Aloe vera

A Natural Approach for Treating Wounds, Edema, and Pain in Diabetes*

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In this research project, the authors extrapolate their earlier findings, and better characterize *Aloe vera* as a therapeutic alternative for physicians to consider. They attempt to evaluate *A. vera* as an effective treatment for some of the most critical manifestations of diabetes.

Diabetes mellitus currently affects nearly 10 million Americans and represents the sixth leading cause of death in the United States.[1] Diabetes mellitus is a complex disease process represented by a variety of clinical findings. These include altered metabolic pathways, microangiopathy, neuron degeneration, and impaired regenerative and host-defense mechanisms.

Diabetic ulcers affecting the lower extremity constitute a major problem for which no specific therapy is available. The manifestations of diabetes mellitus as a systemic disease present a major impact upon podiatric physicians in their care for diabetic patients. In diabetes, an ordinary ulcer can become limb or even life threatening. Annually 14% of all diabetic patients require hospitalization for diabetic foot problems.[2]

Three major factors are related in the development of the diabetic foot. Initially, peripheral neuropathy causes sensory deprivation, weakness of intrinsic muscles of the foot, and joint changes that lead to foot deformities. These deformities lead to altered gait mechanics and abnormal pressure points that result in foot ulcers. Large and small vessels undergo angiopathy that results in ischemia to vital tissues of the feet. Wounds, either traumatic or pressure induced, become infected five times more often in diabetic than in nondiabetic patients.[2]

The wound healing process depends upon adequate local circulation and formation and deposition of collagen, which requires proteins as building blocks. Precise mechanisms of normal wound healing still remain obscure. However, healing of vascularized tissues is impaired in experimental and clinical diabetes. The reasons for this have not been positively identified. Studies by several groups have demonstrated specific factors responsible for delayed wound healing.[3,4] These include poor collagen formation, reduced tensile strength of surgical wounds, diminished inflammatory response for normal phagocytosis of cellular debris, and wound hypoxia associated with microangiopathy. Goldstein and Soelder recently found, "a premature aging of the diabetic fibroblast."[5] The collagen fibers, once secreted, acquire an overabundance of cross-linkages.

In addition to poor wound healing, the diabetic patient experiences peripheral nerve damage. The ischemia of the lower extremity blood vessels decreases circulation with a resulting nerve pathology. Diabetics complain of cramps, pain, and burning sensations of the feet. The mechanism of pain in diabetes remains unknown. Investigators have difficulty explaining the coexistence of spontaneous

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pain with an insensitivity to painful stimuli.[6] The pain may result from hyperactivity of injured small nerve fibers. Most diabetics are so sensitive to sedation that analgesic medications must be reduced as much as 50% of the amount normally used in treatment. In diabetic neuropathy, the peripheral nerves exhibit a loss of sensation. Symptoms include numbness, tingling, and burning. Impaired conduction velocity, loss of Achilles tendon and stretch reflexes, and a decreased sensory perception may cause unperceived injury in diabetics.[7] Hyperglycemia lowers the myo-inositol content of Schwann's cells and axons, resulting in a decreased ATPase activity with a lowered nerve energy. A delayed axon flow with slowed impulse conduction appears to be the result of metabolic rather than structural abnormalities.[8,9]

The wound healing process related to polymorphonuclear lymphocyte's functions, such as phagocytosis, chemotaxis, and intracellular bacteriocidal activity are diminished in diabetic patients.[2] The ability to respond to fluid changes necessary to correct edema and swelling is critical to the normal wound healing process. Osmotic pressure changes and peripheral dehydration observed in diabetics cause additional metabolic and fluid imbalances that directly alter the entire wound healing process. The outpouring of adrenal steroids in response to glucose-starved cells has profound ill effects upon the body's response to edema and swelling observed in injuries. Generally, diabetic wounds display a decrease in the normal swelling and edema that may be necessary for normal wound healing. In addition, edematous conditions once manifested in the diabetic appear to be delayed in returning to a state of normal vascular osmotic pressure. Swelling and edema are part of the diabetic inflammatory picture.[3]

Poor wound healing, diminished ability to respond to fluid changes, and peripheral neuropathy represent some of the most critical manifestations of diabetes. The purpose of this research is to determine the influence of decolorized *A. vera* (removal of anthraquinones) in treating these potential lethal manifestations of diabetes.

Many publications reference the beneficial effects of *A. vera.* Previous research in the authors' laboratory indicates the effectiveness of decolorized *A. vera* in wound healing and mustard-induced edema. Davis, et al[10] demonstrated the remarkable effects of decolorized *A. vera* upon wound healing. *Aloe vera* has anti-inflammatory and antiedemic activity since it contains acetylsalicylic acid, which blocks the synthesis of prostaglandins. Acetylsalicylic acid may be responsible, in part, for some of the analgesic properties demonstrated by *A. vera.* Prostaglandins have a negative effect after physical trauma and have chemotactic activity.[11] Many of the demonstrated biological activities of *A. vera* can help promote wound healing by overcoming prostaglandin's detrimental influences.

