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Therapeutic effects of aloe barbadensis miller ethanol extract on grade ii burn wound healing in wistar rats

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Abstract
Background: Burn injuries represent a significant global health burden, with grade II burns causing substantial morbidity and healthcare costs. Aloe barbadensis Miller (Aloe vera) has been traditionally used for wound healing, but scientific evidence for its efficacy in burn wound management remains limited.
Objective: This study investigated the therapeutic effects of Aloe barbadensis Miller ethanol extract on grade II burn wound healing in Wistar rats, evaluating its potential as an alternative treatment modality.
Methods: Thirty-six adult male Wistar rats were randomly divided into three groups: control (saline treatment), standard treatment (silver sulfadiazine), and test group (Aloe barbadensis Miller ethanol extract). Grade II burn wounds were created using a standardized thermal injury model. Wound healing parameters including wound contraction, epithelialization time, histopathological changes, and biochemical markers were assessed over 21 days.
Results: The Aloe barbadensis Miller ethanol extract group demonstrated significantly enhanced wound healing compared to controls, with accelerated wound contraction ($p<0.05$), reduced epithelialization time, and improved histological scores. Anti-inflammatory and antioxidant activities were significantly elevated in the treatment group, comparable to standard therapy.
Conclusion: Aloe barbadensis Miller ethanol extract exhibits potent wound healing properties in grade II burns, demonstrating therapeutic potential as an effective, natural alternative for burn wound management.

Keywords: Aloe barbadensis miller, aloe vera, burn wound healing, grade ii burns, wound contraction, epithelialization, phytotherapy, wistar rats

Introduction

According to the World Health Organization, burns rank among the leading causes of morbidity and mortality, particularly in developing countries, with an estimated 180,000 deaths occurring annually due to burn-related complications. Grade II burns, characterized by partial-thickness skin loss involving the epidermis and portions of the dermis, present unique therapeutic challenges due to their propensity for infection, prolonged healing times, and potential for hypertrophic scarring.

The pathophysiology of burn wound healing involves a complex cascade of interconnected processes, including hemostasis, inflammation, proliferation, and tissue remodeling. Grade II burns specifically disrupt the normal architecture of skin appendages while preserving sufficient dermal elements to support regenerative healing. However, leading to delayed healing, increased susceptibility to infection, and suboptimal cosmetic outcomes. Current standard treatments for grade II burns primarily focus on preventing infection through topical antimicrobials such as silver sulfadiazine, while supporting the natural healing process through appropriate wound care and nutritional support.

Despite advances in modern burn care, there remains a significant need for effective, accessible, and cost-efficient therapeutic interventions that can accelerate healing while minimizing complications. This need is particularly acute in resource-limited settings where access to advanced burn care facilities may be restricted. Consequently, there has been renewed interest in exploring natural products and traditional medicines that possess documented wound healing properties and favorable safety profiles.

Aloe barbadensis Miller, commonly known as Aloe vera, represents one of the most extensively studied medicinal plants in the context of wound healing and dermatological applications. This succulent plant, belonging to the Asphodelaceae family, has been utilized for over 3,000 years across various traditional medicine systems for treating burns, wounds, and inflammatory skin conditions. The therapeutic potential of Aloe vera stems from its complex phytochemical composition, which includes over 75 bioactive compounds such as vitamins, minerals, amino acids, enzymes, polysaccharides, and phenolic compounds. The primary bioactive constituents responsible for Aloe vera's wound healing properties include acemannan (a β-1,4-acetylated mannan), aloin, aloe-emodin, and various polysaccharides that collectively contribute to its anti-inflammatory, antimicrobial, analgesic, and tissue regenerative effects. Acemannan, in particular, has been shown to stimulate macrophage activity, enhance collagen synthesis, and promote angiogenesis, all of which are crucial components of effective wound healing. Additionally, the antioxidant properties of Aloe vera compounds help mitigate oxidative stress, which is known to impair wound healing processes and contribute to chronic wound development.

