Academic International Journal of Veterinary Medicine
ISSN: 2984-7753
Aca. Intl. J. Vet. Med. 2025;3(2)01-08
Journal homepage: www.aipublishers.org/aijvm

Effect of Aqueous Extract Iraqi Aloe vera on Treatment of Skin Wounds in Rabbits

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(Received 25 April 2025, Revised 8 May 2025, Accepted 25 July 2025, Published 26 August 2025)

Abstract

The objective of this study was to assess how aloe vera extract affected the rabbits' full-thickness skin wounds' histological recovery. A total of sixteen healthy adult male rabbits weighing 1.25 to 2 kg were employed. Each rabbit's back was incised with a 4 cm² full-thickness incision. Animals were divided into two groups: Group A (control) received no treatment, while Group B (treated) had Aloe vera extract applied topically to the wounds. Skin biopsy samples were collected from two rabbits in each group on days 3, 10, 14, and 21 post-surgery for histopathological analysis. There were no discernible variations in the two groups' wound healing rates, according to the clinical evaluation. However, histological analysis revealed notable distinctions. On day 3, Group A exhibited a prominent polymorphonuclear (PMN) cell demarcation line and thickened epidermis with inflammatory cell infiltration around the wound margins. Group B, however, had re-epithelialization early on, granulation tissue formation, and minimal inflammation. On day 10, Group A featured marked dermal inflammation, thickened epidermis, wide granulation tissue, and hemostatic signs. Group B featured wider granulation tissue and collagen fiber proliferation with narrower inflammation. On day 14, Group A featured wide re-epithelialization, keratinocyte proliferation, and fibrosis. Group B also featured wide collagen fiber proliferation, indicating advanced healing. Group A had excessive fibrosis (scar tissue) and chronic granulation tissue by day 21. Group B still had organized epidermal fibrosis, more dermal neovascularization (new blood vessel formation), and new hair follicle formation, which indicated superior tissue regeneration.

Keywords:

Aloe vera, Skin wounds, Aqueous extract

How to cite:
Amaal M. Khudaier, Jassim M. Khalaf Albozachri, Inam Badr Falih. Effect of Aqueous Extract Iraqi Aloe vera on Treatment of Skin Wounds in Rabbits. *Aca. Intl. J. Vet. Med. 2025;3(2)01-08:* https://doi.org/10.59675/V321

Introduction

Over the last few decades, Aloe vera (Aloe barbadensis Miller) has been rapidly attracting scientific attention as a biomedical, therapeutic, and pharmacological compound. A Liliaceae family member with over 360 documented species, A. vera is a succulent crop living in an arid environment and is presently being commercially grown to meet world demand [1]. Among all its various species, A. barbadensis Miller is most medicinally and commercially utilized in North America, Europe, and Asia [2].

A. vera has been used conventionally to treat many conditions, such as inflammatory disorders, burns, ulcers, and acne. Bioactive molecules like vitamins C and E, essential amino acids, polysaccharides, and enzymes have been isolated from their inner gel and are the basis of its anti-inflammatory, antibacterial, and antioxidant properties [1, 3]. The bioactive molecules enhance epithelial healing, collagen production, and oxidative stress attenuation and render the plant an effective choice for wound care products [4].

Hemostasis, inflammation, proliferation, and remodeling of tissue comprise the intricate, multi-phased biological process of healing of a wound. Cellular and molecular cues regulate these phases sequentially [5]. The extent and type of tissue damage, infection, and injured tissue's biological potential decide to a large extent the ultimate outcome of healing [6]. There is an overwhelming number of experimental and clinical studies that have quantified the role of A. In wound healing in humans, results have been contradictory. While some work describes improved healing, accelerated re-epithelialization, and improved fibroblast function [7, 4], others detect no significant benefit over conventional management [8].

Given these variations, further studies are needed to determine the efficacy of A. vera in wound healing, especially when derived from different locations. The purpose of this study is to identify the histopathological effect of locally produced aqueous extract of Iraqi aloe vera on rabbits' ability to close full-thickness skin wounds. This study examines A. vera as a potential new addition to clinical wound therapy and adds to the literature in herbal therapies.

