Kerbala Journal of Veterinary Medical Sciences Issue (2), Volume (2), (2026)

Evaluation of the combined effect of aloe vera extract and platelets on full-thickness skin wound healing in rabbit

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Received:25/4/2026 **Accepted:** 14/5/2026 **Published:** 15/6/2026

Abstract*—**Wound healing is a complex process involving tissue remodeling, cellular proliferation, and inflammatory responses of their antioxidant, anti-inflammatory and collagen-supporting qualities, *Aloe vera* and PRP are widely recognized for their ability to heal wounds. Aims to evaluate the synergistic effect of efficacy of combined *Aloe vera* extract and PRP in healing full-thickness skin wounds in a rabbit model over through microscopic assessment of skin wounds,of skin wounds, including evaluation of wound characteristics and related histopathological indicator and histological indicator analysis using Hematoxylin and Eosin (H&E). Methods Forty male rabbits were split into two groups: the control group received (untreated), while the treatment group received (*Aloe vera* + PRP). Full -thickness incision were created on the dorsum of each rabbit had full-thickness incisions made on its dorsum, and treatments were given every day for three, seven, fourteen, and twenty-one days. Results: When compared to the control group, the combination therapy group had the most wound closure and reduction in the wound area. The histopathological examination revealed accelerated re-epithelization with increased collagen deposition and denser granulation tissue combined therapy group's histological examination revealed increased collagen deposition, thick granulation tissue, and almost total re-epithelialization. The entire surface of the wound is covered in a continuous layer of epidermis, signifying complete re-epithelialization of the separate layers. The dermis beneath the epidermis appeared to be securely bonded. The dermal structure becomes more ordered, and connective tissue resembles the dermis of healthy skin. ***Conclusion: These findings suggest that PRP and AloeVera work in concert to improve tissue repair and speed up the healing of wounds. The combo treatment might be a more effective therapeutic approach for wound care.

***Keywords*:** Platelet-rich plasma, *Aloe vera*, Wound healing, Histopathology, Rabbits

INTRODUCTION

The skin, which covers the outside of the body, carries out a number of vital functions, including protecting the body, sensing stimulation, and controlling body temperature. The dermis, subcutaneous tissues, and epidermis are its three main layers. It is the Largest organ o in the animal (1,2). The epidermis, or outer layer of animal skin, is separated into five layers from the inside to the outside based on morphological traits and the degree of keratinocyte differentiation: basal layer, the spinous layer, granular layer, a transparent layer, and stratum corneum (3,4). The stratum corneum serves as the main skin barrier for some of them. Fibroblasts, collagen, and elastin make up the majority of the dermis, which is located beneath the epidermis. (5,6).In order to protect the body from environmental dangers such as UV radiation, pathogenic agents, and dehydration, the skin is crucial (7, 8)

However, its integrity is also jeopardized by the ongoing exposure to such risks. For higher living things to survive and thrive, wound healing and skin regeneration (9,10). Skin metabolic processes PRP, is essential for hemostasis, tissue regeneration, and host defense in wound healing. The equilibrium of the metabolism is necessary to maintain skin homeostasis. One of an animal's main organs for metabolism is the skin. Platelet-rich plasma and its derivatives are used therapeutically to improve wound healing based on these conditions. The biological processes behind the most

conventional and cutting-edge uses of PRP in wound healing are explained in this article (11,12) .

Aloe vera, a member of the Liliaceae family, is a significant and well-known medicinal plant. Due to its many uses as a medicinal plant, particularly in arid regions, *aloe vera*, also known as Indian aloe, Kunvar pathu, and Ghrit Kumari, is widely grown. It is native to Mediterranean and African nations (13, 14). *Aloe vera*, comes in roughly 150 species. Aloe vera is the only plant in this genus with a lengthy and distinguished medical history. The Arabic word "alloeh," which means "bitter," is thought to have inspired the name of *Aloe vera*, because the leaves contain a bitter liquid. The synthetic substances currently utilized in the cosmetics industry can be successfully replaced by aloe vera.(15). *Aloe vera's* antibacterial, antioxidant, and anti-inflammatory properties work together to speed up wound healing. Aloe vera has long been prized for its ability to heal skin damaged by UV and gamma rays. Many different civilizations have been using *aloe vera*, for thousands of years. However, it has recently been shown to provide therapeutic support for healing (16). Aloe vera can be applied topically for the treatment of burns, psoriasis, dermatitis, eczema, and acne. The body's natural healing processes are accelerated by this cell Tissue regeneration . Aloe vera's therapeutic properties make it unique and beneficial in healthcare (17,18). By measuring epithelialization, angiogenesis, and inflammatory response, this study attempts to assess the histological effects of *Aloe vera*, and platelet-rich plasma (PRP) on skin wound healing. Additionally, their efficacy in promoting tissue regeneration, improving overall health, and accelerating skin repair will be evaluated in comparison to untreated controls

