Received: 07.02.2026 | Revision: 16.02.2026 | Accepted: 16.02.2026 | Published: 25.06.2026

Veterinary Sciences

doi: 10.31210/spi2026.29.01.35
UDC 611-018:616.5-003.93-092.9:636.7

ORIGINAL ARTICLE

Scientific Progress & Innovations
ISSN: 2786-8842 (Print)
2786-8850 (Online)

29 (1)
2026

Comparative histological evaluation of topical repair cream and systemic Omega-3 supplementation on canine skin wound healing

H. N. Alkhalissi

Article info

Correspondence Author
H. N. Alkhalissi
E-mail:
hider.ali@uokerbala.edu.iq

College of Veterinary Medicine, University of Kerbala,
Karbala, 56001, Iraq

Citation: Alkhalissi, H. N. (2026). Comparative histological evaluation of topical repair cream and systemic Omega-3 supplementation on canine skin wound healing. *Scientific Progress & Innovations*, 29(1), 223–230. doi: 10.31210/spi2026.29.01.35

Cutaneous wound management represents a significant clinical challenge in veterinary medicine, directly impacting the quality of life and recovery rate in canine patients. Successful dermal restoration requires advanced therapeutic strategies capable of accelerating tissue regeneration, minimizing scar formation, and restoring the natural structural integrity of the skin barrier. Consequently, evaluating the efficacy of diverse treatments remains essential for optimizing dermatological protocols. This study aimed to evaluate the histological effects of a topical Cicalfate+ repair cream on skin wound healing in dogs and to compare its efficacy with Omega-3 supplementation. Full-thickness cutaneous wounds measuring 3 × 3 cm were experimentally induced in the dorsal back area of twelve healthy male dogs under general anesthesia induced by atropine sulfate (0.04 mg/kg, SC), ketamine hydrochloride (10 mg/kg, IV), and xylazine (2 mg/kg, IM). The animals were randomly divided into three groups: group (A) treated with Cicalfate+ repair cream topically twice daily, group (B) treated with a single daily oral dose of Omega-3 (300 mg), and group (C) left untreated as a control. At designated time a skin biopsies were collected under general anesthesia on days 3, 7, and 14 post-wounding, while animals remained alive throughout the experimental period. Full-thickness skin samples were processed for histological and histometrical examination to assess the thickness of the epidermal layers (stratum corneum and stratum spinosum), dermal thickness, and dermal papillae development. Morphometric analysis on day 14 revealed that Cicalfate+ treatment promoted balanced epidermal maturation, achieving a physiological stratum corneum thickness of 19.22±0.18 µm, which prevented the hyperkeratosis observed in group C (51.03±0.14 µm) and the severe thinning seen in group B (7.35±0.25 µm) (P≤0.05). Furthermore, group A demonstrated the most prominent tissue restructuring, with a significantly greater stratum spinosum thickness (60.37±2.52 µm) and dermal thickness (191.35±0.49 µm) compared to group B (7.34±0.38 µm and 88.32±0.3 µm) and group C (9.26±0.27 µm and (47.18±0.17 µm, respectively; P≤0.05). In conclusion, the topical repair cream significantly enhanced the histological features of skin wound healing in dogs compared with Omega-3 treatment and untreated controls. The findings suggest that the repair cream promotes balanced epidermal regeneration, effective dermal remodeling, and improved dermo-epidermal integration with enhanced vascular supply, nutrient delivery, and increased cellularity, making it a promising therapeutic option for enhancing cutaneous wound healing.

Keywords: Skin wound healing, Histology, Repair cream, Omega-3, dogs.

Порівняльна гістологічна оцінка місцевого відновлювального крему та системного застосування Омега-3 на загоєння ран шкіри у собак

Х. Н. Альхаліссі

Коледж ветеринарної медицини, Університет Кербели,
провінція Кербела, Ірак

Лікування ран шкіри є серйозним клінічним викликом у ветеринарній медицині, що безпосередньо впливає на якість життя та швидкість одужання собак. Успішне відновлення дерми вимагає передових терапевтичних стратегій. Відповідно, оцінка ефективності різних методів лікування залишається важливою для оптимізації дерматологічних протоколів. Дане дослідження мало на меті оцінити гістологічні ефекти місцевого застосування відновлювального крему Cicalfate+ на загоєння ран шкіри у собак та порівняти його ефективність із пероральним введенням Омега-3. Повношарові шкірні рани розміром 3 × 3 см були експериментально змодельовані в ділянці спини дванадцяти здорових кобелів під загальною анестезією. Тварини були випадковим чином розділені на три групи: група (А), де двічі на день місцево застосовували відновлювальний крем Cicalfate+; група (В), де перорально вводили одноразову щоденну дозу Омега-3 (300 мг); та група (С), яка залишалася без лікування як контроль. У визначені терміни на 3-й, 7-й та 14-й дні після моделювання рани під загальною анестезією здійснювали забір біоптатів шкіри, при цьому тварини залишалися живими протягом усього експериментального періоду. Повношарові зразки шкіри піддавали гістологічному та гістометричному дослідженню для оцінки товщини шарів епідермісу (рогового та шипуватого), товщини дерми та розвитку дермальних сосочків. Морфометричний аналіз на 14-й день показав, що застосування Cicalfate+ забезпечує збалансоване дозрівання епідермісу, досягаючи фізіологічної товщини рогового шару 19,22±0,18 мкм, що запобігало розвитку гіперкератозу, характерного для групи С (51,03±0,14 мкм), та вираженого стоншення, спостережуваного в групі В (7,35±0,25±мкм) (P≤0,05). Крім того, у групі А відмічено найбільш виражену перебудову тканин із вірогідно більшою товщиною шипуватого шару (60,37±2,52 мкм) та товщиною дерми (191,35±0,49 мкм) порівняно з групою В (7,34±0,38 мкм та 88,32±0,38 мкм) і групою С (9,26±0,27 мкм та 47,18±0,17 мкм відповідно; P≤0,05). В результаті, місцевий відновлювальний крем значно покращив гістологічні показники загоєння шкірних ран у собак порівняно з групою Омега-3 та контрольними групами без лікування. Отримані результати свідчать про те, що відновлювальний крем сприяє збалансованій регенерації епідермісу, ефективному моделюванню дерми та покращенню дермо-епідермальної інтеграції з кращим судинним забезпеченням, доставкою поживних речовин, що робить його перспективним терапевтичним засобом для покращення загоєння шкірних ран.