Aloe vera contains important ingredients necessary for wound healing, such as ascorbic acid, vitamin E, and zinc.[12] Ascorbic acid enhances the synthesis of collagen and counterbalances collagen breakdown. Ascorbic acid promotes ribosomes to synthesize collagen.[13] Vitamin E is a fat-soluble vitamin found in *A. vera* and has demonstrated potent antioxidant activity. It helps to stabilize lysosomal enzymes and prevents free radical damage that is detrimental to the wound healing process. Engel et al[14] support the role of zinc in new tissue regeneration. They also show that diabetic mice experience decreased wound healing strength, with a histology similar to zinc-deficient mice. *Aloe vera* contains other compounds, including lignins, saponins, minerals, enzymes, and amino acids, all of which may help to accelerate the wound healing process.

The authors have shown that *A. vera* prevents and regresses adjuvant arthritis in experimental animals.[15] It also improves wound healing, reduces mustard-induced edema, and prevents polymorphonuclear leukocytes from migrating into an area of inflammation. However, *A. vera* has no antifibrosis effect in reducing connective tissue around a cotton pellet implanted under the skin.[10] The authors conclude that the anti-inflammatory activity of *A. vera* is not like adrenal steroids.

Because of the positive responses of *A. vera* on wound healing and inflammation, the authors believed it necessary to determine the analgesic effects of decolorized *A. vera* on both normal and diabetic mice. Components within *A. vera* have been effective as pain inhibitors. In addition to acetylsalicylic acid, *A. vera* offers the enzyme bradykinase, an inhibitor of the tissue hormone bradykinin, which is a potent vasodilator and important mediator in pain transmission.[16]

Aloe vera is nonsteroidal. *Aloe vera* possesses antiedemic, anti-inflammatory, and improved wound healing properties. However, these results were only obtained in the physiologically normal animal. As the number of diabetics rise annually, there becomes a need for alternative therapies for the various diabetic manifestations. Thus, the authors believed it necessary to test *A. vera's* activity in the diabetic animal model. It is the purpose of

this research to determine decolorized *A. vera's* effectiveness as an antiedemic, analgesic, and wound healing agent in the presence of diabetes. This would verify that *A. vera* works effectively in an abnormal physiological state.

Materials and Methods

Three studies were conducted to determine the effectiveness of decolorized *A. vera* in a diabetic animal. The diabetic problem areas of wound healing, analgesia, and reduction of edema were the foci of this research.

Prior to each experiment, diabetes was induced in test animals by streptozotocin. The drug was prepared fresh daily with 0.9% saline and mixed just prior to injection to assure the stability of the drug. Each animal received one intraperitoneal injection. The mice were made diabetic with a dose of 200 mg/kg, while the Sprague-Dawley rats received an injection of 65 mg/kg.[17]

Following administration of streptozotocin, a time span of 48 hr was allowed to elapse for the onset of diabetes to occur. Confirmation of the disease was determined by analysis of blood sugar content. A drop of whole blood was taken from each animal's tail and placed on a Chemstrip BG[*1] reagent strip. Serum values of greater than 600 mg/dl were obtained and considered indicative of the onset of diabetes.

At the outset of the wound healing study, a circular piece of skin was removed from the right and left sides of both diabetic and control mice. A 6-mm Baker biopsy punch was used in the procedure. The diameters of the inflicted wounds were measured with a Vernier caliper No. 12 and recorded. As the study progressed, additional measurements of the wound site were taken on day 4 and day 7 to record reductions in diameter of the traumatized area.

Throughout 7 days, treatments of decolorized *A. vera* without anthraquinone were given to three of the diabetic groups (12 animals/group). The treatment regimen consisted of daily subcutaneous injections of the Aloe, in varied doses of 1 mg/kg, 10 mg/kg, and 100 mg/kg. Aqueous solutions of *A. vera* were prepared fresh daily just prior to treatments. Each diabetic test group received one of the designated dose amounts for the duration of the experiment. Control groups (12 animals/group), both diabetic and normal, did not receive the decolorized Aloe. Instead, these groups were given aqueous subcutaneous injections. All wound diameters taken on day 7, the final day of the study, were compared to wound measurements taken on day 1 and day 4 to ascertain if Aloe generated any significant reduction of the traumatized area.

