standard treatment for burn wounds and superior for incision wounds, demonstrating enhanced fibroblast activity and more organized re-epithelialization.

CONCLUSION: *Opuntia cochenillifera* cream effectively improves wound healing in diabetic mice through the enchantment fibroblast activity and organized re-epithelialization. These findings support the potential of this formulation as a natural topical therapy for diabetic wounds, warranting further mechanistic investigation.

KEYWORDS: *Opuntia cochenillifera*, diabetic wound, wound healing, topical cream, phytochemical

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Introduction

Diabetes mellitus (DM) often leads to chronic, slow-healing wounds due to impaired tissue regeneration and sustained inflammation, which incidence and prevalence keep increasing globally.(1,2) Diabetic wound healing is characterized by a complex interplay of chronic low-grade inflammation, microvascular dysfunction, oxidative stress, and neuropathy, which together delay re-epithelialization,

angiogenesis, and granulation tissue formation in patients with DM.(3,4) These pathophysiological disturbances explain why conventional wound care alone is often insufficient to prevent the progression to chronic ulcers, including diabetic foot ulcers (DFU). DFU lesions are characterized by epidermal and dermal loss in the lower extremities and commonly develop as chronic, nonhealing open wounds. Major contributing factors include peripheral neuropathy, peripheral arterial disease, and minor traumas such as cuts, punctures, or burns.(5)

Previous research has shown that topical herbal remedies are more effective in speeding up wound healing as adjunctive therapies, preventing infection, and improving tissue quality than conventional treatments such as antibiotics and steroid ointments.(6) Various efforts based on natural materials have been reported to be able to prevent and treat wounds due to DFU. Recent systematic reviews and meta-analyses of clinical and preclinical studies have shown that several plant-derived formulations can significantly accelerate wound closure, shorten epithelialization time, and improve healing rates in diabetic wounds and DFU when added to standard care.(3,7)

Among these natural candidates, cactus species of the genus *Opuntia* have attracted increasing attention. *Opuntia* polysaccharides possess antioxidant, anti-inflammatory, and anti-glycation activities and have demonstrated protective effects in animal models of diabetes.(5,8) More recently, polysaccharides extracted from *Opuntia stricta* significantly improved wound closure, modulated inflammatory markers, and enhanced re-epithelialization in alloxan-induced diabetic rats, supporting their role in promoting diabetic wound healing.(9,10) In parallel, extracellular vesicles derived from *Opuntia ficus-indica* fruit have been shown to attenuate inflammation and oxidative stress in *in vitro* models of chronic skin wounds, further reinforcing the wound-healing potential of *Opuntia*-based preparations.(11) *Opuntia cochenillifera* is an effective herbal ingredient for diabetics, is easily found in Indonesia, and can be adapted to dry environments. Secondary plant substances that aid in wound healing include flavonoids, alkaloids, tannins, terpenoids and steroids. Particularly, flavonoids have anti-inflammatory, antioxidant, and re-epithelializing.(12,13)

Some studies formulated treatment in the form of oil from various cactus species of the genus *Opuntia* that might be able to aid in wound healing process. Yet, treatment in the form of oil is less stable and more susceptible to oxidation. (14) Therefore, the cream preparations are advantageous because they provide better drug stability, spreadability, and skin absorption, offering an optimal balance between efficacy and patient comfort compared to ointments or oils.(13-16) Furthermore, *in vivo* evaluation of topical formulations specifically based on *Opuntia cochenillifera* in diabetic wound models remains very limited. To address this gap, in this study, an innovative *Opuntia cochenillifera* cream formulation was developed and its effect for diabetic wound healing was explored. In this study, the phytochemical content, physicochemical characteristics, and *in vivo* wound-healing efficacy of *Opuntia cochenillifera* creams were also examined. Given that early traumatic wounds in individuals with DM often fail to heal and subsequently advance into DFU, demonstrating improved healing in murine models might provide an essential translational bridge, supporting the possible application of *Opuntia cochenillifera* cream as a natural, accessible, and preventive topical agent for reducing DFU risk or aiding its early stage management.

Methods

Plant Determination, Preparation and Extraction

The prickly pear cactus (*Opuntia cochenillifera*) was examined at the Biology Laboratory of the Faculty of Science and Mathematics at Universitas Diponegoro. The samples were collected and subsequently dried at the Central Laboratory of the Faculty of Medicine, Universitas Diponegoro. The dried cactus was extracted, and 100 g of the dried sample was weighed and placed in an Erlenmeyer flask, followed by maceration in 400 mL of 70% ethanol to extract flavonoid compounds known to promote wound healing. The mixture was filtered through filter paper and heated at 60°C for 3 days to evaporate the ethanol solvent. Once the extract was thickened, it was formulated into a cream.

