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Wound Healing

Oral and Topical Activity of *Aloe vera*

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The influence of *Aloe vera*, orally and topically, on wound healing was studied. Wounds were induced on both sides of the vertebral column of ICR mice using a biopsy punch. For the oral study, experimental animals received *A. vera* in their drinking water for 2 months, whereas the control animals received only water. In the topical study, experimental animals were given 25% *A. vera* in Eucerin^{®1} cream topically. The control animals received cream only. A 62.5% reduction in wound diameter was noted in mice receiving 100 mg/kg/day oral *A. vera* and a 50.8% reduction was recorded in animals receiving topical 25% *A. vera*. These data suggest that *A. vera* is effective by both oral and topical routes of administration.

Previous studies have amply demonstrated the wound-healing influence of *A. vera*.^{1,2} *Aloe vera* given subcutaneously showed a dose-response relationship on improvement of wound healing. Decolorized *A. vera* (without anthraquinones) was more effective than colorized Aloe. Addition of vitamin C and RNA did not increase the wound-healing potency of *A. vera*. *Aloe vera* is a natural substance containing enzymes, amino acids, and other active ingredients that contain important properties needed for wound healing.^{3,4} Aloe's watery composition may increase the migration of epithelial cells so that an improvement of wound healing is recorded.⁵⁻⁷

Rowe⁸ found that 50% of rats treated with *A. vera* exhibited improved wound healing. Crewe⁹ reported that *A. vera* advanced healing with tissue regeneration. This response could be explained by the fact that Aloe dilated capillaries to increase

blood flow to injured areas.¹⁰ In fact, decolorized *A. vera* improved wound healing in a dose-related fashion even in the diabetic animals,¹¹ in which the healing of vascular tissue was impaired. Possibly, there are specific factors that *A. vera* overcomes to improve wound healing. In normal and diabetic animals, *A. vera* possesses anti-inflammatory, antiedemic, and improved healing properties. This study attempts to show the oral and topical activity of *A. vera* in improving wound healing.

Materials and Methods

In the oral study, adult male ICR mice (35 to 45 gm, 8 animals/group) received food grade *A. vera* for 2 months in their drinking water. The control animals did not receive any *A. vera*. The mice were anesthetized and shaved on both sides of the back. A 6-mm punch biopsy was used to induce two skin wounds on each side of the vertebral column. The diameters of the wounds were measured from anterior to posterior with a Vernier^{®2} caliper. Standard errors and p-values were subsequently calculated.

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^{®1} Beiersdorf, South Norwalk, CT.

^{®2} Glogan Co, Chicago, IL.

For the topical study, the materials and methods were as follows: adult male ICR mice (35 to 45 gm, 10 animals/group) were anesthetized and shaved on both sides of the back, and two wounds were made on either side of the vertebral columns of each animal. The wounds were induced by a 6-mm punch biopsy. Anterior-to-posterior measurements of the wounds were recorded by a Vernier caliper on days 1, 4, and 7. One group of experimental mice received 25% colorized *A. vera* topically on each wound daily for 6 days. The total application was 200 mg. A second experimental control group received topical Eucerin cream alone. Untreated mice served as a non-treatment control. The standard errors were calculated, and the p-values were obtained.¹²

Results and Discussion

Normal wound healing occurs in three stages: inflammation, proliferation, and remodeling. The wound healing process depends on a given provision of local circulation, as well as the formation and deposition of collagen. A considerable amount of evidence has shown that *A. vera* improves wound and burn healing in animals and humans.¹³ Some studies found that 50% of rats showed improved wound-healing over 7 days.^{8,9} Aloe given subcutaneously showed a dose-response relationship on improvement of wounds. A similar response was recorded in diabetics, whose wounds normally are characterized by poor or delayed healing.¹¹

Current methods used to treat difficult wounds include debridement, irrigation, antibiotics, tissue grafts, proteolytic enzymes, and corticosteroids, which possess major drawbacks and unwanted side effects. *Aloe vera* contains important ingredients necessary for wound healing, such as vitamin C (ascorbic acid), amino acids, vitamin E, and zinc.^{13,14} Ascorbic acid enhances the synthesis of collagen and counterbalances collagen breakdown.^{15,16} Vitamin E is a fat-soluble vitamin found in Aloe that has proven anti-oxidant activity. It may help stabilize lysosomal enzymes needed to synthesize collagen and it prevents free radical damage (cross-linkage) that appears to be detrimental to normal wound healing.^{13,17} It was demonstrated in the authors' laboratory that zinc improved the tensile strength of wounds, thus improving healing.¹⁸ *Aloe vera* penetrates, cleanses, and dilates capillaries going to an injured site, which also improves healing. *Aloe vera* may hasten epithelialization of wounds and reduce dehydration necrosis.