The analgesia study involved the use of a hot plate to provide a stimulus of pain. Pain is a sensation dulled in a diabetic individual. The authors attempted to demonstrate if a diabetic mouse treated with Aloe would show a variable response to pain compared to the response of a diabetic mouse without Aloe. A week prior to the actual use of the hot plate apparatus, one group of diabetic animals (12 animals/group) were treated with a 100 mg/kg subcutaneous injection of decolorized *A. vera*. The injections were administered each day, for a total of 7 days. In the same fashion, another group of mice were also pretreated. This group, however, received saline injections instead of *A. vera* and, thus, were labeled as diabetic controls. Three groups of physiologically normal mice (12 animals/group) were also a part of this study. Two of these groups were given subcutaneous injections of decolorized *A. vera* in doses of 10 mg/kg and 100 mg/kg. A third group received saline injections instead of the Aloe, and these mice served as normal controls.

All mice were placed on a hot plate set at 51°C.[18,19] These animals were observed as to when a sign of pain was first demonstrated. The accepted expression of pain required that the mice either lick their front paws, shake their hind feet, or jump off the hot plate entirely. The elapsed time (seconds) for one of these signs of pain was recorded for each individual mouse. All data was compiled for both diabetic and normal animals to determine if Aloe treatments caused an effect in the time for a diabetic mouse to feel a painful stimulus.

In the edema study, decolorized *A. vera* was used in an attempt to reduce an induced edema in a diabetic rat. Sprague-Dawley rats were selected instead of ICR mice in this study because rats respond better to irritants. This sensitivity to irritants allows edema and inflammation to be easily observed.

A day prior to the induction of edema, two diabetic test groups (12 animals/group) received subcutaneous injections of decolorized *A. vera* in doses of 10 mg/kg and 100 mg/kg, respectively. The four remaining test groups received only subcutaneous saline injections. Two of the four groups were diabetic animals and two were physiologically normal.

Edema was induced by 2% mustard injection (0.1 ml) into the plantar surface of the rat's hind paw. Edema induction in this fashion is a common laboratory procedure.[10] The mustard was thoroughly

[*1] Boehringer-Manheim Diagnostics, Inc, Indianapolis, IN.

homogenized into a suspension prior to injection. Four groups of rats received the injection, three diabetic and one normal. Control groups were given plantar injections of saline to produce edema. Also, each rat received a subcutaneous injection of Aloe or saline, exactly as the day before.

Volumetric measurements of the edematous hind paws were taken moments after the mustard or saline injection. The volumes were recorded with a mercury plethysmograph. The device involves a plastic cup filled with mercury into which the rat hind paw is dipped up to the anatomical hairline. The volume displaced by the inflammation is recorded by the device in units of edema. Readings were taken immediately after the paw injection and again 6 hr later. The difference between the initial volume and the 6-hr volume were recorded as change in edema.

In each study conducted, the body weights were taken of each animal and recorded in grams. Standard errors for all data collected were determined by using the formula: $SE = \sqrt{\sum d^2/n\ (n-1)}$, and the Student's t-test was calculated for significant differences.[20]

Results and Discussion

Aloe vera has been used for many years as a wound healing and anti-inflammatory agent. Collins and Collins[21] reported beneficial effects when freshly split leaves of *A. vera* were applied locally to x-ray burns. Although ongoing research with *A. vera* is imperative to better characterize its potential therapeutic effects, the question arises as to whether *A. vera* is effective under abnormal physiological states such as diabetes.

Diabetic Model. Animals with streptozotocin-induced diabetes displayed a generalized decrease in wound healing, an abnormal response to painful stimuli, and poor adaptations to mustard-induced edema. These responses are consistent with the diabetic disease state displayed by known diabetic animals. Male ICR mice and adult male Sprague-Dawley rats were confirmed to be diabetic 48 hr following intraperitoneal streptozotocin injections. By analyzing whole blood samples, the authors consistently obtained serum glucose levels >800 mg/dl in mice and >600 mg/dl in rats. Diabetic animals consumed considerably increased amounts of standard animal chow and excessive quantities of water when compared with normal controls. The cages were saturated with a distinct acetone-like smelling urine. Additionally, diabetic mice underwent a mean body weight decrease of 3.1 g as compared to a 2.4 g body weight increase in normal mice throughout the wound healing experiment. While diabetic mice displayed a 13.1 g decrease in body weight, normal mice had an increase in body weight of 4.12 g throughout the analgesia study. This represents a significant weight loss demonstrated by diabetic animals, most probably indicative of decreased insulin-dependent anabolic pathways.

