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Aloe Vera

Its Chemical and Therapeutic Properties

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Many people admit to self-treating burns or cuts by applying the leaf of a potted Aloe vera houseplant directly to their wounds. Much of the information about Aloe is anecdotal. Unfortunately, only a few controlled clinical studies of Aloe have been reported in the literature. In this review, the historical uses of Aloe will be highlighted and its chemical composition and biologic effects will be described.

History

In Mesopotamia, clay tablets dated 1750 B.C.E. showed that Aloe vera was being used in a pharmaceutical manner (Table 1). Egyptian books from 550 B.C.E. mentioned that infections of the skin could be cured by the application of Aloe. In 74 C.E., a Greek physician, Discordes, wrote a book entitled *De Materia Medica* in which he stated that Aloe could treat wounds, heal infections of the skin, cure chapping, decrease hair loss, and eliminate hemorrhoids.¹ Aloe was used predominantly for eczema around 1200 C.E.² Because Aloe was used mostly as a cathartic medicine, little thought was given to its other uses. Previously reported applications of Aloe vera, which are not well substantiated, include seborrheic dermatitis, thermal burns and sunburn, cystic acne, peptic ulcers, amputation stump ulcers, lacerations,³ colds, tuberculosis, gonorrhea, asthma, dysentery, and headaches. It has also been used as an insect repellent and as a laxative.

The Aloe Vera Plant

There are more than 300 species of Aloe plants.⁴ *Aloe barbadensis* is now referred to by taxonomists as Aloe vera.¹ A major pharmaceutical text indicates that Aloe United States Pharmacopeia is either Cape Aloe (Aloe capensis, South Africa),⁵ otherwise known as *A. ferox*,

or Curacao Aloe, also referred to as *A. barbadensis*.⁶ Therefore, when studying Aloe vera, one should mention the specific species used so that confusion is eliminated.

The Aloe plant has yellow flowers. The leaves are arranged in a rosette configuration; they are triangular and spear-like and have thorny ridges. They are meaty if filled with gel that arises from the clear central mucilaginous pulp. The Arabic word "alloe" means shining and bitter.⁷ The peripheral bundle sheath cells give rise to a bitter, yellow exudate that is responsible for the cathartic effect.⁸ The plant reaches maturity when it measures 1½–4 feet long and has a base of 3 inches or greater in diameter. The most mature leaves are on the outer part of the rosette.¹ Aloe vera was first cultivated for pharmaceutical distribution in 1920.⁹ It matures differently depending on the cultivating conditions.^{8,10} Aloe vera dries to a black powder but will produce a red, gelatinous substance if frozen.

There are conflicting reports in the literature concerning the shelf life of Aloe under varying storage conditions. Lt. Col. Hammitt of the United States Army Medical Research Branch found no evidence of Aloe having a therapeutic value.¹

Chemical Components of Aloe Vera

In 1851, it was discovered that the potency of Aloe was the result of aloin, a bitter juice that dried to a yellow powder and functioned as a cathartic medicine (Fig. 1). It is synonymous with barbaloin, 10-(1',5'-anhydroglucosyl)-aloe-emodin-9-anthrone, which is a glycoside.⁶ Anthraquinone derivatives include anthracenes such as aloe-emodin, which is 1,8-dihydroxy-3(hydroxymethyl)-9,10-anthracenedione. These water-soluble glycosides were separated from the water-insoluble resinous material.

The different species of Aloe have different chemical compositions.¹¹ Unfortunately, many investigations of the constituents found in Aloe do not report the specific species studied. Gjerstad¹² found that the leaves of the Aloe vera plant contained 99.5% water and 0.013% protein. Rowe and Parks¹³ also noted fruc-

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Table 1. History of Aloe Vera Therapy