Several factors delay or reduce wound healing,

including bacterial infections, necrotic tissue, interference with blood supply, lymphatic blockage, and diabetes mellitus. These conditions that inhibit wound healing can be combined under the classification, of "tissue anoxia,"¹⁹ or reduction of oxygen in body tissue below physiologic levels. If tissue anoxia could be altered by regional superoxygenation, an increased healing rate could be achieved.

It was found in the authors' laboratory that *A. vera* was effective orally in promoting wound healing. Oral food-grade *A. vera* (100 mg/kg/day) improved wound healing compared to the healing of control animals receiving only water (Table 1, Fig. 1). The decrease in wound diameters for the control animals was 3.5 ± 0.3 mm (51.1%), whereas the Aloe-treated mice had a decrease in wound diameters by as much as 4.8 ± 0.5 mm (62.5%). The difference was significant at $p < 0.05$.

Moreover, the laboratory found that *A. vera* administered topically also served to improve wound healing. Table 2 and Figure 2 depict the effect of topical, 25% colorized *A. vera* in mice over a period of 7 days. The wounds on the mice that received 25% colorized *A. vera* demonstrated a 3.9 ± 0.4 -mm reduction in diameter, as compared to the wound

Table 1. Effect of Oral *Aloe vera* on Wound Healing in Mice Over a 2-Month Period

	DECREASE IN WOUND DIAMETER	
	MM	% DECREASE
CONTROL	3.5 ± 0.3	51.1 ± 4.2
ALOE (100 MG/KG/DAY)	4.8 ± 0.5	62.5 ± 5.4

8 ANIMALS/GROUP *P < 0.05

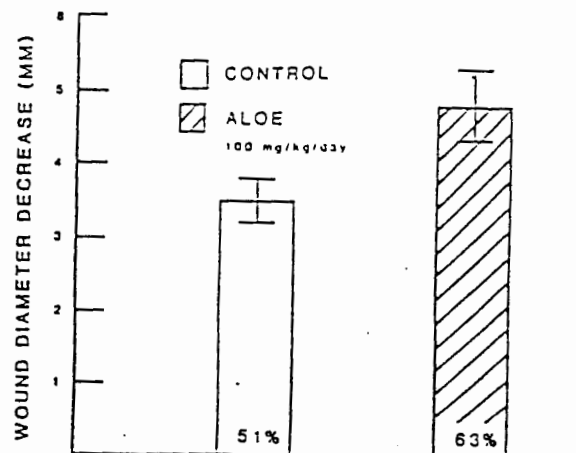


Figure 1. Effect of oral *Aloe vera* on wound healing in mice over a 2-month period.

Table 2. Topical Effect of *Aloe vera* on Wound Healing in Mice Over a 7-Day Period

	DECREASE IN WOUND DIAMETER	
	MM	% DECREASE
CONTROL	2.1±0.4	32.5±4.8
CREAM ALONE	1.9±0.3	25.4±3.4
+25% ALOE	3.9±0.4	50.8±3.6

10 ANIMALS/GROUP

*P<0.001

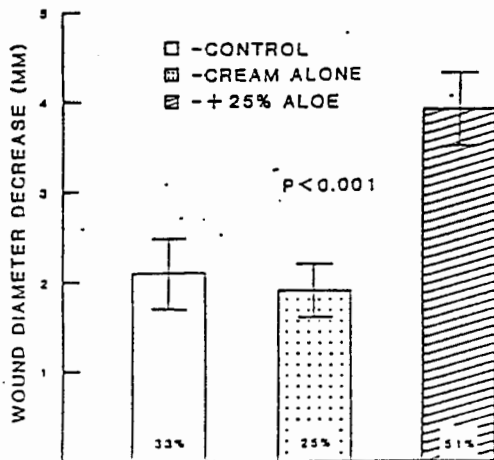


Figure 2. Topical effect of *Aloe vera* on wound healing in mice over a 7-day period.

