

Clinical abstracts

Inflammation

Aloe Vera & Gibberellin, Anti-Inflammatory Activity In Diabetes

Davis RH; Maro NP

J Am Podiatr Med Assoc 79(1):24-6 1989 Jan

Aloe vera inhibits inflammation and adjuvant-induced arthritis. The authors' laboratory has shown that A. 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 A. 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 A. vera.

Anti-Inflammatory Activity Of Extracts From Aloe Vera Gel

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J Ethnopharmacol 55(1):69-75 1996 Dec

We studied the effects of aqueous, chloroform, and ethanol extracts of Aloe vera gel on carrageenan-induced edema in the rat paw, and neutrophil migration into the peritoneal cavity stimulated by carrageenan. We also studied the capacity of the aqueous extract to inhibit cyclooxygenase activity. The aqueous and chloroform extracts decreased the edema induced in the hind-paw and the number of neutrophils migrating into the peritoneal cavity, whereas the ethanol extract only decreased the number of neutrophils. The anti-inflammatory agents indomethacin and dexamethasone also decreased carrageenan-induced edema and neutrophil migration. The aqueous extract inhibited prostaglandin E₂ production from [¹⁴C]arachidonic acid. The chemical tests performed in the aqueous extract for anthraglycosides, reductor sugars and cardiotoxic glycosides were positive. In the ethanol extract, the chemical tests performed for saponins, carbohydrates, naftoquinones, sterols, triterpenoids and anthraquinones were also positive. In the chloroform extract, the chemical tests performed for sterols type delta 5, and anthraquinones were positive. These results demonstrated that the extracts of Aloe vera gel have anti-inflammatory activity and suggested its inhibitory action on the arachidonic acid pathway via cyclooxygenase.

Isolation Of A Stimulatory System In Aloe Extract

Dr. Davis

A set of experiments Dr. Davis and team members conducted involving the “Isolation of a Stimulatory System in Aloe Extract.” This study was done as a follow up on a previous clinical study in which a 50% ethanol extract was done to evaluate a croton oil-induced ear swelling assay. In this test, the Davis research team found that the “supernatant fraction” decreased inflammation when applied topically by 29.2%, and the precipitate decreased inflammation by 12.1%. Even more significantly, the precipitate wound healing activity was increased by an average of 47.5. In the original study the supernatant exhibited a 78% anti-inflammatory activity of Aloe vera, and promised to offer a low-cost, natural substance that could be used to manage inflammation and wounds in the lower extremities.

In the new study, however, the Davis research team did not attempt to alter the original alcohol (or ethanol percentage). Instead, they ultracentrifuged the Aloe compound and then froze the two fractions to approximately -80°C . Then they applied the supernatant (freeze-dried) powder and the Aloe vera freeze dried powder to a test group and control group of white mice. The precipitate (combination of Aloe and ethanol) tested better for wound healing than the supernatant and the Aloe each on their own. In fact the supernatant showed no ability to heal wounds, the Aloe vera showed an ability of wound healing and anti-inflammatory capacities ranging from a 29.4% ratio, yet exhibited a higher anti-inflammatory activity ratio of 37.4 more than that of either the precipitate or the supernatant, and the precipitate combination showed a range of 47.1 in wound healing yet a lower 12.1 anti-inflammatory activity. It was concluded in both these tests that: “Aloe vera has anti-inflammatory components such as amino acids, vitamin C, aspirin like compounds, and mannose which can normalize the acute vascular response. Aloe vera can block the polymorphonuclear leucocyte response, but does not reduce connective tissue formation.”

Part of the process of this particular Davis et al. study also entailed the attempt to isolate a polysaccharide component and glycoprotein (enzyme) constituent in the Aloe vera that might hold the key to all this effective activity. In this case the polysaccharide in question was mannose phosphate. In the singular context, it was determined that the mannose phosphate did serve as a binding agent to the same receptors that formed a positive growth medium for accelerated wound healing, as well as anti-inflammatory activity. However, the researchers arrived at the conclusion that it would be an all but futile determination to credit any complex saccharide or single element for the total activity attributable to the Aloe vera complex itself.

