ALOE VERA: ANATURAL MEDICINE AND ITS EFFECTS: A REVIEW ARTICLE

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Abstract

Aloe vera is a natural product that is now a day frequently used in the field of dermatology. Though there are various indications for its use, controlled trials are needed to determine its real efficacy. The aloe Vera plant, its properties, mechanism of action and clinical uses are briefly reviewed in this article.

Key words: Aloe vera, its effects, Review

Introduction

Aloe is a cactus-like plant that grows in hot, dry climates. In the United States, aloe is grown in Florida, Texas, and Arizona. Aloe produces two substances, gel and latex, which are used for medicines(1). Aloe gel is the clear, jelly-like substance found in the inner part of the aloe plant leaf. Aloe latex comes from just under the plant's skin and is yellow in color. Some aloe products are made from the whole crushed leaf, so they contain both gel and latex. The aloe that is mentioned in the Bible is an unrelated fragrant wood used as incense(2).

Aloe medications can be taken by mouth or applied to the skin. People take aloe gel by mouth for weight loss, diabetes, hepatitis, inflammatory bowel diseases, osteoarthritis, stomach ulcers, asthma, radiation-related skin sores, fever, itching and inflammation, and as a general tonic. A chemical in aloe called acemannan is taken by mouth for HIV/AIDS. Aloe extract is used for high cholesterol(3).

Scientific classification:

Kingdom: Plantae
Clade: Angiosperms
Clade: Monocots
Order: Asparagales

Family: Asphodelaceae

Subfamily: Asphodeloideae

Genus: Aloe

Species: A. Vera

Binomial name

Aloe vera
(L.) Burm.f.

Synonyms

Aloe barbadensis Mill.

Aloe barbadensis var. chinensis Haw.

Aloe chinensis (Haw.) Baker(2)

**Distribution**

The natural range of A. vera is unclear, as the species has been widely cultivated throughout the world. Naturalised stands of the species occur in the southern half of the Arabian Peninsula, through North Africa (Morocco, Mauritania, Egypt), as well as Sudan and neighbouring countries, along with the Canary, Cape Verde, and Madeira Islands. This distribution is somewhat similar to the one of Euphorbia balsamifera, Pistacia atlantica, and a few others, suggesting that a dry sclerophyll forest once covered large areas, but has been dramatically reduced due to desertification in the Sahara, leaving these few patches isolated. Several closely related (or sometimes identical) species can be found on the two extreme sides of the Sahara: dragon trees (Dracaena) and Aeonium being two of the most representative examples.(4)

The species was introduced to China and various parts of southern Europe in the 17th century. The species is widely naturalized elsewhere, occurring in temperate and tropical regions of Australia, South America, Mexico, the Caribbean and southeastern US states. The actual species' distribution has been suggested to be the result of human cultivation (anthropogenic(5))

**Cultivation:** Aloe vera can be grown as an ornamental plant. Aloe vera has been widely grown as an ornamental plant. The species is popular with modern gardeners as a putatively medicinal plant and for its interesting flowers, form, and
succulence. This succulence enables the species to survive in areas of low natural rainfall, making it ideal for rockeries and other low water-use gardens. The species is hardy in zones 8–11, although it is intolerant of very heavy frost or snow. The species is relatively resistant to most insect pests, though spider mites, mealy bugs, scale insects, and aphid species may cause a decline in plant health. This plant has gained the Royal Horticultural Society's Award of Garden Merit(6). In pots, the species requires well-drained, sandy potting soil and bright, sunny conditions; however, Aloe plants can burn under too much sun or shrivel when the pot does not drain water. The use of a good-quality commercial propagation mix or packaged "cacti and succulent mix" is recommended, as they allow good drainage. Terra cotta pots are preferable as they are porous. Potted plants should be allowed to completely dry before rewatering. When potted, aloes become crowded with "pups" growing from the sides of the "mother plant", they should be divided and repotted to allow room for further growth and help prevent pest infestations. During winter, Aloe vera may become dormant, during which little moisture is required. In areas that receive frost or snow, the species is best kept indoors or in heated glasshouses(7).

There is large-scale agricultural production of Aloe vera in Australia, Bangladesh, Cuba, the Dominican Republic, China, Mexico, India, Jamaica, Kenya, Tanzania and South Africa, along with the USA to supply the cosmetics industry(8).