diameter reduction of 1.9 ± 0.3 mm ($p < 0.001$) for the animals that received cream alone. No significant difference was observed between the untreated wounds and the wounds treated with Eucerin cream alone ($p > 0.5$). Therefore, the percentages of decrease in wound diameters for the nontreatment control group, cream-alone control group, and cream plus 25% *A. vera* group were $32.5\% \pm 4.8\%$, $25.4\% \pm 3.4\%$, and $50.8\% \pm 3.6\%$, respectively. These findings clearly suggest that 25% colorized *A. vera* was a significant factor in the healing of the wounds. Since oxygen is required for the synthesis of collagen by fibroblasts,²⁰ *A. vera* may improve the vascular supply and make more oxygen available to improve collagen formation for wound healing.

It also was observed that the animals not receiving topical Aloe had hard and crusty wounds, which generally appeared unclean. However, the Aloe-treated wounds were clean, with healthy granulation tissue. The presence of Aloe seemed to reduce the amount of dead tissue at the wound site and provide better wound healing. Previous studies by the authors have shown that the wounds of mice

receiving 100 m/kg of colorized *A. vera* had better vascularity and healthier looking granulation tissue. Mice receiving decolorized *A. vera* had an even firmer connective tissue and the appearance of more vascularization.

During the wound-healing process, epithelial cells proliferate, migrate from the edges of the wound, and eventually cover the wound with skin. By lysing collagen with enzymes, the epithelial cells move across the wound and attach to viable tissue. The proliferation and migration of the epithelial cells are dependent on an adequate supply of oxygen. Therefore, the increased presence of oxygen, caused by the *A. vera* improving microcirculation, should greatly improve the wound-healing process.²¹ It is hypothesized that catecholamines (epinephrine and norepinephrine) retard epithelial cell proliferation.²² When a wound is sustained, the supply of catecholamines is interrupted, and the barrier to mitosis is removed. Thus, cells begin to grow and divide. Possibly, some constituents of *A. vera* may either block catecholamines or directly stimulate epithelialization to improve wound healing.

During early wound healing, the vascular and lymphatic systems are of primary importance. Failure or delay of vascular regeneration decreases oxygen transport to the wound, which subsequently depresses the mobilization of excessive fluids from the wound site. The wound becomes edematous, leading to further damage, infection, and eventually cell death. In wound healing, new blood vessels sprout up from platelets or macrophages to keep the wound open-ended. Hypoxia may be a stimulant to revascularization. Aloe may, thus, achieve the following effects to improve tissue healing: an increased blood supply, and, hence, an increased oxygen supply to the wound by blocking vasoconstrictive compounds (inflammation stage); greater migration of epidermal cells over moist tissue caused by factors and enzymes present in *A. vera* (proliferation stage); and extensive reorientation of collagen fibers caused by a stronger cross-linking (remodeling stage).²³ *Aloe vera* also provides for a clean wound free of excess exudate and contamination, making it a favorable treatment for wounds.

The authors' histologic work indicates that *A. vera* stimulates and enhances vascularity around the wound area. As a result, the general appearance of the wound is, in all respects, healthier than the untreated control wound. It may be that *A. vera* increases the supply of oxygen to the wound. This is further evidence to support the theory that an increase in oxygen availability improves wound healing. Furthermore, *A. vera* can topically reduce

inflammation and depress the symptoms of adjuvant arthritis.

Summary

* The authors' studies have shown that *A. vera* improves wound healing when administered either orally or topically. It not only contributes to a decrease in wound diameter, but also leads to better vascularity and healthier granulation tissue. The fact that Aloe is effective orally suggests that it is not broken down by the gastrointestinal tract and is absorbed into the blood. Aloe possibly improves wound healing by increasing the availability of oxygen and by increasing the synthesis and the strength of collagen. *Aloe vera* has become a subject of scientific study concerning inflammation and wound healing. As knowledge about Aloe increases, significant benefits of a practical nature in the management of healing wounds can be expected.

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