1750 B.C.E.	Aloe pictured as medicinal treatment on Mesopotamian clay tablets
550 B.C.E.	Egyptian books refer to the treatment of skin infections
74 C.E.	Greek physician writes about his success in treating wounds, hair loss, and hemorrhoids
700 C.E.	Aloe used for sinusitis and eczema in the Orient
1200 C.E.	Predominantly used as a cathartic medicine
1935 C.E.	Modern experimentation begins with radiation-induced ulcerations

tose, ash, and amylase. Although they did not find vitamins A or D, Coats and Ahola¹ indicate that Aloe contains beta carotene and alpha-tocopherol. Many other organic compounds and inorganic elements have been found by others^{7,14} and are listed in Table 2. Both fresh and commercial Aloe preparations were found to contain high levels of lectin-like substances.¹⁵ Lectins, which are found in some plant seeds, are hemagglutinating proteins that bind to glycoproteins and decrease inflammation. Lignin, which is similar to cellulose, is believed to provide Aloe with the ability to penetrate skin, whereas saponin offers antiseptic properties. Gibberellin acts as a growth hormone¹⁶; it decreases inflammation, but, unlike steroids, stimulates protein synthesis. The central gel mucilage is thought to contain the growth hormone-like substance, whereas the yellow sap has been found to decrease cell growth.

In Vitro Properties of Aloe Vera

Some researchers claim that Aloe vera has both antibacterial¹⁷ and anti-inflammatory properties.¹⁸ The anti-inflammatory properties can be explained by three mechanisms. First, Fujita and Teradaira¹⁹ found that a carboxypeptidase in Aloe could inactivate bradykinin. An analogy was made to a peptidase known as bromelain that exists in the stem of pineapples.²⁰ Second, salicylates were shown to be byproducts of emodin, aloemodin, and aloin.¹⁴ Finally, magnesium lactate is known to inhibit histidine decarboxylase, thereby preventing the formation of histamine from histidine in mast cells.⁴

The production of both thromboxane B₂ and prostaglandin F₂ alpha has been shown to decrease because of competitive inhibition when Aloe is added.^{14,21} A commercial preparation of Aloe was reported to decrease the amount of thromboxane A₂ that formed in a monkey that had been scalded accidentally.²²

Decolorized, or anthraquinone-free, Aloe has been reported to inhibit inflammation more than the color-

ized form of Aloe.²³ Whereas high concentrations of anthraquinones have been shown to increase the production of prostaglandins by an irritant effect, trace amounts can decrease the inflammatory response.⁸ If given by the oral route, Aloe depends on anthraquinone for it to be absorbed effectively.²⁴

The growth of normal human cells was promoted by the *in vitro* exposure to fresh Aloe leaves.²⁵ Commercially stabilized Aloe gel, however, was cytotoxic to normal cells. Penneys²⁶ hypothesized that compounds inhibiting oxidation of arachidonic acid might decrease inflammation. Using an *in vitro* assay, he noted that increasing concentrations of a commercial preparation effected increased inhibition. This study also showed that vehicles used in Aloe preparations (eg, petrolatum, mineral oil, and aquaphor) all inhibited prostaglandin production. This emphasizes the importance of designing vehicle-controlled studies. Thermal and radiation burns have healed slightly quicker and with less necrosis when treated with a control ointment versus Aloe ointment.²⁷ Aloe-emodin inhibits a murine leukemic lymphocyte strain known as P-388,²⁸ but the vehicle, which is polysorbate 80, may be responsible for this action.

Antibacterial properties of Aloe vera include *in vitro* inhibition of *Mycobacterium tuberculosis*^{29,30} and *Bacillus subtilis*. Lorenzetti et al.³¹ demonstrated that the juice of Aloe vera was bacteriostatic against *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Salmonella paratyphi*, but also unstable. An Aloe vera extract of 60% concentration was found to be bactericidal against *Streptococcus agalactiae*, *Enterobacter cloacae*, *Citrobacter* species, *Serratia marcescens*, *Klebsiella pneumoniae*, and even *Pseudomonas aeruginosa*. A 70% concentration inhibited *Staphylococcus aureus*. To inhibit *Escherichia coli*, an 80% concentration of Aloe extract was required, whereas a 90% concentration was needed for *Streptococcus faecalis* and *Candida*