Ключові слова: загоєння ран шкіри, гістологія, відновлювальний крем, Омега-3, собаки.

Бібліографічний опис для цитування: *Альхаліссі Х. Н.* Порівняльна гістологічна оцінка місцевого відновлювального крему та системного застосування Омега-3 на загоєння ран шкіри у собак. *Scientific Progress & Innovations*. 2026. № 29 (1). С. 223–230.

Introduction

The skin is the largest organ in the body, providing the first line of physical, chemical, and immunological defense against external insults. It is composed of three main layers-the epidermis, dermis, and hypodermis-with each layer serving unique roles in protection, thermoregulation, sensation, and metabolic functions [1].

The epidermis, in turn, is histologically divided into five structural strata (from deep to superficial: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum). In contrast, the dermis is of mesodermal origin and composed largely of connective tissue matrix and cellular elements [2].

A skin wound is defined as damage to the structural integrity of the tissue following a rupture caused by physical, chemical, thermal, or biological agents. These injuries disrupt the protective skin barrier, triggering a complex sequence of biological events aimed at restoring tissue homeostasis [3].

Such disruptions in tissue continuity can involve one or multiple layers of the skin. Wounds are typically categorized by their etiology, depth, and duration. For instance, acute wounds-such as simple surgical incisions and traumatic injuries-undergo a normal, orderly, and timely reparative process. Conversely, chronic wounds, including diabetic ulcers and pressure sores, fail to progress through the typical stages of healing, usually due to persistent inflammation or underlying systemic diseases [4].

Thus, cutaneous wound healing is a highly regulated biological process that aims to restore tissue architecture and function [2]. During this process, multiple cell types, extracellular matrix components, cytokines, and growth factors interact with each other in a highly orchestrated manner [3].

Depending on the severity, acute wounds can vary from minor superficial scratches to extensive tissue injuries. However, they are all characterized by a predictable physiological healing pathway, which normally results in complete tissue restoration within approximately three weeks [5–7].

Dogs are among the most commonly used experimental models in biomedical and veterinary sciences. They are utilized either to address specific canine diseases or to serve as a translational model to enhance human health research, with their close physiological and clinical similarities to humans providing strong justification for this model choice [8, 9].

To optimize wound care, a variety of treatment strategies have been suggested, including hyperbaric oxygen therapy, modern wound dressings, and advanced antimicrobial agents [10].

Omega-3 fatty acids are essential polyunsaturated fatty acids required for normal physiological functions, naturally found in marine products-particularly fish and fish oil-as well as certain plant seed oils. While widely used for their dietary benefits and anti-inflammatory properties, such as reducing the severity of rheumatoid arthritis [11], marine Omega-3 fatty acids (EPA/DHA) can also modulate the early inflammatory phase of cutaneous wound healing. For instance, a randomized, double-blind study using standardized suction-blister wounds demonstrated that a 4-week omega-3 dietary supplementation reduced the plasma AA : EPA ratio and elevated local IL-1β levels in blister fluid at 24 hours, showing a trend toward a slower time to complete wound closure compared to a placebo [12].

In the search for innovative products capable of modulating the immune response, postbiotics have emerged as promising candidates. These soluble bioactive compounds, which are secreted by probiotics, represent a relatively underexplored category of therapeutic agents in the context of tissue repair [13, 14].

Previous research has demonstrated that postbiotics exhibit a broad spectrum of biological activities, including anti-inflammatory, antimicrobial, immunomodulatory, and antioxidant effects. Nevertheless, many aspects of the mechanisms underlying these activities, as well as their full biological potential, remain insufficiently understood or largely unexplored [15].

There is considerable growing interest in the application of postbiotics in wound care, as this novel and safer delivery of microbe-derived bioactivity does not require adding live organisms to already-compromised tissue. In short, the International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus describes a postbiotic as a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host when administered in adequate amounts. This inactivation may be associated with beneficial metabolites; however, purified metabolites per se are not considered postbiotics [12]. Such a framework facilitates topical postbiotic development where safety and stability are paramount, especially in infected or chronic wounds where the systemic entry of live microbes into the bloodstream is a real clinical concern [16].

Cicalfate⁺® repair cream features a distinct composition of four dermal restorative and protective active ingredients designed to restore the skin barrier. Within this formulation, zinc sulfate and copper sulfate exert a potent physical antibacterial effect, while zinc oxide acts as a protective agent by forming a reliable film barrier directly on the skin surface.

Additionally, Avène Thermal Spring Water is incorporated for its well-documented soothing, anti-irritant, and anti-inflammatory properties. The formulation also utilizes *Aquaphilus dolomiae*, a unique bacterium naturally present in Avène Thermal Spring Water. Through a specialized biotechnological extraction process, this microorganism yields a bioactive postbiotic compound known as C+ Restore™. Collectively, these synergistic components enhance epidermal repair and promote accelerated skin recovery, with reported healing occurring up to four times faster [17, 18].

