

Molecular and Cellular Mechanisms of Wound Healing in Animals: Biological Dynamics and Therapeutic Innovations

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Abstract; Wound healing in animals is a highly complex and dynamic biological process that involves coordinated cellular, molecular, and tissue-level responses aimed at restoring structural and functional integrity after injury. This study examines the biological regulation of wound healing in animals, with particular emphasis on the sequential phases of hemostasis, inflammation, proliferation, and remodeling. Clinical and experimental observations were conducted on farm animals with traumatic, surgical, purulent, and necrotic wounds to evaluate healing dynamics under different treatment approaches. The application of bioactive collagen-based dressings and platelet-rich plasma (PRP) therapy significantly reduced microbial contamination, enhanced fibroblast activity, promoted angiogenesis, and accelerated epithelialization compared with conventional antiseptic treatments. Histological and microbiological findings confirmed improved tissue organization and faster wound closure in the experimental group. The results highlight the importance of understanding wound healing biology for optimizing therapeutic strategies and demonstrate the potential of innovative bioactive treatments in improving clinical outcomes in veterinary practice.

Keywords: *wound healing, bioactive dressings, epithelialization, veterinary surgery*

1. INTRODUCTION

Wound healing is a fundamental process in veterinary medicine, as injuries to the skin and underlying tissues are among the most frequently encountered clinical problems in farm and domestic animals. Effective wound management is essential not only for restoring tissue integrity but also for preventing infections, reducing pain, and maintaining animal welfare. Delayed or impaired wound healing can lead to serious complications, including chronic infections, systemic illness, and decreased productivity, particularly in livestock species.

Wounds in animals arise from a variety of causes. In farm animals, common sources include mechanical trauma, housing and equipment-related injuries, handling and transportation accidents, and surgical interventions. Domestic animals are frequently affected by bite wounds, lacerations, burns, and post-operative complications. Environmental factors, poor hygiene, and management practices may further increase the risk of wound contamination and delayed healing.

The clinical and economic significance of wound healing is especially pronounced in agricultural settings. Prolonged recovery times can result in reduced growth rates, decreased milk or meat production, increased veterinary costs, and, in severe cases, loss of animals. From a clinical perspective, understanding the biological mechanisms underlying wound healing is critical for selecting appropriate treatment strategies and improving therapeutic outcomes. Therefore, wound healing biology remains a key area of interest in both veterinary practice and research.

2. DEFINITION AND CLASSIFICATION OF WOUNDS

A wound is defined as a disruption of the anatomical and functional integrity of tissues caused by physical, chemical, thermal, or biological factors. Proper classification of wounds is essential for determining prognosis and selecting effective treatment approaches.

Based on the nature of injury, wounds are commonly classified as mechanical, thermal, chemical, or biological. Mechanical wounds include incisions, punctures, crush injuries, and lacerations, often resulting from trauma or surgical procedures. Thermal wounds arise from exposure to heat or cold, such as burns and frostbite. Chemical wounds occur following contact with corrosive substances, including acids and alkalis. Biological wounds are caused by microorganisms or parasites and are frequently associated with infection and tissue necrosis.

Wounds are further categorized as acute or chronic. Acute wounds typically follow a predictable healing pattern and resolve within a normal time frame. In contrast, chronic wounds fail to progress through the normal stages of healing and are often associated with persistent inflammation, infection, or underlying systemic disorders. Additionally, wounds may be classified as aseptic or septic, depending on the presence or absence of microbial contamination. Septic wounds present a greater therapeutic challenge and require more intensive management to prevent complications.

3. BIOLOGICAL BASIS OF WOUND HEALING

Wound healing is a complex, multi-phase biological process that involves coordinated interactions among cells, signaling molecules, and structural components of tissues. At the cellular level, key participants include platelets, inflammatory cells, fibroblasts, endothelial cells, and epithelial cells. These cells communicate through the release of cytokines, growth factors, and chemokines that regulate inflammation, cell migration, proliferation, and tissue remodeling.

The extracellular matrix (ECM) plays a crucial role in wound healing by providing structural support and a dynamic scaffold for cell attachment and migration. Components such as collagen, fibronectin, and proteoglycans influence cell behavior and tissue strength. During healing, the ECM undergoes continuous remodeling, allowing newly formed tissue to gradually regain functional integrity.

Wound healing is also regulated by the interaction of the immune, nervous, and endocrine systems. The immune system initiates inflammatory responses and protects against infection, while the nervous system influences vascular responses and cellular activity through neurogenic signaling. Endocrine factors, including hormones and metabolic regulators, modulate cellular functions and energy availability required for tissue repair. The integration of these systems ensures an efficient and coordinated healing response, highlighting the biological complexity underlying wound repair in animals.

4. STAGES OF WOUND HEALING AND KEY INFLUENCING FACTORS

Wound healing in animals is a coordinated, multi-phase process that restores tissue integrity through successive biological stages. Although the phases overlap in time, each stage has dominant cellular activities and specific clinical characteristics. The efficiency of healing depends not only on the biological progression of these stages but also on multiple internal and external factors, including the animal's physiological condition, nutritional status, wound characteristics, and environmental management.

