

Producing *Aloe barbadensis* in the old-fashioned way – a botanic excursion to the Dominican Republic

Anthony C. Dweck FLS FRSC FRSH
Technical Editor

Introduction

The author has worked on the benefits of Aloe since the early 1980s with the climax of his work being the honour to assist with a paper that was published by Tom Reynolds, the Royal Botanic Gardens Kew [T. Reynolds, A.C. Dweck: Aloe vera leaf gel - a review update. *Journal of Ethnopharmacology*, **68** (1999) 3-37]. Despite the many years of work and the accumulation of a huge data base of knowledge, the author had never seen Aloe grown on a commercial scale. A dream came true with an invitation to visit and inspect a commercial plantation that was growing and harvesting of Aloe gel in the old and traditional way.

There are many producers of Aloe vera gel (*Aloe barbadensis*) and not all of them are the same.

“Aloe vera gel is the fresh mucilaginous gel obtained from the parenchymatous tissue in the leaf centre, used for its emollient and wound healing activity.”

Clearly, any method that produced Aloe by any means other than from the central gel would not be an aloe produced in the traditional way. It is also important to remember that all of the literature referring to the beneficial properties of *Aloe barbadensis* refers to the carefully extracted Aloe vera gel.

Ways in which Aloe has been produced

Squashing out the gel from the leaf through large rollers – the method is quick, saves lots of process time and gives a gel that abounds in ruptured cells from the inner surface of the outer leaf. This surface is rich in anthraquinones and other undesirable chemical species that spoil the composition of the final product.

Maceration of the whole leaf – a method that has no historical or traditional basis. The literature always refers to the inner gel and never to the whole leaf extract. The only time when the outer leaf is used is for the preparation of dried aloes used as a purgative.

Growing of the Aloe



The fields examined were in the Dominican Republic. Our journey across the island led from a verdant, fresh and lush landscape into a much more arid and barren topography.

The fields of Aloe stretched out before us as far as the eye could see. The plant has few predators with the tough outer skin providing excellent resistance to insects and other potential attackers. It is likely that the bitter anthraquinones



and other polyphenolic materials contained in the outer leaf make the plant unattractive to these attacks. The need for insecticides and anti-feedants is therefore not required.

The remaining complication might have been the weeds, but in this case there are many hungry goats eager to help out in the fields and so keep the number of weeds down to a minimum. The use of strip irrigation and accurate placement of water directly onto the Aloe plants makes it tougher still for the weeds to survive.



Aloe leaves are cut by hand, with three leaves being harvested from each plant. The plant will not be harvested again for at least three months once the leaves have been taken.

This is arduous and intensive work, the cut leaves being put in wire baskets for transportation to the next phase of the operation.



The baskets are transferred directly to the washing station, where most of the mud and other debris are washed off in the first water bath. The leaves are then transferred to another bath where they receive another

rinse to leave them looking fresh and clean.



The washed and rinsed leaves are then transferred to baskets and taken inside the factory where the filleting process is started.



The outer leaf is tough and leathery and it takes a very sharp knife to top and tail the leaf and to cut off the sides in order to leave a gel sandwiched between the outer sides of the leaf. These pre-prepared fillets are placed into drums and then pass on through the factory to the next stage



where the gel is separated from the back and the front of the leaf. The skill and speed of the operators is breath-taking, and those of a nervous disposition when around sharp knives would be well advised not to watch!



The final gel extracted from the leaf is totally untainted and shows no yellow or green colouration from the inner surface of the outer leaf. As can be seen from the photograph, the gel is water-white, totally colourless and odourless. This central parynchomal gel is collected into white buckets and transferred to the next stage of the

process. A single leaf yields around 500g of gel.

It is always a warming sight to see a production process seeking perfection. The gel (that is already of superb quality by any standards) is then hand inspected to remove any traces of outer leaf that may have been missed inadvertently during the various filleting processes. This operation is carried out on an inspection table and the mucilaginous stringiness of the fillets makes touching



it almost irresistible! The gel that is free of any imperfections or impurities is then passed through a macerating cutter to break down the natural polymeric polysaccharide bonds to break down the gel into a free flowing liquid.