MATERIALS AND MTHODS

Ethical Approval

The University of Karbala College of Veterinary Medicine's Research Ethics Committee (ethics number UOK.VET.AN 2025.147) accepted the experimental design and techniques used in this work in compliance with animal welfare ethics

Experimental design

Rabbits This study included forty adult male rabbits weighing between 1100 and 1800 grams. They were given water and green feed and housed in separate cages with a daily light cycle of 12:12. The animals were kept in separate cages for acclimatization. each stage that comes before the surgery. conducted in this study were approved by the scientific committee. anesthesia was induced by intramuscular injection of a mixture containing 20% xylazine (5 mg/kg b.w.) and 80% ketamine (40 mg/kg b.w.) (19). College of Veterinary Medicine. September through December of 2025 at the University of Kerbala. At random, the rabbits were divided into two equal categories. Group A (control group)(n = 20) did not receive treatment for the dorsal injury. Group B (the treatment group) received platelet-rich plasma and aloevera extract (n = 20). Skin samples were collected at four time points: 3, 7, 14, and 21 days post-surgery for histological examination .Hematoxylin and Eosin stains were used in the histological investigation for cellular details (20).

Preparation of aloevera alcoholic extract:

Aloevera plant complete leaves were cleaned with distilled water, then chopped into small pieces, shade-dried for seven days, and then thoroughly ground into a powder. (21)

The powdered leaves were placed into the Soxhlet thimble, which was then closed and placed within the Soxhlet main chamber. The Soxhlet equipment was heated until the solvent vapour filled the main chamber after one litre of 100% ethanol was added. After that, the solvent vapour condensed and trickled back into the chamber holding the extract of aloe vera leaves. (*22*). where the extraction process lasted for a full day. After then, the ethanolic extract was given time to filter. However, a residue was produced in the water bath (Labtech, Korea) For later usage, the final residue was put in airtight containers and kept in a refrigerator.(23)

preparation of platelet rich plasma:

A 9-ml sample of blood was drawn from the rabbits in the PRP group via heart penetration in order to prepare the platelet-rich plasma. (24).and use falcon tubes filled with 10% sodium citrate (25).For the separation of the cells into layers, the collected blood was centrifuged for seven minutes at 2700 rpm Red blood cells, platelet rich plasma (PRP), and platelet deficient plasma (PPP) are the three primary elements of the blood that are separated by this process. Using a spinal needle connected to a syringe, the section containing platelets and mononuclear cells was carefully extracted and re-suspended with the remaining plasma. After PRP and plasma were mixed, the final solution was put in a sterile tubes. Then centrifuged for 15 minutes at 3600 rpm to better extract the platelets from the PPP supernatant layer. PPP was at the top of the container was while platelets were gathered at the bottom. Only the PRP was left when the PPP was eliminated. A syringe was used to draw up the finished PRP. (26)

STATISTICAL ANALYSIS

Graph Pad Prism (Version 7.04, Graph Pad Software Inc., San Diego, CA) was used to statistically analyse the data using two-ways ANOVA. the results were expressed as (Mean± SE). The statistical significance level was ($P < 0.001$). (24)

