Academic International Journal of Veterinary Medicine
ISSN: 2984-7753
Aca. Intl. J. Vet. Med. 2025;3(1)44-53
Journal homepage: www.aipublishers.org/aijvm

Morphological Comparative Changes in Skin Healing by Using Postbiotic Cream and Antibiotics in Rabbit

Hayder Nadhim Alkhalissi

Department of Anatomy and Histology, College of Veterinary Medicine, University of Kerbala-Iraq
Email: hider.ali@uokerbala.edu.iq

(Received 10 January 2025, Revised 25 February 2025, Accepted 27 April 2025, Published 21 May 2025)

Abstract

The present study was done at the College of Veterinary Medicine, Kerbala University. The purpose of the study was to examine the properties of antibiotics (penicillin-streptomycin) and a postbiotic cream (Cicalfate+ cream) on the shape of rabbits' healing processes in full-thickness skin wounds. In forty-five healthy adult bucks weighing 1.3 and 1.8 kg, full-thickness wounds measuring 2.5 x 2.5 cm were made in the dorsal back area. Intramuscular injections of xylazine hydrochloride (5 mg/kg), ketamine hydrochloride (35 mg/kg) were given very quickly (IM), along with 1 mg/kg of diazepam. In group A, one group received a daily intramuscular injection of procaine penicillin G (80,000 U/kg of body weight) along with probenecid (25 mg/kg of body weight) and streptomycin (20 mg/kg of body weight) for five days. In group B, participants applied cicalfate+ cream topically twice a day. Group C served as a control group and did not receive any treatment. On the 3rd, 7th, and 14th days after wounding, the fifteen male adult rabbits that were chosen for the morphological investigation were separated into three subgroups of five. All groups showed different rates of epidermal re- and de-generation, although the one using Cicalfate+ cream showed the fastest skin wound healing progress, according to the morphological results.

Keywords: Postbiotic cicalfate+ cream, penicillin-streptomycin, wound healing, rabbits.

How to cite:
Hayder Nadhim Alkhalissi. Morphological Comparative Changes in Skin Healing by Using Postbiotic Cream and Antibiotics in Rabbit. *Aca. Intl. J. Vet. Med. 2025;3(1)44-53*: https://doi.org/10.59675/V316

Introduction

The first stage in learning is to evaluate the nonfiction on the typical on which to achieve the research. When a study is done on the suitable creatures, the data obtained must estimate what can be probable in human actualities [1]. Traditional experimental uses of rabbits include antibody manufacturing, the development of new surgical techniques, and the study of medication toxicity and physiology [2].

Various ecosystems across the world are home to rabbits, a group of tiny mammals that belong to the family Leporidae and the order Lagomorpha [3, 4]. Physical damage disrupts the natural continuity or integrity of an organ, part, or system in the body [5]. From a pathophysiologic perspective, the epithelial barrier can be breached by mechanical, chemical, or biological processes,

which in turn activate a biological cascade that constitutes wound healing [6, 7]. After injecting several antibacterial drugs into rats, researchers looked at how they affected the healing process. An elongated incised and sutured healing skin wound's tensile strength was used as a measure of healing [8]. One such alternative to antibiotics for the treatment and prevention of certain diseases is postbiotics, which are produced by metabolites of Lactobacillus species [9]. Probiotics produce soluble chemicals and metabolites that offer physiological benefits for persons who have not been tested or investigated, which is known as postbiotics [10, 11]. A cicalfate+ cream, which is a restorative, repairing, protective cream this product is a part of the ongoing quest for natural agents that might modulate immune response. This cream was designed to speed up the skin's recovery fourfold. It contains a variety of beneficial ingredients, including copper sulfate and zinc sulfate, which act as physical antibacterial; zinc oxide acts as a protectant; Avene thermal spring water has calming, anti-irritant, and anti-inflammatory properties; and finally, a biotechnological extraction of the revolutionary bacteria *Aquaphilus dolomiae*, which is found exclusively in Avene thermal spring water, has resulted in a new postbiotic called C+ Restore finally this cream for its composition makes skin recovery four times faster [12]. One billion microorganisms per square centimeter connect to the human body through the skin [13]. According to popular belief, the cutaneous microbiome plays a role in immune-mediated homeostasis maintenance [14, 15]. Similar changes in the skin microbiome, which cause pathogenic bacterial overgrowth due to stimuli inside and outside the body, can cause inflammatory and infectious skin diseases [16, 17, 18, 19].