The aim of the study

The present study aimed to evaluate the histological effects of a topical *Cicalfate⁺* repair cream on cutaneous wound healing in dogs and to compare its therapeutic efficacy with systemic Omega-3 supplementation.

Materials and methods

Animals and Experimental Design

A total of twelve adult male dogs, weighing 18–25 kg, were utilized in this study. The animals were randomly allocated into three groups (n = 4) dogs per group). All dogs were housed individually under standard laboratory conditions at the animal facility of the College of Veterinary Medicine, University of Kerbala. The animals had ad libitum access to water and a standard diet under uniform environmental and management conditions throughout the experimental period. To ensure optimal health, all dogs underwent a complete clinical examination every two days. Prior to surgery, the animals were fasted for 6–12 hours, with water withheld for 5 hours.

Anesthesia and Surgical Procedure

The animals were placed in a ventral recumbent position to aseptically expose the interscapular region of the dorsal back surface. Premedication was achieved with atropine sulfate (0.04 mg/kg, SC), followed by the induction of general anesthesia using a combination of ketamine hydrochloride (10 mg/kg, IV) and xylazine (2 mg/kg, IM). A full-thickness cutaneous wound measuring 3×3 cm was surgically induced in the mid-dorsal thoracic region of each animal. To prevent self-trauma and interference with the wound site, an Elizabethan collar was fitted immediately after the procedure.

Experimental Groups and Treatment Protocol

The experimental animals were assigned to three distinct groups:

- *Group A*: received topical application of Cicalfate⁺ repair cream twice daily for 14 days.
- *Group B*: received a single daily oral dose of 300 mg Omega-3 for 14 days [20].
- *Group C*: remained untreated, serving as a negative control group.

The commercial Cicalfate⁺ repair cream utilized in this study is composed of the following active ingredients: 1 % C+ Restore™ postbiotic, 0.2 % copper sulfate, 0.1 % zinc sulfate, 4 % zinc oxide, and 45 % Avène Thermal Spring Water. This postbiotic formulation is characterized by its therapeutic, antibacterial, soothing, and anti-inflammatory properties.

Tissue Sampling and Histological Processing

Histological assessment was conducted on days 3, 7, and 14 post-wounding for all groups [19]. At designated time points, animals were euthanized under general anesthesia, and full-thickness skin specimens 3×3 cm encompassing the wound site were obtained immediately after death. The tissue samples were fixed by immersion in a 10 % formalin solution, subjected to routine tissue processing, and stained with hematoxylin and eosin (H&E) [21].

Results and discussion

The present study demonstrated distinct and statistically significant histological dynamics across the experimental groups during the 14-day cutaneous wound healing period.

Stratum Corneum Thickness

In Group A (Cicalfate⁺), the thickness of the stratum corneum showed a gradual and significant time-dependent increase from day 3 to day 14 ($P \leq 0.05$), measuring 8.25±0.33 µm, 10.18±0.26 µm, and 19.22±0.18 µm, respectively (***Table 1***; ***Figs. 1***, ***2***, and ***3***).

Table 1

Stratum corneum thickness across experimental groups (µm, Mean±SD)

Groups	Day 3	Day 7	Day 14
Cicalfate⁺ (Group A)	8.25±0.33^{a}	10.18±0.26^{b}	19.22±0.18^{c}
Omega-3 (Group B)	10.11±0.15^{a}	12.17±0.15^{b}	7.35±0.25^{c}
Control (Group C)	25.25±0.49^{a}	43.85±0.76^{b}	51.03±0.14^{c}

Note: Means within the same row with different superscript letters (^{a,b,c}) are statistically significantly different according to ANOVA ($P \leq 0.05$).

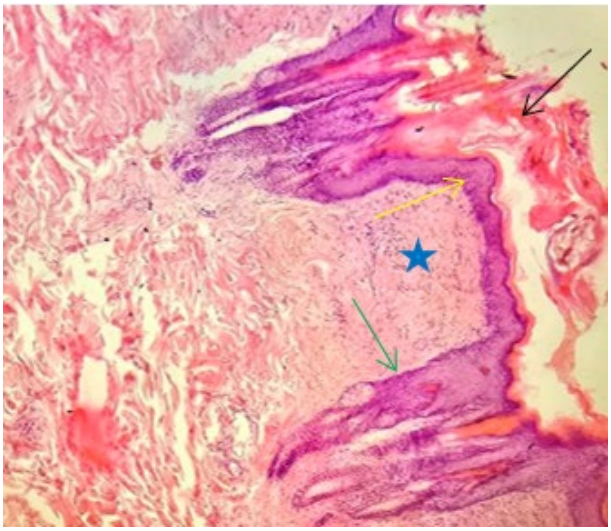

Fig. 1. Histological cross-section of group (A) at day 3 showed stratum corneum (black arrow), stratum spinosum (yellow arrow), dermis (blue star), and dermal papillae (green arrow). (H&E 100x).