The diabetic animals also displayed extreme lethargy, a generalized weakness, and a random thinning of body hair as compared to normal animals. The precise mechanisms of polyuria, polydipsia, and polyphagia, with associated body weight reductions, represent a complex group of biochemical abnormalities, which are still not fully understood. Their association with diabetes mellitus, however, is well documented.[22]

Wound Healing. In the authors' first study with diabetic mice, a general pattern of wound healing in the groups treated with varied doses of decolorized *A. vera* was observed. As the doses of *A. vera* were increased on a milligram per killogram basis, a proportionate increase in percentage of wound reduction was observed, up to the maximum 100 mg/kg dose. Normal control mice showed an 18.40% ± 3.57% wound reduction on day 4, while the untreated diabetic mice showed a similar rate of healing of 20.58% ± 3.12% wound reduction at the same time in the study ($p > 0.5$). This showed no significant difference on day 4 between untreated, normal, and diabetic mice. However, on day 7, normal mice progressed from day 1 to a 35.00% ± 4.94% wound reduction resulting in a marked 16.6% increase in wound reduction from day 4, compared to only an 8.16% increase in wound reduction in diabetic control mice. (The percentage value changes from day 4 to day 7). Untreated diabetic mice showed a total percentage of wound reduction of only 28.42% ± 3.45% from day 1 to day 7. These preliminary results possibly suggest an altered secondary response to wound healing in the streptozotocin-treated animal. These secondary responses represent collagen synthesis and ability to adapt and dissipate associated edema and inflammation necessary for normal healing of wounds.[23]

The three diabetic test groups received daily doses of 1 mg/kg, 10 mg/kg, and 100 mg/kg of decolorized *A. vera* for 6 days. The diabetic animals treated with *A. vera* showed significantly increased rates of healing on both day 4 and day 7 measurements. The wound healing response based on the varied doses of decolorized *A. vera* administered on a daily milligram/killogram regimen exhibited a

classic dose response curve as demonstrated by Figure 1. As doses of *A. vera* were increased, the percentage of wound reduction values increased from 32.30% ± 3.28% (1 mg/kg) to 38.30% ± 2.40% (10 mg/kg) to 42.90% ± 3.16% (100 mg/kg) on day 4. These results are significant in comparison to the normal control group ($p < 0.001$) and, more importantly, in comparison with the untreated diabetic control group ($p < 0.001$). The animals receiving a 100 mg/kg decolorized *A. vera* showed a percentage of wound reduction of 42.90% ± 3.16% on day 4 while the diabetic control mice had a percentage of wound reduction of only 28.42% ± 3.45% on day 7. These results exhibited by the diabetic control group were significantly decreased even after 7 days, as compared with only 3 days of treatment with 10 mg/kg and 100 mg/kg decolorized *A. vera*. While the test group receiving 1 mg/