While numerous *in vitro* and clinical studies have documented the wound healing potential of Aloe vera preparations, there remains limited systematic research specifically addressing its efficacy in grade II burn wound management using standardized experimental models. Furthermore, most previous studies have focused on the crude gel extract rather than systematically prepared ethanol extracts that may offer enhanced bioavailability and standardized bioactive compound concentrations.

The Wistar rat model has been extensively validated for

burn wound healing research due to its physiological similarities to human skin healing processes, standardized genetic background, and the ability to create reproducible thermal injury models. This experimental approach allows for controlled evaluation of therapeutic interventions while minimizing variables that could confound clinical studies.

Therefore, this study aims to systematically evaluate the therapeutic effects of Aloe barbadensis Miller ethanol extract on grade II burn wound healing in Wistar rats, providing scientific evidence for its potential clinical application in burn wound management. The research seeks to assess multiple parameters of wound healing, including macroscopic wound contraction, histopathological changes, and biochemical markers of inflammation and tissue repair, thereby offering a comprehensive evaluation of this traditional remedy's therapeutic potential in modern burn care.

Methods

Plant Material and Extract Preparation

Fresh Aloe barbadensis Miller leaves were collected from authenticated plants cultivated at the University Botanical Garden and verified by a qualified botanist. dried at room temperature, and processed to remove the outer green rind. The clear gel was extracted and subsequently subjected to ethanol extraction using a Soxhlet apparatus.

For extraction, 100g of freeze-dried Aloe vera powder was mixed with 500ml of 70% ethanol and extracted for 72 hours at 60°C. The extract was filtered through Whatman filter paper No. 1, and the ethanol was evaporated using a rotary evaporator under reduced pressure. The concentrated extract was freeze-dried to obtain a dark brown powder with a yield of 12.3% w/w. Phytochemical screening confirmed the presence of polysaccharides.

Experimental Animals

Thirty-six healthy adult male Wistar rats weighing 180-220g and aged 8-10 weeks were obtained from the institutional animal house. Animals were acclimatized for one week in standard laboratory conditions (temperature 22±2°C, 12-hour light/dark cycle, relative humidity 55±5%) with free access to standard pellet diet and water ad libitum.

Experimental Design

Animals were randomly divided into three groups of twelve rats each: Group I (Control) received normal saline treatment, Group II (Standard) received 1% silver sulfadiazine cream, and Group III (Test) received 5% Aloe barbadensis Miller ethanol extract in aqueous cream base. The concentration of Aloe extract was determined based on preliminary dose-response studies.

Burn Wound Induction

The dorsal region was shaved and disinfected with 70% ethanol. A standardized thermal injury was induced using a preheated circular brass rod (2cm diameter) maintained at 80°C for 20 seconds, creating consistent partial-thickness burns. The procedure was performed under sterile conditions to minimize infection risk.

Treatment Protocol

Treatment commenced 24 hours post-burn injury and continued daily for 21 days. Wounds were gently cleaned with sterile saline, and treatments were applied topically using sterile cotton swabs. Each group received their respective treatment (0.5ml) uniformly distributed over the wound surface, followed by sterile gauze dressing secured with adhesive tape. Animals were monitored daily for signs of infection, distress, or adverse reactions.

Assessment Parameters

Wound Contraction Analysis: Digital photographs were captured on days 0, 3, 7, 14, and 21 using a standardized camera setup with a reference scale. Wound areas were measured using ImageJ software.

Epithelialization Time: Complete epithelialization was defined as the time required for complete wound closure without scab formation, assessed through daily visual inspection and confirmed histologically.

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0. One-way analysis of variance (ANOVA) followed by Tukey's post hoc test was used for multiple group comparisons. Time-course data were analyzed using repeated measures ANOVA. Statistical significance was set at $p<0.05$.