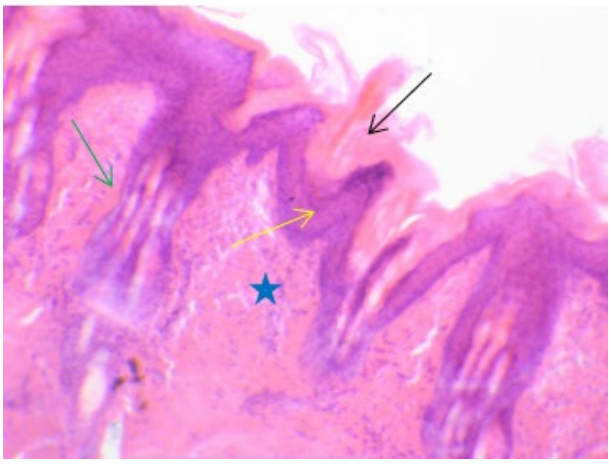

Fig. 2. Histological cross-section of group (A) at day 7 showed stratum corneum (black arrow), stratum spinosum (yellow arrow), dermis (blue star), and dermal papillae (green arrow). (H&E 100x).

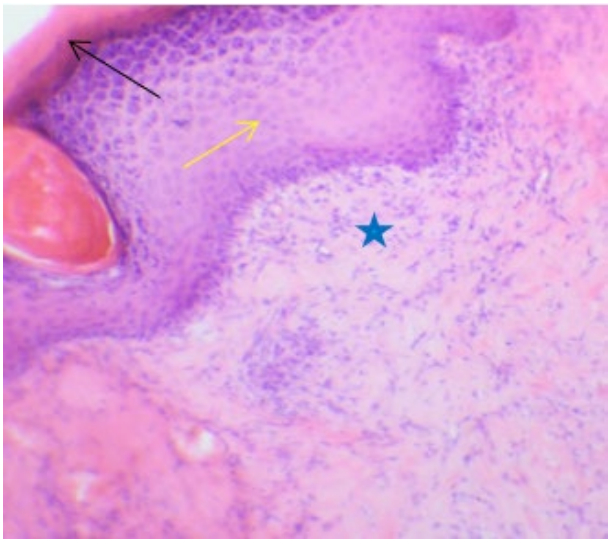

Fig. 3. Histological cross-section of group (A) at day 14 showed stratum corneum (black arrow), stratum spinosum (yellow arrow), and dermis (blue star). (H&E 100x).

Conversely, histopathological assessment of Group B (Omega-3) showed a gradual increase in stratum corneum thickness from day 3 (10.11±0.15 µm) to day 7 (12.17±0.15 µm) post-wounding (P≤0.05; ***Figs. 4*** and ***5***), followed by a significant thinning to 7.35±0.25 µm by day 14 (***Fig. 6***).

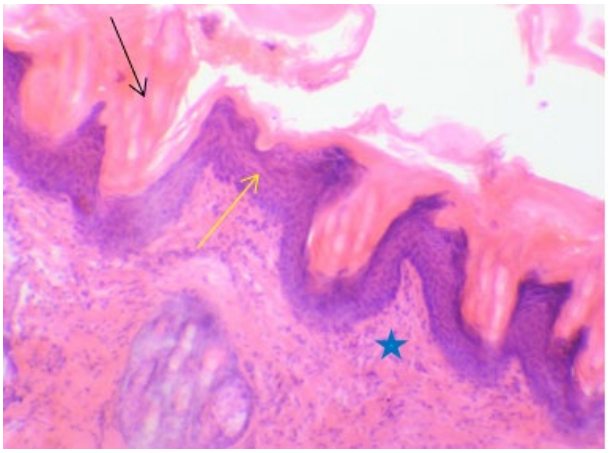

Fig. 4. Microscopic cross-view of group (B) at day 3 showed stratum corneum (black arrow), stratum spinosum (yellow arrow), and dermis (blue star). (H&E 100x).

In Group C (Control), the stratum corneum thickness in untreated wounds increased progressively after the third day, reaching its maximum value of 51.03±0.14 µm on day 14 (P≤0.05). The values were recorded at 25.25±0.49 µm on day 3, 43.85±0.76 µm on day 7, and 51.03±0.14 µm on day 14 (***Figs. 7***, ***8***, and ***9***).

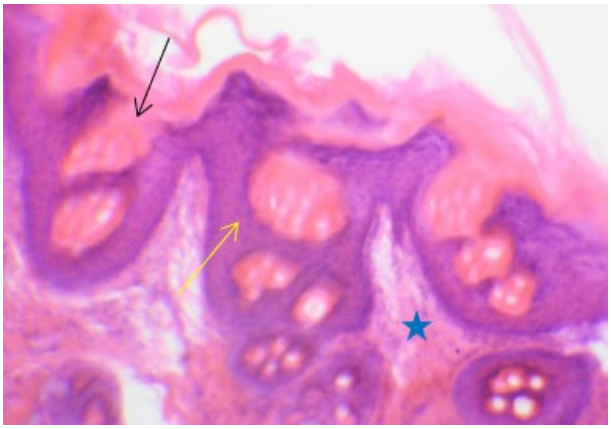

Fig. 5. Microscopic cross-view of group (B) at day 7 showed stratum corneum (black arrow), stratum spinosum (yellow arrow), and dermis (blue star). (H&E 100x).

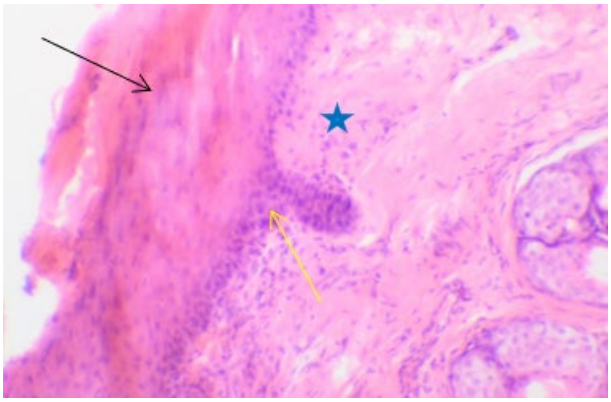

Fig. 6. Microscopic cross-view of group (B) at day 14 showed stratum corneum (black arrow), stratum spinosum (yellow arrow), and dermis (blue star). (H&E 100x).