This pure 1:1 Aloe gel is pumped to a holding tank ready for the next stage of the process to prepare 10:1 gel, or is taken



through to finished bulk. The product is further refined by sieving and filtration according to the specification and filled into foil-pouched drums for shipping once the preservation of the bulk has

been completed.

The transition to a 10:1 strength gel is achieved using an evaporimeter that gently removes 90% of the water from the harvested gel.

This process is quite confidential as the removal of the water has to be done very carefully in order to preserve the integrity and chemical composition of the original gel.



The water used in irrigation comes from bore holes and also from the water reclaimed from the evaporimeter. All of the material removed during the fillet-making process is used as a green compost and so can be considered an environmentally friendly process.

The harvesting is carried out by Haitians who are able to cope with the warmer temperatures in the fields and the processing is carried out by local Dominicans. The production of Aloe helps the local economy and so may be considered community traded.

There are many species of Aloe and identification can be very difficult, the surest method is to study the flowers, but be warned, the Aloe flowers quite infrequently!



Since there is no use of herbicides and pesticides this material has been certified as being of organic quality.

CLINICAL STUDIES

A summary of the clinical and animal studies carried out on *Aloe barbadensis* Miller and related species.

ASTHMA AND RELATED CONDITIONS

Afzal et al.¹ reports that the present study was prompted by a report on the efficacy of *A. barbadensis* extracts in treating adult bronchial asthma and pharyngitis. Extracts of

above-ground parts contained endogenous arachidonic acid, a potential precursor for prostanoid synthesis. The presence of endogenous cyclooxygenase was established by radiometric assay. Relatively high proportions of PGE₂ (a bronchodilator) and TXB₂ (a bronchoconstrictor) and low proportions of other prostaglandins were identified in the plant extract when incubated with [¹⁴C]-arachidonic acid. There were also high percentages of phosphatidylcholine and cholesterol. It has been suggested that the enhancement of phagocytosis in adult bronchial asthma is due to the nondialysable material from the pulp fraction of the plant. However, this activity was only exhibited if the plant extracts were kept in the dark at 4-30°C for a period of 3-10 days. These storage conditions were just right for the hydrolysis of phospholipids, thus releasing arachidonic acid to synthesize prostanoids involving endogenously present cyclooxygenase as indicated by the results.

Yagi et al.² showed that a mixture of cysteine and proline (1:1) extracted from *Aloe arborescens* var. *natalensis* significantly enhanced the depressed phagocytosis of neutrophils in adult bronchial asthma.

WOUND HEALING

Swaim³ et al. describe the healing of open pad wounds in dogs, the Aloe-treated wounds had a smaller unhealed area than did untreated control wounds and wounds treated with antibiotics.

Davis⁴ reports that 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.

Fulton⁵. Full-face dermabrasion provided an ideal opportunity to document the effects of dressings on wound healing management. Following the procedure, the abraded face was divided in half. One side was treated with the standard polyethylene oxide gel wound dressings. The other side was treated with a polyethylene oxide gel dressing saturated with stabilized aloe vera.

The polyethylene oxide dressing provided an excellent matrix for the release of aloe vera gel during the initial 5 days of wound healing. By 24-48 hours there was dramatic vasoconstriction and accompanying reduction in edema on the aloe-treated side. By the third to fourth day there was less exudate and crusting at the aloe site, and by the fifth to sixth day the reepithelialization at the aloe site was complete. Overall, wound healing was approximately 72 hours faster at the aloe site. This acceleration in wound healing is important to reduce bacterial contamination, subsequent keloid formation, and/or pigmentary changes. The exact mechanism of acceleration of wound healing by aloe vera is unknown.

Davis et al.⁶. 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 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.