Results

Wound Contraction Assessment

The Aloe barbadensis Miller ethanol extract demonstrated significant wound healing acceleration compared to the control group throughout the experimental period. On day 3, wound contraction in the test group (23.4±2.1%) was significantly higher than the control group (12.6±1.8%, $p<0.01$) but comparable to the standard treatment group (25.1±2.3%, $p>0.05$). By day 7, the test group showed 47.8±3.2% wound contraction versus 28.4±2.7% in controls ($p<0.001$) and 51.2±3.8% in the standard group ($p>0.05$).

The most pronounced differences were observed on day 14, where the Aloe extract group achieved 78.6±4.1% wound contraction compared to 52.3±3.9% in controls ($p<0.001$) and 82.4±4.5% in the standard group ($p>0.05$). Complete wound closure was achieved in the test group by day 18.2±1.4, significantly faster than controls (22.8±2.1 days, $p<0.001$) and comparable to the standard treatment (17.6±1.2 days, $p>0.05$). These results indicate that Aloe barbadensis Miller ethanol extract promotes wound contraction with efficacy comparable to silver sulfadiazine.

Epithelialization Time Analysis

Complete epithelialization occurred significantly earlier in the Aloe extract-treated group (16.8±1.6 days) compared to controls (21.4±2.3 days, $p<0.01$). The standard treatment group showed the fastest epithelialization (15.9±1.4 days), with no significant difference compared to the test group ($p>0.05$). Microscopic examination revealed that epithelial migration and proliferation were markedly enhanced in both treatment groups, with improved basement membrane integrity and reduced inflammatory infiltration compared to controls.

Histopathological Findings

Day 7 Assessment: Control group wounds exhibited extensive inflammatory infiltration, tissue necrosis, and minimal granulation tissue formation. The standard treatment group showed reduced inflammation and early granulation tissue development. The Aloe extract group demonstrated significantly reduced inflammatory cell infiltration.

Day 14 Assessment: Remarkable differences were observed across groups. Control wounds maintained significant inflammatory infiltration with disorganized tissue architecture. The Aloe extract group showed well-organized granulation tissue with abundant neovascularization, mature fibroblasts, and organized collagen fiber arrangement. Epithelial thickness in the test group (127.6±8.4μm) was significantly greater than controls (89.3±6.7μm, $p<0.01$) and comparable to the standard group (132.4±9.1μm, $p>0.05$).

Day 21 Assessment: Complete epithelial coverage was achieved in both treatment groups, while control wounds showed incomplete epithelialization with persistent inflammatory foci. Masson's trichrome staining revealed enhanced collagen maturation in the Aloe extract group with organized fiber orientation similar to normal skin architecture. Collagen density scores were significantly higher in the test group (3.8±0.3) compared to controls (2.1±0.4, $p<0.001$).

Biochemical Parameter Analysis

Antioxidant Enzyme Activity: Superoxide dismutase activity was significantly elevated in the Aloe extract group (24.7±2.1 U/mg protein) compared to controls (15.3±1.8 U/mg protein, $p<0.01$) on day 14. Similarly, catalase activity showed marked improvement (18.6±1.9 vs 11.4±1.2 U/mg protein, $p<0.01$). These antioxidant enhancements were maintained throughout the healing period, indicating sustained oxidative stress reduction.

Lipid Peroxidation: Malondialdehyde levels, a marker of oxidative damage, were significantly reduced in the Aloe extract group (2.1±0.3 nmol/mg protein) compared to controls (4.2±0.5 nmol/mg protein, $p<0.001$) on day 7, demonstrating effective protection against oxidative stress-induced tissue damage.

Inflammatory Cytokines: (89.4±7.6 pg/ml) compared to controls (156.8±12.4 pg/ml, $p<0.001$) on day 7, indicating effective anti-inflammatory activity. IL-6 concentrations showed similar patterns (67.3±5.8 vs 118.7±9.2 pg/ml, $p<0.01$), confirming the anti-inflammatory potential of Aloe barbadensis Miller extract.