Materials and Methods

Experimental Animals

This study employed 45 mature male rabbits, divided to three groups of 15 from each group, ranging in weight from 1.3 to 1.8 kg. Animals were housed in individual cages at the Veterinary Medicine College of University of Kerbala and maintained under conventional hygienic circumstances over the duration of the experiment. These settings included a controlled atmosphere, food, and handling.

Procedure

In the six to twelve hours leading up to surgery, the mice were not given food or water. Collective anesthesia was established with diazepam as a preanesthetic in a dose of 1 mg/kg b.w. after shaving and washing the dorsal-back region of the area. ten minutes later. A dosage of 5 mg/kg body weight of xylazine hydrochloride was administered to the animals to put them to sleep. Together with 35 mg of ketamine hydrochloride per kilogram of body weight. they were all given intramuscularly [20]. The rabbits were prepared for aseptic surgery by placing them in ventral recumbency and preparing their dorsal surface, or back. The animals were all created a full-thickness skin wounds of 2.5×2.5 cm as a square in the dorsal back area (fig.1). There were three groups of rabbits used in the experiment: one group got an intramuscular injection of (penicillin-streptomycin) once a day for five days, with probenecid and streptomycin added at doses of 25 mg/kg and 20 mg/kg, respectively [21]; another group got cicalfate+ cream applied topically twice a day for fourteen days, and the control group got no treatment at all. With its postbiotic composition of (C+ Restore 1% postbiotic, copper sulfate 0.2%, zinc sulfate 0.1%, zinc oxide 4%, and Avene thermal water 45%), cicalfate+ cream can heal wounds, soothe irritated skin, and reduce inflammation. In this investigation, a complete clinical examination was performed on each rabbit every two days during the experiment. To ensure that the wound boundaries were checked, digital cameras were used to take pictures of all wounds. A picture was taken after the region was carefully shaven to get a clearer picture of the granulation tissue and the epithelization area, and the scab was scraped gently. The wound borders, wound length and width, were all measured using the digital caliper to follow wound healing progress, on the third, seventh, and fourteenth days, we measured the length and width of each group's wounds and photographed them.

Aca. Intl. J. Vet. Med. 2025;3(1)44-53: https://doi.org/10.59675/V316

Results:

The effects of present study showed that changes in medical declaration of wounds seem like really that the group (B) were displayed rapidly declined in wound dimension (length and width) through the current study more than other groups, and this decrease in wound size was to a less degree in group (A) and lesser in wound of group (C) (table 1).

The change was started at 3rd day in control and treated groups, which became clear at day 14th, especially in group (B) in both length and width of wound (table 1) due to its properties which acts as a repair cream with anti-inflammatory, soothing anti-irritant effects. In addition, the wound size of each group observed a decrease in the same group from 3rd day until 14th days (table 2, 3 and 4). The indistinct variances seemed in overall wound healing among treated & controlled wounds mostly at the completion of the study (fig.4,7 and 10). The morphological assessment exposed that the amount of wound reduction (closer) in group (A) found a significant difference (P≤0.05) in wound length and width in 3rd, 7th and 14th days respectively (table 2) (fig.2,3 and 4), while in group (B) there was a significant difference (P≤0.05) in 3rd and 7th days for length of wound and a significant difference (P≤0.05) in 3rd, 7th and 14th days for width of wound respectively (table 3) (fig.5,6 and 7), and in group (C) also there was a significant difference (P≤0.05) in 3rd, 7th and 14th days for both length and width of wounds respectively (table 4) (fig.5,9 and 10). On other hand the contraction zone or margin of wound more clear in group (B) than other groups and this believed to the activity of wound to heal due to the fibers and epithelia proliferation at this margin (fig.5 and 6). Our results revealed there was hyperemia at the end of this study in group (A) more than other groups (fig.4).