Watcher et al.⁷. Eight topical agents in current use were studied for their effects on wound contraction and rate of reepithelialization of full-thickness excisions using a porcine animal model. The following agents were applied daily for a period of 27 days: scarlet red ointment, benzoyl peroxide lotion, bacitracin ointment, silver sulfadiazine cream, aloe vera gel, tretinoin cream, capsaicin cream, and mupirocin ointment. The rate of reepithelialization was significantly enhanced by treatment with capsaicin, bacitracin, silver sulfadiazine, and scarlet red, and was markedly retarded by treatment with tretinoin. Wound contraction was significantly retarded by mupirocin, bacitracin, and silver sulfadiazine. Knowledge of the effects of topical agents on various aspects of healing allows the clinician to choose the most appropriate material to use in a given clinical situation to optimize the healing process and produce the best final result.

Davis et al.⁸. 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.

Davis⁹ further examines wound healing in a further paper.

Fan et al.¹⁰ looked at hepatic lesions. The injection(10-15 ml/kg/d, ip x 4), total glycoside (125-225 mg/kg/d, ip x (3-4); 600 mg/kg/d, ig x 3) and crystal III (120 mg/kg/d, ip x 4) of Aloe vera var. chinensis were found to be effective in lowering the elevated sGPT induced by CCl₄, thioacetamide and D-aminogalactose in mice or rats. It was also observed that these agents could protect hepatic cells from the CCl₄-induced injury. When dogs were given in with Aloe injection of 0.1 ml/kg/d x 180, no toxicity was noted. The total effective sGPT-lowering rate of Aloe injection on 38 patients of chronic hepatitis with positive HBsAg was 86.8%.

Zawahry et al.¹¹ describe the use of aloe in treating leg ulcers.

Kligman¹² writes in his conclusions: It is our opinion that the Aloe vera materials tested did not interfere with the normal rate of superficial dermal wound re-epithelialisation nor did they enhance the process any faster than the covered non-treated control wounds at the end of three weeks. It can be stated that the wounds treated with Aloe vera healed better than uncovered wounds and were more cosmetically gratifying.

RADIOTHERAPY

Sato et al¹³ report on the protective qualities of *Aloe arborescens* against radiation. Protective effects of *Aloe arborescens* (AA) on mouse skin injury induced by soft X-irradiation were examined. The mechanisms on radiation protection by measuring scavenge activity of activated oxygen, protective effects of nucleic acid, induction of antioxidative protein and so on were further investigated. Consequently a significant protective effect of skin injury was observed in AA S6-3-b. As the mechanisms of radiation protection in AA, the following matters were found. AA S6-3-b showed scavenge activity of hydroxyl radicals generated by Haber-Weiss reaction. AA S6-3-b suppressed the changes of activity in superoxide dismutase and glutathione peroxidase at 7d after soft X-irradiation. Metallothionein was induced in the skin and liver against normal mice at 24 h after administration of AA S6-3-b.

Iena¹⁴ gives formulae of mixtures with aloe which may be used in domestic conditions for increasing the defensive forces of the body during radiation lesions.

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Lushbaugh and Hale¹⁶ looked at the experimental acute radiodermatitis following Beta Irradiation versus histopathological study of the mode of action of therapy with *Aloe vera*.

Their experiments showed objectively that *Aloe vera* has a remarkably curative effect upon radiodermatitis in the rabbit. It was found to increase greatly the development of the lesion by apparently doing away with the so-called latent period. Either as a result of earlier development of necrosis and ulceration, or from a specific effect upon the adjacent epithelium, re-epithelialisation occurred much earlier than usual and was more hypoplastic in character. The inhibition of the fibroplasia was also overcome earlier than usual so that new connective tissue was produced throughout the dermis as re-epithelialisation was occurring.

As a result of the enhancement of the healing processes, the damage to the original connective tissue seemed to be restricted and usually did not proceed so extensively as the untreated lesions. While in occasional treated specimens what appeared to be new capillaries were seen, granulation tissue did not actually develop, and defects were obliterated by fibroplasia and contraction of the connective tissue. No histological explanation could be found for the absence of telangiectatic vessels in the healed treated lesions other than that the treated ulceration, being shallower, might not have led to the exposure and subsequent elevation to the surface of the larger vessels of the deep dermis. Degenerative vascular changes secondary to the radiation

appeared to be the same with or without treatment. These experimentally observed beneficial alterations in the course of the radiodermatitis treated with *Aloe vera* would seem to substantiate firmly previous clinical experiences with this plant in the treatment of human radiodermatitis.