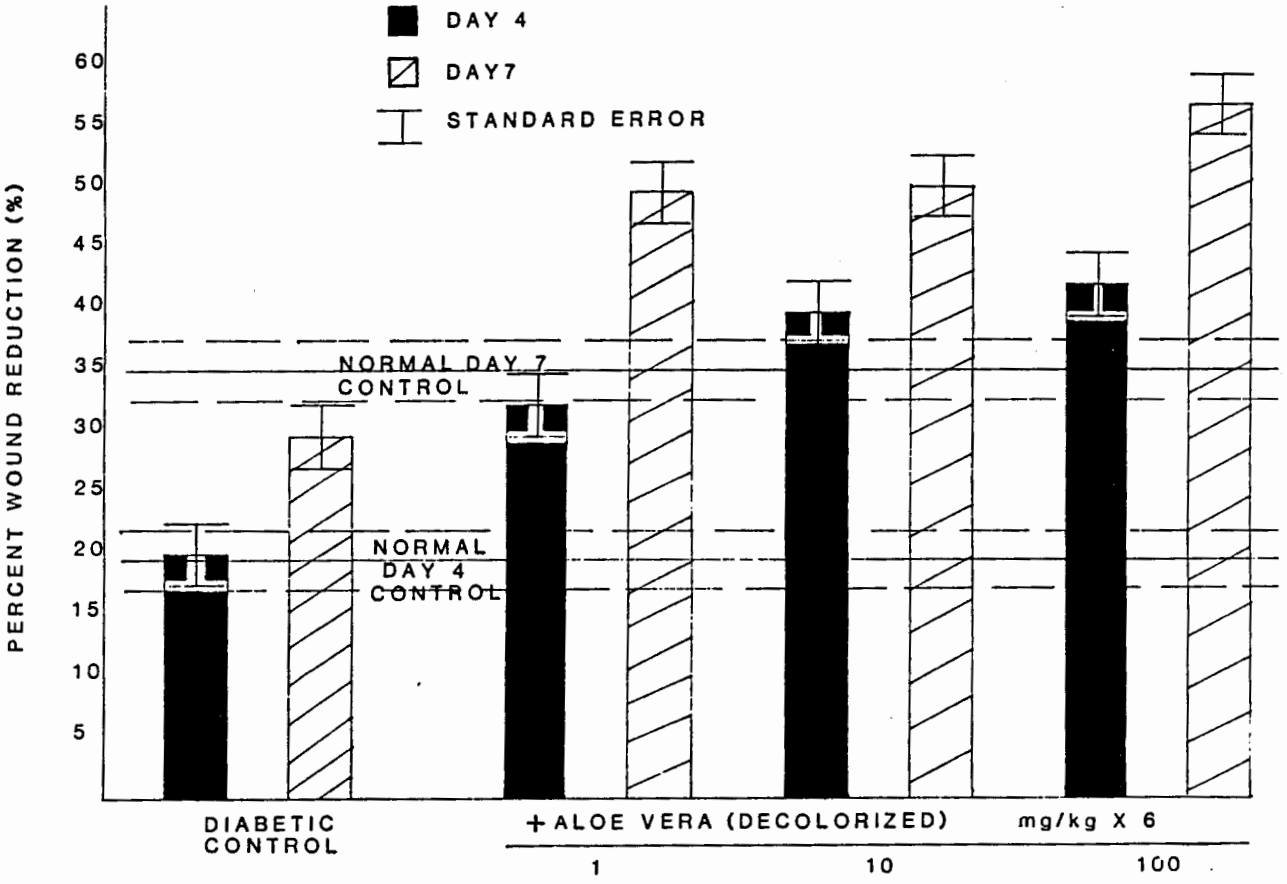

Figure 1. Effect of decolorized *A. vera* on wound healing in diabetic mice after 7 days.

Table 1. Effects of Decolorized *A. vera* on Wound Healing in Diabetic Mice.

Treatment	Number of Mice	Body Weight Change (gm)	Wound Reduction (%)	
			Day 4[a]	Day 7
Normal control[b]	10	+2.40	18.40 ± 3.57	35.00 ± 4.94
Diabetic control[b]	12	−4.40	20.58 ± 3.12	28.42 ± 3.45
A. vera (1 mg/kg)	12	−3.22	32.30 ± 3.28	47.08 ± 3.78
A. vera (10 mg/kg)	12	−1.55	38.30 ± 2.40	50.00 ± 2.61
A. vera (100 mg/kg)	12	−3.32	42.90 ± 3.16	56.58 ± 3.50

[a] ±, standard error.
[b] Aqueous injections.

kg decolorized *A. vera* showed significant results of 47.08% ± 3.78% wound reduction after 7 days *versus* the diabetic control.

On day 7, the diabetic treatment groups receiving 1 mg/kg, 10 mg/kg, and 100 mg/kg all indicated profound wound reduction values of 47.08% ± 3.78%, 50.00% ± 2.61%, and 56.58% ± 3.50%, respectively ($p < 0.001$). Table 1 shows that the diabetic group treated with 100 mg/kg decolorized *A. vera* showed a doubling in wound healing after 7 days with a percentage of wound reduction of 56.58% ± 3.50% compared to 28.42% ± 3.45% ($p < 0.02$) in diabetic controls. Accelerated rates of wound healing over normal controls were also shown by the treatment groups.

The data suggest that the lower dosing regimens of 1 mg/kg and 10 mg/kg showed their most outstanding percentage of wound reduction values after 6 days of treatment, while the treatment group receiving 100 mg/kg showed significant wound healing effects after only 3 days of treatment compared to control groups. These results may be related to the fact that *A. vera* is primarily water soluble, and, at lower doses, it takes additional time for therapeutic levels to be achieved. Additionally, *A. vera's* pharmacokinetic profile suggests the use of higher doses to achieve maximum beneficial effects with a subsequent faster onset of action. This proposal is only a speculation based on the fact that water soluble drugs are usually excreted from the body at increased rates compared to lipid soluble agents that tend to accumulate in adipose tissues.[24]

Analgesia and Pain. The diabetic syndrome progressively affects all areas of the nervous system. Diabetic patients may initially complain of burning and painful feet, but their inability to respond to painful stimuli becomes a life-threatening long-term complication.[5] Diabetic peripheral neuropathy is a compromising factor that must be considered when administering any type of medication or performing a surgical procedure. Currently, available analgesic medications provide effective pain relief, but cause side effects that are magnified many times in the diabetic patient. *Aloe vera's* constituents, which include acetylsalicylic acid and bradykinase, provide a basis for studying the analgesic activity of *A. vera* in both normal and diabetic animals.[10,16]

