

Aloe vera and Wound Healing*

ROBERT H. DAVIS, PhD†
JOSEPH M. KABBANI, BS‡
NICHOLAS P. MARO, BS‡

The authors present a study of the wound healing effects of *Aloe vera*. Special emphasis is given to combined RNA and vitamin C with Aloe because of their effectiveness against arthritis. Consideration is given to anthraquinones because their influence is not clearly understood. As a result of the preliminary findings in the study, the authors recommend Aloe for the treatment of wounds.

The dynamic state of an untreated open wound may take on critical manifestations. It may even result in disabling an individual. The limitations of steroidal and some nonsteroidal agents upon wound healing led the authors to study the wound healing effects of *Aloe vera*. *Aloe vera* is a natural substance containing enzymes, amino acid, and other active ingredients that provide emulsifying and emollient properties needed for wound repair. Healing may also be accelerated by the transfer of water from *A. vera* (gel is 96% H₂O) to injured tissue.¹ *Aloe vera*'s watery consistency exerts a major effect by increasing epithelial cell migration of wounds. Desiccation retards wound healing.

The healing of skin wound involves repair elements from two main sources: epithelium coming from undamaged surrounding epidermis, which occurs in three phases, ie, migration, proliferation, and maturation. The second source occurs in the dermis that gives rise to connective tissue. For years, steroids have been used in treatment of inflammation and wound healing. However, steroid utility is limited because of the adverse side effects. Corticosteroids may proliferate and mature keratinocytes, inducing epidermal atrophy. Fourtanier et al² observed that topical steroids decrease epidermal DNA synthesis in skin.

Crewe³ reported *A. vera* caused improved wound healing with tissue regeneration. This response

could be explained by the fact that Aloe dilates capillaries to increase blood flow to injured areas.⁴ *Aloe vera* hastens the "contractile response" in open wounds. Tensile forces originate from collagen formation. Fiber shortening accounts for changes in granulation tissue of the wound bed.⁵ Furthermore, Rowe's experiments demonstrated the effectiveness of *A. vera* on burns in rats. He found 50% of the rats showed increased healing in areas treated with Aloe.

The pharmacodynamics of the plant gel⁷⁻¹⁰ have not been well established in the literature. The mechanism, of action comes in part from barbolin, emodin, and acetylsalicylic acid, components of *A. vera*. Barbolin and emodin block prostaglandins and thromboxanes. *Aloe vera* overcomes prostaglandin's destructive effect after physical trauma.¹¹ Davis et al¹² reported that topical *A. vera* inhibits adjuvant arthritis by 72%. The acetylsalicylic acid of Aloe may account, in part, for some of the analgesic properties.

Unlike steroids, Aloe may effect the synthesis and breakdown of hydroxyproline to reduce inflammation and improve wound healing. Ryan¹³ observed that hydrocortisone decreased free amino acids in connective tissue on administration. Hydrocortisone increases the amino acid pool in the liver. It inhibits protein synthesis as well as inflammation. Houck¹⁴ believed that adrenal steroids were antianabolic and catabolic on skin. Cushing's syndrome is a perfect example of this theory.

The physician's concern is to reduce the size of the wound as quickly as possible after an injury, with minimal side effects. This lessens the chance of infection. The purpose of this study primarily is

* Bronze Medal, 1986 William J. Stickel Award for Research and Papers in Podiatric Medicine.

† Professor of Physiology, Pennsylvania College of Podiatric Medicine, Eighth at Race St, Philadelphia, PA 19107.

‡ Submitted during second year, Pennsylvania College of Podiatric Medicine, Philadelphia.

to show the tissue-related influence of *A. vera* on wound healing. Consideration was given to a basic experimental model. The punch biopsy technique measures wound healing as a function of reduced diameter with time. Special emphasis was given to combining RNA and vitamin C because of its effectiveness against arthritis.¹⁵ Also, consideration was given to the anthraquinones because their influence in Aloe is not clearly understood.