Cream Formulation

The cream formulation consisted of two phases: an oil phase and an aqueous phase, with a total batch size of 100 g each. The oil phase comprised cetyl alcohol (4% w/w), stearic acid (8% w/w), and paraffin oil (0.1% w/w). The aqueous phase contained triethanolamine (2% w/w), glycerin (20% w/w), methylparaben (0.2% w/w), and distilled water (65.7% w/w). The oil and aqueous phases were separately heated to 50°C and then combined under continuous stirring at 400 rpm using a magnetic stirrer until a homogeneous cream base formed. Subsequently, Opuntia cochenillifera extract was incorporated at a final concentration of 30% w/w, replacing an equivalent portion of distilled water to maintain a total formulation weight of 100 g.

Phytochemical and Physicochemical Evaluation of *Opuntia cochenillifera* Cream

The cream was then evaluated based on its organoleptic properties, homogeneity, pH, adhesion, and dispersion. The parameters used in determining the optimization of the cream were organoleptic tests, which include color, smell, and texture.(17) Stability testing was conducted using a six-cycle heating–cooling test (4–40°C) and centrifugation at 3,000 rpm for 30 min to assess the phase separation. The final cream should have pH between 6.0–7.0 and a viscosity range of 3,000–5,000 cP, which was suitable for topical applications. Microbial limit test was also performed to confirmed whether the total plate count was within the acceptable limits for topical formulations. Animal irritation tests on BALB/c mice indicated no visible signs of erythema or edema 24 h after application.

Animal Grouping

In this study, 48 male BALB/c mice (25–30 g; 2–3 months old) were used and randomly allocated into healthy control (HC), negative control (C−), positive control (C+), and treatment (T) groups. To avoid repetition and improve clarity, the animals were then organized according to both treatment assignment and observation period, resulting in two parallel sets of groups; for the 7-day observation: HC-7d, C(–)-7d, C(+)-7d, and T-7d; and for the 14-day observation: HC-14d, C(–)-14d, C(+)-14d, and T-14d. Each group consisted of six mice, which was consistent with the common practice for exploratory wound-healing studies. To justify the sample size, the use of six mice per group/time point was deemed adequate based on previous exploratory diabetic wound-healing studies that reported detectable differences in re-epithelialization, fibroblast activity, and wound closure with group sizes ranging from five to eight animals. Randomization was performed using a computer-generated sequence, in which all mice were randomly assigned to their respective groups after diabetes-induction and wound-creation.

Diabetes-induction and Wound-creation

For the acclimatization process, all mice were kept under standard feeding conditions for 7 days before receiving any treatment. After the acclimatization, initial blood glucose levels were measured, with normal values of mice ranging from 62.5–175 mg/dL, which were considered normal. The mice in HC groups did not receive any diabetes-induction and wound-creation, but their blood glucose was measured after 3 days to make sure that the blood glucose was kept in the normal range.

Meanwhile, to create a diabetes mice model, the mice in C−, C+, and T groups were given a single intraperitoneal injection of streptozotocin (STZ) at a dose of 180 mg/kgBW dissolved in a 1 mL syringe and then provided sugar water. After 3 days of STZ-injection, the glucose levels were measured again to confirm whether the mice have been diabetes-induced successfully. Hyperglycemia was confirmed since all diabetic-induced mice showed blood glucose levels above 175 mg/dL. Next, an incision wound of ±1 cm length, fascia-depth, was made and burn wound with a diameter of ±1 cm was created for the mice in C−, C+, and T groups.

Treatment of Experimental Animals

Since HC groups represent healthy mice, mice in this group were further left without receiving any treatment until euthanized after 7 and 14 days for HC-7d group and HC-14d group, respectively. Mice in C− groups also did not receive any treatment after receiving diabetes-induction and wound-creation until euthanized after 7 and 14 days for (C−)-7d group and (C−)-14d group, respectively.

After the diabetes-induction and wound-creation, mice in C(+)-7d were treated with povidone iodine 10% for their incision wounds and with Bioplacenton (Kalbe Farma, Jakarta, Indonesia) for their burn wounds in the dorsal region. The treatment was given once daily for 7 days, and then the mice were euthanized. Same treatment was received by the C(+)-14d once daily for 14 days, and then the mice were euthanized.

