

**ALOE VERA: A REVIEW OF ITS CLINICAL EFFECTIVENESS**

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**INTRODUCTION**

_Aloe vera_ is a species of _Aloe_ that is particularly popular for its medicinal properties. The name _Aloe vera_ derives from the Arabic word “Alloeh” meaning shining bitter substance, while _vera_ in Latin means true. 2000 years ago, the Greek scientists regarded _Aloe vera_ as the universal panacea. The Egyptians called _Aloe_, the plant of immortality. In India the whole leaves, exudates and fresh gel of _Aloe_ are used as a cathartic, stomachic, Emenogogue and anthelmintic. In China, Mexico and the West Indies, it has become a common household remedy for a variety of uses. In India, it is found in Rajasthan, Andhra Pradesh, Gujarat, Maharashtra and Tamil Nadu. It is commercially cultivated in Aruba, Bonaire, Haiti, India, South Africa, the United States of America and Venezuela.1,2

**Taxonomy**

Kingdom - Plantae
Order - Asparagales
Division - Spermatophyta
Subdivision - Angiospermae
Class - Monocotyledoneae
Family - Liliaceae
Genus - Aloe
Species - _barbadensis_ Mill1,3,4

**Vernacular Names** 5,6

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Chinese - Lu Hui
Cuba - Sabilla
Dutch - Aloe
French - Aloeos
German - Aloe
Greek - Aloi
Haiti - Laloii
Italian - Aloe
Japanese - Rokai
Korian - Nohwa
Russian - Aloe, Aloi, Sabur
Thai - Wan hang Jo
Vietnam - Lohoi

**Botanical Description**

The plant is a coarse looking perennial with short, thick somewhat divided stem, 30-60 cm high. The leaves are glaucous green, sessile, crowded, lanceolate, Erect spreading rather than concave, spiny toothed at margin, about 30-60 cm long, 10 cm broad and 1.8 cm thick full of juice. The scape is longer than leaves and is scaly and branched. The flowers are pendulous, imbricated and yellow in colour. The plant reaches maturity after four years and has leaves with a length averaging between two and three feet and a base width from three to five inches, each leaf weighing from two to four pounds. The plant’s complete life cycle is twelve years. It produces an average of twelve to thirty leaves. The odour is characteristic while the taste is nauseous and bitter.

**Chemical Constituents**

_Aloe_ is made up of a vast range of compounds which can be divided into three large groups. The first group, complex sugars (among which acemannan stands out), are inside the leaves gel and have an immunostimulating action. Next are the anthraquinones, contained in the outermost part of the skin, with a strong laxative action. Last of all are several substances with a wide array of actions such as minerals, vitamins, essential, non-essential and semi-essential amino acids, organic acids, phospholipids, enzymes, lignin and saponins.7-15
The anthraquinones are a vast group of substances very widespread in the plant kingdom, possessing a wide range of pharmacological properties, both curative and toxic. The exact mechanism for this substance’s ability to have indirect and yet potent effects on the body is not yet known. What is clear, however, is that these substances regulate intestinal motility (i.e., norepinephrine and acetylcholine) and thereby cause peristalsis and, hence, a laxative action. The peristaltic action is closely related to the chemical structure of the molecule. In fact, the anthraquinones present in Aloe are many and the effects differ slightly between them. They include aloetic-emodin, aloetic acid, anthranol, chrysophanic acid, and an ester of cinnamic acid and resistanoll. The typical bitter taste of Aloe is due to these compounds. Their effect on the body is slow, taking between six and twenty-four hours. Botanically, the anthraquinones are found in high concentrations in the sap that runs through the trunk of the plant, with a smaller amount of sap evidenced in the outer layer of the cuticle or skin of the Aloe leaves. Anthraquinones in fresh plants are in a reduced form called anthranols. When these anthranols go through the drying process, the drug quickly converts and is reduced to an oxidized state. Prolonged use of plants containing these drugs can eventually cause the loss of colonic tone. Excessive doses cause diarrhea with imbalances in intestinal absorption of food or nutritional malabsorption, and electrolyte imbalances. These substances are, therefore, not recommended for pregnant women, exactly because of the strong peristalsis which can occur in the lower abdomen. According to recent research findings, aloins in an isolated form destroy the herpes and influenza viruses by deactivating the protein membrane (coating shell) of the virus. The anthraquinones are part of the aromatic polyene hydrocarbons and originate from two main substances: anthracene and fenantrene. In their structure, comprised of three joined benzene rings, eventual substitutions preferentially occupy positions 9 and 10, which are the most chemically active.