Fig.1 Grossly the area of full thickness wound were created in dorsal back region

Fig.2 Morphologically, skin wound of group (A), 3rd day.

Aca. Intl. J. Vet. Med. 2025;3(1)44-53: https://doi.org/10.59675/V316

Fig.3 Morphologically skin wound of group (A), 7th day.

Fig.4 Morphologically skin wound of group (A), 14th day.

Fig.5 Morphologically skin wound of group (B), 3rd day.

Aca. Intl. J. Vet. Med. 2025;3(1)44-53: https://doi.org/10.59675/V316

Fig.6 Morphologically skin wound of group (B), 7th day.

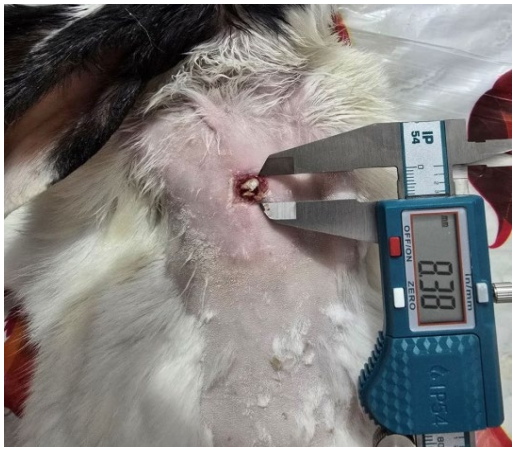

Fig.7 Morphologically skin wound of group (B), 14th day.

Fig.8 Morphologically skin wound of group (C), 3rd day.

Aca. Intl. J. Vet. Med. 2025;3(1)44-53: https://doi.org/10.59675/V316

Fig.9 Morphologically skin wound of group (C), 7th day.

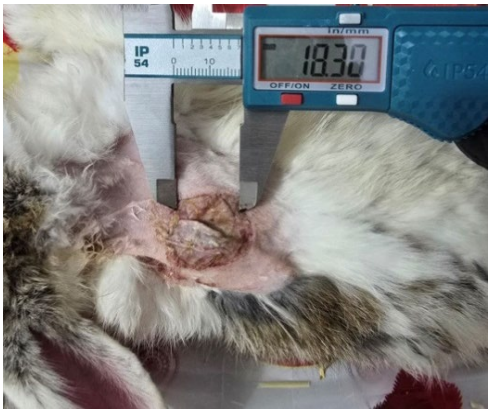

Fig.10 Morphological skin wound of group (C), 14th day.

Table (1) Length and width of wounds of groups (A, B and C) in 3rd, 7th and 14th days.

Wound dimensions	Day	Penicillin-streptomycin (Group A) (unit mm) Mean ± SE	Cicalfate+ cream (Group B) (unit mm) Mean ± SE	Control (Group C) (unit mm) Mean ± SE	P value
Length	3 days	24.17 ± 0.14 A	23.03 ± 0.12 a	22.57 ± 0.09 B	0.016
Length	7 days	21.26 ± 0.09 A	23.02 ± 0.22 a	21.54 ± 0.06 A	0.064
Length	14 days	17.61 ± 0.19 B	9.16 ± 0.06 c	19.76 ± 0.08 A	0.023
Width	3 days	22.08 ± 0.17 A	21.43 ± 0.17 a	21.73 ± 0.15 A	0.075
Width	7 days	21.35 ± 0.13 A	22.09 ± 0.34 a	21.47 ± 0.15 A	0.058
Width	14 days	13.68 ± 1.35 B	9.14 ± 0.10 c	19.45 ± 0.19 A	0.014

Aca. Intl. J. Vet. Med. 2025;3(1)44-53: https://doi.org/10.59675/V316

Table (2) Length and width of wounds of group (A) in 3rd, 7th and 14th days.