Materials and Methods

A 6-mm Baker punch was used to remove a circular piece of skin from both shaven sides of ICR mice (35 to 40 g; 12 animals/group) and adult male Sprague-Dawley rats (180 to 270 g; 12 animals/group). The animals were placed under ether anesthesia. A #12 vernier caliper was used to measure diameters as evidence of wound healing. Mice were subcutaneously injected 1, 10, or 100 mg/kg each day for 7 days with either regular colorized *A. vera*, with anthraquinone, or with decolorized *A. vera*, without anthraquinone. *Aloe vera* color bodies (anthraquinones) were extracted from the decolorized sample. Colorized *A. vera* was stabilized by an antioxidant stabilizer. Solutions were prepared fresh each day with the appropriate Aloe powder dissolved in distilled water. Rats were injected subcutaneously (basis of 10 mg/kg powder or 10 ml/kg fluid) each day for 12 days with either regular *A. vera* (colorized) or with added 150 mg/kg L-ascorbic acid-sodium salt and RNA-sodium salt, each homogenized into the Aloe solution. Solutions were prepared fresh each day. Rat and mouse control groups received no injections. Treated mice and rats were injected daily for 7 days and rats for 12 days, respectively. A 6-mm wound was made in both sides of all the animals, and an average diameter was recorded on days 0 and 7 for the mice and days 0, 7, and 12 for the rats.

The percentage of reduction of wound size was calculated for *A. vera* treated animals, with and without anthraquinone in mice and with and without vitamin C and RNA in the rats, in reference to day 0. This represents a horizontal and vertical comparison. A dose-response curve was constructed within the two experimental groups of mice, with the control as the baseline. Histologic sections were obtained through the middle of the wound, randomly picked from each group among the rats and mice on the final day. Tissues were stained with hematoxylin and eosin. The authors obtained pictures of the wounds at various times over the experimental period. Standard errors were calculated

for mean wound diameter and percentage reduction of wound diameter within the groups, using the formula

$$SE = \frac{d^2}{N(N-1)}$$

The Student's t test, was used to obtain the p values.

Results and Discussion

According to the literature, the most optimal time to record wound healing reduction is on day 7. *Aloe vera* increases the tensile strength of normal wounds by this time.^{5,16}

Colorized *A. vera* treated mice given doses of 1, 10, and 100 mg/kg had no significant reduction ($p > .5$) in wound diameters on day 7 relative to day 0. However, mice treated with decolorized *A. vera* showed a dose-response relationship exhibiting wound diameter differences on day 7 of 2.36 ± 0.44 mm for 1 mg/kg, 3.40 ± 0.10 mm for 10 mg/kg, and 4.33 ± 0.30 mm for 100 mg/kg ($p < .01$), respectively (Table 1, Fig. 1). A maximum of $56.5 \pm 3.2\%$ reduction was observed at the high treatment dose of decolorized *A. vera*.

The percentage of reduction of wound diameters in reference to day 0 for *A. vera* treated rats receiving no vitamin C and RNA was $61.1\% \pm 1.6\%$ on day 7 as compared to the mean control value of $40.3\% \pm 4.1\%$ ($p < .001$). A similar percentage of reduction of $69.9\% \pm 1.9\%$ was recorded on day 12 (Table 2). This demonstrates the wound healing effectiveness of colorized *A. vera* in both mice and rats. For Aloe-treated rats receiving RNA and vitamin C, the percentage of reduction for wound diameter on day 7 ($34.8\% \pm 4.6\%$) was similar to control rats ($40.3\% \pm 4.1\%$) ($p > .1$). On day 12, rats receiving *A. vera* with RNA and vitamin C showed a $57.1\% \pm 3.4\%$ reduction in wound size as compared to $46.6\% \pm 4.1\%$ for untreated animals ($p > .05$). However, when the responses were compared relative to control values, the 7-day and 12-day percentage of reduction of wound diameters for animals receiving only Aloe were 31.3% and 40.1%, respectively.