Materials and Methods

Ethical Approval

This study was approved by the Research Ethics Committee of the College of Veterinary Medicine, University of Kerbala (Ethics Approval No. 1305 P.G., issued January 18, 2024). All experimental procedures were conducted in compliance with institutional guidelines and animal welfare regulations.

Experimental Animals

Sixteen adult male rabbits weighing 1.25 to 2.0 kg and in good clinical health were acquired from the University of Kerbala's College of Veterinary Medicine's animal farm. The animals were kept separately in typical lab cages with regulated surroundings, fed a commercial pellet diet, and given unlimited access to water. Before anesthesia, food was denied for 6–12 hours and drink for 5 hours.

Animals were given a premedication dose of diazepam (1 mg/kg body weight, b.w.) to induce anesthesia. After abdominal shaving and aseptic preparation, ketamine (50 mg/kg b.w.) and xylazine (10 mg/kg b.w.) were given intramuscularly to induce general anesthesia 10 minutes later [9]. Using a sterile template cut from X-ray film, a single, full-thickness, square skin wound measuring 4 cm^2 was made on the back of each rabbit. Eight animals each were randomly assigned to one of two groups: group A (control), which received no therapy for their wounds, and group B (treatment), which received topical application of aloe vera extract.

Preparation of *Aloe vera* Extract

Mature leaves of *Aloe vera* were harvested and the outer rind carefully removed [10]. The inner gel was allowed to partially dry at room temperature in a shaded area to concentrate the mucilaginous content. The gel was then blended with a small volume of distilled water, followed by centrifugation to separate fibers. The supernatant was filtered through standard filter paper, and the resulting aqueous extract was stored at 4 °C until use [11]. Prior to application, the extract was equilibrated to room temperature.

Skin Tissue Biopsy and Histological Analysis

On days 3, 10, 14, and 21 following injury, two animals per group had full-thickness skin tissue samples taken. The biopsy samples were dried, embedded in paraffin, and preserved in 10% neutral buffered formalin. For histological assessment, sections 5 µm thick were cut with a microtome, stained with hematoxylin and eosin (H&E), and seen under a light microscope [12].

Result and Discussion

During the postoperative phase, no animals showed any clinical indications of infection. The use of aseptic surgical procedures was validated by microscopic inspection. Numerous cell types, including fibroblasts, endothelial cells, neutrophils, keratinocytes, lymphocytes, and macrophages, coordinate the intricate and dynamic process of wound healing, which includes inflammation, tissue proliferation, and remodeling [13, 14].

Day 3 Post-Wounding: By day 3, the control group (A) exhibited acute inflammatory responses characterized by extensive tissue necrosis, polymorphonuclear (PMN) cell infiltration, and epidermal thickening at the wound margins. These findings align with the initial inflammatory phase of wound healing following mechanical injury [15]. In contrast, the Aloe vera-treated group (B) showed signs of

granulation tissue formation and partial re-epithelialization, with a notably reduced presence of inflammatory cells (Fig. 1). Aloe vera is known to suppress inflammatory cytokines and oxidative stress, which may explain the attenuated inflammatory response [16, 17].

Day 10 Post-Wounding: On day 10, histological evaluation of group A revealed dense granulation tissue, marked dermal inflammation, hemostasis, and epidermal thickening. However, group B demonstrated enhanced organization of collagen fibers, milder inflammation, and more advanced granulation tissue development (Fig. 2). The improved collagen arrangement suggests better tensile strength and faster tissue remodeling, likely influenced by Aloe vera's known stimulatory effect on fibroblasts [18, 19]. Collagen alignment is essential for functional recovery, and Aloe vera may enhance this process by promoting fibroblast activity and regulating matrix metalloproteinases [20, 21].