Role Of Thromboxane In Experimental Inadvertent Intra-Arterial Drug Injections

Zachary LS; Smith DJ Jr; Heggers JP; Robson MC; Boertman JA; Niu XT; Schileru RE; Sacks RJ

J Hand Surg [Am] 12(2):240-5 1987 Mar

Inadvertent intra-arterial injection of drugs produces a well-defined clinical syndrome whose pathophysiology remains unclear. This study was designed to determine the role of the inflammatory mediator, thromboxane, in intra-arterial drug injections. The rabbit ear model, as described by Kinmonth and Sheppard, was used. Five of the experimental groups were treated with specific or nonspecific thromboxane blocking agents and two groups served as

controls. Immunohistochemical staining of the control ears showed elevated levels of thromboxane within the first 6 hours postinjury. The specific thromboxane blocking agents, methimazole and Aloe vera, showed almost complete blockade of thromboxane production. The percentage of ear survival was significantly greater in the group treated with topical Aloe vera (p less than 0.05) and even greater survival was achieved in the combined Aloe vera/methimazole group (p less than 0.01). On the basis of these results, we have begun treatment of such injuries with specific and nonspecific thromboxane blocking agents.

Effects Of Low Molecular Constituents From Aloe Vera Gel On Oxidative Metabolism & Cytotoxic & Bactericidal Activities Of Human Neutrophils **t' Hart LA; Nibbering PH; van den Barselaar MT; van DiJk H; van den Berg AJ; Labadie RP**

Department Of Pharmacognosy, Faculty Of Pharmacy, University Of Utrecht
Int J Immunopharmacol Vol 12, ISS 4, 1990, P427-34

In traditional South-East Asian medicine the therapeutic value of the parenchymous leaf-gel of Aloe vera for inflammatory-based diseases is well-reputed. The aim of this study is to investigate at which level gel-constituents exert their activity. We show here that low –Mr constituents of an aqueous gel-extract inhibit the release of reactive oxygen species (ROS) by PMA-stimulated human PMN. The compounds inhibit the ROS-dependent extracellular effects of PMN such as lysis of red blood cells. The capacity of the PMN to phagocytose and kill micro-organisms at the intracellular level is not affected. The inhibitory activity of the low-Mr compounds is most pronounced in the PMA-induced ROS production, but is significantly antagonized by the Ca-ionophore A23187. It is shown that the inhibitory effect of the low-Mr compounds is the indirect result of the diminished availability of intracellular free Ca-ions.

Aloe Jelly Decomposes Bradykinin **Yagi, Akiar**

Akiar Yagi confirmed that the enzyme (glycoprotein) in Aloe jelly decomposes bradykinin which causes inflammation. He also confirmed the fact that aloe has a splendid action to promote DNA (=deoxyribonucleic acid) synthesizing which will accelerate cell multiplication. It is certain that these aloeuclin and enzyme are rendering great service to treatment for burns.

Anti-Inflammatory Activity Of Aloe Vera Against A Spectrum Of Irritants **Davis RH; Leitner MG; Russo JM; Byrne ME**

J Am Podiatr Med Assoc Vol 79, ISS 6, 1989, P263-76

The authors have evaluated the spectrum of anti-inflammatory activity of A. vera in a number of models of inflammation in the hind paw of the experimental rat induced by kaolin, carrageenan, albumin, dextran, gelatin, and mustard. Croton oil was used in a topical model of

inflammation to determine the oral activity and time-dependent dosing of A. vera. The authors found that A. vera was active in all models of inflammation. Of the various irritants tested, A. vera was especially active against gelatin-induced and kaolin-induced edema and, in contrast, had minimal activity when tested against dextran-induced edema. Oral activity of A. vera was demonstrated to be dependent on the presence of anthraquinones. The various irritant-induced edema models provided a broad spectrum of anti-inflammatory activity for A. vera.

The Isolation Of An Active Inhibitory System From An Extract Of Aloe Vera **Davis RH; Parker WL; Samson RT; Murdoch DP**

Pennsylvania College Of Podiatric Medicine

J Am Podiatr Med Assoc 81(5):258-61 1991 May

An Aloe vera extract was prepared with 50% ethanol. The resultant supernatant and precipitate were tested for anti-inflammatory activity using the croton oil-induced ear-swelling assay. The supernatant fraction decreased inflammation, when applied topically, by 29.2%, and the precipitate decreased inflammation by 12.1%. The authors have shown that the anti-inflammatory activity (inhibitory system) resides in the supernatant of a 50% ethanol extract.