Acemannan
Acemannan is biologically active in both humans and animals, and is absorbed through the intestine unchanged by digestion. This mucopolysaccharide deals with the damaging processes of the body by acting as an immune stimulant, principally by stimulating the production of T lymphocytes and macrophages from the thymus and the beta cells of the pancreas. Acemannan has bactericidal and germicidal actions as well as an antifungal action that combats intestinal Candidiasis. Acemannan has the ability to coat and permeate all the gastrointestinal surfaces, increasing the fluidity and the permeability of these membranes. In this way, it allows the easy expulsion of toxins and an even faster absorption of nutritive factors. The chemical name of acemannan is beta-(1,4) acetylpolymannose, because it contains a long chain polymer made up of glucose and mannose, and reaches a molecular weight of about 18,000 to 20,000 units of molecular mass.

Anthraquinones
The anthraquinones are a vast group of substances very widespread in the plant kingdom, possessing a wide range of pharmacological properties, both curative and toxic. The exact mechanism for this substance’s ability to have indirect and yet potent effects on the body is not yet known. What is clear, however, is that these substances regulate intrinsic intestinal motility (i.e., not due to the sympathetic or parasympathetic nervous systems, but due to the stimulation of intestinal plexuses, with a subsequent increase of intestinal motility). This action is closely related to the chemical structure of the molecule. In fact, the anthraquinones present in Aloe are many and the effects differ slightly between them. They include aloetic-emodin, aloetic acid, anthranol, chrysophanic acid, and an ester of cinnamic acid and resistanoll. The typical bitter taste of Aloe is due to these compounds. Their effect on the body is slow, taking between six and twenty-four hours. Botanically, the anthraquinones are found in high concentrations in the sap that runs through the trunk of the plant, with a smaller amount of sap evidenced in the outer layer of the cuticle or skin of the Aloe leaves. Anthraquinones in fresh plants are in a reduced form called anthranols. When these anthranols go through the drying process, the drug quickly converts and is reduced to an oxidized state. Prolonged use of plants containing these drugs can eventually cause the loss of colonic tone. Excessive doses cause diarrhea with imbalances in intestinal absorption of food or nutritional malabsorption, and electrolyte imbalances. These substances are, therefore, not recommended for pregnant women, exactly because of the strong peristalsis which can occur in the lower abdomen. According to recent research findings, aloins in an isolated form destroy the herpes and influenza viruses by deactivating the protein membrane (coating shell) of the virus. The anthraquinones are part of the aromatic polyene hydrocarbons and originate from two main substances: anthracene and fenantrrene. In their structure, comprised of three joined benzene rings, eventual substitutions preferentially occupy positions 9 and 10, which are the most chemically active.

Aloetic Acid
The aloetic acid present in Aloe has an antiseptic and germicidal action. This acid also has a role in inflammatory processes, producing an anaesthetic and analgesic effect. Lastly, this acid has a strong detergent action because its molecular structure is very similar to a saponin. This explains why cinnamic acid is present throughout the cosmetics industry and in anaesthetic medicine. Cinnamic acid is an organic acid whose identifying formula is R-COOH, where R is a radical made up of long and short chained carbons of varying complexity. In this case, the radical is a modified anthracenic compound. The radical –COOH represents the group that gives the compound its main characteristic, which in this case, is an acid.

Chrysophanic Acid
Chrysophanic acid is a naturally occurring organic acid which, like cinnamic acid, has an anthraquinoid radial. Its properties are similar to those described for the anthraquinones. It is a good purifying agent, laxative, diuretic, and it stimulates bile secretion. Its strong, bitter taste gives it a tonic and digestive effect. The chrysophanic acid present in Aloe also functions as a fungicide, especially in the intestine.