No information was gained from these experiments concerning the mechanism by which *Aloe vera* produced these changes.

CHEMOTHERAPY

Nersesian et al.¹⁷. General and local nonspecific immunity was studied in 143 new cases of pulmonary tuberculosis (71 and 72 persons, respectively). The results showed that combination of chemotherapy using desensitizing agents and tissue preparations according to V. P. Filatov (a suspension of placenta tissue and aloe) had an immunomodulating effect. The efficacy of the combined chemotherapy amounted to 87 per cent with an account of the general immunity status.

IMMUNOLOGY

L.A. 't Hart et al.¹⁸ showed that biological activity of the polysaccharides was shown by the opsonization of zymosan in human pooled serum, their adjuvant activity on specific antibody production and the induction of delayed type hypersensitivity in mice.

REVIEW ARTICLES

Klein et al.¹⁹ reviews the literature on *Aloe vera* (*A. barbadensis*) and its products. *A. 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. Results of some studies offer evidence for antibacterial and antifungal properties of substance(s) in *A. vera*. Studies and case reports provide support for the use of *A. 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 *A. vera* is sufficient to warrant the design and implementation of well-controlled clinical trials.

Grindlay and Reynolds²⁰ - A review and discussion. The literature reviewed here provides evidence that *A. vera* [*A. barbadensis*] gel is of value for treating burns and certain other dermatological conditions and that it has definite physiological effects (although there is no certain correlation between these and the identified gel components).

GASTRIC ULCERS

Parmar et al.²¹ say that despite previous reports, no activity was found with *A. vera* [*barbadensis*] exudate or gel.

Davis et al.²² recommends Aloe vera as a natural approach for treating wounds, edema, and pain in diabetes.

BIOLOGICAL ACTIVITY

Yagi et al.²³ reported that three neutral polysaccharides (A, B and C) and a glycoprotein were isolated by gel filtration from a nondialyzable fraction of leaf extract. In vitro assays showed that polysaccharide C (which had a structural profile similar to that of the anti-tumour compound aloemmannan) and the glycoprotein had phagocytic activity.

Erazo et al.²⁴ reported on the humectant properties of a related aloe species. The gel and mucilage of *A. perryi* closely resembled those of *A. barbadensis*. The mucilages of both species were incorporated into oil/water emulsions (10%). Both increased the hydration of human skin to a similar extent when applied for 30 days.

Ralamboranto et al.²⁵. An immuno-modulator fraction (Alva) extracted from an endemic plant, in the south of Madagascar, the *Aloe vahombe*, significantly protects mice against bacterial, parasitic and fungal infections. Wishing to verify whether the fraction Alva was active in tumour reduction, we studied its effect on the development of experimental fibrosarcoma and melanoma in mice by intravenous and intracutaneous injections and injections directly into the tumour of the immunostimulant fraction. We have observed cures, only in the case of the McC3-1 tumour but it is encouraging to note that under different experimental conditions the rate of growth of tumours in animals which were treated is slower than in those not treated. The Alva fraction is a substance which is hydrosoluble, thermostable, having a molecular weight exceeding 30,000 and is a polysaccharide. The predominant sugars are glucose and mannose in 3:1 ratio. Preliminary studies of its action seem to indicate that the Alva fraction acts upon non-specific response and could possibly stimulate the phagocyte activity of the peritoneal macrophagus.

Michel, Pignon et al.²⁶ looked at a prospective study of the immunomodulator properties of i.m. administered "ALVA" extract in patients with solid tumors under a course of chemical immunosuppressive therapy.