The pain response (seconds) in diabetic mice seems to be higher than normal (Table 2 and Figure 2). A value of 6.3 ± 0.5 sec was recorded for normal control mice while the untreated diabetic control group had a pain response time of 8.3 ± 0.8 sec on day 3 of our study ($p < 0.05$). On day 7, the pain reaction time of normal control mice was 5.5 ± 0.5 sec, consistent with day 3 values. In contrast, the untreated diabetic mice progressed to a pain response time of 10.7 ± 1.2 sec ($p < 0.001$). The day 7 value for the diabetic group represents nearly a 100% increase in pain response time over normal controls, thereby supporting the presence of peripheral neuropathy in streptozotocin-treated animals. Subcutaneous administration of 10 mg/kg decolorized *A. vera* increased the pain response in normal mice from 6.3 ± 0.5 to 10.6 ± 1.1 sec on day 3 ($p < 0.02$). A further increase was observed at the 100 mg/kg dose with a pain response time of 14.3 ± 0.5 seconds ($p < 0.01$). Administration of 10 mg/kg and 100 mg/kg *A. vera* for 7 days demonstrated pain response values of 11.9 ± 0.9 sec and 15.7 ± 1.2 sec, respectively ($p < 0.001$). The day 7 pain response values were again increased over normal controls but were similar to day 3 values.

One group of streptozotocin-treated mice received a dose of 100 mg/kg for 7 days, with usual day 3 and day 7 pain reaction times being recorded. On day 3, diabetic mice receiving 100 mg/kg showed a slightly increased reaction time to painful stimuli, progressing from 8.3 ± 0.8 sec to 10.7 ± 0.6 sec ($p < 0.05$). This demonstrates only a 22.4% increase in pain response as compared to untreated (control) diabetic mice. Day 7 values again only represented small increases in pain reaction times as they progressed from 10.7 ± 0.6 to 13.7 ± 0.5 sec (100 mg/kg Aloe), demonstrating a 21.8% differentiation ($p < 0.05$).

Although analgesia achieved in normal mice receiving varied doses of *A. vera* was significantly increased as compared to diabetic treatment groups, some pain relief was observed in this group. The analgesic activity of decolorized *A. vera* shows a dose response relationship in normal animals. Decolorized *A. vera* conclusively showed an increased potency in normal mice when compared to similarly treated diabetic mice. However, higher doses of *A. vera* might indicate a dose response relationship in streptozotocin-treated animals as well. Thus, Aloe activity appears to be different from most analgesic medications in that the dose must be increased in diabetic animals. Further research is necessary to determine whether Aloe treatment helps the impaired impulse conduction, sensory perception, and reflex action in diabetes. However, this study proves that *A. vera* does inhibit pain, even in diabetes.

Edema. Evidence suggests that diabetes causes a severe metabolic and fluid change that directly alters the entire wound healing process.[25] Previous experiments by Davis et al[10] has provided evidence

Table 2. Analgesic Effect of Decolorized *A. vera* in Normal and Diabetic Mice

Treatment	Number of Mice	Body Weight Change (gm)	Pain Response (sec)	
			3 Days[a]	7 Days
Normal control[b]	12	+4.1	6.3 ± 0.5	5.5 ± 0.5
A. vera (10 mg/kg × 6)	12	+1.5	10.6 ± 1.1	11.9 ± 0.9
A. vera (100 mg/kg × 6)	12	+1.0	14.3 ± 0.5	15.7 ± 1.2
Diabetic control[b]	10	−10.3	8.3 ± 0.8	10.7 ± 1.2
A. vera (100 mg/kg × 6)	12	−8.8	10.7 ± 0.6	13.7 ± 0.5

[a] ±Standard error.
[b] Aqueous injections.