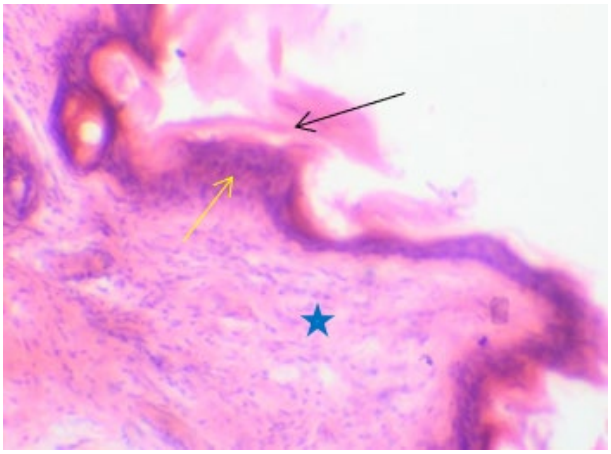

Fig. 7. Microscopic cross view of group (C) at day 3 showed stratum corneum (black arrow), stratum spinosum (yellow arrow) and dermis (blue star). (H&E 100x).

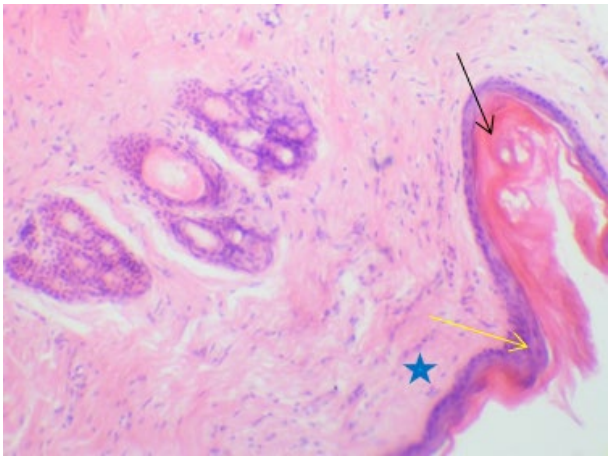

Fig. 8. Microscopic cross view of group (C) at day 7 showed stratum corneum (black arrow), stratum spinosum (yellow arrow) and dermis (blue star). (H&E 100x).

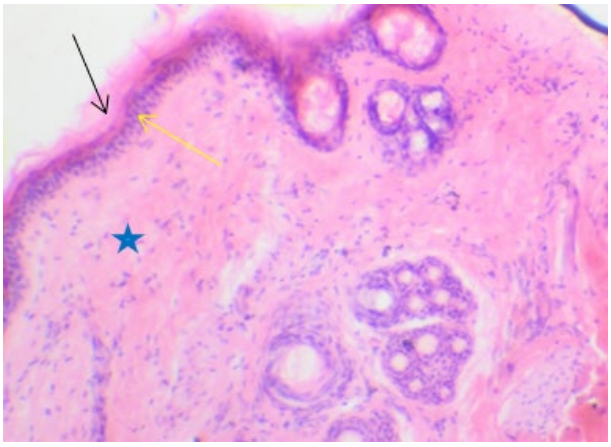

Fig. 9. Microscopic cross-view of group (C) at day 14 showed stratum corneum (black arrow), stratum spinosum (yellow arrow), and dermis (blue star). (H&E 100x).

Stratum Spinosum Thickness

Histologically, Group A exhibited a progressive and highly significant increase in stratum spinosum thickness over the course of the study (P≤0.05), with measurements reaching 13.04±0.13 µm on day 3, 21.25±0.36 µm on day 7, and peaking sharply at 60.37±2.52 µm on day 14 (***Table 2***; ***Figs. 1***, ***2***, and ***3***).

Table 2

Stratum spinosum thickness across experimental groups (µm, Mean±SD)

Groups	Day 3	Day 7	Day 14
Cicalfate+ (Group A)	13.04±0.13^{a}	21.25±0.36^{b}	60.37±2.52^{c}
Omega-3 (Group B)	9.28±0.3^{a}	20.35±0.43^{b}	7.34±0.38^{c}
Control (Group C)	7.18±0.30^{a}	8.16±0.26^{a}	9.26±0.27^{b}

Note: Means within the same row with different superscript letters (^{a,b,c}) are statistically significantly different according to ANOVA (P≤0.05).

In Group B, the stratum spinosum gradually grew thicker from day 3 (9.28±0.31 µm) to day 7 (20.35±0.43 µm) (P≤0.05; ***Figs. 4*** and ***5***), but a significant decline to 7.34±0.38 µm was observed at the end of the experimental period (***Fig. 6***).

In Group C, the untreated wounds revealed only a minimal and stagnant increase in stratum spinosum thickness between day 3 and day 14 (P≤0.05), with recorded values of 7.18±0.30 µm, 8.16±0.26 µm, and 9.26±0.27 µm, respectively (***Figs. 7***, ***8***, and ***9***).

Dermal Thickness and Dermal Papillae

Histological alterations showed a significant thickening of the dermis in Group A, particularly during the latter part of the study (P≤0.05). The dermal thickness values were measured at 163.18±0.81 µm, 173.30±0.49 µm, and 191.35±0.49 µm for days 3, 7, and 14, respectively (***Table 3***; ***Figs. 1, 2***, and ***3***), representing the highest overall values among all groups.