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RESULT AND DISCUSSION

Macroscopic result

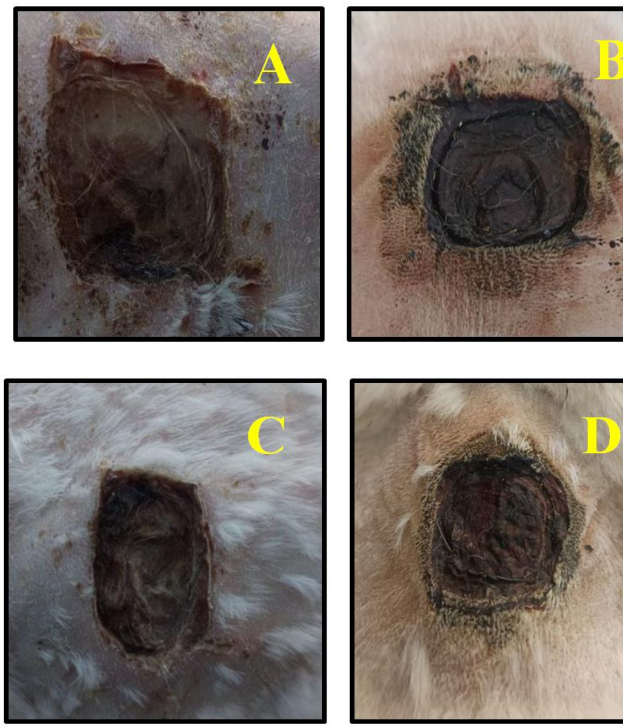

Figure 1. Macroscopic result A. Control macroscopic view in Day3, B. Treatment macroscopic view in Day3 , C. Control macroscopic view in Day7, D. Treatment macroscopic view in Day7

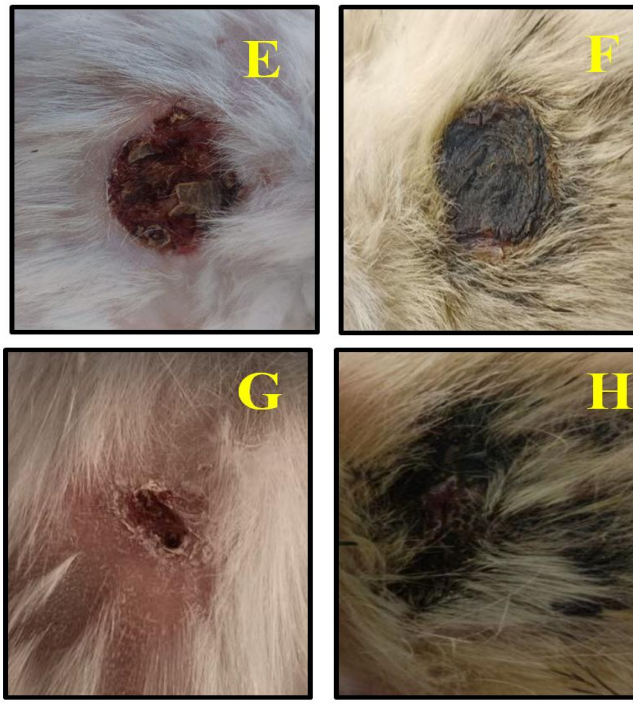

Figure 2. Macroscopic result E. Control macroscopic view in Day14, F. Treatment macroscopic view in Day14, G. Control macroscopic view in Day21, H. Treatment macroscopic view in Day21

Histological Examination

Control Group: Histological examination of skin injury sites in the 3-day control group showed that the keratinocytes have migrated from the injury's edges, the outer layer of the wound is not yet entirely covered in cells (Figure, 3). These results correspond with the findings of (27) Histological examination of control group at 3 days post injury showed initial keratinocytes from wound margins to ward the center. However ,reepithelization remain incomplete.At 7 days ,the control group showed that thinner and more uneven than typical skin. In certain places, it lacks complete differentiation at the edges of wounds, Incomplete epidermal differentiation of cells continues to be visible (Figure, 4). 14day control group show that the damaged epidermis active basal cell proliferation intact. In certain places, there was slightly thinner or more substantial skin than usual, The keratin layer could be uneven (Figure, 5). 21day control group show Epidermis that has fully Keratinization The thickness of the epidermis is Similar to the typical surrounding skin A slight deviation might continue (Figure, 6). According to (28) histopathology, the non-treated group showed a typical crust on the skin's typical surface following of treatment. In certain areas, the skin had lost its epidermal layer, and in other areas, a promoting epidermal palate had grown over the granulation forming tissues.

