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Aloe Vera And Gibberellin Anti-Inflammatory Activity In Diabetes

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Abstract

Aloe vera inhibits inflammation and adjuvant-induced arthritis. The authors' laboratory has shown that Aloe vera improves wound healing, which suggests that it does not act like an adrenal steroid. Diabetic animals were used in this study because of their poor wound healing and anti-inflammatory capabilities. The anti-inflammatory activity of Aloe vera and gibberellin was measured in streptozotocin-induced diabetic mice by measuring the inhibition of polymorphonuclear leukocyte infiltration into a site of gelatin-induced inflammation over a dose range of 2 to 100 mg/kg. Both Aloe and gibberellin similarly inhibited inflammation in a dose-response manner. These data tend to suggest that gibberellin or a gibberellin-like substance is an active anti-inflammatory component in Aloe vera.

Aloe Vera inhibits inflammation and adjuvant-induced arthritis.

Aloe vera inhibits inflammation and adjuvant-induced arthritis. The authors' laboratory has demonstrated that Aloe vera improves wound healing in a dose-response fashion, reduces edema and pain, but does not decrease the granuloma tissue around a foreign substance under the skin.¹⁻³ This suggests that Aloe acts on an acute anti-inflammatory basis and does not act like a steroid.

Aloe vera is a clear mucilaginous gel within the leaf of the spiny Aloe barbadensis plant. Investigation of the chemical composition of the gel indicates that it includes minerals, vitamins, monosaccharides, polysaccharides, and enzymes. Other ingredients believed to be responsible for Aloe's healing powers are lignins, which, with cellulose, penetrate human skin; saponins, with antiseptic capabilities; and anthraquinones, which are believed to be a pain-related component.⁴ The authors focus on the carbohydrate



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fraction of Aloe vera. Based on evidence in the literature and the authors' studies, the authors wondered if a main, active component in Aloe is glycoside. Corbin et al⁵ found that indole acetic acid, a plant auxin, appears to have anti-inflammatory properties.

Diabetic animals were used in the study because of their poor healing and anti-inflammatory capabilities. Biochemical alterations in the microvasculature of diabetics make them vulnerable to injections and prolong the healing response.

The authors determine if gibberellin, a glycolic and growth hormone found in plants, could account for some of the anti-inflammatory activity Aloe vera possesses. The antiphlogistic activity of colorized (with anthraquinones) Aloe vera and gibberellin in streptozotocin-induced diabetic mice at 2, 20, and 100 mg/kg subcutaneously was determined by measuring the inhibition of polymorphonuclear leukocyte infiltration into a 2% gelatin-induced inflammation. The reduction of polymorphonuclear leukocyte cells at the site of inflammation is a standard technique to measure acute inflammatory activity.

Materials And Methods

Adult male ICR mice (20 to 30 g, eight animals group) were injected intraperitoneally with 200 mg/kg streptozotocin to induce diabetes. The streptozotocin (powder basis) was mixed into a solution with 0.9% saline. The control animals received injections. Five days later, two animals from each group, with the exception of the control groups, were randomly chosen to test for diabetes. Blood sugars were determined to certify that the animals were diabetic. Under ether anesthesia, all mice were shaven on one side. A marking pencil was used to outline an area the size of a nickel. Each animal was injected subcutaneously within this area with 0.2 cc of 2% gelatin (0.4% NaCl, 1% ethanol) solution to form a bleb. This was immediately followed by a second subcutaneous injection of 2, 20, and 100 mg/kg colorized Aloe vera or gibberellic acid A. The Aloe vera and gibberellin were injected into an area outside the designated circle. A nondiabetic and a diabetic control group each received saline injections in place of the gelatin irritant, as well as the Aloe vera or gibberellin. A third nondiabetic control group received the gelatin injection and saline in place of the Aloe vera or gibberellin.

The animals were killed 3 hr. following the second injection. Incisions were made along the indicated circumscribed area so that subdermal tissue could be removed and stained.

Polymorphonuclear leukocyte infiltration in the circumscribed inflamed area was determined by staining the subdermal tissue with Wright stain. Three separate sections of each excised tissue were randomly chosen for viewing under a light microscope, high



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power. Mean and standard errors were calculated for polymorphonuclear leukocyte cell counts. The Student t-test was used to determine p values.⁶

Table 1
Comparison of Aloe vera & Gibberellin on Polymorphonuclear Leukocyte Infiltration in Diabetic Mice^a