Table 1. Comparisons of the Effects of Colorized *A. vera* and Decolorized *A. vera* on Wound Healing in Mice Over 7 Days.*

Dose	Wound Diameter Decrease (mm)	
	Colorized <i>A. vera</i>	Decolorized <i>A. vera</i>
Control	2.48 ± 0.48	2.48 ± 0.48
1 mg/kg	2.65 ± 0.36	2.36 ± 0.44
10 mg/kg	2.53 ± 0.33	3.40 ± 0.10
100 mg/kg	2.85 ± 0.34	4.33 ± 0.30

* 12 animals/group.

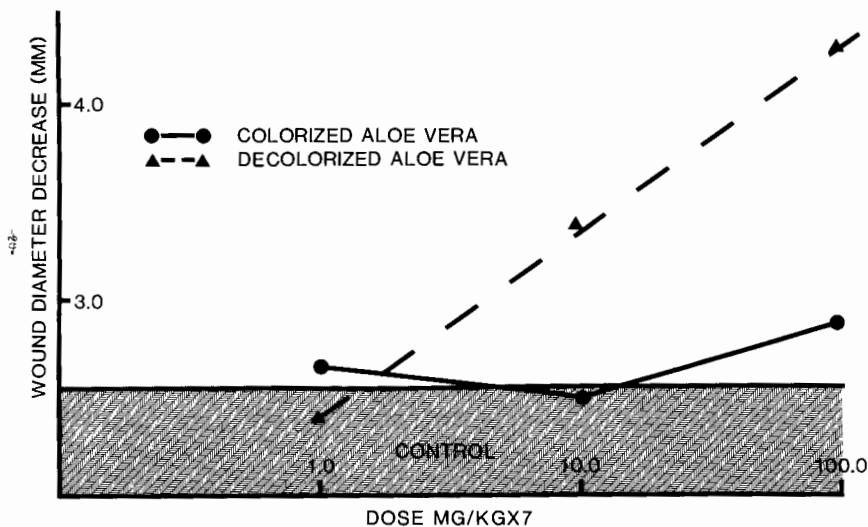


Figure 1. The effect of *A. vera* on mouse wound healing over 7 days.

Table 2. Effect of Colorized *A. vera* with and without RNA and Vitamin C on Wound Healing in Rats^a

Group	Dose	Reduction of Wound Diameter Relative to (%)			
		Day 0		Control	
		Day 7	Day 12	Day 7	Day 12
Control		40.3 ± 4.1	46.6 ± 4.1		
<i>A. vera</i>	10 mg/kg	61.1 ± 1.6	69.9 ± 1.9	31.3	40.1
Combination		34.8 ± 4.6	57.1 ± 3.4	0.0	14.3
<i>A. vera</i>	10 mg/kg				
RNA	150 mg/kg				
Vitamin C	150 mg/kg				

^a 12 rats/group.

When RNA and vitamin C treatments were added to Aloe, a maximum 14.3% reduction was observed on day 12 with a 0% response by day 7 (Table 2 and Fig. 2). This indicates that RNA and ascorbic acid did not improve the wound healing ability of *A. vera*, even though RNA and vitamin C are effective against adjuvant arthritis. The best healing response as measured by wound diameter was observed by *A. vera* treatment alone in the rats.

Within the *A. vera* treated mouse and rat groups, an increase in skin circulation was observed with redness in the wounded area. Aloe also seems to continue its effectiveness even after wound closure by avoiding contracture and hypertrophic scarring. Sections were made through the wound area 7 days and 12 days after the punch biopsy for the mice and rats, respectively. The control wound without treatment in mice and rats contained a thin growing layer of epithelium observed microscopically. Connective tissue, capillaries, and smooth muscles were recorded in the dermis. Wounds from the rats receiving 10 mg/kg *A. vera* (powder basis) injections appeared to have a greater amount of vasculature in the dermis with a better defined germination layer. Those animals receiving 150 mg/kg *A. vera*

with RNA and vitamin C appeared to present the same picture as Aloe alone, except that dermis connective tissue appeared to be somewhat tighter and more compact. Wounds of mice treated with 100 mg/kg of colorized *A. vera* exhibited a healthier looking connective tissue and better vascularity than controls. Qualitatively, no dose-response relationships were observed from a histologic viewpoint between colorized and decolorized *A. vera* in the mice. However, a rough observation confirms that the decolorized *A. vera* wound has a better looking epithelium and dermis versus the colorized *A. vera* wound.