Treatment Group: The current study's three-day results indicate a slight improvement in the epidermis layer when compared to the untreated group, with edema between dermal collagen fibers (Figure7,8). In contrast, the current study demonstrates that after seven days, the wound is usually in the proliferative phase of healing, and the epidermis is experiencing active regeneration, partial to nearly complete re-epithelialization, and increased epidermal thickness as a result of basal keratinocyte proliferation (Figure 9,10). After 14 days, the wound surface is completely covered by a continuous layer of epidermis, indicating complete re-epithelialization. To seal the wound, keratinocytes have moved and multiplied (Figure 11,12). 21 days, the wound surface is completely covered by a continuous layer of epidermis, demonstrating the well-defined layers' full re-epithelialization. The epidermis and underlying dermis seemed to be firmly attached. Connective tissue resembles the dermis of normal skin, and the dermal structure becomes more ordered (Figure 13,14). These findings are consistent with (29), who reported that the mixed-treated group's epidermal thickness was noticeably greater compared to that of each of the other medicated groups. The placement and thickness of the epidermal layers, as well as the stratum corneum thickness of the compositely treated wounds, resembled normal skin layers.

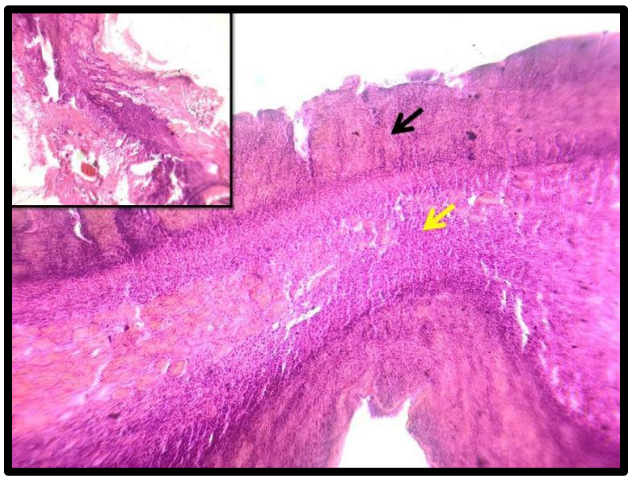

Figure 3. Histological section of skin in rabbit (control 3 day) revealed that the keratinocytes have migrated from the injury's edges, the outer layer of the wound is not yet entirely covered in cells (black arrow). The dermis layer highly intercellular edema with granulation tissue formation (yellow arrow). 100X. H&E stain.

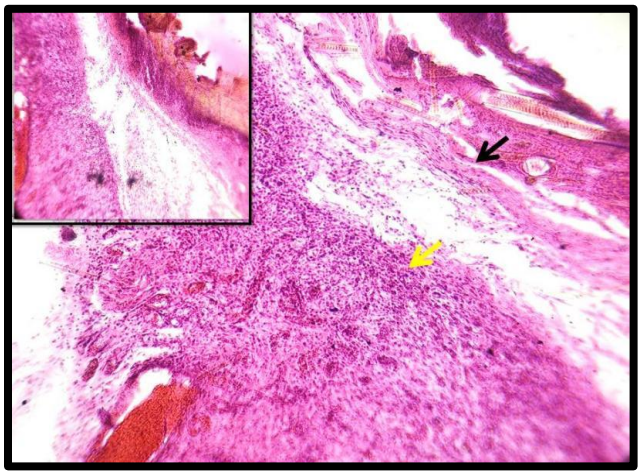

Figure 4. Histological section of skin in rabbit (control 7 day) revealed that the thinner and more uneven than typical skin. In certain places, it lacks complete differentiation at the edges of wounds, basal proliferation of cells continues to be visible (black arrow). The majority of the surface of the wound is made up of granulation tissue, and the dermal framework is still chaotic. reduced invasion of inflammatory cells (yellow arrow). 100X. H&E stain.