Meanwhile for the T groups, after the diabetes-induction and wound-creation, mice in T-7d were treated with treated with 1 g *Opuntia cochenillifera* cream for both incision and burn wounds. The cream was applied evenly to the full wound area in the dorsal region once daily for 7 days, and then the mice were euthanized. The formulation remained in contact for 24 hours without occlusion throughout the treatment period. Same treatment was received by the T-14d group until 14 days of cream application before the mice were euthanized by neck dislocation.

Ethical clearance for this study protocol was obtained from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Diponegoro (No. 284/EC/KEPK/FK UNDIP/X/2025). All experimental procedures were conducted in accordance with the international guidelines for the care and use of laboratory animals, following the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE) guidelines and WHO recommendations to ensure ethical and humane treatment of animals.

Wound Measurements

Before being terminated, mice were assessed macroscopically for their wound size, including burn diameter and incision length and width, using a calibrated ruler after 7 and 14 days for the 7-day observation and the 14-day observation groups, respectively. The wound measurements were performed by two independent blinded observers to minimize assessment bias, and inter-observer reliability was ensured through prior calibration and consistency testing. To maintain methodological rigor, the allocation concealment was implemented by having an independent researcher, who was not involved in treatment administration or outcome evaluation, who was preparing for the coded group labels. The observers who performed wound measurements and histological assessments remained blinded to each subject' group identity throughout the study, to ensure that both allocation and outcome assessment were unbiased.(18)

Histopathological Analysis

After terminated, the skin tissue samples were obtained from all mice to examine the microscopic indicators for the evaluation of fibroblast percentage and re-epithelialization. Skin tissue samples were fixed in 10% buffered formalin for 48 hours at room temperature and subsequently processed for paraffin embedding using standard histological procedures, as described previously. Sections were stained with hematoxylin and eosin following established protocols, and microscopic evaluation was performed under a light microscope.

To assess the percentage of fibroblasts, five representative high-power fields (HPF) (400×) were examined using a semi-quantitative ordinal scoring system: 1 = <25% (1–5 cells/HPF); 2 = 25–50% (6–10 cells/HPF); 3 = 50–75% (11–15 cells/HPF); and 4 = 75–100% (>15 cells/HPF). Epidermal thickness (re-epithelialization) was evaluated on day-7 and -14, for the 7-day observation and the 14-day observation groups, respectively, using an Olympus microscope connected to the Olympus CellSens imaging software (Olympus, Tokyo, Japan). Measurements were performed in micrometers (μm) and independently assessed by two blinded observers to reduce the observer bias.(19) Because the fibroblast scoring method is inherently semi-quantitative, its precision might be limited compared with that of full morphometric quantification. However, it could represent a widely accepted technique in exploratory *in vivo* wound-healing research when more advanced quantitative morphometry was not feasible. Scale calibration was performed before imaging.(15)

Statistical Analysis

Data were analyzed using SPSS software (IBM Corporation, Armonk, NY, USA). Statistical evaluation was conducted using one-way analysis of variance (ANOVA) for normally distributed macroscopic parameters (length), while non-normally distributed data were analyzed using the Kruskal–Wallis test followed by the Mann–Whitney post hoc test. A p-value<0.05 was considered statistically significant, whereas p-value≥0.05 were regarded as not significant.

Results

Phytochemical and Physicochemical Characteristics of *Opuntia cochenillifera*

Qualitative phytochemical screening identified flavonoids, tannins, terpenoids, and alkaloids in *Opuntia cochenillifera* simplicia. The cactus-based cream exhibited acceptable characteristics for topical use, including a semi-solid texture, dark green color, distinctive aroma, and good homogeneity. The pH of 6.44 was within the safe range for skin application, while the adhesion (4.97 s) and spreadability (5.10 cm) indicated good usability and comfort. Microbial limit tests confirmed that the total plate count was within the acceptable limits for topical formulations (<10^3 CFU/g).

Macroscopic Assessment of Incision Wound Healing

Significant differences in wound length and width were observed among 7-day observation and 14-day observation groups (p<0.05). Both among the 7-day observation or the 14-day observation groups, the T groups had shorter incision length (2.80±0.83 and 1.00±1.41 mm, respectively) compared to C(–) and C(+) groups. A similar pattern was observed for wound width, the T groups had shorter incision wound (1.00±0.00 and 0.27±0.43, respectively) compared to C(–) and C(+) groups, with C(–) groups having the longest incision wound width (Figure 1, Table 1).