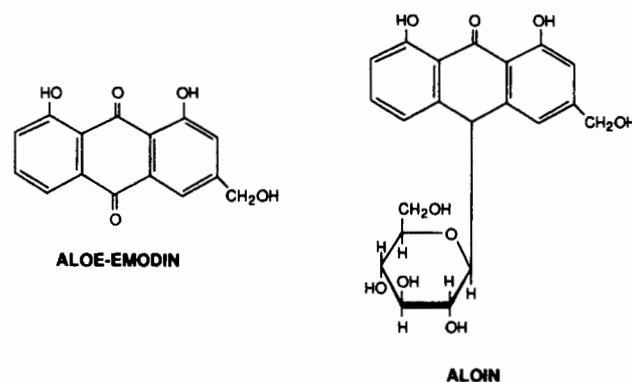


Figure 1. Molecular structures of aloe-emodin and aloin. Structures reproduced from Budavari S, O'Neil MJ, Smith A, et al., eds. The Merck Index. 11th ed. 1989. Permission granted by copyright owner, Merck & Co., Inc., Rahway, NJ, USA © Merck & Co., Inc., 1989.

Table 2. Chemical Composition of Aloe Vera

Anthraquinones		Inorganic	
Aloin	Ester of cinnamic acid	Calcium	
Barbaloin	Aloe-emodin	Sodium	
Isobarbaloin	Emodin	Chlorine	
Anthranol	Chrysophanic acid	Manganese	
Aloetic acid	Ethereal oil	Magnesium	
Anthracene	Resistannol	Zinc	
		Copper	
		Chromium	
		Potassium sorbate	
Saccharides	Enzymes	Vitamins	
Cellulose	Oxidase	B1	Folic acid
Glucose	Amylase	B2	C
Mannose	Catalase	B6	Alpha-tocopherol
L-rhamnose	Lipase	Choline	Beta carotene
Aldopentose	Alkaline phosphatase		
Essential amino acids		Nonessential amino acids	
Lysine	Leucine	Histidine	Proline
Threonine	Isoleucine	Arginine	Glycerine
Valine	Phenylalanine	Hydroxyproline	Alanine
Methionine		Aspartic acid	Tyrosine
		Glutamic acid	
Miscellaneous			
Cholesterol		Uric acid	
Triglycerides		Gibberellin	
Steroids		Lectin-like substance	
Beta-sitosterol		Salicylic acid	
Lignins			

albicans. *B. subtilis* was not inhibited in this study. An 80% concentration of Aloe vera was shown to inhibit growth of *Trichophyton rubrum* and *Trichophyton mentagrophytes*.³² Aloe vera was also noted to be virucidal against herpesvirus.

In Vivo Studies of the Effect of Aloe Vera

In 1935, Collins and Collins published the first credible report of a medicinal use of Aloe vera.³³ A woman experienced acute radiodermatitis after receiving a depilatory x-ray dose to her scalp. Eight months later, when she was still unable to receive relief from various treatments, she applied the inner, gelatinous side of a fresh Aloe vera leaf directly to her wound. Within 24 hours she noted relief from itching and burning, and in 5 weeks her dermatitis healed. Shortly thereafter, three similar cases were reported^{34,35}; no control subjects were used in these studies. In 1937, Crewe³⁶ treated palmar eczema and pruritus vulvae effectively with whole-leaf gel topically. An ulcer that resulted from the

administration of intraoral radium healed after 10 weeks of treatment with topical Aloe leaf therapy.³⁷ Crewe noted satisfactory to good results when Aloe powder mixed with mineral oil was used to treat thermal burns.³⁸

In 1941, Rowe et al.³⁹ treated radiation-induced ulcers in rats with fresh Aloe pulp and observed an increased rate of healing. Although an ointment made from dried Aloe powder was not effective, a decomposed form produced beneficial results. In 1943, Aloe was shown to be successful in the treatment of thermal second-degree burns and radium burns.⁴⁰ One study, which was not a double-blind study, incorporated a control using 50% fresh Aloe vera leaves in petrolatum to treat abrasions of the fingers. The wounds treated with the Aloe reportedly healed better than those treated with a petrolatum base.⁴¹

Lushbaugh and Hale⁴² studied beta irradiation-induced ulcers in rabbits and the histopathologic effects of Aloe vera therapy. There was no vehicle control. Aloe vera juice in aquaphor was more effective than

whole-leaf Aloe. Although the treated sites had necrosis before the untreated sites, the treated sites healed more rapidly. This was hypothesized to occur by increasing the rate of degeneration and repair. There was also an increase in the collagen deposition of the treated wounds.

