

Biological Activity of Aloe Vera

An examination of the biological activity of steroids and synthetics revealed that they are both active yet toxic. In the search for natural substances, such as vitamins and amino acids, that have biological activity, we serendipitously discovered that Aloe Vera had many biologically active compounds that had anti-inflammatory, wound healing, analgesic and anti-arthritic activity.

Ingredients in Aloe Vera Gel

Mannose and glucose are the most significant sugars found in the Aloe Vera gel, and they can be used to assay the activity of Aloe Vera. The gel contains important sterols which can have anti-inflammatory activity. Amino acids such as tryptophane and phenylalanine reduce inflammation. Studies have shown that vitamin C & B complex can maintain adrenalectomized animals, and that minerals such as zinc are very important in wound healing. Anthraquinones have good anti-inflammatory activity, but their activity is usually obtained by working through an inflammation pattern. Salicylic acid and aspirin are also highly biologically active.

The Aloe Leaf

The rind is the manufacturing plant for carbohydrates, fats, proteins and vitamins. These Aloe Vera constituents are transported throughout the leaf by the phloem, and other materials are brought up from the roots by way of the xylem. These two mechanisms aid in transporting the Aloe Vera under the influence of the wind. Mucilage was

once thought to take part in this transport process, but researchers now feel that it acts as a container for the gel fillet or the storage of Aloe Vera.

If one takes the liquid mucilage and freeze dries it, one finds that the mucilage looks and acts like a bandage. It has occlusive »coverlike« properties as well as biological activity. The topical anti-inflammatory activity of mucilage at the 1% dosage is 3.8% in decreasing edema, whereas at the 5% dose level, it is 33.7%.

A consideration of the sol-gel transformation becomes very evident as an animal bites the Aloe leaf. The sol which is a colloidal system under the influence of many factors can be converted into a colloidal gel. If this system could be transported to the human wound, one would have an excellent topical wound healing treatment.

In the Aloe leaf synthesis, carbon dioxide and water are converted to an »active carbon« that is used to make carbohydrates, lipids, protein and vitamins. The Aloe Vera cell, visible at a magnification of about 40,000, is surrounded by a cell wall, has a large nucleus and two cell membranes the cytoplasm of which manufacturers mucopolysaccharide. The mucopolysaccharide is stored within the lumen of the cell.

Biological Activity

Aloe Vera could prevent adjuvant arthritis 72%, and cause a regression of 22 to 26% at a dosage of 150 mg/kg per day. In another experiment, we proved that Aloe Vera was effective in reducing inflammation over a broad spectrum of irritants in experimental animals. The percent inhibition by Aloe Vera ranged from 76.9% against gelatin to 22.7% against dextran. In evaluating vitamin C's influence on localized adjuvant arthritis, we found that it could reduce

edema 80%, inhibit PMN infiltration, and decrease the pain induced by the adjuvant arthritis. However, there was no influence on the paw temperature. Anthranilic acid, a metabolite of tryptophane, could inhibit PMN infiltration as was evident in the peritoneal fluid of adjuvant arthritic rats.

The topical treatment of adjuvant arthritis with combined Aloe, RNA and vitamin C produced a 25.2% prevention inhibition and 45.1% regression inhibition at a dosage of 1.5% concentration of each.

Phenylalanine synergized with hydrocortisone acetate in reducing localized edema. We also obtained a good vehicle response on anti-inflammatory activity using Aloe Vera for hydrocortisone acetate. The combination of Aloe Vera and hydrocortisone was definitely additive in nature. We observed the vehicle effect of Aloe Vera for hydrocortisone acetate on inhibiting the infiltration of PMN's as well as the topical application of the steroid.

Aloe Vera is also a good vehicle for vitamin C and other important agents. Tryptophane and phenylalanine had good local anti-inflammatory activity in inhibiting PMN infiltration. In fact, the inhibition effect approaches that of the steroid. While phenylalanine was able to inhibit granuloma tissue weight in adrenalectomized animals synergistically with cortisone, tryptophane did not synergize with the steroid.

When we placed a cotton pellet under the skin of a rat we found that Aloe Vera was unable to inhibit the growth of granuloma tissue. Aloe Vera had no antifibrosis effect over a dosage range of 50 to 400 mg/kg administered for 12 days.

While Aloe Vera had no chronic anti-inflammatory influence, we wondered if it could inhibit the detrimental effects of the steroid on wound healing. Aloe Vera could inhibit edema in diabetic animals in a dose-response fashion up to 80% over a dosage range from 10 to 100 mg/kg.

A similar response was obtained in diabetic animals by Aloe Vera in inhibiting

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Aloe Vera

the infiltration of PMN's. Aloe Vera definitely can block the vasoactive substances responsible for inflammation, can constrict small blood vessels, can block PMN filtration, as well as inhibit production of oxygen radicals.

We evaluated the influence of mucilage in Aloe Vera on skin penetration of 5% trypan blue over six hours. We found that Aloe Vera at a 10% dose could increase the trypan blue penetration 24%. However, 10% mucilage was occlusive, that is it acts as a cover for wounds and blocks the penetration of trypan blue. A combination of Aloe Vera and mucilage revealed that the mucilage could block the penetrating ability of Aloe Vera. Mucilage acts as a cover for wounds but does not increase the penetrability through the skin.