**Treatment of inflammation**

Inflammation is a tissue reaction by the body to injury and typically follows burns or other skin insults. It is classically characterized by swelling (tumor), pain (dolor), redness (rubor) and heat (calor) as well as loss of function. It is thus a complex process and investigations into the therapeutic properties of the gel should take account of its effects on these various symptoms. In addition, the gel may have more than one active constituent, which may be addressing different parts of the healing process. Failure to take all this into account may be responsible for ambiguities which may have arisen in the past about the efficacy of the gel. Although inflammatory processes are a natural response to injury and may hinder healing it may also be undesirable to suppress them in an unstructured way before their purpose is accomplished(9). Leucocytes accompanied by fluid accumulate in the damaged tissues producing the swelling, these movements being the result of increased capillary permeability. Pain is a complex reaction following the release of short peptides and prostaglandins(10). The redness and heat are caused by vasodilatation which reduces blood pressure and
increases circulation, although this gradually slows. Inflammation can be either caused, or intensified by invasion with micro-organisms. As well as in wounds, inflammation is involved in conditions such as arthritis. Continuing research into inflammation has shown that it is a complex process involving many biochemical pathways and a variety of agents and mediators. In particular these authors distinguish three components.\(^{11-13}\)

1. Vasoactive substances; agents causing dilation of blood vessels and opening of junctions between cells of the ultimate capillaries, produced by altering contractile elements in endothelial cells. These factors include vasoactive amines, bradykinin and also prostaglandins\(^{14}\).

2. Chemotactic factors; these agents cause increased cell motility, especially of white blood cells (leucocytes) into stressed areas. These include several proteins and peptides\(^{15}\).

3. Degradative enzymes; these are hydrolytic enzymes breaking down tissue components. Proteases in particular participate in inflammatory states causing chemotactic factors to be released. It was also shown that aloe gel contained both an inhibitory system and a stimulatory system that influenced both inflammatory and immune responses\(^{16}\).

The healing effects of A. vera gel are therefore now being seen as more complex than previously realized. It now appears that several activities are operating each with its own part to play in the overall therapy. These activities may well reflect the presence of several different active agents in the gel. There seems to be a need for two types of investigation. The first, the academic, analytical approach, seeks to dissect the processes and reveal the individual biochemical and physiological reactions, while the second, the clinical approach, puts the various processes back together and studies their interactions. The second can only be ultimately successful when the first is well known. In the best, recent, precise experimentation, care has been taken to separate the inner parenchyma of the aloe leaf completely from the outer layers rich in phenolics, both experimentally and conceptually. However in some trials this separation has not been complete and two preparations were deliberately made and tested, one decolorized and the other containing anthraquinones from the outer layers. These substances were to some degree toxic and reduced for instance suppression of polymorphonuclear lymphocyte infiltration. They also greatly reduced the healing of croton oil-induced inflammation.

A component extracted from whole Aloe barbadensis (sic) leaves and probably originating from the exudate rather than the gel was characterized as a cinnamic acid ester of aloesin and shown to reduce croton oil-induced inflammation. A low molecular weight component claimed to be extracted from the gel but probably also of exudate origin, was shown to
have cytotoxic effects similar to barbaloin. This raises the possibility of both irritating and healing agents in the exudate as well as the gel. Even this comparison is not strictly accurate as it is not clear how the anthraquinone-free gel is made and if other substances are removed, or not, at the same time. Mannose-6-phosphate was shown to have anti-inflammatory activity and this was said to resemble the known activity of acetylated mannan, a gel component.

Two aspects of inflammation reduction following aloe gel treatment by injection in rats were observed. Mustard induced oedema of the paw was reduced by between 445 and 70% while infiltration of polymorphonuclear lymphocytes into a skin blister was reduced by 58%. Two other substances, RNA and vitamin C synergized with the gel in inhibiting oedema. Similarly mouse ear inflammation induced with croton oil was reduced by up to 67% following topically applied aloe gel. In another study these workers tested the action of topical or injected aloe gel against inflammation produced by a variety of agents which were considered to induce different types of inflammation. Thus the gel relieved the inflammatory effects of kaolin, carrageenan (an algal polysaccharide), albumin, gelatin, mustard and croton oil which were said to act either by promoting prostaglandin synthesis or by increasing infiltration of leucocytes. Elsewhere, aqueous or chloroform extracts of the gel reduced a carrageenan-induced inflammation and migration of neutrophils. Aloe gel was less effective against inflammatory agents which produced allergic reactions through the action of bioactive amines such as histamine, even if their synthesis might be inhibited by magnesium lactate. In other ways aloe gel was found to show immunomodulatory properties so the full picture is still not clear. Another aspect is the use of the gel as a vehicle for application of other active substances to which it may additionally impart its own activity(17).