Treatment	PMN Count Number/HPF ^b	p Value	Reduction (%)
Saline control	17.4 +/- 0.6		
Saline diabetic	10.8 +/- 0.5	<0.001	
2% Gelatin	28.4 +/- 0.8	<0.001	
+ Aloe vera 2 mg/kg	28.2 +/- 0.7	>0.5	0.7
+ Aloe vera 20 mg/kg	17.0 +/- 0.6	<0.001	40.1
+ Aloe vera 100 mg/kg	9.1 +/- 0.5	<0.001	68.0
Saline control	18.1 +/- 0.7		
Saline diabetic	9.5 +/- 0.6	<0.001	
2% Gelatin	28.3 +/- 0.5	<0.001	
+ Gibberellin 2 mg/kg	28.8 +/- 0.8	>0.5	0.0
+ Gibberellin 20 mg/kg	21.2 +/- 0.8	<0.001	25.1
+ Gibberellin 100 mg/kg	11.3 +/- 0.7	<0.001	60.1

^aEight animals/group.

^bPMN, polymorphonuclear; HPF, high power field.

Results And Discussion

Gibberellin may be an active anti-inflammatory ingredient in Aloe vera. Two percent gelatin caused an increase in polymorphonuclear leukocyte infiltration in inflammation. This response was reduced by Aloe vera in a dose-response fashion to 68% and as much as 60.1% with the maximum dose of gibberellin in diabetic animals. These responses were significant at $p < 0.001$ (Table 1). By substituting gibberellin, a growth hormone glycoside, for Aloe vera, virtually identical results were obtained. Gelatin-treated diabetic mice receiving 2 mg/kg of gibberellin had a polymorphonuclear leukocyte count of 28.8 +/- 0.8 ($p > 0.05$) neutrophils, showing no significant effect at this dosage relative to the diabetic 2% gelatin control group that received no gibberellin injection. The experimental animals receiving 20 mg/kg of gibberellin showed a significant decrease in polymorphonuclear leukocyte infiltration. The neutrophil cell count was 21.2 +/- 0.8 ($p < 0.001$), which is a 25.1% reduction in neutrophil infiltration, while Aloe vera showed



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a similar count of 17.0 +/- 0.6 ($p < 0.001$) at the same dosage. At 100 mg/kg, Aloe vera reduced the polymorphonuclear leukocyte cell count 68% below the 2% gelatin control, showing a mean value of 9.1 +/- 0.5 ($p < 0.001$) neutrophils/high power field. At this same dose, gibberellin reduced the count 60.1%, with a mean count of 11.3 +/- 0.7 ($p < 0.001$). These data show that Aloe vera and gibberellin are parallel in activity and possibly could suggest that the activity of each has similar origin.

The growth of root tips has demonstrated the dependence of the root on the shoot for carbohydrates, vitamins, and enzymes. The chemical determinant for growth and differentiation depends on plant growth hormones called auxins. These are essential for growth. Gibberellin was first isolated from mass cultures of fungus by Japanese investigators⁷ who observed an increase in elongation growth in dwarfed plants. This hormone is universally distributed in taller plants. Gibberellic acid (GA_3) tends to be the most active of all the chemically identified gibberellins.^{8,9} Key¹⁰ indicates that the auxin-like substance, gibberellic acid, is a significant mediator in plant tissue growth because it enhances cell enlargement. The ability of gibberellic acid to enhance the rate of cell elongation is dependent on new RNA and protein synthesis.^{11,12} These data would tend to suggest a wound-healing property. Since gibberellin stimulates protein synthesis as well as the DNA-RNA system in cells, it may have a value in healing wounds as it reduces inflammation.¹³⁻¹⁶

Infiltration of polymorphonuclear leukocyte cells into the wound area is an important cellular response to injury. Polymorphonuclear leukocyte activity might be a chemotactic response to hydrolysis products from the protein of the injured tissues.¹⁷ These cells first marginate to the walls of the microcirculation in the injured area, then emigrate between the endothelial cells of the vessel wall, and, finally, migrate from the vessel through the ground substance to the site of the injury. Phagocytes, found in acutely traumatized tissue, are responsible for release of tissue-damaging lysosomal enzymes.¹⁸ The auxins present in certain plant extracts are probably related to steroid-like compounds. This would account for the anti-inflammatory effect gibberellin has on gelatin-induced edema. Unlike steroids, which are antianabolic, gibberellins increase protein synthesis.¹⁹ They would, therefore tend to heal wounds. Microsomes from auxin-treated tissue incorporate amino acid into protein at a higher rate than untreated tissue.

Aloe vera and gibberellin have similar anti-inflammatory activity in diabetic animals. The activity of gibberellin-like substances possibly plays a major role in the wound healing and anti-inflammatory activity of Aloe vera. Unlike steroids, Aloe vera and gibberellin inhibit inflammation but do not retard wound healing. This study helps redefine inflammation as it relates to wound healing.