Day 14 Post-Wounding: On day 14, both the groups showed maturation of the wound. Group A showed re-epithelialization, proliferation of keratinocytes, and moderate deposition of collagen. But in Aloe-treated group (B), increased proliferation of collagen fibers and improved dermal architecture (Fig. 3) were seen. All these findings suggest that Aloe vera increases the deposition of extracellular matrix and tensile strength of the skin [5]. The bioactive constituents of Aloe vera, such as acemannan and glucomannans, are found to increase growth factors that induce re-epithelialization and fibroplasia at increased rates [22, 19].

Day 21 Post-Wounding: The control group wounds at day 21 exhibited dense fibrosis and residual granulation tissue—characteristics of scar formation. Group B, however, revealed additional epidermal regeneration, dermal neovascularization, and neoformed hair follicles (Fig. 4). The findings reveal that Aloe vera improves not only tissue repair but also functional restoration and cosmetic appearance of the healed skin. Angiogenesis and hair follicle neogenesis are vital for the complete restoration of wound healing, and Aloe vera has been shown to enhance these processes by inducing vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) pathways [12, 6]Our findings demonstrate that Aloe vera extract enhances wound healing through accelerated epithelial migration, reduced inflammation, improved collagen organization, and enhanced angiogenesis. These results are consistent with previous studies in both veterinary and human medicine, highlighting the therapeutic value of Aloe vera for wound care [23, 24, 7].

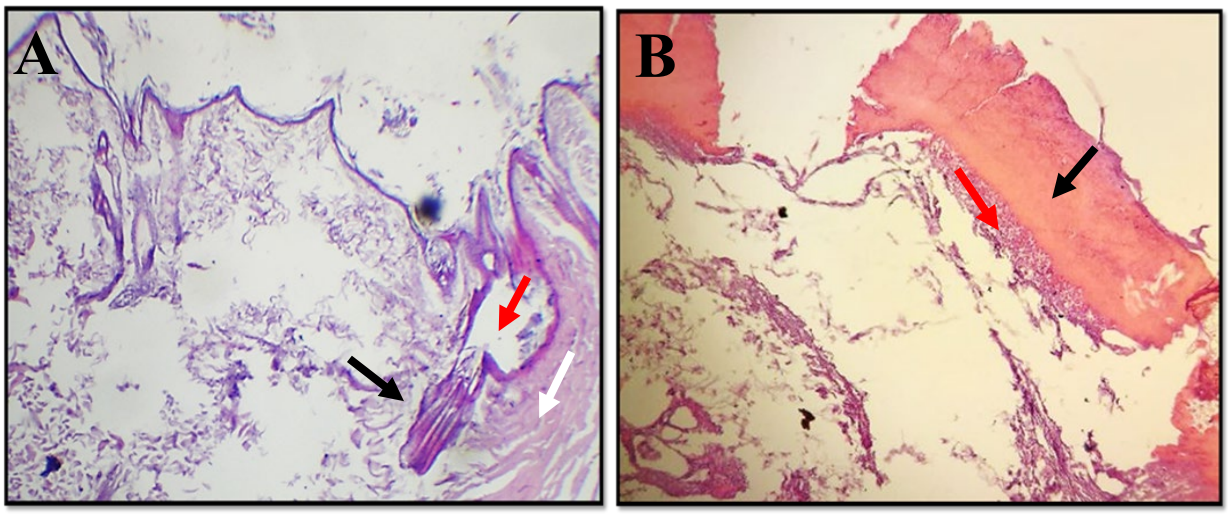

Figure (1): Histological cross section of skin show: (A) 3rd day wound healing slight thickness in epidermis (red arrow), formation of demarcation line (black arrow) and significant hemostasis (white arrow), (B) 3rd day wound healing Aloe Vera treated group animal revealed the re-epithelization (black arrow) with granulation tissue and inflammation (red arrow). (H &E stain) 10X.