Peng et al.²⁷ An extract from the parenchyma of *Aloe barbadensis* Miller shown to contain long chain polydispersed beta (1,4)-linked mannan polymers with random O-acetyl groups (acemannan, Carrisyn) was found to initiate the phagocyte production of monokines that supported antibody dependent cellular cytotoxicity and stimulated blastogenesis in thymocytes. Acemannan, in both enriched and highly purified forms, was administered intraperitoneally to female CFW mice into which murine sarcoma cells had been subcutaneously implanted. The rapidly growing, highly malignant and invasive sarcoma grew in 100% of implanted control animals, resulting in mortality in 20 to 46 days, dependent on the number of cells implanted.

Approximately 40% of animals treated with acemannan at the time of tumor cell implantation (1.5×10^6 cells) survived. Tumors in acemannan-treated animals exhibited vascular congestion, edema, polymorphonuclear leukocyte infiltration, and

central necrosing foci with hemorrhage and peripheral fibrosis. The data indicate that in vivo treatment of peritoneal macrophages stimulates the macrophage production of monokines, including interleukin-1 and tumor necrosis factor. The data further indicate that sarcomas in animals treated i.p. with acemannan at the time of tumor cell implantation were infiltrated by immune system cells, became necrotic, and regressed. The combined data suggest that acemannan-stimulated synthesis of monokines resulted in the initiation of immune attack, necrosis, and regression of implanted sarcomas in mice.

Sydiskis et al.²⁸ determined the extent of antiviral activity present in a number of plant extracts, hot glycerin extracts were prepared from *Rheum officinale*, *Aloe barbadensis*, *Rhamnus frangula*, *Rhamnus purshianus*, and *Cassia angustifolia* and their virucidal effects were tested against herpes simplex virus type 1. All the plant extracts inactivated the virus. The active components in these plants were separated by thin-layer chromatography and identified as anthraquinones. A purified sample of aloe emodin was prepared from aloin, and its effects on the infectivity of herpes simplex virus type 1 and type 2, varicella-zoster virus, pseudorabies virus, influenza virus, adenovirus, and rhinovirus were tested by mixing virus with dilutions of aloe emodin for 15 min at 37 degrees C, immediately diluting the sample, and assaying the amount of infectious virus remaining in the sample. The results showed that aloe emodin inactivated all of the viruses tested except adenovirus and rhinovirus. Electron microscopic examination of anthraquinone-treated herpes simplex virus demonstrated that the envelopes were partially disrupted. These results show that anthraquinones extracted from a variety of plants are directly virucidal to enveloped viruses.

Fujita et al.²⁹ looked at the effect of leaf extracts of *Aloe arborescens* Mill subsp. *natalensis* Berger on growth of *Trichophyton mentagrophytes*.

Brossat et al.³⁰ A partially purified extract of leaves of *Aloe vahombe*, a plant endemic in the south of Madagascar, administered intravenously to mice, protects them against infection of bacteria (*Listeria monocytogenes*, *Yersinia pestis*), parasites (*Plasmodium berghei*) and fungus (*Candida albicans*). The protective fraction must be administered two days before inoculation of the pathogenic agent. These results significantly confirm those we obtained in earlier study on mice infection by *Klebsiella pneumoniae*. Currently we are testing the protective action of the purified extract on the experimental development of sarcomas, and we are in the process of analysing the mode of action of this non specific immunostimulant.

Winters et al.³¹ Fractions of leaf extracts from *Aloe barbadensis* (AVB) and *A saponaria* were prepared by differential centrifugation and tested by in vitro assays for the presence of lectin-like activities. Fractions were also tested for effects on the attachment and growth of human normal fetal lung (HFL) and human cervical carcinoma (ME180) cells grown on confluent plates and monitored by hemagglutination (HA) and immunodiffusion (ID) tests. Comparable fractions from all Aloe sources after separation had approx the same ratio of recoverable supernatant fluids to high speed pellet materials. In ID tests all Aloe sources reacted with human and baboon sera, and none of the fractions reacted with canine sera from normal and two tumor-bearing adult dogs.