Table 3

Dermal thickness across experimental groups (µm, Mean±SD)

Groups	Day 3	Day 7	Day 14
Cicalfate+ (Group A)	163.18±0.81^{a}	173.30±0.49^{b}	191.35±0.49^{c}
Omega-3 (Group B)	120.24±0.31^{a}	244.27±1.20^{b}	88.32±0.38^{c}
Control (Group C)	80.60±0.76^{a}	83.14±0.72^{a}	47.18±0.17^{b}

Note: Means within the same row with different superscript letters (^{a,b,c}) are statistically significantly different according to ANOVA (P≤0.05).

In Group B, dermal thickness significantly increased to 120.24±0.31 µm on day 3 and peaked markedly at 244.27±1.20 µm on day 7 (P≤0.05; ***Figs. 4*** and ***5***), but declined again by day 14 to 88.32±0.38 µm (***Fig. 6***).

Group C exhibited a slight but statistically significant increase between day 3 (80.60±0.76 µm) and day 7 (83.14±0.72 µm) (P≤0.05; ***Figs. 7*** and ***8***), followed by a notable decrease to a minimum of 47.18±0.17 µm by day 14 (***Fig. 9***).

Additionally, the development and frequency of the Dermal Papillae at the dermo-epidermal junction were found to be significantly higher in Group A than in the other experimental groups (***Figs. 1*** and ***2***).

The present study provides a detailed histological comparison of wound healing in canine skin treated with a repair cream, Omega-3 supplementation, and untreated controls. The observed variations among the experimental groups reflect distinct effects on epidermal regeneration, dermal remodeling, and dermo-epidermal integration, which collectively determine the quality and efficiency of wound healing.

Compared to their respective controls, administration of the repair cream led to an increase in the thickness of the stratum corneum in group (A) as early as day 3 post-wounding, and the increase was also time-dependent over the course of 14 days ($p<0.01$). This regulated thickening seems to reflect a beneficial adaptation in the course of healing. At the same time, we know that low levels of SC thickening early on can aid in keratinocyte migration and lateral spreading, necessary processes in re-epithelialization and wound closure [22]. The clearly marked stratum corneum thickening at day 14 indicates

restoration of epidermal barrier function, which is vital to limit transepidermal water loss, provide a homeostatic level of skin hydration, and prevent entry of microorganisms [23].

The favorable effect seen in group (A) could be due to the moisturizer and repair cream ingredients (Avène thermal spring water, zinc oxide, copper sulfate, and zinc sulfate). Notably, zinc ions are crucial for keratinocyte proliferation, epithelial differentiation, and the antimicrobial defense involved in wound healing activities [24]. In addition, the appearance of postbiotic entities such as C+ Restore™ may influence local inflammatory responses and facilitate epidermal repair by increasing cellular metabolism and accelerating barrier repair mechanisms [25].

Conversely, group (B), in which the model was treated with Omega-3, only showed a slight increase in stratum corneum thickness in the early post-healing phase. Moreover, a significant decrease in stratum corneum thickness could be observed at day 14 post-healing. The anti-inflammatory effects of Omega-3 fatty acids are well established and they can also modify wound healing pathways [26], but the thinning of the stratum corneum at 2-week timepoints interpreted within the context of epidermal barrier function raises questions about the appropriateness of high Omega-3 fatty acid for certain wound types. A poorly formed stratum corneum may put the wound bed at risk for fluid loss and bacterial colonization, thus impairing the signaling required for best tissue repair [27].

In addition to that, group (C) appeared to have a very thickening stratum corneum early and gradually throughout the experiment period. This hyperkeratosis is usually related to migration dysfunction of keratinocytes and delayed re-epithelialization, which results in prolonged healing time and promotion of scar formation [28]. This was the first indication that, without therapeutic intervention, epidermal repair may be random rather than regenerative.

In group (A), stratum spinosum clearly increased in thickness, especially on day 14, which indicates increased keratinocyte proliferation and upward migration. This reaction is characteristic of epidermal healing and effective re-epithelialization, important processes required for recover of normal skin structure after skin injury [3]. This sustained elevation also indicates that the repair cream drove a leveled augmentative response without causing deleterious hyperplasia. In group (B), the stratum spinosum thickness decreased at the end of the study, while it increased at the middle stage. This pattern suggests a transient, and not a sustained, epidermal response to the intervention, which could result from the anti-proliferative effects ascribed to sustained Omega-3 activity [29], whereby excess cellular proliferation is inhibited, but epidermal regeneration is slowed in isolation. For group (C), we recognized only slight changes in stratum spinosum thickness, notwithstanding a statistical significance there. Such weak epidermal response was associated with delayed wound healing and indicates insufficient keratinocyte activation, which in natural circumstances requires supportive therapeutic agents.

Background Dermal remodeling reflects fibroblast activity, collagen deposition, and neovascularization, and is an important determinant of wound healing quality. In group (A), dermal thickness showed a gradual and marked increase until day 14. Such a result indicates better angiogenesis as well as the supply of nutrients to the neo-formation of epidermis that is essential for maintaining tissue regeneration [30]. The increase in dermal thickness is frequently accompanied by well-organized collagen and a restored functional dermal architecture. In group (B), dermal thickness increased at first but thereafter showed a pronounced decrease during the course of the experiment. These variations potentially reflect an initial stimulation of dermis repair subsequently compromised by inadequate maintenance of vascular and structural support that ultimately impair epidermal regeneration [31]. In contrast group (C) showed only modest early increases in dermal thickness followed by a marked decrease. Such a pattern suggests impaired fibroblast activity and low vascularization which has been reported to prolong wound healing and weaken the tissue [32].