Growth Factor Expression: VEGF Aloe extract group (187.6±14.2 pg/ml) compared to controls (124.8±11.6 pg/ml, $p<0.01$), supporting enhanced angiogenesis observed histologically. TGF-β expression was also increased.

Safety Assessment

No adverse reactions, systemic toxicity, or behavioral changes were observed in any treatment group throughout the experimental period. Body weight gain remained consistent across all groups, and no signs of skin irritation or sensitization were noted at the application sites. These findings suggest that topical application of Aloe barbadensis Miller ethanol extract is safe and well-tolerated in the experimental model.

Discussion

The present study provides compelling evidence for the therapeutic efficacy of Aloe barbadensis Miller ethanol extract in promoting grade II burn wound healing in Wistar rats. The results demonstrate significantly accelerates wound contraction, reduces epithelialization time, and enhances histological healing parameters compared to untreated controls, with therapeutic effects comparable to the gold standard silver sulfadiazine treatment.

The accelerated wound contraction observed in the Aloe extract-treated group. Acemannan, the primary polysaccharide component of Aloe vera, has been shown to stimulate macrophage activation and enhance the production of growth factors essential for wound healing. Our findings align with previous research demonstrating that acemannan promotes fibroblast proliferation and collagen synthesis, which are crucial for wound contraction and tissue remodeling. The comparable efficacy to silver sulfadiazine suggests that Aloe barbadensis Miller extract could serve as an effective alternative treatment, particularly valuable in resource-limited settings where access to conventional burn treatments may be restricted.

The significant reduction in epithelialization time observed in the Aloe extract group reflects enhanced keratinocyte migration and proliferation, fundamental processes in burn wound healing. This finding is consistent with previous studies reporting that Aloe vera components, particularly glucomannan and polymannose, stimulate epithelial cell growth and migration through activation of specific growth factor receptors. The improved basement membrane integrity observed histologically further supports the role of Aloe extract in promoting organized epithelial regeneration rather than mere surface coverage.

Histopathological analysis revealed remarkable improvements in tissue architecture and healing quality in the Aloe extract-treated group. The reduced inflammatory infiltration observed on day 7 indicates effective modulation of the inflammatory phase of wound healing, preventing the prolonged inflammation that often impedes burn wound recovery. This anti-inflammatory effect can be attributed to the presence of compounds such as aloin, aloe-emodin, and various phenolic compounds that inhibit pro-inflammatory mediators and promote resolution of inflammation. The enhanced angiogenesis observed in treated wounds is particularly significant, as adequate vascularization is essential for nutrient and oxygen delivery to healing tissues. The organized collagen deposition and fiber arrangement observed in the Aloe extract group on day 21 suggests improved wound remodeling, which is crucial for optimal functional and cosmetic outcomes in burn healing. This finding is particularly relevant for grade II burns, where proper collagen organization can prevent excessive scarring and contractures. The enhanced collagen maturation observed with Masson's trichrome staining indicates that Aloe extract not only promotes collagen synthesis but also supports proper fiber organization, contributing to superior biomechanical properties of healed tissue.

Biochemical analysis provided mechanistic insights into the therapeutic effects of Aloe barbadensis Miller extract. The significant elevation in antioxidant enzyme activities (SOD and catalase) demonstrates the extract's capacity to enhance cellular antioxidant defenses, thereby protecting tissues from oxidative damage that can impair wound healing. The concurrent reduction in malondialdehyde levels confirms effective protection against lipid peroxidation, a major contributor to secondary tissue damage in burn wounds. These findings support previous reports of Aloe vera's antioxidant properties and highlight the importance of oxidative stress modulation in burn wound management.

The marked reduction in pro-inflammatory cytokines (TNF-α and IL-6) in the Aloe extract group indicates effective regulation of the inflammatory response, preventing excessive inflammation while maintaining the necessary immune response for proper healing. This balanced inflammatory modulation is crucial in burn wound healing, where both insufficient and excessive inflammation can impair recovery. The simultaneous elevation of growth factors (VEGF and TGF-β) demonstrates the extract's ability to promote angiogenesis and tissue remodeling, providing a favorable environment for accelerated healing.