Anti-Inflammatory C-Glucosyl Chromone From Aloe Barbadensis **Hutter JA; Salman M; Stavinoha WB; Satsangi N; Williams RF; Streeper RT;** **Weintraub ST**

Department Of Pharmacology, Research Imaging Center, University Of Texas Health Science Center

J Nat Prod Vol 59, ISS 5, 1996, P541-3

A new anti-inflammatory agent identified as 8-[C-beta-D-[2-O-(E)-cinnamoyl]glucopyranosyl]-2- [(R)-2-hydroxypropyl]-7-methoxy-5-methylchromone (1) has been isolated from Aloe barbadensis Miller. At a dose of 200 microg/mouse ear, 1 exhibited topical anti-inflammatory activity equivalent to 200 microg/ear of hydrocortisone. There was no reduction in thymus weight caused by treatment with 1 for any of the doses tested, while 200 microg/ear of hydrocortisone resulted in a 50% decrease in thymus weight.

Anti-Inflammatory & Wound Healing Properties Of Aloe Vera **Udupa SL; Udupa AL; Kulkarni DR**

Dep. Biochem., Kasturba Med. Coll.

Fitoterapia 65 (2). 1994 141-145

The fresh juice of the indigenous drug A. vera (0.2 ml/100 g, i.p.) was studied for its anti-inflammatory and wound healing properties in rats. Anti-inflammatory action was studied by observing percent reduction in carrageenin-induced paw oedema at 3 h. Wound healing effects were studied on incision (skin breaking strength), excision (percent wound contraction and epithelization time) and dead space (granuloma breaking strength and biochemical

parameters) wound models. A. vera showed significant anti-inflammatory activity in acute inflammatory model without any significant effect on chronic inflammation. Significant increase in breaking strength (skin and granuloma tissue), enhanced wound contraction and decreased epithelization period were observed. An increase in lysyl oxidase activity and mucopolysaccharide content were also seen. This drug could therefore increase tensile strength by increasing cross-linking in collagen and interactions with the ground substance.

Processed Aloe Vera Administered Topically Inhibits Inflammation

Davis RH; Rosenthal KY; Cesario LR; Rouw GA

J Am Podiatr Med Assoc Vol 79, ISS 8, 1989, P395-7

Aloe vera preparations were evaluated for topical anti-inflammatory activity using the croton oil-induced edema assay. The results show that small amounts of A. vera given topically will inhibit inflammation induced by a moderate amount of irritant. In general, the decolorized Aloe was more effective than the colorized Aloe (with anthraquinone). A 47.1% inhibition of inflammation was obtained by 5% decolorized irradiated Aloe. These results may be used as a baseline to assess the biologic activity of A. vera in the treatment of inflammation by podiatric physicians.

Pharmacological Studies On A Plant Lectin Aloctin A. II. Inhibitory Effect Of Aloctin A On Experimental Models Of Inflammation In Rats

Saito H; Ishiguro T; Imanishi K; Suzuki I

Jpn J Pharmacol 32(1):139-42 1982 Feb

A glycoprotein, Aloctin A, which was isolated from Aloe arborescens Mill, markedly inhibits adjuvant arthritis in rats and carrageenin-induced edema in rats.

Anti-Arthritic Activity Of Anthraquinones Found In Aloe For Podiatric Medicine

Davis RH; Agnew PS; Shapiro E

J Am Podiatr Med Assoc 76 (2). 1986. p61-66

Rheumatoid arthritis is a painful and crippling systemic disease for which there is no cure. The best experimental model for studying rheumatoid arthritis in humans is the adjuvant-induced arthritis in rats. One of the group of compounds found in Aloe is the anthraquinones. These substances have been recognized for their use in veterinary medicine against inflammation. The authors evaluate the anti-inflammatory and anti-arthritic activity of anthraquinone, anthracene, cinnamic acid, and anthranilic acid found in the Aloe vera plant, and show what contribution each ingredient makes toward the total activity found in Aloe.

Prof. Davis and his group at Medical College on Podiatry, Pennsylvania discovered that Aloe vera contains anthraquinone and anthranilic acid both of which are quite efficacious against

arthritis and articular rheumatism. These two constituents can restrict the biosynthetic function of bradykinin, a substance causing pain or inflammation.

Prof. Davis further explains when supplemented with RNA (ribonucleic acid) and vitamin C, Aloe vera can accomplish a tremendous feat. The professor received an academic award for this achievement.