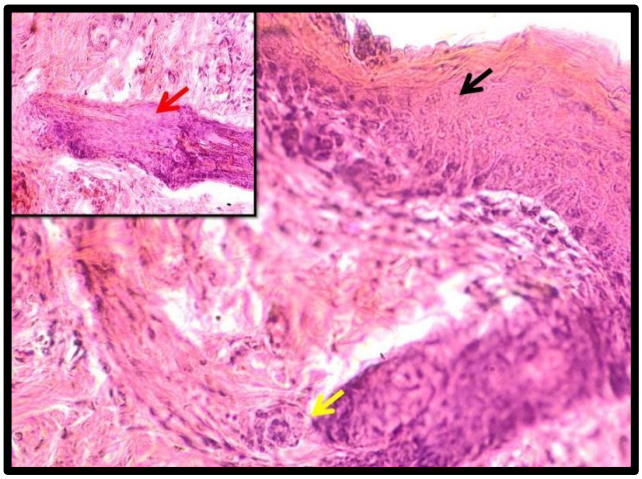

Figure 5. Histological section of skin in rabbit (control 14 day) revealed that the damaged epidermis seems intact (black arrow). In certain places, there was slightly thinner or more substantial skin than usual The keratin layer could be uneven or immature. Granulation tissue has been primarily substituted by newly created connective tissue (yellow arrow), and epidermal separation improved but not entirely restored. 100X. H&E stain.

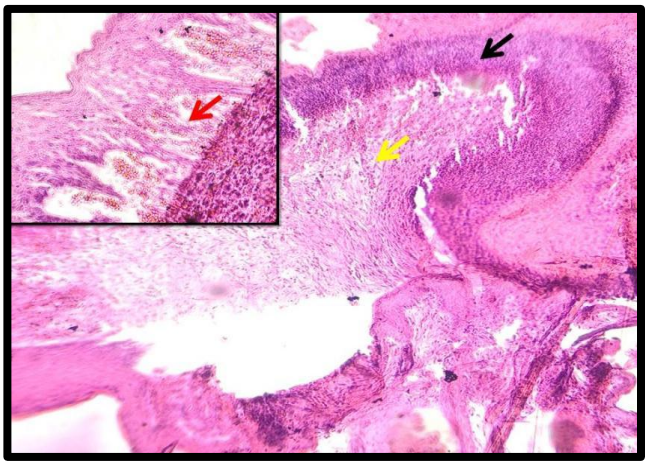

Figure 6. Histological section of skin in rabbit (control 21day)Epidermis that has fully regenerated its epithelium The thickness of the epidermis is Similar to the typical surrounding skin A slight deviation might continue. Epidermal layer stratification that is clearly defined substantial neovascularizationreduction.400x.H&

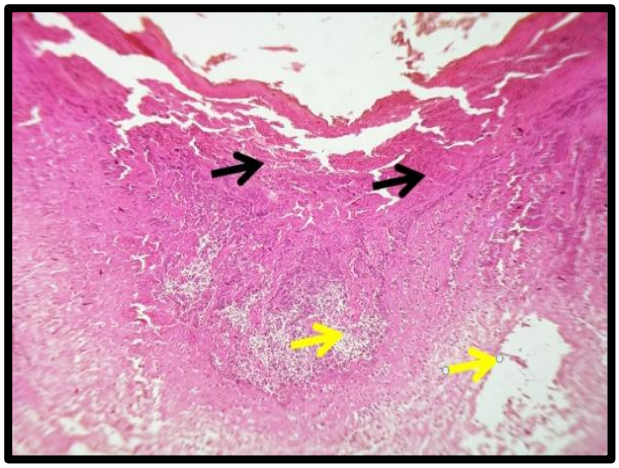

Figure7. Histological section of skin in rabbits (treat 3 day) showing the epidermis layer slightly enhancement compared with untreated group (black arrow) with presence of edema between dermal collagen fibers (yellow arrow). 100X. H&E stain.

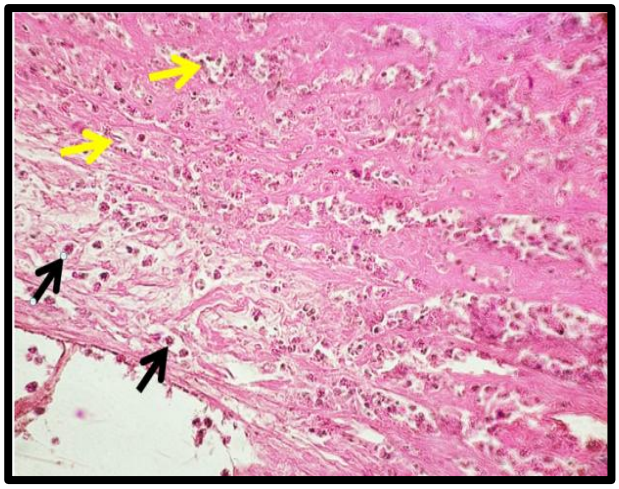

Figure8. Histological section of skin in rabbits (treat 3 day) showing the slight reduction in inflammatory cell infiltration compared with untreated (black arrows). Early fibroblast activation begins around the wound margins. (yellow arrow). 400X. H&E stain.