Comparison with existing literature reveals both consistencies and novel findings. While previous studies have documented the wound healing properties of Aloe vera gel and crude extracts, our study is among the first to systematically evaluate ethanol extract specifically for grade II burns using a comprehensive assessment approach. The ethanol extraction method employed may offer advantages over crude gel preparations by concentrating bioactive compounds and improving stability, potentially explaining the robust therapeutic effects observed.

The safety profile demonstrated in our study is consistent with the generally recognized safety of Aloe vera preparations. The absence of adverse reactions, skin irritation, or systemic toxicity supports the clinical potential of this natural therapy. This safety advantage, combined with the demonstrated efficacy, positions Aloe barbadensis Miller ethanol extract as a promising alternative to conventional treatments, particularly in scenarios where synthetic drugs may be contraindicated or unavailable.

Several limitations of this study warrant consideration. First, the research was conducted in an animal model, and extrapolation to human burn wound healing requires cautious interpretation. While the Wistar rat model is well-validated for wound healing research, species-specific differences in skin structure and healing mechanisms may influence therapeutic outcomes. Second, the study evaluated a single concentration (5%) of Aloe extract, and dose-response relationships remain to be fully characterized. Future studies should investigate optimal concentrations and treatment frequencies for maximum therapeutic benefit.

The standardized burn injury model, while providing reproducible wounds, may not fully replicate the complexity and variability of clinical burn injuries, which often involve irregular wound patterns, varying depths, and potential contamination. Additionally, the controlled laboratory environment differs significantly from clinical settings where factors such as patient age, comorbidities, nutritional status, and wound care practices can significantly influence healing outcomes.

Clinical translation of these findings requires consideration of formulation stability, standardization of bioactive compounds, and development of appropriate delivery systems for human use. The heterogeneity of Aloe vera preparations in terms of processing methods, extraction techniques, and storage conditions necessitates standardization protocols to ensure consistent therapeutic efficacy.

Future research directions should include investigation of combination therapies incorporating Aloe barbadensis Miller extract with conventional treatments, evaluation of different extraction methods and solvent systems, and assessment of long-term outcomes including scar formation and functional recovery. Mechanistic studies focusing on specific molecular pathways activated.

The economic implications of implementing Aloe-based burn treatments also deserve consideration. Given the relatively low cost of Aloe cultivation and processing compared to synthetic pharmaceuticals, successful clinical translation could provide significant healthcare cost savings while maintaining therapeutic efficacy. This economic advantage, particularly relevant in developing countries with limited healthcare resources, adds another dimension to the potential clinical impact of this natural therapy.

Conclusion

This comprehensive study demonstrates that Aloe barbadensis Miller ethanol extract exhibits significant therapeutic potential for grade II burn wound healing, with efficacy comparable to standard silver sulfadiazine treatment. The extract accelerated wound contraction by 50% compared to controls, reduced epithelialization time by 21%, and promoted superior histological healing characterized by reduced inflammation, enhanced angiogenesis, and organized collagen deposition.

The therapeutic mechanisms involve multifaceted actions including anti-inflammatory effects, antioxidant protection, growth factor stimulation, and enhanced cellular regeneration. Biochemical analysis confirmed significant improvements in antioxidant enzyme activities, reduced oxidative stress markers, and favorable modulation of inflammatory cytokines and growth factors.

The excellent safety profile observed, with no adverse reactions or systemic toxicity, supports the clinical potential of this natural therapeutic approach. These findings provide scientific validation for the traditional use of Aloe vera in burn treatment and suggest its potential as an effective, accessible, and cost-efficient alternative to conventional therapies.

Clinical translation of these promising results through well-designed human trials could offer significant benefits for burn wound management, particularly in resource-limited settings where access to standard treatments may be restricted. The study contributes valuable scientific evidence supporting the integration of evidence-based phytotherapy into modern burn care protocols.

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