Aloe Vera

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Department Of Dermatology, University Of Miami School Of Medicine

J Am Acad Dermatol, 18(4 Pt 1):714-20 1988 Apr

We reviewed the scientific literature regarding the Aloe vera plant and its products. Aloe vera is known to contain several pharmacologically active ingredients, including a carboxypeptidase that inactivates bradykinin in vitro, salicylates, and a substance(s) that inhibits thromboxane formation in vivo. Scientific studies exist that support an antibacterial and antifungal effect for substance(s) in Aloe vera. Studies and case reports provide support for the use of Aloe vera in the treatment of radiation ulcers and stasis ulcers in man and burn and frostbite injuries in animals. The evidence for a potential beneficial effect associated with the use of Aloe vera is sufficient to warrant the design and implementation of well-controlled clinical trials.

Aloctin A, Active Substance Of Aloe Arborescens Miller As An Immunomodulator

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Department Of Microbiology & Immunology, Tokyo Women's Medical College

Phytotherapy Research (1993) Vol 7, No. Special issue, pp. S20-S22. 15 ref.

Aloctin A (Alo A), an active substance isolated from the leaves of *A. arborescens*, has many biological and pharmacological activities, such as mitogenic activity for lymphocytes, binding of human alpha 2-macroglobulin, complement activation via the alternative pathway, anti-inflammatory activity, anti-ulcer activity and antineoplastic activity. Alo A exhibited immunomodulatory activities on the immune responses of murine and human lymphoid cells in vivo and in vitro.

An Anti-Complementary Polysaccharide With Immunological Adjuvant Activity From The Leaf Parenchyma Gel Of Aloe Vera

t' Hart LA; van den Berg AJ; Kuis L; van Dijk H; Labadie RP

Planta Med 55(6):509-12 1989 Dec

The aim of the study is to develop new substances with immunomodulatory activity. To this end, extracts from plants used in traditional medicine are used as starting material. This study deals with the mucilagenous leaf-gel of Aloe vera which is well reputed for its therapeutical

effect on inflammatory-based disorders. The purification of an aqueous gel-extract guided by inhibition of complement activity in HPS is described. Using anion-exchange and gel permeation chromatography a highly active polysaccharide fraction was isolated, that is present in the gel in various chain lengths. The polysaccharides consist of several monosaccharides of which mannose is dominant. The inhibition is based on alternative pathway activation, resulting in consumption of C3. With respect to their biological activity the polysaccharides inhibit the opsonization of zymosan in HPS and display adjuvant activity on specific antibody production and the induction of delayed type hypersensitivity in mice.

Aloe Vera, Hydrocortisone, & Sterol Influence On Wound Tensile Strength & Anti-Inflammation

Davis RH; DiDonato JJ; Johnson RW; Stewart CB

Pennsylvania College Of Podiatric Medicine

J Am Podiatr Med Assoc 84(12):614-21 1994 Dec

Aloe vera at doses of 100 and 300 mg/kg daily for 4 days blocked the wound healing suppression of hydrocortisone acetate up to 100% using the wound tensile strength assay. This response was because of the growth factors present in A. vera masking the wound healing inhibitors such as sterols and certain amino acids. The sterols showed good anti-inflammatory activity (-36%) in reducing the croton oil-induced ear swelling. This activity displayed a dose-response relationship.

Anti-Inflammatory & Wound Healing Activity Of A Growth Substance In Aloe Vera

Davis RH; Donato JJ; Hartman GM; Haas RC

Department Of Biomedical Sciences, Pennsylvania College Of Podiatric Medicine

J Am Podiatr Med Assoc 84(2):77-81 1994 Feb

Aloe vera improves wound healing and inhibits inflammation. Since mannose-6-phosphate is the major sugar in the Aloe gel, the authors examined the possibility of its being an active growth substance. Mice receiving 300 mg/kg of mannose-6-phosphate had improved wound healing over saline controls. This dose also had anti-inflammatory activity. The function of mannose-6-phosphate in A. vera is discussed.

Aloe Plant For Promotion Of Wound Healing

Davis, Robert H

The present invention describes a compn. derived from the Aloe plant which when used as an adjuvant for the healing of wounds exhibits increased anti-inflammatory and wound-healing activity. An open wound is treated by (1) applying a first wound-healing compn. comprising Aloe vera and gibberellin or micronized aspirin to an open wound and (2) overlaying the first compn. with a bandaging mixt. comprising an 1:1 ratio of whole leaf Aloe vera and Aloe vera mucilage. The compn., an Aloe vera mucilage at approx. 1:1 ratio, preferably with Aloe pulp fibers, increased open wound healing activity and tensile strength by 131% over controls.