Macroscopic Assessment of Burn Wound Healing

Among the 7-day observation, the C(–)-7d group showed the largest burn diameter, whereas both the C(+)-7d and T-7d groups demonstrated significantly smaller diameters (p<0.05), indicating effective early wound contraction. After 14 days of treatment, both the C(+)-14d and T-14d groups achieved significantly greater wound closure than the C(–)-14d group (Figure 2, Table 2). No significant difference was observed between the T-7d and C(+)-7d groups or T-14d and C(+)-14d groups, suggesting that *Opuntia cochenillifera* cream was comparable to the standard treatment.

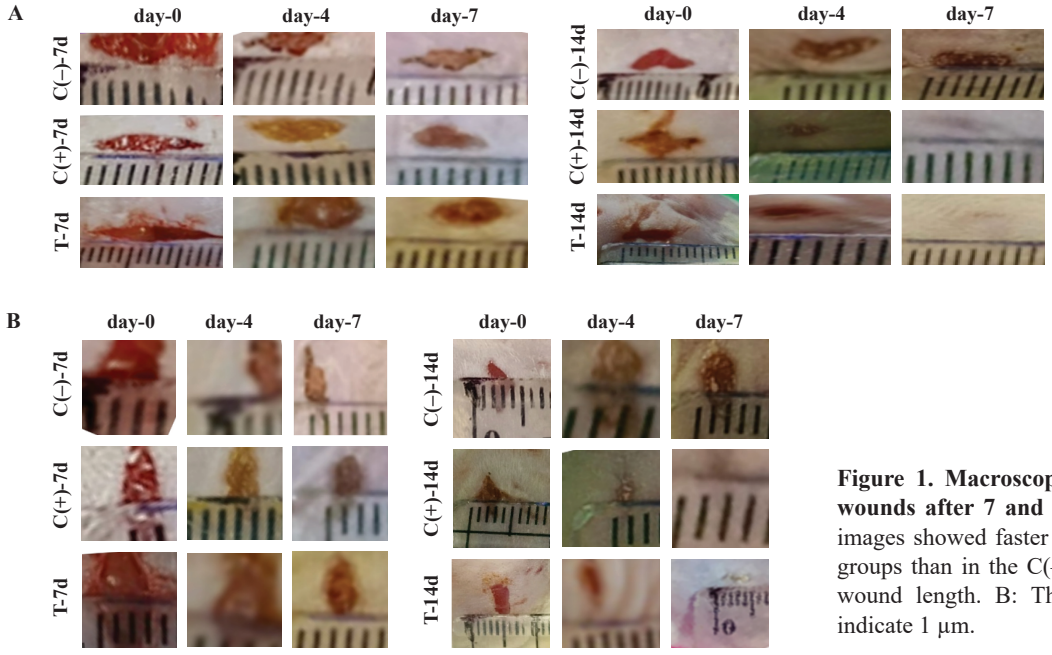

Figure 1. Macroscopic appearance of incision wounds after 7 and 14 days of treatment. The images showed faster wound contraction in the T groups than in the C(–) and C(+) groups. A: The wound length. B: The wound width. Each bar indicate 1 µm.

Microscopic Assessment of Incision Wound Healing

Histopathological analysis results revealed significant enhanced re-epithelialization in the T-7d and T-14d groups. Although fibroblast scores increased in the T-7d group (2.32±1.06), the values of T-14d group converged between the groups owing to tissue maturation (Figure 3, Table 3). Meanwhile for the re-epithelialisation, both T-7d and T-14d groups consistently showed more organized epithelial layers (55.95±58.60 and 52.92±27.97 µm) than the C(–), C(+), and even HC groups (Figure 4, Table 3).

Microscopic Assessment of Burn Wound Healing

Between the 7-day observation and the 14-day observation groups, the T groups showed accelerated epithelial regeneration compared to the C(–) and C(+) groups. The epithelial layer in the T-14 group (50.59±37.02 µm) was more continuous and organized compared to T-7d group (49.08±38.25 µm) (Figure 4, Table 4). The fibroblast score was also higher in the T-7d group compared to C(–)-7d and HC-7d. Although in T-14d group the fibroblast score was lower than T-7d group, but it was still higher compared to the C(–)-14d and HC-14d (Figure 3, Table 4).