**Wound healing**

If inflammation is a complex process, then wound healing is much more so and the intervention of aloe gel is likely to be multifaceted. A wound to the skin may pierce two layers, the epidermis and dermis as well as damaging appendages. A temporary repair is effected by fibrin clot which is then invaded by a variety of cells, some of which produce the inflammatory response and which eventually carry out a permanent repair(9). It may well be that the repair is not perfect in that scar tissue is produced and appendages do not regenerate. The epidermis is repaired in three phases, migration of cells, proliferation and maturation, while new connective tissue is found in the dermis. As well as repair of structure there is an urgency to avoid microbiological entry which can retard wound contraction. Increased speed of repair was seen in an early detailed study of healing of a surgical cut which showed that ‘A. vera extract in an ointment base’
speeded repair but did not alter the ultimate result. Perhaps aloe gel removes delaying effects rather than accelerating healing as such. The use of aloe gel to heal wounds is the classic use of the material and one of the first explanations of its efficacy was its high water content which kept the wound moist and increased epithelial cell migration, although even this has been questioned. Indeed the beneficial effects on oral wounds where moisture is abundant, indicates that other factors operate. A report of effective aloe gel healing of pressure sores recorded rapid granulation, an effect also noted with various incision wounds in rats and attributed to more rapid maturation of collagen (18).

In a more detailed study, a skin punch wound healed more rapidly when treated with ‘decolorized’ gel than with ‘colorized’ gel. These observations were made on the 7th day after wounding a mouse or rat skin which was said to be optimal for recording healing. Treatment by daily injection of the gel reduced wound diameter, increased skin circulation and seemed to reduce scarring (Davis et al., 1987a and Davis et al., 1989a)(1, 19). Acute inflammation was also inhibited. The colour mentioned is due to anthraquinones from the aloe leaf exudate but details of their removal (‘decolorized’ gel) were not given. Elsewhere, trials using cultures of human endothelial cells or fibroblasts demonstrated cytotoxicity in gel samples contaminated with leaf exudate. In contrast, cytotoxicity was shown to be reduced in neutrophils treated with a low molecular weight fraction of gel, probably exudate-derived, although this was not stated, following inhibition of release of reactive oxygen species (20). In a further study, ‘A. vera’ (sic), presumably the gel, was administered orally over two months or applied to the wounded skin in a cream. Both treatments improved wound healing. It was suggested that one of the factors, out of several, enhanced by aloe gel was increased oxygen access as a result of increased blood supply. In another trial using topical application, stimulation of fibroblast activity and collagen proliferation was demonstrated. Angiogenesis, the growth of new blood capillaries, is a necessary part of tissue regeneration and vascularity of burn tissue of a guinea pig was shown to be reestablished by topical application of aloe gel. A low molecular weight component of freeze-dried aloe gel was shown to stimulate blood vessel formation in a chick chorioallantoic membrane, while a methanol-soluble fraction of the gel was shown to stimulate proliferation of artery endothelial cells in an in vitro assay and to induce them to invade a collagen substrate. Activation of matrix proteinases, which allow penetration, was thought to be involved. Tissue survival following arterial damage in a rabbit ear, which mimicked drug abuse damage, was maintained by topical aloe gel application (21). Healing of an experimental excision wound was promoted by topically applied aloe preparation and this was enhanced when the gel was combined
with a nitric oxide inhibitor. Subsequent work showed that another important impediment to wound healing, microbiological activity, infection, was also addressed by aloe gel treatment. Here, cuts to rat skin were more rapidly healed by topical applications of aloe gel compared with an untreated control or by applications of potential antimicrobials. Many antibiotic agents are more toxic to fibroblasts than to bacteria and seem to retard the healing process.

The gel was thought to contain a growth factor which enhanced the breaking strength of wounds. Only buffered sodium hypochlorite solution (0.025%) had therapeutic effects similar to aloe gel. Macrophages play a considerable part in controlling microorganisms and it was shown that young active macrophages accelerated the rate of wound healing in aged rats, compared with rates where senescent cells in these animals were left alone to act. Activation of macrophages by acemannan, an aloe gel polysaccharide, was claimed. This followed previous observations on the healing powers of acemannan on wounds in elderly or obese rats also attributed to macrophage stimulation. Total regeneration of the skin also requires that ‘difficult’ cells such as neurons are replaced. Proliferation of neuron-like cells and also perhaps cell adhesion, in a culture of rat adrenal cells was stimulated by gel preparations(22, 23).