Treatment	Wound dimensions	Day	Measurements Mean ± SE (unit mm)	Tukey pairwise	P value
Penicillin-streptomycin (Group A)	Length	3 days	24.17 ± 0.14	A	
Penicillin-streptomycin (Group A)	Length	7 days	21.26 ± 0.09	B	0.023
Penicillin-streptomycin (Group A)	Length	14 days	17.61 ± 0.19	C	
Penicillin-streptomycin (Group A)	Width	3 days	22.08 ± 0.17	A	
Penicillin-streptomycin (Group A)	Width	7 days	21.35 ± 0.13	B	0.014
Penicillin-streptomycin (Group A)	Width	14 days	13.68 ± 1.35	C	

Table (3) Length and width of wounds of group (B) in 3rd, 7th and 14th days.

Treatment	Wound dimensions	Day	Measurement Mean ± SE (unit mm)	Tukey pairwise	P value
Cicalfate+ cream (Group B)	Length	3 days	23.03 ± 0.12	A	
Cicalfate+ cream (Group B)	Length	7 days	23.02 ± 0.22	A	0.048
Cicalfate+ cream (Group B)	Length	14 days	9.16 ± 0.06	B	
Cicalfate+ cream (Group B)	Width	3 days	21.43 ± 0.17	A	
Cicalfate+ cream (Group B)	Width	7 days	22.09 ± 0.34	B	0.033
Cicalfate+ cream (Group B)	Width	14 days	9.14 ± 0.10	C	

Aca. Intl. J. Vet. Med. 2025;3(1)44-53: https://doi.org/10.59675/V316

Table (4) Length and width of wounds of group (C) in 3rd, 7th and 14th days.

Treatment	Wound dimensions	Day	Measurements Mean ± SE (unit mm)	Tukey pairwise	P value
Control (Group C)	Length	3 days	22.57 ± 0.09	A	0.025
Control (Group C)	Length	7 days	21.54 ± 0.06	B	
Control (Group C)	Length	14 days	19.76 ± 0.08	C	
Control (Group C)	Width	3 days	21.73 ± 0.15	A	0.017
Control (Group C)	Width	7 days	21.47 ± 0.15	B	
Control (Group C)	Width	14 days	19.45 ± 0.19	C	

Discussion

Wound healing is a complicated and dynamic biological process initiated in response to the disruption of the epithelial barrier caused by physical, chemical or biological factors [22] [23].

This study set out to examine the effects of antibiotics and postbiotics on rabbits' ability to heal full-thickness cutaneous wounds and good re-epithelialization. The results showed that, while the effects of each group were not identical, the treated groups showed a marked improvement in wound healing compared to the control group, with a marked decrease in incidence and an increase in epithelization. Based on the clinical observations and gross measurements of the wounds in this study, it appears that inflammation in progress quickly in individually the control and treatment groups. However, the postbiotic group (group B) in the treated group progressed more rapidly than the control group due to the pronounced action of the cicalfate+ cream that containing C+ restore, zinc sulfate, and thermal spring water. This finding extends to the previous research [24]. Who observed that zinc plays a role in wound healing as an activator and cofactor for many metalloenzymes that are involved in cell proliferation, growth and membrane repair, I also agreed with [25] their work established the significance of zinc levels in patients' wound healing processes. Also [26] suggested the zinc in topical treatment for Auto debridement, anti-infective action, and epithelialization were all found to be benefits of topical zinc treatment. In contrast, they found that zinc oxide in paste bandages reduced inflammation around ulcers and helped to keep them from spreading.

Through encouraging re-epithelialization and fiber re-deposition in the dermis, [27] found that apigenin cream which is a postbiotic cream, significantly improved wound healing on the 4th and 7th days compared to the other groups. But [28] in wild rabbits given an oral postbiotic, researchers found no discernible change in any of these bodily processes, serological reactions, or other metrics; nevertheless, they did find some intriguing alterations and modulation of the immunological response.