Discussion

The healing dynamics of incisional and burn wounds demonstrated distinct tissue responses in this study. In the diabetes and incised mice model, which involved deeper dermal disruption and extension to the fascia, wound healing progressed in a structured manner and reached the remodelling phase by day-14. Histopathological findings

Table 1. Macroscopic assessment of incision wound healing after 7 and 14 days of treatment.

Wound Size	HC	C(–)	C(+)	T
Day-7				
Length (mm)	0.00±0.00^{a}	5.20±1.09^{c}	5.00±0.70^{c}	2.80±0.83^{b}
Width (mm)	1.40±0.54^{a}	2.00±0.00^{c}	1.00±0.00^{b}	1.00±0.00^{b}
Day-14				
Length (mm)	0.00±0.00^{a}	3.00±0.70^{c}	2.80±0.44^{b}	1.00±1.41^{b}
Width (mm)	0.00±0.00^{a}	1.00±0.00^{c}	0.27±0.43^{b}	0.27±0.43^{b}

Values are presented as mean±SD. Different superscript letters (^{a,b,c}) indicate statistically significant differences between groups ($p<0.05$). Means sharing the same letter are not significantly different.

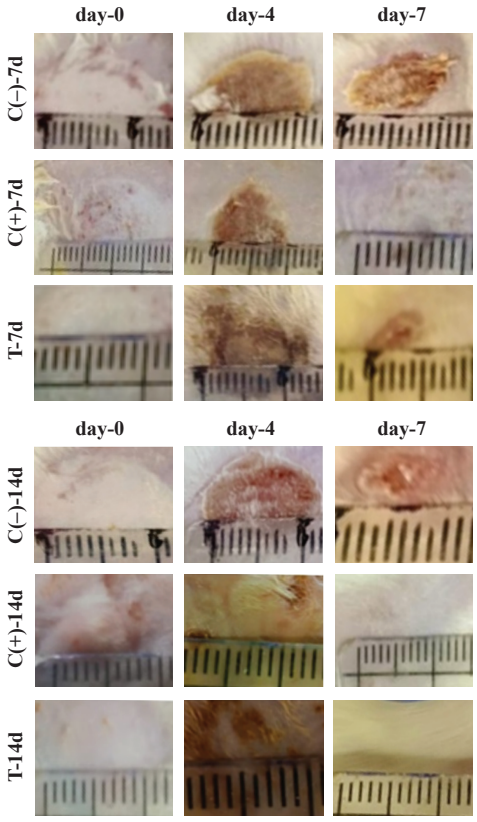

Figure 2. Macroscopic appearance of burn wounds after 7 and 14 days of treatment. The images showed that the T group demonstrates smaller wound diameters than C(–) at both time points. Each bar indicate 1 µm.

showed increased fibroblast activity during the early phase, followed by a reduction in fibroblast counts on day-14, indicating matrix reorganization and tissue maturation. In our findings, there are the more ordered epithelial structure and decreased fibroblast activity observed in the later stages. In contrast, burn wounds exhibit a different progression pattern. Although fibroblast activity and collagen formation indicated that dermal remodelling had begun, epidermal thickness remained elevated through day-14, suggesting incomplete epithelial maturation. The broader surface area and more diffuse tissue injury characteristic of burn wounds likely contribute to a more prolonged inflammatory response. Studies indicate that burn injuries often elicit persistent neutrophil infiltration, elevated interleukin (IL-6) and tumor necrosis factor (TNF)-α expression, and delayed transition from pro-inflammatory M1 to reparative M2 macrophages. (18-20) In this study, these mechanisms were not directly measured; however, the delayed epithelial maturation observed in the C(–) and C(+) groups is consistent with these established inflammatory patterns.

Overall, the findings of this study showed that *Opuntia cochenillifera* cream improved wound contraction, epithelial regeneration, and early fibroblast activation in incision wounds and produced healing effects comparable to those of standard treatment in burn wounds. These outcomes suggest that the topical formulation enhances multiple aspects of tissue repair, although the molecular pathways involved were not directly assessed in this study. Hyperglycaemia-induced impairment of fibroblast proliferation, collagen formation, angiogenesis, and extracellular matrix stability is well documented in diabetic wounds.(21)

These findings align with those of a previous study that reported that chronic hyperglycemia and oxidative stress in diabetic wounds impair fibroblast migration and keratinocyte proliferation. Persistent M1 macrophage activity and inadequate M2 polarization prolong inflammation and hinder progression to the proliferative phase, thereby delaying tissue remodelling.(22) This mechanism is consistent with the histopathological observations in this study, where epithelial regeneration in the control group remained incomplete and inflammation persisted longer. In contrast, the T group exhibited enhanced keratinocyte migration and fibroblast activation, which was attributed to the synergistic bioactive compounds of *Opuntia cochenillifera*, which modulate inflammatory signalling, stimulate angiogenic and growth factor pathways and promote extracellular matrix stabilisation.(23) These combined effects create a favorable wound microenvironment that accelerates epithelial recovery, collagen organization, and overall tissue regeneration compared with the control groups.