The manner in which Aloe could expedite the healing of skin ulcers may be related to its occlusive properties. Blitz et al.⁴³ suggest that Aloe vera may function as a protective barrier. Vehicle control was not used in a study where a greater percentage of frostbite injuries healed if Aloe vera was applied to the wounds.⁴⁴ Based on a controlled, non-blind study of frostbite injuries in rabbit ears, Raine et al.⁴⁵ noted that tissue survival was increased when the wounds were treated with Aloe vera cream. Similar results were obtained in a study by McCauley et al.,⁴⁶ but no control group was included.

Increased capillary perfusion has been observed after application of Aloe vera to skin,^{47,48} which may explain how Aloe could help heal chronic ulcers. Both thromboxane A₂³⁶ and thromboxane B₂, along with PGF₂ alpha,⁴⁹ have been shown to be decreased as a result of Aloe therapy. Zawahry et al.⁴⁸ included steroids as a component of Aloe vera gel. This explains the decreased amount of prostaglandins. The full-thickness thermal burns of Guinea pigs healed better with Aloe vera gel than with silver sulfadiazine,⁵⁰ but no vehicle control was used in this study. Conflicting evidence is offered by Kaufman et al.⁵¹ who thought that Aloe hindered the healing process.

A controlled, *in vivo* study used rats in which both a primary inflammatory and a secondary immunologically induced arthritis were the parameters measured.¹⁴ Aloe africana, the species studied, significantly decreased inflammation and prevented arthritis. Whereas Davis et al.⁵² noted that the wounds of rats healed more rapidly when anthraquinone-free Aloe vera was applied, an additional adjuvant arthritis study⁵³ showed that the anthraquinone complex had the greatest preventative antiarthritic activity and good healing properties.

Aloe vera improved re-epithelialization in full-thickness wounds, but to an insignificant extent.⁵⁴ A marked increase in the rate of partial-thickness wound re-epithelialization was noted in a controlled study using a commercially prepared Aloe product.⁵⁵

Davis et al.⁵⁶ mention that the Food and Drug Administration has approved Aloe vera for the treatment of inflammation; however, the dosage is questionable. Aloe vera has been approved by the Food and Drug Administration as a flavoring substance in food.⁵⁷ Gottlieb³ states that a 70% concentration of Aloe is required for healing and anti-inflammatory effects.

There are few reports of adverse reactions caused by topical application of Aloe vera; however, this may

represent under-reporting. Aloe arborescens was the cause of contact dermatitis in two reports.^{58,59} Widespread dermatitis was noted after aloe vera was applied to stasis dermatitis.⁶⁰ An acute bullous allergic reaction and contact urticaria have been reported to result from the use of Aloe vera.⁶¹ One patient experienced a cathartic effect from the topical use of Aloe vera on the mucosal surface²⁶; in this study two cases of "allergic" erythema resulted from the treatment.

Conclusions

An excellent topical medication would be a welcome addition to our armament of topical anti-inflammatory agents. Several studies investigating the components of Aloe vera have had conflicting results. Therefore, there is a need for a definitive study to eliminate the discrepancies. The component of Aloe vera that is most responsible for its effects must be identified. *In vitro* antimicrobial effects often do not correlate well with *in vivo* results; better designed clinical studies that incorporate vehicle controls are necessary.

Stabilization has been a major problem in the past for pharmaceutical companies. Different investigations should study the same species of Aloe and use the same prepared form; otherwise, these variables will create confusion when results are interpreted.

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