Studies Of The Status Of Antioxidant Enzymes & Metabolites Following Burn Injury, & The Presence Of Antioxidant Enzymes In The Aloe Vera Plant (Tumor Necrosis Factor Glutathione)

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Dissertation Abstracts International (1995) Vol. 56, No. 12B, p. 6728

Part I. The effects of skin burn injury on the levels of oxidized and reduced glutathione, malondialdehyde, and on the activities of glutathione peroxidase, glutathione S-transferase, and glutathione reductase were determined in liver and lung of rabbit models, 24-h post-burn. The data obtained are indicative of a major oxidative stress in liver and lung tissues due to burn injury at a remote site. Tumor necrosis factor (TNF), a mediator in the pathogenesis of endotoxic shock and burn injury, is associated with decreased glutathione levels. Depletion of cellular glutathione by chemical agents enhanced the release of TNF from lipopolysaccharide (LPS) - stimulated rabbit lung macrophages. Glutathione repletion of macrophages, using glutathione diesters, inhibited LPS - stimulated TNF secretion. Thus, glutathione diesters may have therapeutic value in treating endotoxic shock and burn injury.

Part II. Two antioxidative enzymes, glutathione peroxidase (GSHPx) and superoxide dismutase (SOD), which are involved in scavenging reduced oxygen species, have been purified and characterized from the Aloe vera plant. GSHPx activity was purified to homogeneity by ion exchange and gel filtration chromatography. The enzyme is apparently a tetramer with a sub-unit molecular mass of 16 kD, with one atom of selenium per subunit. The Km values are 3.2 mM for glutathione and 0.26 mM for cumene hydroperoxide. The enzyme is competitively inhibited by N, S, bis-fluorenylmethoxy-carbonyl glutathione. Superoxide dismutases from both the gel and the rind of Aloe vera were purified by ion exchange chromatography. Seven SOD activities were detected, with identifiable differences in their relative distribution in rind and gel. Two of these contain manganese with native molecular masses of 42 and 43 kD and five others are copper/zinc SODs with molecular masses of 31-33 kD. Aloe vera SODs have high specific activities; these high activities may relate to the plant's healing properties of inflammatory disorders.

Purification Of Active Substances Of Aloe Arborescens Miller & Their Biological & Pharmacological Activity

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Phytother Res. (1993) 7 (Spec. Issue, Proceedings of the International Congress of Phytotherapy, 1991), S14-S19

The authors purified Aloctin A from Aloe arborescens Miller and defined its chem., biol. and pharmacol. activities. Aloctin A consists of two discrete bands, a and b with a combined S-S bond. Its mol. wt. for a is 7500 and the mol. wt. for b is 10,500. Aloctin A has many biol. and pharmacol. activities as follows: 1. hemagglutinating activity; 2. cytoagglutinating activity; 3. mitogenic activity of lymphocytes; 4. ppt. - forming reactivity with α 2-macroglobulin; 5. complement C3 activating activity; 6. inhibition of heat-induced hemolysis of rat

erythrocytes; 7. anti-tumor effect; 8. anti-inflammatory effect; 9. inhibition of gastric secretion and gastric lesions.

Aloe-Derived Carbohydrates Reduce Inflammation By Blocking Neutrophil Emigration Mediated By Certain Beta2 Integrins

Tizard, Ian

Texas A&M University

It has been recognized for many years that some Aloe-derived products have significant anti-inflammatory activity. Published evidence has shown that this is mediated, at least in part, by inhibition of prostanoid production in damaged tissue. Studies conducted at Texas A&M University and Texas Children's Hospital by Drs. Bob Bowden and Wayne Smith have now demonstrated that Aloe extracts mediate a second anti-inflammatory mechanism by blocking certain integrins.

Integrins are proteins that mediate cell adherence. Thus in inflamed tissues, defensive cells such as blood neutrophils must first bind to endothelial cells on blood vessel walls before entering the tissues. This binding is integrin-mediated. Neutrophils, although critical for host defense, are unfortunately able to cause significant tissue damage as a result of the release of potent enzymes and oxygen metabolites. Thus compounds that block neutrophil emigration will prevent tissue damage and so reduce inflammation.

Evidence has been presented to show that certain Aloe-derived carbohydrates bind specifically to carbohydrate-binding sites on two β 2-integrins called LFA-01 and Mac-1. In doing this, they significantly reduce neutrophil emigration in some models of experimental inflammation.