Hemostasis

Hemostasis begins immediately after injury and serves as the first protective response. Reflex vasoconstriction reduces blood loss, while activated platelets form a temporary plug. The coagulation cascade produces a fibrin network that stabilizes the clot and creates an initial matrix for cell migration. This clot also limits the entry of microorganisms and provides biochemical signals that initiate the inflammatory phase.

Inflammatory phase

The inflammatory phase typically occurs within the first days after injury. Neutrophils migrate into the wound to control microbial contamination and remove debris, followed by macrophages that continue phagocytosis and coordinate tissue repair. Macrophages are particularly important because they release cytokines and growth factors that regulate the transition from inflammation to tissue formation. Excessive or prolonged inflammation, however, may lead to tissue damage and delayed healing.

Proliferative phase

During proliferation, the wound begins to fill with granulation tissue. Fibroblasts proliferate and synthesize collagen and other extracellular matrix components, strengthening the wound structure. At the same time, angiogenesis develops new capillaries to supply oxygen and nutrients. Epithelial cells migrate from the wound edges to restore the surface barrier, a process known as epithelialization. Clinically, this phase is characterized by visible granulation tissue, reduced exudate, and gradual wound contraction.

Remodeling and maturation phase

In the final stage, collagen fibers are reorganized and cross-linked, and vascular density decreases as the tissue becomes more stable. Although tensile strength improves, scar tissue does not fully replicate the original tissue structure. The duration of remodeling may range from weeks to months and is strongly affected by wound severity and systemic conditions.

Factors affecting wound healing in animals

Several factors can accelerate or delay healing. Species differences influence tissue repair capacity and inflammatory responses. Age is also critical, as young animals often heal faster than older ones due to better cell proliferation and circulation. General physiological condition, including endocrine balance and stress levels, affects immune response and tissue regeneration.

Nutrition and immune status are among the most important systemic determinants. Deficiencies in protein, energy, vitamins, and minerals can reduce fibroblast activity, collagen synthesis, and immune defense, increasing susceptibility to infection. Similarly, immunosuppression or metabolic disorders may prolong inflammation and impair granulation and epithelialization.

Local wound factors also play a major role. Large, deep, or highly contaminated wounds require more time to heal and are more likely to become chronic. Poor blood supply, extensive tissue necrosis, and repeated trauma to the wound area can significantly delay progress through the healing stages. Environmental and management conditions—such as hygiene, housing quality, moisture, bedding, and handling practices—may either support clean healing or promote contamination and reinjury.

5. INFECTION AND INFLAMMATION IN WOUNDS

Infection is one of the most common causes of delayed wound healing in veterinary practice. Microbial contamination may occur at the time of injury or during subsequent management. When bacteria multiply in the wound, they intensify inflammatory responses, increase tissue necrosis, and reduce the effectiveness of repair mechanisms.

Microbial contamination and biofilm formation

A major challenge in chronic or non-healing wounds is biofilm formation. Biofilms are structured communities of microorganisms attached to the wound surface and protected by an extracellular matrix. This structure reduces bacterial sensitivity to antiseptics and antibiotics and makes infection more persistent. As a result, wounds with biofilms may show prolonged exudation, persistent odor, weak granulation tissue, and delayed epithelialization.

Role of cytokines and inflammatory mediators

Cytokines and inflammatory mediators regulate both protective and harmful outcomes in wound healing. In a normal response, cytokines recruit immune cells and support tissue repair. However, excessive production of inflammatory mediators can maintain the wound in an inflammatory state, preventing progression to the proliferative and remodeling phases. This imbalance can lead to chronic inflammation, impaired collagen formation, and prolonged healing time.

Impact on delayed healing

Infected wounds typically show increased swelling, heat, pain sensitivity, and purulent discharge. Clinically, infection slows granulation tissue formation, damages newly formed vessels, and interrupts epithelial migration. Therefore, effective control of infection—through debridement, appropriate antiseptics, and targeted therapy—is essential for restoring normal healing dynamics.

6. MATERIALS AND METHODS

Clinical examination and wound modeling

The study involved clinical observation and treatment of mechanically induced traumatic wounds as well as purulent and necrotic open wounds in farm animals. Wounds were assessed by type, depth, size, degree of contamination, and clinical signs such as temperature, edema, and exudate characteristics. Wound healing stages were recorded daily to evaluate progression and response to treatment.

Surgical procedures and treatment protocols

Standard wound management procedures were applied, including cleaning, disinfection, and when necessary, surgical intervention such as debridement to remove necrotic tissue. Treatment was continued for 21 days, and wound dynamics were monitored throughout the study period.

Experimental design and animal grouping

A total of 30 calves were included and divided into two groups:

1. **Control group:** Treated with conventional antiseptics and standard dressings.
2. **Experimental group:** Treated using PRP therapy and bioactive collagen-based dressings.