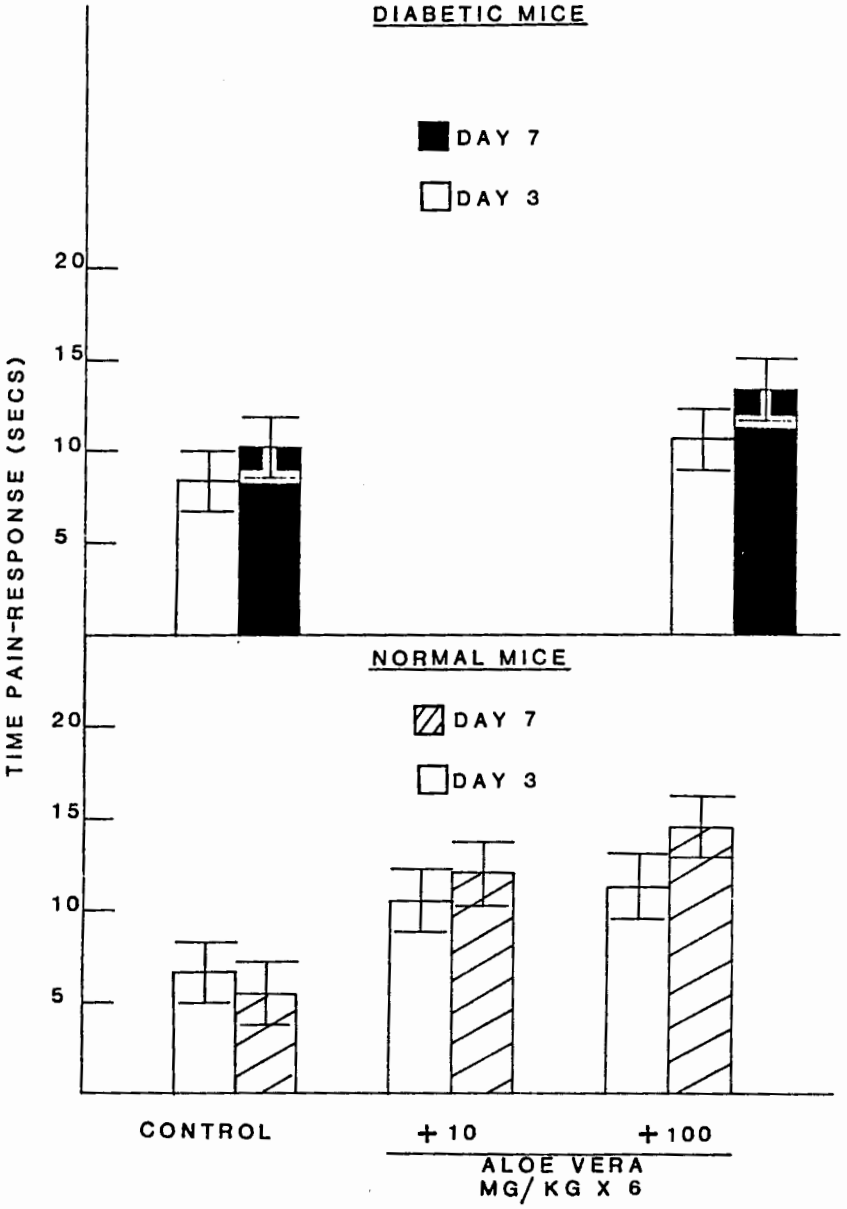

Figure 2. Analgesic effect of decolorized *A. vera* in normal and diabetic mice.

that decolorized *A. vera* is effective in reducing edema and inflammation in the nondiabetic rat. *Aloe vera* provides the substances alotocin A and magnesium lactate, which may possess anti-inflammatory qualities. In addition, *A. vera* offers the enzyme bradykinase, a potent inhibitor of the tissue hormone bradykinin and a potent vasodilator.[16] These provide the basis for studying *A. vera* as an antiedematous agent.

Table 3. Effect of Decolorized *A. vera* on Mustard-Induced Edema in the Diabetic Rat

Treatment	Number of Rats	Edema Volume[a]	Inhibition (%)
Normal control[b]	12	0.12 ± 0.24	
Normal + 2% mustard	12	4.60 ± 0.55	
Diabetic control	12	0.78 ± 0.23	
Diabetic + 2% mustard[b]	12	2.15 ± 0.37	
Diabetic + 2% mustard, + *A. vera*[c] (10 mg/kg)	12	0.86 ± 0.35	60
Diabetic + 2% mustard, + *A. vera*[c] (100 mg/kg)	12	0.44 ± 0.43	80

[a] ±, Standard error.
[b] Saline injection.
[c] Subcutaneous injection × 6.

When injected with saline, normal control rats showed an inflammatory response of 0.12 ± 0.24 units of edema, while the diabetic control rats showed a response of 0.78 ± 0.23 units. Animals having diabetes tend to have an elevated foot volume compared to normal controls, suggesting a decreased ability of diabetic animals to compensate for fluid imbalances. Injections of an irritant of 2% mustard into both normal and diabetics once again demonstrates a decreased inflammatory response in the diabetic state. With equal amounts of 2% mustard injected, the normal rats showed an edema of 4.60 ± 0.55 units, while the diabetics only showed an edema of 2.15 ± 0.37 ($p < 0.02$). These results suggest that there is a decreased inflammatory response in hyperglycemic rats as opposed to normal rats (Table 3 and Figure 3).