Human RBC were more sensitive indicators of HA than canine RBC for tests of Aloe fractions, while both human and canine RBC were equally sensitive in HA tests of the control lectin, Concanavalin A. Neither HFL or ME180 cells in single cell suspensions were aggregated when mixed with dilutions of AVB fractions.

Attachment of HFL cells was markedly enhanced by 1:10 dilutions of concentrated, particle-free supernatant. Counts Of cells at the edges of wounds in monolayer HFL and ME180 cell cultures treated with AVB were higher than cell densities at wound edges in other cultures treated with high speed supernatant and pellet fractions or those in untreated cultures. Treatment of monolayer cultures of both cells with fractions of a 'stabilized' commercial A vera gel caused marked cellular granularity and inhibition of attachment of cells within 2 days. These cytotoxic responses prevented the completion of cell attachment and growth experiments using A vera gel fractions. (17 Refs)

BURNS

Yagi et al.³² reported on the effect of aloe lectin on deoxyribonucleic acid synthesis in baby hamster kidney cells. It is suggested that this lectin may be responsible for the therapeutic effect of aloe gel on burns.

Strickland³³ investigated the ability of Aloe barbadensis gel extract to prevent suppression of contact hypersensitivity (CHS) and delayed-type hypersensitivity (DTH) responses in mice by ultraviolet (UV) irradiation. Topical application of 0.167-1.67% Aloe gel after each irradiation significantly reduced this suppression. Aloe treatment partially preserved the number and morphology of Langerhans and Thy-1+ dendritic epidermal cells in skin, compared to those in the skin of mice given only UVR or UVR plus the vehicle. Experiments using a single (2 kJ/m²) dose of UVR followed by Aloe treatment showed that the effect of Aloe was not due to screening of the UVR. Treatment of the UV-irradiated skin with Aloe immediately after irradiation prevented suppression of both DTH to Candida and CHS to FITC. Aloe treatment did not prevent the formation of cyclobutyl pyrimidine dimers in the DNA of UV-irradiated skin or accelerate the repair of these lesions. These studies demonstrate that topical application of Aloe barbadensis gel extract to the skin of UV-irradiated mice ameliorates UV-induced immune suppression by a mechanism that does not involve DNA damage or repair.

Crowell et al.³⁴. Aloe vera does not affect cutaneous erythema and blood flow following ultraviolet B exposure.

Rodriguez-Bigas³⁵. An experimental study was designed using Hartley guinea pigs, who received full-thickness burns covering 3 percent of their body surface area by direct contact with a hot plate. A total of 40 animals were equally divided among four modalities of closed burn wound management as follows: group I: silver sulfadiazine (Silvadine); group II: aloe vera gel extract (Carrington Dermal Wound Gel); group III: salicylic acid cream (aspirin); and group IV: plain gauze occlusive dressing only. The dressings were changed daily, and the size and appearance of each burn wound were recorded until complete healing. On the sixth postburn day, quantitative burn wound cultures were made. The average time to complete healing in the control group was 50

days, and the only significant difference was found in the aloe vera-treated animals, which healed on an average of 30 days (p less than 0.02).

Wound bacterial counts were effectively decreased by silver sulfadiazine ($p = 0.015$) and by aloe vera extract ($p = 0.015$). From our data it appears that aloe gel extracts permit a faster healing of burn wounds.

McCauley³⁶ says that if frostbite is to be treated successfully, direct and indirect effects of injury must be understood. Rapid rewarming helps to preserve tissue by limiting the amount of direct cellular injury. Selective management of blisters helps protect the subdermal plexus, and application of Aloe vera cream (eg, Dermaide Aloe Cream) combats the local vasoconstrictive effects of thromboxane. Oral administration of ibuprofen decreases systemic levels of thromboxane.

Cera et al³⁷. A therapeutic protocol that included topical and systemic administration of a thromboxane inhibitor was used to successfully treat a burned Rhesus monkey. Accidental exposure of the animal to steam and water (180°C) for 5 minutes had caused full-thickness dermal injury to its entire body surface area (BSA). Animals with full-thickness burns involving more than 50% BSA are generally regarded as having remote chances of recovery. Based on the favourable outcome obtained, the therapeutic protocol that was used for this monkey is advocated for general use.