The authors have found that *A. vera* inhibits acute inflammation while improving wound healing. The addition of RNA and vitamin C did not improve wound healing in rats, but colorized *A. vera* with RNA and vitamin C inhibited 2% mustard-induced paw edema 67%, whereas *A. vera* alone decreased edema 44%. Colorized *A. vera* at subcutaneous daily doses up to 400 mg/kg × 12 has no antifibrosis effect. Hence, *A. vera*, unlike the steroid, did not reduce the growth of granuloma connective tissue around cotton pellets implanted under the skin. This demonstrates that *A. vera*

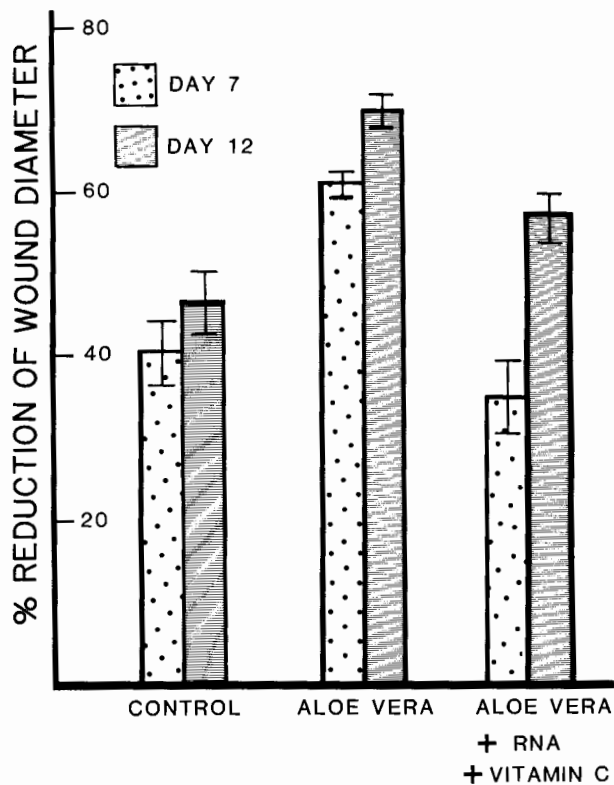


Figure 2. The effect of colorized *A. vera* with RNA and vitamin C on wound healing in rats.

removes acute inflammation and improves wound healing so that a chronic anti-inflammatory connective tissue response becomes unnecessary. This is a major discovery in the treatment of inflammation and wound, because both end points are positively influenced at the same time. This is not true for synthetic drugs and steroids.

A comparison of colorized and decolorized *A. vera* (2 mg/kg dose) produced a 58% and 41% inhibition, respectively, of polymorphonuclear leukocyte infiltration into a 2% gelatin-induced infiltration site in mice (Davis et al, unpublished manuscript). This proves that *A. vera* has good acute anti-inflammatory activity, with or without the anthraquinones, as suggested by the reduction of polymorphonuclear leukocytes found in an area of inflammation. The polymorphonuclear leukocytes infiltration method is a reliable method of testing antiphlogistic activity and reflects the vascular dilation, increased permeability, hyperemia, and edema of an inflamed area. The role of polymorphonuclear leukocytes action in inflammation and the defense against bacterial invasion is generally accepted.