Previous work by Davis et al,[10] on normal test

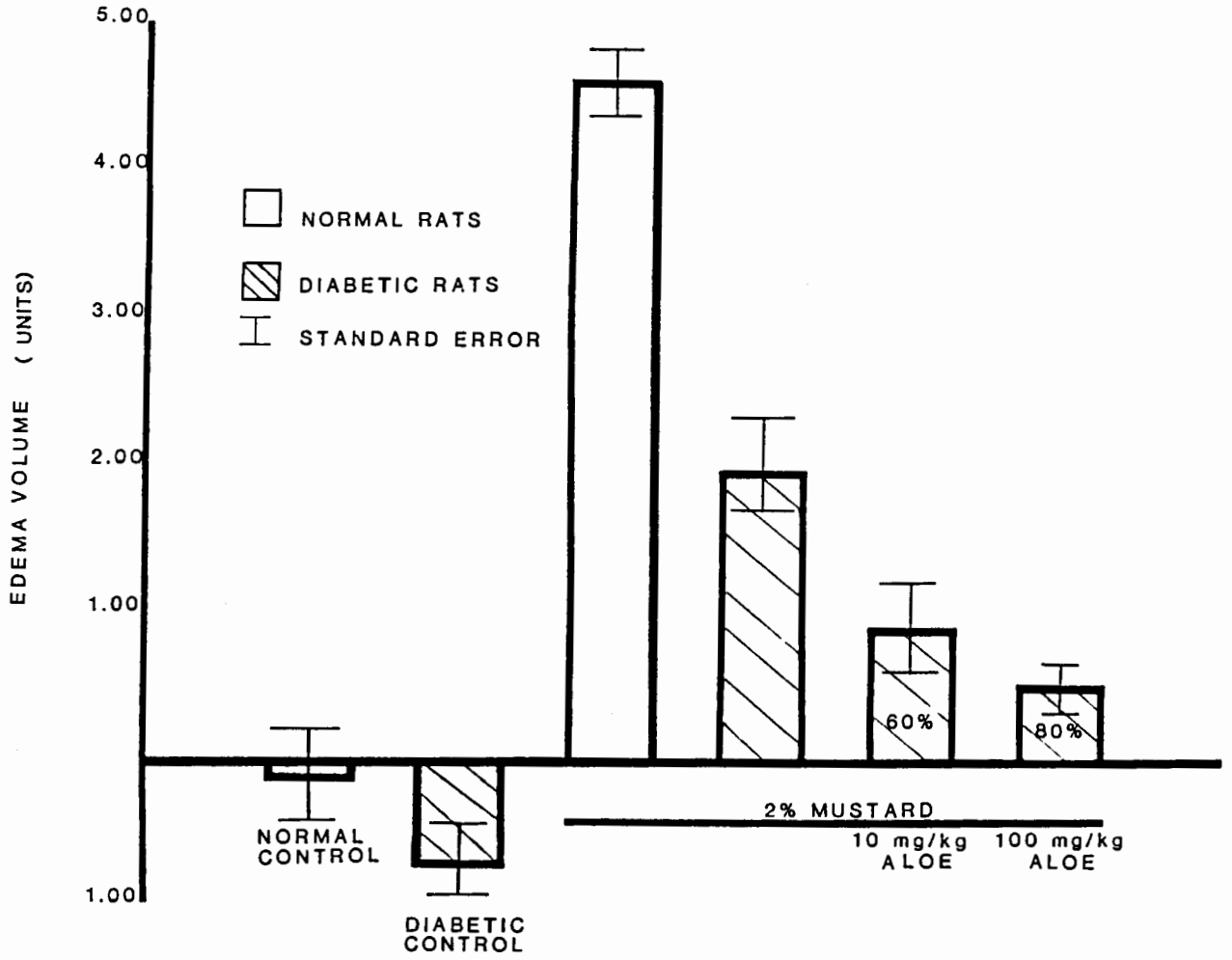

Figure 3. Inhibition of edema in the diabetic rat by decolorized *A. vera*.

subjects verified *A. vera's* antiedemic qualities. Therefore, in this experiment, *A. vera* was only administered to diabetic animals. It appears that *A. vera* reduced edema in diabetic animals in a dose response fashion similar to normals. Treatment of the diabetic rat with a 10 mg/kg of decolorized *A. vera* showed a 60% decrease in edema when compared to the mustard-treated diabetic controls. When the dose of *A. vera* was increased to 100 mg/kg, edema was reduced to 0.44% ± 0.43% ($p < 0.05$). This represents an 80% reduction in edema when compared to the mustard-treated diabetic control. The antiedemic and possibly the anti-inflammatory properties of *A. vera* have been demonstrated; however, the complex mechanisms of its actions are still somewhat unclear.

Summary

The diabetic patient suffers from a diminished wound healing mechanism, an insensitivity to pain perception, and altered fluid dynamics, resulting in a prolonged edema response. This study dealt with *A. vera* (decolorized) as a mode of treatment to alleviate some of the consequences associated with diabetes. The results in each area tested were favorable. As an aid in promoting diabetic wound healing, test groups treated with *A. vera* displayed nearly a 100% increase in wound size reduction as compared to their untreated counterparts.

In the area of analgesia, diabetic mice receiving *A. vera* were able to tolerate a painful stimulus a full 3 sec longer than suitable controls without the total obliteration of responsiveness to stimuli. Additionally, physiologically normal mice treated with Aloe represented nearly 3 times the tolerance to painful stimuli as compared to untreated animals.

As an antiedemic agent, Aloe-treated animals experience a five-fold reduction in the edema response as compared to untreated diabetic groups. *Aloe vera* has been proven to be an effective agent in the treatment of wounds, edema, and pain associated with diabetes.

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