Consistent with previous research showing significant differences in wound healing when using thermal water, the present study demonstrated that group B exhibited significantly more re-epithelialization and the fibrous zone were more effective than other groups. This was attributed to the constituents of [29] who observed that was statistically significant wound healing differences used thermal water which had an effective role in wound healing.

Based on the morphological aspect of the wounds in all groups, there was no inflammation. In group A, there was hyperemia, in group B, it was nearly normal skin with hyperemia, and in group C, the wounds were wide and pale without end closure. As a result of this study and the results of the previous one [30] it was assumed that a combination of penicillin or ampicillin and curcumin may have a racing action without inflammatory reactions. In addition, I concur with [31] who claimed that applying an apigenin cream topically reduced changes to the stratum corneum and the skin's surface.

The clinical follow-up demonstrated that both the treatment and control groups' wounds shrank quickly throughout the trial. However, the clinical examination found that the treated groups, and the postbiotic group in particular, had a substantially higher percentage of wound contracture (closure) than the control group did throughout the observation period, and these differences persisted until day 14 after treatment. These results were in line with those of [32], which also showed that the postbiotic strain considerably reduced the skin wound size. It also belongs to the [33] that studied the effects of omega-3 on the healing of oral mucosal wounds in albino rats.

Conclusions

Cicalfate+ cream can be used for speeding up and improvement of cutaneous wounds healing more than antibiotics in rabbits. The healing in the treated groups appeared to be effective more than control group.

References

1. Liebschner MA. Biomechanical considerations of animal models used in tissue engineering of bone. Biomaterials. 2004;25:1697–714.
2. Bõsze Zs, Houdebine LM. Application of rabbits in biomedical research: a review. World Rabbit Sci. 2006;14:1–14.
3. Pearce AI, Richards RG, Milz S, Schneider E, Pearce SG. Animal models for implant biomaterial research in bone: A review. Eur Cell Mater. 2007;13:1–10.
4. Mapara M, Thomas BS, Bhat KM. Rabbit as an animal model for experimental research. Dent Res J. 2012;9.(1)
5. Weledji EP. Perspectives on wound healing. Austin J Surg. 2017;4(3):1104.
6. Tonnesen MG, Feng X, Clark RA. Angiogenesis in wound healing. J Invest Dermatol Symp Proc. 2000;5(1):40–6.
7. Clark RA. Fibrin and wound healing. Ann N Y Acad Sci. 2001;936:355–67.
8. Zimmermann A, Truss F. The effect of antibiotic drugs on wound-healing. Urol Res. 1974;2:73–7.
9. Díaz Cano JV, Argente MJ, García ML. Effect of postbiotic based on lactic acid bacteria on semen quality and health of male rabbits. Animals. 2021;11(4):1007.
10. Aguilar-Toalá JE, Garcia-Varela R, Garcia HS, Mata-Haro V, González-Córdova AF, Vallejo-Cordoba B, et al. Postbiotics: An evolving term within the functional foods field. Trends Food Sci Technol. 2018;75:105–14.
11. García-Vicente EJ, Rey-Casero I, Martín M, Pérez A, Benito-Murcia M, Risco D. Oral supplementation with postbiotics modulates the immune response produced by myxomatosis vaccination in wild rabbits. Vaccine. 2024;42:125978.
12. Avene. Cicalfate Sell Sheet Cream Scar Gel Hand Lips [Internet]. Available from: https://www.avene.com/media/marketing/assets/Cicalfate_Sell_Sheet_Cream_Scar_Gel_Hand_Lips.pdf
13. Kong HH, Segre JA. Skin microbiome: looking back to move forward. J Invest Dermatol. 2012;132(3 Pt 2):933–9.