In wounds, prostaglandins and thromboxanes produce platelet and leukocyte aggregation with vasoconstriction. *Aloe vera* blocks these products of

arachidonic acid to prevent inflammation.¹⁷⁻¹⁹ *Aloe vera*, unlike steroids, improves wound healing but does not initiate connective tissue breakdown nor inhibit connective tissue formation while exhibiting this acute anti-inflammatory activity. Steroidal activity is clearly seen in the diabetic patient who has acquired too much circulating steroid, which tends to prevent collagen formation and wound healing. The authors' results indicate that *A. vera* may be an appealing steroidal substitute (Fig. 3).

When a wound is made on the surface of the skin, the slight bleeding forms a clot.²⁰ In 24 hr, the clot forms a crust. The wound swells because of the increased fluid between the fibers of the dermis. Blood vessels dilate in the area and fill with polymorphonuclear leukocytes. The clot covering the wound becomes dissolved in fluid oozing from the dermis. Epidermal cells become ameboid and move toward the center of the wound. These cells are guided by fibers from the dermis. The epidermal recovery proceeds from the wound edges. A new dermis containing collagen fibers is formed. The stimulus for regeneration of the epidermis and dermis is the wound itself. Since *A. vera* contains

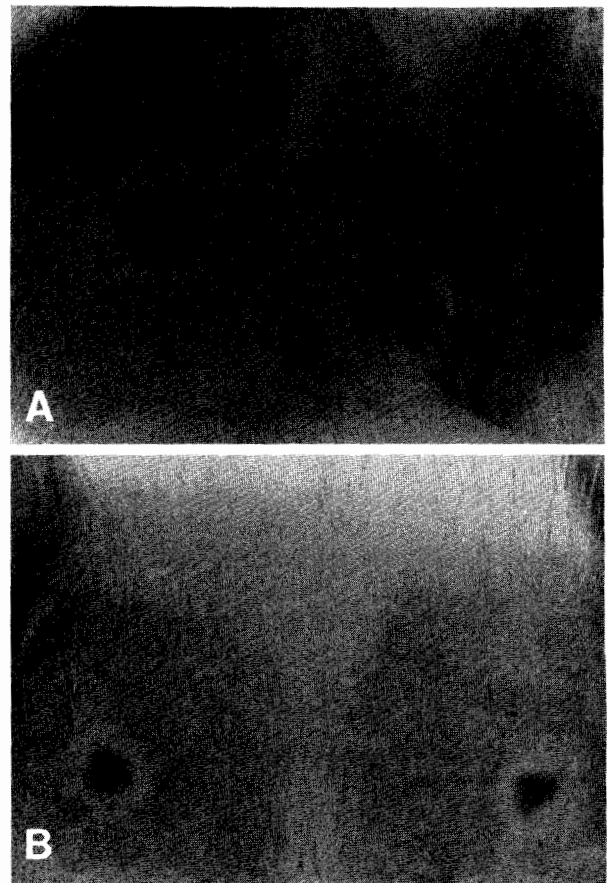


Figure 3. Comparison of an untreated control (A) and the *A. vera*-treated wound (B).

growth factors, anti-inflammatory substances and many normalizing physiologic agents, the authors believe that *A. vera* stimulates this entire process to improve wound healing. It normalizes connective tissue and epithelial elements but, at the same time, prevents inflammation from proceeding without the inhibition of connective tissue (antifibrosis effect). *Aloe vera* bridges the gap between inflammation and wound healing, which should contribute to the treatment of podiatric patients.

Conclusions

Wound healing and inflammation in patients present a major problem for podiatrists in the treatment of foot conditions. Pressure on skin from tight shoes causes ulcers that heal with difficulty. Heavy steroids and strong synthetic drugs provide major drawbacks because they inhibit wound healing and increase the spread of infection. The present data clearly indicate that Aloe in small doses improves circulation and wound healing. The decolorized *A. vera* (without anthraquinones) was more active than the colorized powder, and the authors found no increase in wound healing of Aloe by the adding of vitamin C and RNA to the treatment. Because of these results, the authors recommend *A. vera* for the treatment of wounds.

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