Rovatti et al.³⁸ looked at a comparative study of the immediate and delayed histopathological changes of the skin in untreated and treated thermal burns. Their conclusions based on gross and microscopic observations showed that in deep dermal burns an eschar forms and separates microscopically in 24 to 48 hours and grossly the eschar separated in 10 to 14 days if the skin is not treated with ointment after burning.

The study of the burned skin in the untreated group, showing this clear cut separation and demarcation, suggest that early treatment should be directed toward the prevention of the changes which produce the eschar within the first 24 hours.

The first group I (treated with Aloe-Creme ointment): The skin burned and treated with Aloe-Creme ointment remained pliable and soft during the first week with slight and continuous superficial debridement of the upper dermis and without gross or microscopic separation of an eschar. These lesions healed in two weeks without gross evidence of scarring.

The second group II (treated with Aloe-Creme Ointment containing cysteine): Identical burns treated with Aloe-Creme Ointment containing 5% cysteine showed during the second week more superficial debridement than observed in animals of group I. There was no gross or microscopic separation of an eschar and no gross scarring occurred. There was little or no difference between this group and group I.

The third group, (treated with trinitrophenol ointment): the appearance of the skin was comparable during the first 24 hours to that observed in Groups I and II. Then these lesions became grossly and microscopically haemorrhagic and the separation of an

eschar was evident microscopically at 24 hours. None of the animals survived the tenth day and haemorrhages were found in the skin at the end of the first week.

The fourth group IV (treated with petrolatum and gauze): during the first three days there was a gradual development of congestion, oedema and focal haemorrhages of the skin area in these burns. Microscopically an eschar did develop and separate during the first 48 hours. By the end of the first week there were numerous haemorrhages and several small abscesses. At the end of the second week the entire dermis was debriding in large masses and the lesions healed by scarring during the third and fourth week.

Cera et al.³⁹. It is generally accepted that in the canine species with a 50% or more partial or full thickness burn over the body surface area (BSA), recovery is remote and euthanasia is recommended.

They presented two case histories where a therapeutic modality employing an Aloe vera cream (Dermaide Aloe) and tablets, reversed the dermal ischemia of burns due to prostaglandins and abrogated a *Pseudomona aeruginosa* infection in animals with over a 35% burn.

Both bacteriological and immunohistochemical data presented confirms the bactericidal and antiprostaglandin effect of Aloe cream/ Dermaide Aloe) and substantiates its efficacy in the management and treatment of thermal injuries in the canine species.

ANTI-INFLAMMATORY

Davis⁴⁰ showed that administration of air under the skin produced a pouch wall that closely resembled a synovium in that the inner lining was made up of macrophages and fibroblasts. Administration of 1% carrageenan directly into the 7-day-old air pouch produced an inflammation characterized by an increased number of mast cells in pouch fluid as well as an increase in wall vascularity. A punch biopsy weight of the pouch wall did not reveal an increase in 1% carrageenan-treated animals. However, a 10% Aloe vera treatment of carrageenan-inflamed synovial pouches reduced the vascularity 50% and the number of mast cells in synovial fluid 48%. The pouch wall punch biopsy weight was increased by A. vera, which was verified by histologic examination of the inner synovial lining. Aloe vera stimulated the synovial-like membrane, as evidenced by an increased number of fibroblasts, suggesting that A. vera stimulated fibroblasts for growth and repair of the synovial model. The synovial air pouch can be used to study simultaneously the acute anti-inflammatory and fibroblast stimulating activities of A. vera.

Davis et al.⁴¹. 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.

Davis et al.⁴² found in the present work, the precipitate fraction decreased the wound diameter by an average of 47.1% (stimulatory system). Little or no wound healing activity was found in the supernatant. Aloe vera appears to act as a modulatory system toward wounds and inflammation and is a potentially valuable tool for managing lower extremity conditions.