14. Lai Y, Di Nardo A, Nakatsuji T, et al. Commensal bacteria regulate toll-like receptor 3-dependent inflammation after skin injury. Nat Med. 2009;15(12):1377–82.
15. Gallo RL, Nakatsuji T. Microbial symbiosis with the innate immune defense system of the skin. J Invest Dermatol. 2011;131(10):1974–80.
16. Shimizu K, Ogura H, Asahara T, et al. Gut microbiota and environment in patients with major burns—a preliminary report. Burns. 2015;41(3):e28–33.
17. Grice EA, Kong HH, Conlan S, et al. Topographical and temporal diversity of the human skin microbiome. Science. 2009;324(5931):1190–2.
18. Malic S, Hill KE, Playle R, Thomas DW, Williams DW. In vitro interaction of chronic wound bacteria in biofilms. J Wound Care. 2011;20(12):569–77.
19. Thomson CH. Biofilms: do they affect wound healing? Int Wound J. 2011;8(1):63–7.
20. Albozachri JMK, Hameed FM, Al-Tomah HM, Muhammid HA. Evaluation of two general anesthetic regimes using xylazine and ketamine with atropine and diazepam in rabbits. J Univ Kerbala. 2017;15:21–30.
21. Pujadas R, Escriva E, Jane J, Fernandez F, Fava P, Garau J. Comparative capacity of orally administered amoxicillin and parenterally administered penicillin-streptomycin to protect rabbits against experimentally induced streptococcal endocarditis. Antimicrob Agents Chemother. 1986;29(5):909–12.
22. Tonnesen MG, Feng X, Clark RA. Angiogenesis in wound healing. J Invest Dermatol Symp Proc. 2000;5(1):40–6.
23. Clark RA. Fibrin and wound healing. Ann N Y Acad Sci. 2001;936:355–67.
24. Lin PH, Sermersheim M, Li H, Lee PHU, Steinberg SM, Ma J. Zinc in wound healing modulation. Nutrients. 2018;10(1):16.
25. Henzel JH, DeWeese MS, Lichti EL. Zinc concentrations within healing wounds: significance of postoperative zincuria on availability and requirements during tissue repair. Arch Surg. 1970;100:349–57.
26. Lansdown IBG, Mirastschijski U, Stubbs N, Scanlon E, Agren MS. Zinc in wound healing: theoretical, experimental, and clinical aspects. Wound Repair Regen. 2007;15:2–16.
27. Rajab AM, Al-Wattar WT, Taqa GA. The roles of apigenin cream on wound healing in rabbit models. J Appl Vet Sci. 2022;7(1):1–5.
28. García-Vicente EJ, Rey-Casero I, Martín M, Pérez A, Benito-Murcia M, Risco D. Oral supplementation with postbiotics modulates the immune response produced by myxomatosis vaccination in wild rabbits. Vaccine. 2024;42:125978.
29. Ersoz M, Koc A, Ulutas PA, Serefoglu F. [Title missing]. J Biol Life Sci. 2017;8(2). [Please provide full title].
30. Sukandar EY, Kurniati NF, Anggadiredja K, Kamil A. In vitro antibacterial activity of Kaempferia pandurata Roxb. and Curcuma xanthorrhiza Roxb. extracts in combination with certain antibiotics against MSSA and MRSA. Int J Pharm Sci. 2016;8:108–11.
31. Man MQ, Hupe M, Sun R, Man G, Mauro TM, Elias PM. Topical apigenin alleviates cutaneous inflammation in murine models. Evid Based Complement Alternat Med. 2012;2012:912028.
32. Nam Y, Kim J, Baek J, Kim W. Improvement of cutaneous wound healing via topical application of heat-killed Lactococcus chungangensis CAU 1447 on diabetic mice. Nutrients. 2021;13:2666.
33. Soha B, Sahar ME, Mervet M. Assessment of the topical and systemic effects of omega-3 on oral mucosal wound healing in albino rats: a histopathological and biochemical study. Madridge J Case Rep Stud. 2018;2(1):26–31.