Table 2. Macroscopic assessment of burn wound healing after 7 and 14 days of treatment.

Diameter (mm)	HC	C(–)	C(+)	T
Day-7	0.00 ± 0.00^{a}	11.0 ± 0.70^{c}	7.00 ± 1.41^{b}	7.40 ± 1.81^{b}
Day-14	0.00 ± 0.00^{a}	9.60 ± 0.54^{c}	0.60 ± 0.54^{b}	4.80 ± 3.83^{b}

Values are presented as mean±SD. Different superscript letters (^{a,b,c}) indicate statistically significant differences between groups ($p<0.05$). Means sharing the same letter are not significantly different.

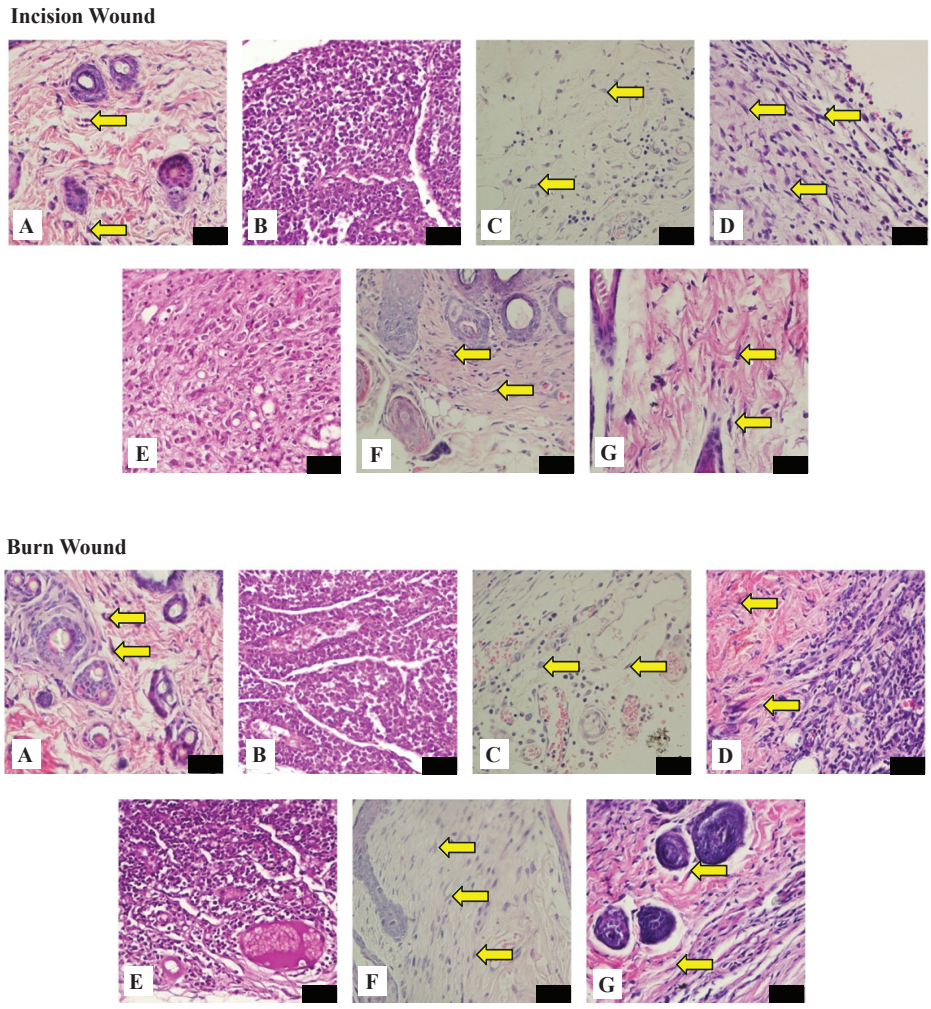

Figure 3. Dermal fibroblast distribution in incision and burn wounds after 7 days and 14 days of treatment. Yellow arrows indicate fibroblast cells within the dermal layer. The images demonstrate higher fibroblast density in the T group during early wound healing. Black bar: 100 µm.