't Hart et al.⁴³. 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.

There exists some conflicting data...

Schmidt et al.⁴⁴ evaluated the time interval required for wound healing using a standard wound management protocol with and without aloe vera gel. Twenty-one women were studied who had wound complications requiring healing by second intention after cesarean delivery or laparotomy for gynecologic surgery. Wounds treated with standard management healed in a mean (+/- SD) time interval of 53 +/- 24 days, whereas those treated with aloe vera gel required 83 +/- 28 days (P = .003). The use of aloe vera dermal wound gel was associated with a significant delay in wound healing compared with treatment with an otherwise identical regimen that did not include aloe vera.

Hunter et al.⁴⁵ Three women and one man aged forty-one to sixty-five years experienced a severe burning sensation following the application of aloe vera or vitamin E preparations to a skin area that had been subjected to a chemical peel or dermabrasion. Subsequently, a severe dermatitis occurred that required hospitalization of one patient and intravenous administration of steroids. The dermatitis abated very slowly in all patients: full recovery took three months or more. One patient resumed the use of vitamin E creams two years after the episode of dermatitis and experienced no adverse effect. Patients undergoing dermabrasion or chemical peel procedures should be cautioned specifically against the use of aloe vera or vitamin E topically in the first weeks after surgery.

Davis et al.⁴⁶. 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 colored 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.

Davis et al.⁴⁷ 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*.

Davis et al.⁴⁸ 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*.

Davis et al.⁴⁹ 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.

Davis et al.⁵⁰ Aloe vera, as a biological vehicle for hydrocortisone 21-acetate, was tested topically and systemically against acute inflammation. Systemically, the combination of *A. vera* and hydrocortisone produced a maximum 88.1% inhibition of edema. Polymorphonuclear leukocyte infiltration was reduced 91.1%. The topical inhibition of edema peaked at 97%. The possibility that *A. vera* has significant potential as a biologically active vehicle for steroids is discussed.

Davis et al.⁵¹ examines topical anti-inflammatory activity of Aloe vera as measured by ear swelling.

Davis^{52,53} examines another aspect of the anti-inflammatory activity in relation to arthritis.

Saito et al.⁵⁴ found a glycoprotein, Aloctin A, which was isolated from *Aloe arborescens* Mill, markedly inhibits adjuvant arthritis in rats and carrageenin-induced edema in rats.

Timchenko et al.⁵⁵ described a complex method of treating chronic inflammatory diseases of the internal female genitalia of nonspecific etiology.

Swingle et al.⁵⁶ look at the anti-inflammatory effects of aloe vera on various induced inflammations using croton oil and cantharidin.

BLOOD

Ajabnoor⁵⁷. The acute and chronic effects of the exudate of *Aloe barbadensis* leaves and its bitter principle were studied on plasma glucose levels of alloxan-diabetic mice. Aloes was administered orally, 500 mg/kg, and the bitter principle was administered intraperitoneally, 5 mg/kg. The hypoglycemic effect of a single oral dose of aloes on serum glucose level was insignificant whereas that of the bitter principle was very highly significant and extended over a period of 24 h with maximum hypoglycemia observed at +8 h. In chronic studies, aloes was administered twice daily and the bitter principle was administered once a day for 4 days. The maximum reduction in plasma glucose level was observed at the 5th day in both cases. The hypoglycemic effect of aloes and its bitter principle may be mediated through stimulating synthesis and/or release of insulin from the beta-cells of Langerhans.

CORNEAL or OCULAR

Lawrence⁵⁸ recommends aloe vera for treatment for flash burns of the conjunctiva.

Bakurskaia⁵⁹ examined the effects of tissue therapy and vitamin therapy on unconditioned vascular reflexes and intraocular pressure in glaucomatous patients.

Dumbrova et al.⁶⁰ examined the effect of aloe on the resistance of the optic nerve system of the eye.

Mortada et al.⁶¹ describe the use of aloe extracts in the treatment of experimental corneal ulcers.

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