Perhaps the most important observation from the current work was that dermal papillae height increased in the group (A). Greater number of dermal papillies increases dermal – epidermal contact surface, allowing for a stronger adhesion and resisting mechanical shear forces [33]. Such a structural adaptation enhances mechanical stability, and allows the facilitation of oxygen and nutrient diffusion from dermal microvasculature to the epidermis, thus allowing continuous maintenance of epidermal turnover. In contrast, the less developed dermal papillae seen in (B) and (C) indicate weaker dermo-epidermal interactions, which may in part explain their poorer wound healing phenotype.

Histology results highly correlated. At all sections, the histological features indicate a synergic environment created by group (A) of the repair cream for optimal wound healing including balanced rate of epidermal proliferation with full restoration of barrier, adequate remodeling of dermis and strong dermal-epidermal integration. Omega-3 supplementation alone (group B) had minimal transient effects and absence of treatment (group C) resulted in delayed but incomplete healing. These findings highlight the importance of topical reparative agents in modulating cellular and structural processes during canine skin wound healing.

Conclusions

The present study demonstrates that the topical application of Cicalfate$^+$ repair cream creates a highly synergistic microenvironment that significantly optimizes cutaneous wound healing in dogs compared to systemic Omega-3 supplementation and untreated controls. By day 14 post-wounding, Cicalfate$^+$ treatment promotes a balanced and controlled maturation of the epidermal barrier, achieving a physiological stratum corneum thickness of 19.22±0.18 µm, which successfully prevents hyperkeratosis seen in the control group (51.03±0.14 µm) and severe epidermal thinning observed in the Omega-3 group (7.35±0.25 µm). Furthermore, the repair cream

drives robust tissue restructuring, significantly maximizing both stratum spinosum thickness (60.37±2.52 µm) and dermal thickness (191.35±0.49 µm) by the end of the experimental period. This is structurally reinforced by an enhanced development of dermal papillae, which ensures superior mechanical stability and dermo-epidermal adhesion. Collectively, these findings establish the postbiotic-containing Cicalfate+ repair cream as a highly effective and safe therapeutic agent for accelerating and enhancing structured cutaneous wound regeneration in veterinary dermatology.

DECLARATIONS

Ethical Statement

The research plan was approved by the committee of the College of Veterinary Medicine, University of Kerbala [UOK.VET.AN.179] in [8.1.2026].

Funding

This research received no external funding.

Conflict of Interest

The author declares no conflict of interest.

Acknowledgements

None.

Declaration of AI and AI-assisted technologies

The author declares that no artificial intelligence or AI-assisted technologies were used in the preparation of this manuscript.