Evaluation methods included visual clinical assessment, planimetric measurement of wound area, microbiological examination, histological analysis (hematoxylin-eosin staining), and immunohistochemical methods. Outcomes were compared between the two groups to assess differences in epithelialization speed, microbial load, granulation quality, and tissue organization.

7. MODERN TREATMENT APPROACHES

Effective wound management in veterinary practice aims to control bleeding, prevent infection, remove devitalized tissue, and create optimal local conditions for tissue repair. In recent years, modern approaches such as **bioactive dressings** and **platelet-rich plasma (PRP) therapy** have gained attention because they support healing not only through protection but also through direct biological stimulation of repair processes.

Conventional antiseptic and dressing methods

Traditional wound care typically includes mechanical cleaning, disinfection, removal of necrotic tissue when necessary, and application of standard dressings. Antiseptics help reduce microbial load, while dressings protect the wound surface from further contamination and trauma. Although conventional methods are effective in many cases, they may be less successful in wounds with high contamination, necrosis, or prolonged inflammation, where healing often becomes delayed.

Bioactive dressings

Bioactive dressings are designed to provide more than physical coverage. In addition to maintaining an optimal moist environment, they can promote epithelial migration, support granulation tissue formation, and reduce microbial contamination. Collagen-based bioactive dressings, in particular, act as a scaffold for cell adhesion and fibroblast activity, which may enhance collagen deposition and improve tissue organization during the proliferative phase.

Platelet-rich plasma (PRP) therapy

PRP therapy involves the application of a concentrated platelet fraction derived from the animal's own blood. Platelets release multiple growth factors that can stimulate angiogenesis, fibroblast proliferation, extracellular matrix production, and epithelialization. PRP is especially relevant in chronic or complicated wounds because it may shorten the inflammatory phase and accelerate the transition to active tissue repair.

8. EXPERIMENTAL RESULTS

Clinical observations and wound size reduction

During the 21-day observation period, wounds in both groups showed progressive healing; however, the **experimental group (PRP + bioactive dressings)** demonstrated faster improvement in key clinical parameters. Compared with the control group, wounds in the experimental group showed earlier reduction in edema and exudate, cleaner wound beds, and quicker appearance of healthy granulation tissue. Overall, epithelialization was observed to progress approximately **30–40% faster** than in the control group, and necrotic tissue was recorded less frequently.

Histological and microbiological findings

Microbiological examination indicated that the experimental approach reduced wound contamination more effectively, supporting a cleaner local environment for repair. Histological assessment (hematoxylin-eosin

staining) showed increased fibroblast activity, denser and more organized collagen fiber deposition, and a higher number of newly formed capillaries (angiogenesis) in the experimental group. These findings corresponded with stronger granulation tissue development and a more active proliferative phase.

Comparison between control and experimental groups

- **Control group:** Healing progressed under standard antiseptic care, but inflammation and exudation tended to persist longer, and epithelial closure was slower.
- **Experimental group:** Faster transition from inflammation to proliferation, improved tissue organization, reduced microbial burden, and accelerated epithelial coverage.

9. DISCUSSION

Interpretation of experimental outcomes

The results indicate that wound healing in animals is strongly influenced by local wound conditions—especially microbial load and moisture balance—as well as by biological stimulation of repair mechanisms. The experimental group’s faster epithelialization and improved histological architecture suggest that PRP and bioactive dressings support a more favorable healing trajectory by promoting earlier granulation and more efficient tissue remodeling.

Advantages of bioactive dressings and PRP

Bioactive dressings likely improved outcomes by maintaining an optimal moist environment and supporting fibroblast migration and collagen synthesis through structural scaffolding. PRP therapy likely enhanced healing by delivering growth factors that stimulate angiogenesis and cellular proliferation, improving oxygen and nutrient supply to the wound bed and accelerating repair. The combined use of both approaches may therefore provide a synergistic benefit, particularly for traumatic, necrotic, and purulent wounds where classical methods may be slower.

Comparison with previous studies

The observed improvements align with broader veterinary surgical literature emphasizing the importance of moisture-balanced wound environments, microbial control, and biologically active therapies for enhanced regeneration. The findings support the growing clinical trend toward integrating regenerative techniques and advanced dressings into routine veterinary wound management, especially for complicated wounds.

10. CONCLUSION

This study confirms that wound healing in animals is a complex, multi-stage biological process regulated through coordinated cellular and molecular mechanisms across the phases of hemostasis, inflammation, proliferation, and remodeling. The experimental application of **bioactive collagen-based dressings** and **PRP therapy** reduced microbial contamination, promoted fibroblast activity and angiogenesis, improved collagen organization, and significantly accelerated epithelialization compared with conventional antiseptic care.

These results highlight the practical value of combining innovative wound-healing technologies with standard veterinary management. Implementing bioactive dressings and PRP-based strategies can improve clinical outcomes, shorten recovery time, and support animal welfare and productivity, particularly in farm

animals with traumatic or infected wounds. Further controlled studies with expanded sample sizes and standardized wound models would strengthen evidence for broader clinical adoption.

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