Combining advanced-platelet-rich fibrin (A-PRF) with hyaluronic acid (HA) reduced IL-6 levels and improved granulation in patients with DFU, indicating faster inflammation resolution and enhanced angiogenesis and fibroblast proliferation. This supports the anti-inflammatory role in wound healing, that might be similar to the effects of terpenoids and flavonoids in Opuntia cochenillifera.(24) The addition of HA to A-PRF increased VEGF and PDGF release, enhancing fibroblast proliferation and angiogenesis in diabetic wound environments. This mechanism closely aligns with the effects of Opuntia cochenillifera phytochemicals, particularly flavonoids and alkaloids, which upregulate vascular endothelial growth factor (VEGF) and transforming growth factor (TGF)-β expressions. Since flavonoids and alkaloids are known to have anti-inflammatory and antidiabetics properties (25), it was known that fibroblast proliferation and collagen organization were enhanced after treatment, indicating

Table 3. Microscopic assessment of incision wounds after 7 and 14 days of treatment.

Microscopic Variables	HC	C(–)	C(+)	T
Day-7				
Re-epithelialisation (µm)	22.94±6.54^{a}	26.94±4.97^{a}	32.19±8.07^{a}	55.95±58.60^{b}
Fibroblast score	1.60±0.50^{a}	1.36±0.48^{a}	1.60±0.81^{a}	2.32±1.06^{b}
Day-14				
Re-epithelialisation (µm)	22.94±6.54^{a}	27.42±5.66^{a}	30.96±13.84^{a}	52.92±27.97^{b}
Fibroblast score	1.60±0.50^{a}	1.24±0.43^{a}	1.72±0.45^{a}	1.28±0.45^{a}

Values are presented as mean±SD. Different superscript letters (^{a,b}) indicate statistically significant differences between groups ($p<0.05$). Means sharing the same letter are not significantly different.