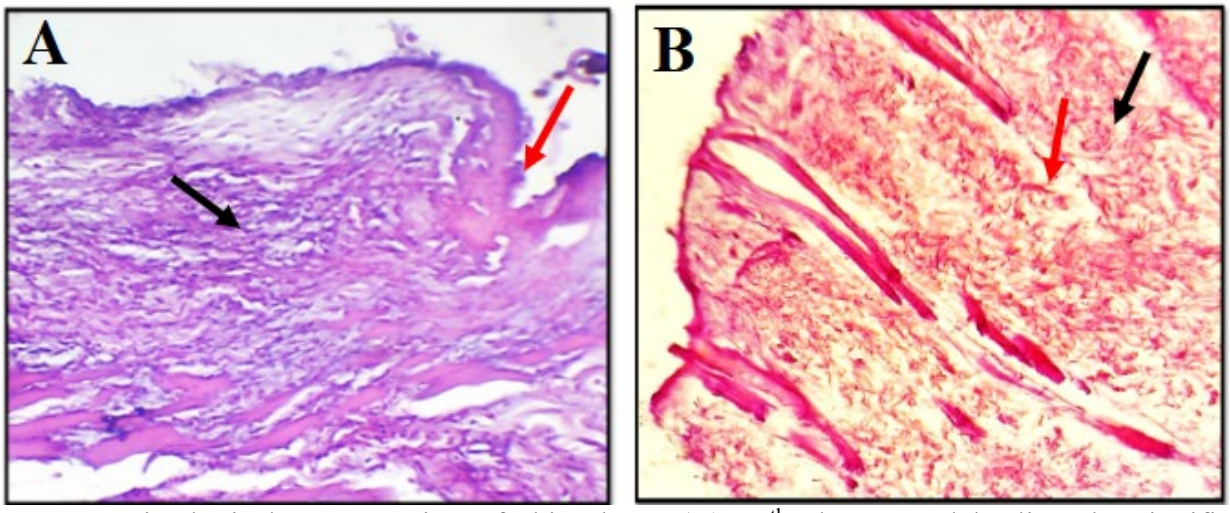

Figure (2): Histological cross section of skin show: (A) 10th day wound healing the significant hemostasis with thickness in epidermis (red arrow), sever dermal inflammation and marked granulation tissue (black arrow) (B) 10th day wound healing the severity of granulation tissue and inflammation has increased (black arrow), collagen fibers proliferation (red arrow) (H &E stain) 10X.

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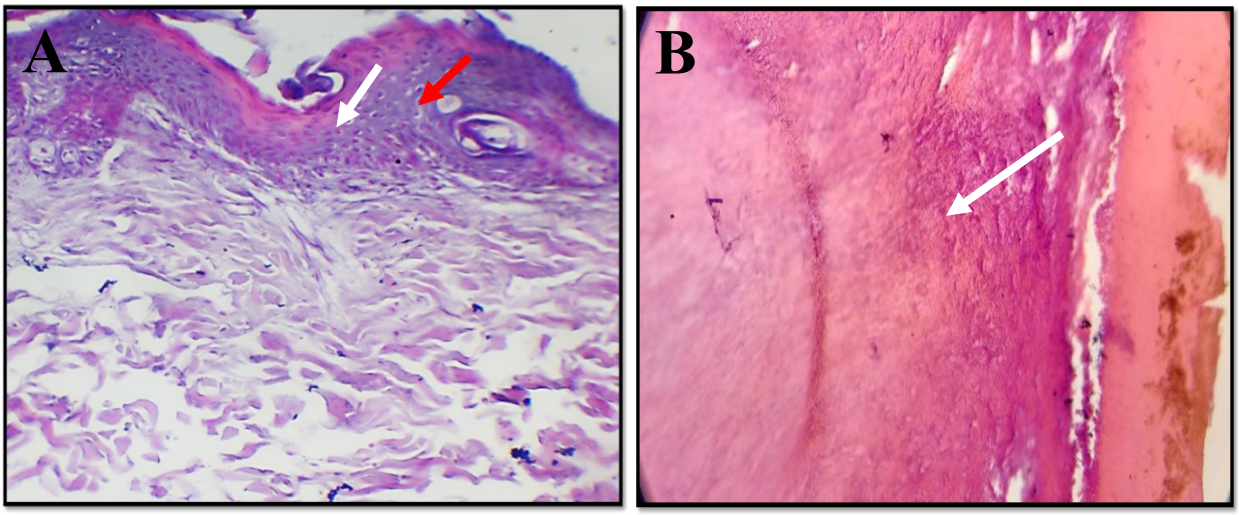