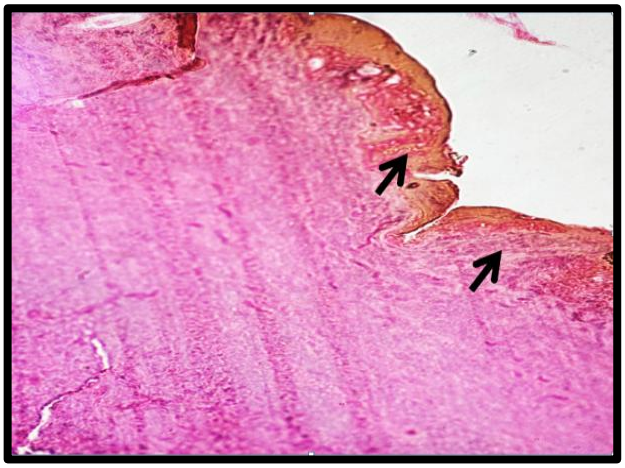

Figure9. Histological section of skin in rabbits (treat 7 day) showing the wound is typically in the proliferative of healing, and the epidermis, active regeneration, partial to nearly complete re-epithelialization, Increased thickness of the epidermis due to rapid proliferation of basal keratinocytes (Black arrows). H&E stain.40x.

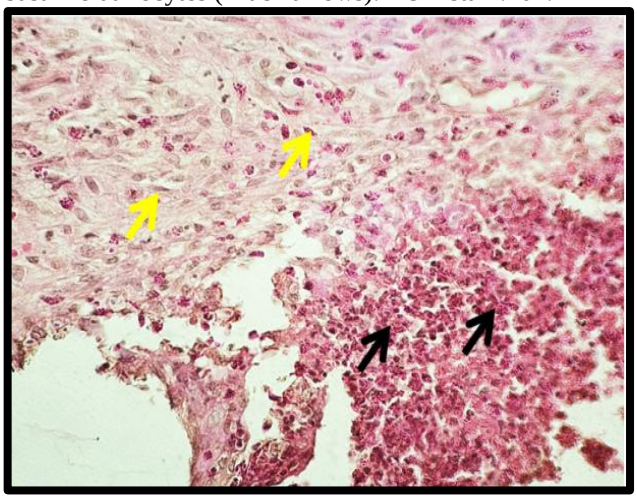

Figure10. Histological section of skin in rabbits (treat 7 day) showing the active granulation tissue formation, This tissue consists of fibroblasts, newly formed blood vessels, and inflammatory cells (black arrows). Fibroblast proliferation, Large numbers of activated fibroblasts are present within the dermis (yellow arrows). H&E stain. 40X.

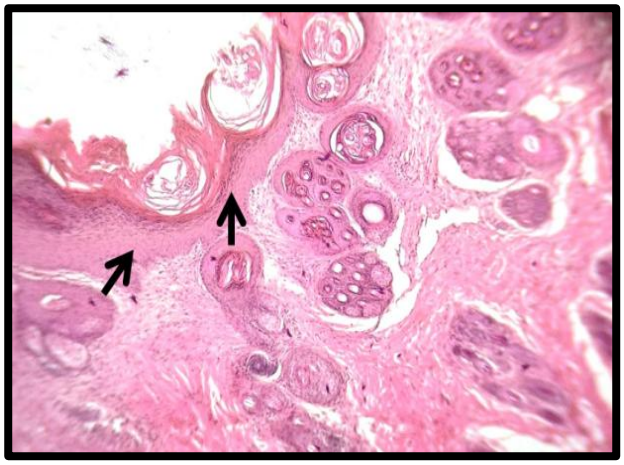

Figure11. Histological section of skin in rabbits (treat 14 day) showing the complete re epithelialization the wound surface is fully covered by a continuous epidermal layer. Keratinocytes have migrated and proliferated to close the wound. Hyperkeratosis with hair follicle formation H&E stain. 40X.