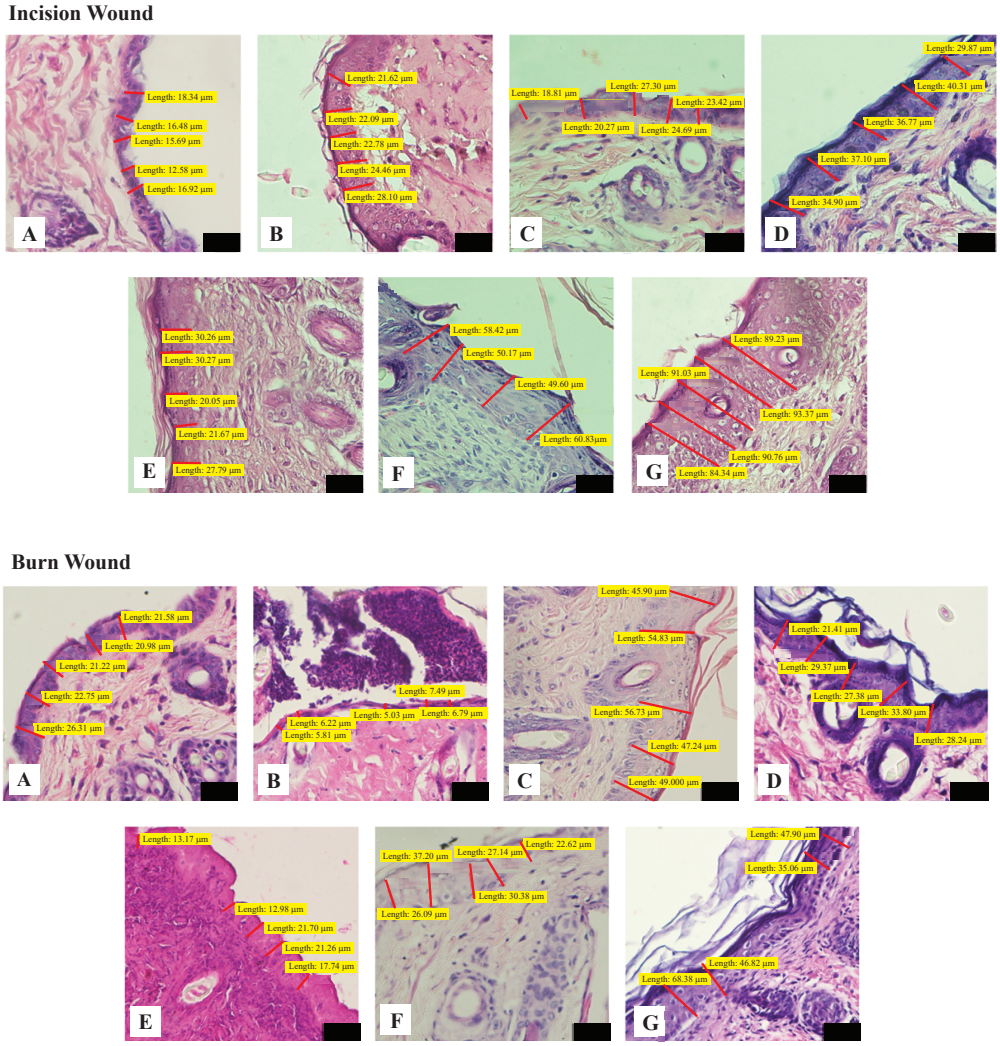

Figure 4. Epidermal thickness and re-epithelialisation in incision and burn wounds after 7 days and 14 days of treatment. The images demonstrate that the T group shows a more continuous and thicker epithelial layer at day-7 and -14. Black bar: 100 µm.

improved angiogenesis and extracellular matrix (ECM) remodelling comparable to HA + A-PRF therapy.(26)

This study did not include molecular analyses of inflammatory or growth factor markers (such as IL-6, TNF-α, VEGF, and TGF-β), nor did it perform antibacterial testing of *Opuntia cochenillifera* cream, which limits the deeper mechanistic interpretation of the observed healing effects. In addition, macroscopic wound assessment relied on manual ruler-based measurements, which may introduce observer-dependent variation and reduce precision compared with digital planimetry measurements. Future studies should incorporate molecular marker profiling, quantitative image-based wound assessment, and antibacterial assays to better characterize the pharmacological activity of *Opuntia cochenillifera*. Moreover, dose–response studies are needed to determine the optimal concentration and formulation parameters for maximal therapeutic benefit, as the present study evaluated only a single topical dose. Long-term safety

Table 4. Microscopic assessment of burn wounds after 7 and 14 days of treatment.

Microscopic Variables	HC	C(–)	C(+)	T
Day-7				
Re-epithelialisation (µm)	22.94±6.54[a]	34.57±37.25[a]	52.76±23.14[b]	49.08±38.25[b]
Fibroblast score	1.60±0.50[a]	1.44±0.50[a]	2.64±0.63[b]	2.40±0.63[b]
Day-14				
Re-epithelialisation (µm)	22.94±6.54[a]	18.91±8.79[a]	21.17±6.73[a]	50.59±37.02[b]
Fibroblast score	1.60±0.50[a]	1.36±0.48[a]	2.36±0.63[b]	1.72±0.79[a]

Values are presented as mean±SD. Different superscript letters ([a,b]) indicate statistically significant differences between groups ($p<0.05$). Means sharing the same letter are not significantly different.

and toxicity assessments, including repeated application studies and dermal irritation testing, are also essential to ensure that *Opuntia cochenillifera* cream is suitable for prolonged clinical use in patients with diabetes. These additional approaches will provide a more comprehensive understanding of the therapeutic potential and translational value of diabetic wound management.

Conclusion

This study demonstrates that the topical application of *Opuntia cochenillifera* cream improved wound healing outcomes in both incision and burn models under diabetic conditions. The treatment group showed faster wound contraction, more organized epithelial regeneration, and enhanced early fibroblast activity than the control groups, with efficacy comparable to standard therapy in burn wounds and superior effects in incision wounds. Therefore, these findings indicate that *Opuntia cochenillifera* cream might be a promising adjunctive topical agent for enhancing wound healing under diabetic conditions.

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Authors Contribution

IA assisted in the preparation of the formulation and manufacture of creams, animal observations, STZ-induced diabetes, scripting, wound creation, and removal of wound tissue from animals. DA assisted in the planning of experimental mental studies, scriptwriting, wound tissue retrieval from animals, animal observation, experimental data collection, wound creation, and induction of diabetes with STZ. RV, JW, and SH assisted in the manufacture of creams, treatment and observation of experimental animals, preparation of microscopic slides, and writing of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest or competing interests related to the content of this manuscript.

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