Figure (3): Histological cross section of skin show: (A) 14th day wound healing which significant re-epithelialzation in epidermis (black arrow), keratocytes proliferation (red arrow) and collagen fibers proliferation (fibrosis) (white arrow), (B) 14th day wound healing significant collagen fibers proliferation (fibrosis) (white arrow). (H &E stain) 10X.

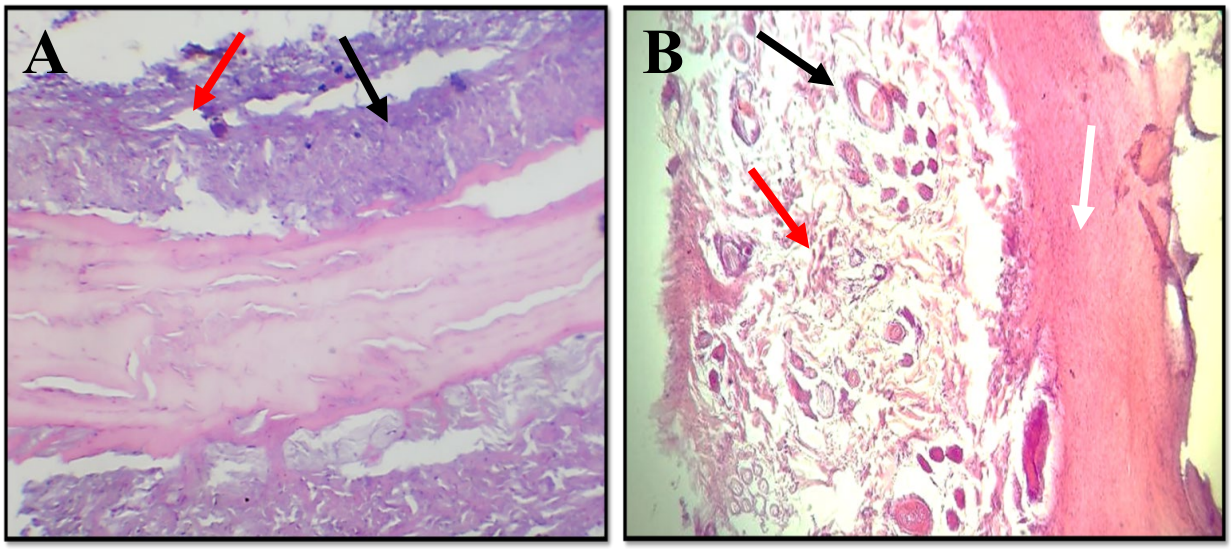

Figure (4): Histological cross section 21th day wound healing show:(A) sever fibrosis (scar tissue formation) (black arrow) with granulation tissue (red arrow), (B) marked epidermal fibrosis (white arrow) with more dermal vascular formation of newly formed blood vessels (red arrow) and more newly hair follicles (black arrow). (H &E stain) 10X

Conclusions

Topical application of *Aloe vera* extract enhanced wound healing in rabbits by reducing inflammation, promoting collagen formation, accelerating re-epithelialization, and improving vascularization and hair follicle regeneration. These effects suggest that *Aloe vera* can be a beneficial natural agent in promoting tissue repair.

Author's Contributions

Amaal M. Khudaier conceived and planned the experiments and contributed to sample preparation. Jassim M. Khalaf Albozachri has had surgery. Inam Badr Falih has analysis histopathology. Khalid A. Hadi and all authors analyzed the data and shaped the study, analysis, and manuscript.

Abbreviations

PMN: polymorphonuclear
Av: Aloe vera
H&E: hematoxylin and eosin

Conflict of Interest

No conflicts of interest are disclosed by the authors.

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