Wound Healing and the Aloe Vera Molecule

The effect of Aloe Vera on skin fibroblasts was measured by Danhof in 1983 (Danhof 1987). He found that tritiated thymidine uptake by skin fibroblasts was increased in a dose-response fashion by Aloe Vera. He also found that the anthraquinones in the yellow sap killed the fibroblasts. This »killing of fibroblasts« has potential as an anti-inflammatory assay if Aloe Vera was used to protect against this »killing effect.« Years ago we felt that wounds should not be covered. However, we found that dry wounds drop, and prevent the

migration of cells and the influence of wound healing growth factors. With Aloe Vera acting as a cover, the wound remains moist, and there is an excellent migration of epidermal and fibroblast cells. So, there is an increase in covered wound healing over that of uncovered wounds. Aloe Vera increased the wound healing over a dosage range of 1 to 100 mg/kg in a dose-response fashion.

This was the first study that demonstrated that Aloe Vera was effective in animals.

Aloe Vera is a modulator. It has an inhibitor system capable of blocking the immune system observed in the adjuvant arthritic animal, and it can block the mediators responsible for inflammation.

Aloe Vera also has a stimulatory system in which it can increase antibody production and stimulate wound healing by means of growth factors such as gibberellin, auxin and mannose phosphate. The isolation of the wound healing and anti-inflammatory activities using the 50% ethanol extraction of Aloe Vera revealed that the supernatant contained 78% of the anti-inflammatory activity whereas the precipitate had only 32%.

On the other hand, the supernatant had 0% wound healing activity whereas the precipitate had 160% wound healing activity in reference to the original Aloe Vera. This 160% value is likely due to the fact that the anti-inflammatory activity is masking some of the wound healing effect seen in the original Aloe Vera.

All of our studies seem to indicate that Aloe Vera is both orally and topically active on wound healing and inflamma-

tion even in the diabetic animal. For example, studies show that Aloe Vera can improve wound healing in the diabetic in a clear cut dose-response fashion over a dosage of 1 to 100 mg/kg.

Gowda demonstrated that mannose phosphate is the significant constituent in the 50% Aloe Vera extract (Gowda 1979). At the same time, Morgan showed that the mannose phosphate will bind to the insulin like growth factor receptor (Morgan 1987). Willenberg's study exhibited the anti-inflammatory activity of mannose phosphate (Willenberg 1989). Its ability to improve wound healing is evident.

The effect of mannose phosphate on topical croton-oil-induced inflammation was dose-related. The plateau of the dose-response curve was seen, however, at 25% inhibition. Glucose-6-phosphate had no effect and served as a control. Mannose phosphate improved wound healing in a dose-response straight-line fashion, but not response was seen with glucose-6-phosphate. The mannose phosphate of Aloe Vera activates the insulin like growth factor receptor.

The »Aloe Vera molecule« consists of a protein at one end and mannose-6-phosphate at the other end. The polysaccharide chain contains one glucose which is covalently linked to the protein with six mannose sugars moving toward the insulin, like the growth factor receptor of the fibroblast. The »Aloe Vera molecule« can stimulate the fibroblast to increase collagen and proteoglycans. We feel that the protein part of the Aloe Vera molecule acts to guide the polysaccharide chain into the receptor. The mechanism of action of Aloe Vera at the present time seems to inhibit

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pain and inflammation, but also can, by means of the growth factors, stimulate the fibroblast to increase wound tensile strength.

We have developed a wound tensile strength assay in which the length of the curve extends from day three to day ten. A dose-response relationship with Aloe Vera on wound tensile strength was obtained on a two-day treatment as well as on a four-day treatment basis at doses of 50 to 300 mg/kg per day.

The slopes of both curves were similar. However, we have decided to use the four-day treatment as the curve on which to best assay Aloe Vera on wound tensile strength. Gibberellin, a plant growth hormone, stimulated wound healing in a dose-response straight-line fashion over a dosage range from 2 to 100 mg/kg. Auxin was also shown to have good biological activity. Gibberellin could also block PMN infiltration even in diabetic animals up to 60%.

Aloe Vera may have an additive or a synergistic relationship with over 100 compounds to produce biological activity. It is possible that Aloe Vera acts as a kind of conductor which produces music with an orchestra of many biological active ingredients. It seems presumptuous for us to consider, or even to postulate, that any one substance is responsible for the biological activity seen in the Aloe Vera gel.

The Air Pouch Synovium

We made an air pouch in animals by administering 30 ml of air under the skin. In seven days we administered 1% carrageenan into the pouch, and two hours later we administered 10% Aloe Vera to determine what effect Aloe Vera would have on the air pouch synovium.

We found that Aloe Vera could stimulate the pouch wall weight by increasing the number of fibroblasts. This agrees with previous findings that the alcohol precipitate of Aloe had its greatest effect on wound healing by stimulating the fibroblast. Aloe Vera decreased by 60% the mass cell count and wall vascularity.

The effect of Aloe Vera on a 1% carrageenan-irritated simulated joint synovium model proves conclusively that Aloe Vera stimulates the fibroblasts, as seen in the wound healing studies, and inhibits inflammation, as evidenced by the decrease in vascularity and the reduction in mass cell count.

Summary

We have shown that some of the constituents of Aloe Vera have biological activity similar to amino acids, vitamin C and growth factors like gibberellin and auxin. Some attention was given to how the Aloe leaf makes and stores the gel. Mention was also made of the fact that we have seen what we call the »Aloe Vera Cell« in our laboratory at 40,000 magnification. In addition we have shown that the »Aloe Vera molecule« probably does not act alone, but rather acts in either an additive or synergistic fashion with some of the 100 constituents of the Aloe Vera.

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