References

1. Ross, M. H., & Pawlina, W. (2020). *Histology: A text and atlas: With correlated cell and molecular biology* (8th ed.). Wolters Kluwer
2. Eroschenko, V. P. (2013). *di Fiore's atlas of histology with functional correlations* (11th ed., South Asian ed., pp. 216–224). Wolters Kluwer; Lippincott Williams & Wilkins.
3. Gurtner, G. C., Werner, S., Barrandon, Y., & Longaker, M. T. (2008). Wound repair and regeneration. *Nature*, 453 (7193), 314–321. https://doi.org/10.1038/nature07039
4. Guo, S., & DiPietro, L. A. (2010). Factors affecting wound healing. *Journal of Dental Research*, 89 (3), 219–229. https://doi.org/10.1177/0022034509359125
5. Sen, C. K. (2021). Human wound and its burden: Updated 2020 compendium of estimates. *Advances in Wound Care*, 10 (5), 281–292. https://doi.org/10.1089/wound.2021.0026
6. Martin, P., & Nunan, R. (2015). Cellular and molecular mechanisms of repair in acute and chronic wound healing. *British Journal of Dermatology*, 173 (2), 370–378. https://doi.org/10.1111/bjd.13954
7. Dreifke, M. B., Jayasuriya, A. A., & Jayasuriya, A. C. (2015). Current wound healing procedures and potential care. *Materials Science and Engineering: C*, 48, 651–662. https://doi.org/10.1016/j.msec.2014.12.068
8. Schulte, E., & Arlt, S. P. (2022). What kinds of dogs are used in clinical and experimental research? *Animals*, 12 (12), 1487. https://doi.org/10.3390/ani12121487
9. Ward, S. (2022). Dog as the experimental model: Laboratory uses of dogs in the United States. *Altex*, 39 (4), 605–620. https://doi.org/10.14573/altex.2109101
10. Akita, S. (2019). Wound repair and regeneration: mechanisms, signaling. *International Journal of Molecular Sciences*, 20 (24), 6328. https://doi.org/10.3390/ijms20246328
11. Kremer, J. M. (2000). n−3 Fatty acid supplements in rheumatoid arthritis. *The American Journal of Clinical Nutrition*, 71 (1), 349S–351S. https://doi.org/10.1093/ajcn/71.1.349s
12. McDaniel, J. C., Belury, M., Ahijevych, K., & Blakely, W. (2008). Omega-3 fatty acids effect on wound healing. *Wound Repair and Regeneration*, 16 (3), 337–345. https://doi.org/10.1111/j.1524-475x.2008.00388.x
13. Aguilar-Toalá, J. E., Garcia-Varela, R., Garcia, H. S., Mata-Haro, V., González-Córdova, A. F., Vallejo-Cordoba, B., & Hernández-Mendoza, A. (2018). Postbiotics: An evolving term within the functional foods field. *Trends in Food Science & Technology*, 75, 105–114. https://doi.org/10.1016/j.tifs.2018.03.009
14. García-Vicente, E. J., Rey-Casero, I., Martín, M., Pérez, A., Benito-Murcia, M., & Risco, D. (2024). Oral supplementation with postbiotics modulates the immune response produced by myxomatosis vaccination in wild rabbits. *Vaccine*, 42 (20), 125978. https://doi.org/10.1016/j.vaccine.2024.05.026
15. Wang, P., Wang, S., Wang, D., Li, Y., Yip, R. C. S., & Chen, H. (2024). Postbiotics-peptidoglycan, lipoteichoic acid, exopolysaccharides, surface layer protein and pili proteins-Structure, activity in wounds and their delivery systems. International *Journal of Biological Macromolecules*, 274, 133195. https://doi.org/10.1016/j.ijbiomac.2024.133195
16. Salminen, S., Collado, M. C., Endo, A., Hill, C., Lebeer, S., Quigley, E. M. M., Sanders, M. E., Shamir, R., Swann, J. R., Szajewska, H., & Vinderola, G. (2021). The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nature Reviews Gastroenterology & Hepatology*, 18 (9), 649–667. https://doi.org/10.1038/s41575-021-00440-6
17. Eau Thermale Avène. (n.d.). *Cicalfate+: Innovation in postbiotic skincare* [Product brochure]. https://www.avenederm.com/media/marketing/assets/Cicalfate_Sell_Sheet_Cream_Scar_Gel_Hand_Lips.pdf
18. Ribet, V., Mielewczyk, E., Sirvent, A., Georgescu, V., & Rossi, A. B. (2018). A novel dermo-cosmetic product containing thermal spring water, sucralfate, copper sulfate, and zinc sulfate in the management of hand eczema. *Clinical, Cosmetic and Investigational Dermatology*, 11, 373–381. https://doi.org/10.2147/ccid.s157849
19. Hargis, A. M., & Lewis, T. P. (1999). Full-thickness cutaneous burn in black-haired skin on the dorsum of the body of a Dalmatian puppy. *Veterinary Dermatology*, 10 (1), 39–42. https://doi.org/10.1046/j.1365-3164.1999.00109.x
20. Hameed, F. M. (2020). Effect of Omega-3 on induced cutaneous wounds healing in rabbits. *Medico Legal Update*, 20 (3), 1316–1320. https://doi.org/10.37506/mlu.v20i3.1583
21. Luna, L. G. (1992). *Histopathologic methods and color atlas of special stains and tissue artifacts*. American Histolabs.
22. Singer, A. J., & Clark, R. A. F. (1999). Cutaneous wound healing. *New England Journal of Medicine*, 341 (10), 738–746. https://doi.org/10.1056/nejm199909023411006
23. Proksch, E., Brandner, J. M., & Jensen, J.-M. (2008). The skin: an indispensable barrier. *Experimental Dermatology*, 17 (12), 1063–1072. https://doi.org/10.1111/j.1600-0625.2008.00786.x
24. Lansdown, A. B. G., Mirastschijski, U., Stubbs, N., Scanlon, E., & Ågren, M. S. (2007). Zinc in wound healing: Theoretical, experimental, and clinical aspects. *Wound Repair and Regeneration*, 15 (1), 2–16. https://doi.org/10.1111/j.1524-475x.2006.00179.x
25. Prajapati, S. K., Lekkala, L., Yadav, D., Jain, S., & Yadav, H. (2025). Microbiome and postbiotics in skin health. *Biomedicines*, 13 (4), 791. https://doi.org/10.3390/biomedicines13040791
26. Calder, P. C. (2010). Omega-3 fatty acids and inflammatory processes. *Nutrients*, 2 (3), 355–374. https://doi.org/10.3390/nu2030355
27. Elias, P. M. (2005). Stratum corneum defensive functions: An Integrated view. *Journal of Investigative Dermatology*, 125 (2), 183–200. https://doi.org/10.1111/j.0022-202x.2005.23668.x
28. Martin, P. (1997). Wound healing-aiming for perfect skin regeneration. *Science*, 276 (5309), 75–81. https://doi.org/10.1126/science.276.5309.75

29. Alexander, J. W., & Supp, D. M. (2014). Role of arginine and Omega-3 fatty acids in wound healing and infection. *Advances in Wound Care*, 3 (11), 682–690. https://doi.org/10.1089/wound.2013.0469
30. Tonnesen, M. G., Feng, X., & Clark, R. A. F. (2000). Angiogenesis in wound healing. *Journal of Investigative Dermatology Symposium Proceedings*, 5 (1), 40–46. https://doi.org/10.1046/j.1087-0024.2000.00014.x
31. Broughton, G., Janis, J. E., & Attinger, C. E. (2006). The basic science of wound healing. P*lastic and Reconstructive Surgery*, 117 (7 S), 12S–34S. https://doi.org/10.1097/01.prs.0000225430.42531.c2
32. Falanga, V. (2005). Wound healing and its impairment in the diabetic foot. *The Lancet*, 366 (9498), 1736–1743. https://doi.org/10.1016/s0140-6736(05)67700-8
33. Mescher, A. L. (2010). *Junqueira's basic histology: Text & atlas* (12th ed.). McGraw-Hill Medical.

ORCID

H. N. Alkhalissi https://orcid.org/0000-0003-4905-6235

2025 by the author(s). This is an open-access article distributed under the Creative Commons Attribution License http://creativecommons.org/licenses/by/4.0, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.