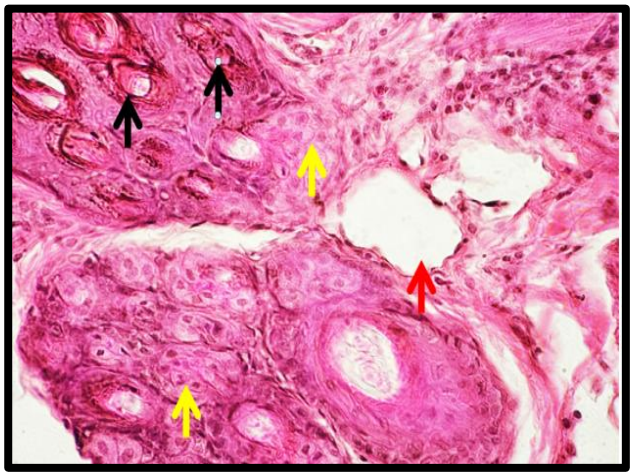

Figure12. Histological section of skin in rabbits (treat 14 day) showing the hair follicles, early regeneration of hair follicles may be observed near the wound margins. Hair follicles appear as invaginations of the epidermis extending into the dermis (black arrows). Sebaceous glands are seen associated with hair follicles (yellow arrows). sweat glands may appear intact or gradually re-establishing normal structure (red arrow). H&E stain. 40X.

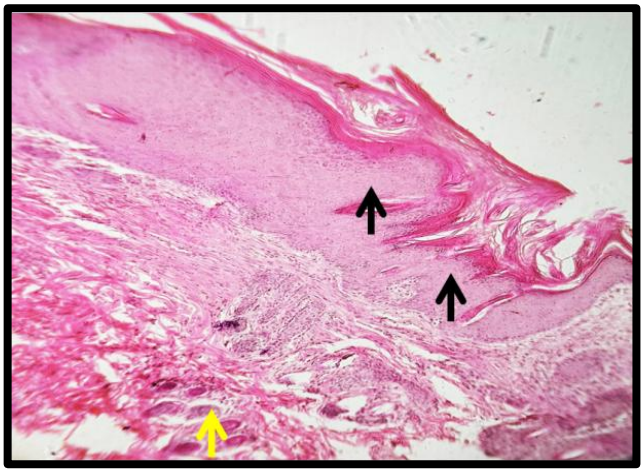

Figure13. Histological section of skin in rabbits (treat 21 day) showing the well-defined layers complete re-epithelialization, the wound surface is fully covered by a continuous epidermal layer. The epidermis appeared well attached to the underlying dermis (black arrows). The dermal structure becomes more organized, and connective tissue resembles normal skin dermis (yellow arrow). H&E stain. 40X.

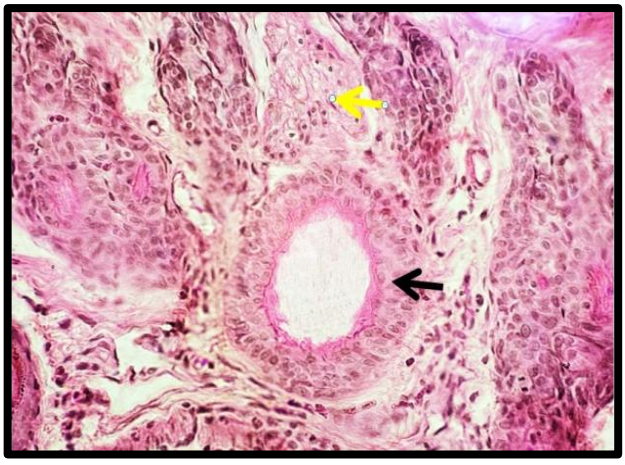

Figure14. Histological section of skin in rabbits (treat 21 day) showing the Hair follicles appear regenerated or well preserved within the dermis (black arrow). Sebaceous glands are present and associated with hair follicles, follicles may be more numerous and structurally organized, indicating improved tissue regeneration (yellow arrows).H&E stain.

CONCLUSION

The combined application of Aloe vera extract and PRP significantly accelerated full-thickness wound healing in rabbits, as evidenced by enhanced re-epithelialization, increased collagen deposition, and organized dermal structure compared to untreated controls. These results support the therapeutic potential of this combination for wound management. Further studies with larger sample sizes, quantitative measurements, and evaluation in other animal models are recommended.

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