**Burn Healing**

Burn healing can be regarded as a special type of wound healing and most of the skin reactions are the same. It has been pointed out however that conditions for healing would differ according to the depth of the burn wound and that several factors can interfere with the healing process. Thus three zones have been recognized in a burn, an inner zone (coagulation zone) where cell damage is irreversible, a middle zone (statis zone) where damage is severe and an outer zone (hyperemic zone) where recovery is likely(9). In addition there are three degrees of burns, the first in which the epidermis only is damaged, the second where some dermal damage also occurs but where epithelial regeneration is possible and the third where both epidermis and dermis are irreversibly damaged. Like wound healing it is one of the classic subjects for aloe gel treatment, although as for wound healing some studies demonstrate little benefit. In a large, double-blind trial using 194 patients with radiation burns, no difference to a placebo was observed. However other samples of the preparation used in this trial (Fruit of the Earth) were found elsewhere to have no mucopolysaccharide content(24). The existence of diverse components of a burn and the diverse components of aloe gel which might be healing the burn, were soon recognized. Here the gel was said to possess an anaesthetic effect, a bactericidal action and an anti-thromboxane effect. Recognizing the possible multifarious activities of Aloe constituents, a series of tests of aloe...
gel on heat burns, electrical burns and frostbite in guinea pigs, rabbits and in clinical studies with humans demonstrated a therapeutic potential across the wide variety of soft tissue injuries. The gel was shown to penetrate tissue, relieve pain, reduce inflammation and increase blood supply by inhibiting the synthesis of thromboxane A2, a potent vasoconstrictor (25). Hotplate burns to guinea pig skin healed more quickly after topical aloe gel application and interestingly, the bacterial count was reduced by 60% (11, 18). A recent study demonstrated healing activity towards gamma-radiation burns but only if applied quickly, when it produced more rapid healing than controls but only because peak reaction levels were reduced. Here it was speculated that aloe gel affected the induction of the skin reaction but not the later healing phases. In a similar trial using mice, differences were seen in the effect on first, second and third degree burns. Gel preparations delayed the inflammatory response and speeded the recovery time for first and second degree burns and epithelialization was rapid. Third degree burns proved more intractable. A synergism was noted between the gel and the cream base used. Elsewhere, partial thickness burns were observed to heal more rapidly when treated with aloe gel, compared with vaseline, both growth of epithelial cells and organization of fibro-vascular and collagen tissue being stimulated (26).

**Frostbite:** Direct and indirect cellular injury arising from frostbite can be regarded as a type of burn, although the stages described differ. One classification distinguished four degrees, the first with numbness and erythema, the second where oedema and blisters occur and thromboxane is released, the third where damage extends to the subdermis and the fourth with full tissue thickness damage. Another classification recognized four phases, the first (pre-freeze phase) with chill but no ice crystal formation, the second (freeze–thaw phase) with ice formation, The third (vascular stasis phase) with plasma leakage and the fourth (ischemic phase) with thrombosis, blood loss and even gangren (9). Topical application of *A. vera* cream (sic) enhanced tissue survival of frost-bitten rabbit ear. In an accompanying clinical trial with humans, 68% of the aloe-treated patients achieved full healing, while only 33% of those receiving other treatments were fully healed. In the first group 7% required amputation, compared with 33% in the second group. In another trial with rabbit ears, 24% survived from those treated with *A. vera* cream while only 6% of the untreated ears survived (27).

**Adjuvant arthritis**

One very troublesome instance of inflammation is rheumatoid arthritis where the joints become inflamed and a complex syndrome of pathological effects appears. An experimental model set up to probe this disorder is the so called adjuvant
arthritis produced by injection of a substance which unspecifically intensifies the immune response without itself being antigenic. In one experimental design the adjuvant is injected into the right hand paw of a rat where it soon produces inflammation, whereas later inflammation in the left hand paw is held to be an immunologic phenomenon. A whole leaf extract from A. africana (sic), strictly A. ferox Mill. or a hybrid, but probably in fact A. vera, was injected and decreased inflammation (48%) in the right paw also inhibiting the immunological response (72%) in the left paw(28). It was speculated without experimental evidence that these effects resulted from inhibition of prostaglandin synthesis. In another test A. vera extract, described as a 5% leaf homogenate, (also called A. africana in parts of the text) together with ascorbic acid and RNA was applied topically in a hydrophilic cream base, again produced reduction of both immediate inflammation (39%) and subsequent arthritis (45%). The gel itself, included in this mixture produced 45% regression. A further study attempting to pinpoint active ingredients found that injected aqueous suspensions of anthraquinone, anthracene, cinnamic acid or anthranilic acid inhibited inflammation to various extents, while anthraquinone and cinnamic acid had some effect on the immune response(29).

Another experimental model attempting to simulate the synovial cavity in a joint, where inflammatory reactions occur and produce arthritis is the ‘synovial pouch’ where air is injected under the skin to form a cavity. The walls of the cavity are said to resemble the synovial membrane and the action of carrageenan on this is said to resemble arthritic inflammation. Subsequent injection of Aloe gel reduces this inflammation rapidly and then induces fibroblast growth. The number of mast cells migrating from surrounding connective tissue was also reduced(30).

References


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