Salicylic Acid
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Alo-emodin
Alo-emodin is a molecule present in the yellow exuded matter, rich in anthraquinones, found in the lining or under the cuticle of the Aloe leaf. It possesses bactericidal and laxative properties and can boast a marked anti-tumoural effect, especially in pre-cancerous and cancerous cells of ectodermic tissues, as is being demonstrated in some of the recent research. Alo-emodin’s chemical description is that of a methoxanthraquinone derived from the splitting of aloin to form a simple sugar called arabinose and a composite called anthracene.

Aloin or Barbaloin
Aloin is an active principle exclusive to the Aloe plant and made up of anthraquinone glycosides. Aloin is the conventional name given to molecules which most represent this class of compounds. If this compound is derived from the barbadensis variety, there is a predominance of Barbaloin. Its therapeutic effects are summed up as purging, detoxifying, and markedly antibiotic. Its chemical composition and physical properties are similar to one another and vary according to the source from which they are derived. Pure Barbaloin is a crystalline solid made up of small needles prismatically coloured, varying from yellow to a yellow-brown and the odour may vary from none to the typical green plant smell, with a decisively bitter taste. The two aloins are distinguished from each other by the differences present in some of their chemical and physical properties, and are recognized by whether they are soluble in water, alcohol, ether, or in inorganic acids.

Isobarbaloin
Isobarbaloin possesses a marked analgesic effect and acts as a natural antibiotic. Isobarbaloin is also part of the anthrocyanic glycosides. It is specifically a geometric isomer of aloin, meaning that it has the same molecular weight as aloin, but with differently arranged atoms. They are therefore slightly different in their physical and chemical characteristics.

Vitamins
It is rich in all vitamins excluding Vitamin D, especially the antioxidant Vitamins A (beta-carotene), C and E and even contains a trace of Vit. B12, one of the very few plant sources of this vitamin. This is important for vegetarians.

Enzymes
Several different types of these biochemical catalysts when taken orally aid digestion by breaking down fat. Bradykinase helps to reduce excessive inflammation when applied to the skin topically and therefore reduces pain, whereas others help digest any dead tissues in wounds. Lipases and proteases which break down foods and aid digestion are present.

Minerals
Several minerals such as Calcium, Sodium Potassium, Manganese, Magnesium, Copper, Zinc, Chromium and Selenium are found in Aloe vera. Although minerals and trace elements are only needed in very small quantities, they are essential for the proper functioning of various enzyme systems in different metabolic pathways.

Uses Based on Scientific Evidence
Antifungal, Antidiabetic, Anti-inflammatory, Analgesic, Anticancer, Antimicrobial, Antioxidant, Antiproliferative, Gastric mucosal protection, Hepatoprotective, Neuroprotective, Hypolipidaemic, Immunomodulatory, Antimitogenic, Antileishmanial, Radioprotective and Wound healing.15,16

Analgesic Properties
The analgesic action of Aloe is dominated by three different molecules, all of which collaborate with the beneficial action of anthraecnes and anthraquinones on the cell. To these, an enzyme is added. They are the ester of cinnamic acid, isoabarbaloin, and salicylic acid. The enzyme added is bradykinase. The second molecule is one of the bitter compounds of Aloe and the third is a natural anesthetic yielding the well-known acetylsalicylic acid or aspirin. Bradykinase stimulates the immune system, particularly the macrophages, and becomes a part of the pain system on which it has an analgesic action. It inhibits bradykinin, responsible for post-traumatic pain and swelling, called to action by the liposomal enzymes after an elevated loss of granulocytic macrophages that are unable to block the invading foreign bodies that may enter the body. Used topically, Aloe, and the enzyme bradykinase contained in it, is an effective analgesic and anti-inflammatory remedy.17

Immuno-modulating Property
This property is carried out by the Glucomannan, a class of long-chained sugars derived from plants, which have demonstrated in clinical and laboratory studies to have a wide variety of protective and immunostimulating effects in the human body. At the intestinal level, Glucomannan acts as a powerful anti-inflammatory and neutralizer of the many enzymes responsible for damage to the mucosal membranes. It acts much like a fire extinguisher, lessening the effects of these harmful enzymes. This occurs due to a reduction of the number of leaks in the intestinal wall and a diminishing of the foreign protein absorption that can stimulate allergic reactions in the body. Acemannan, therefore, clearly carries out direct viricidal, bactericidal, and fungicidal properties through which it can help the body to control the production and growth of Candida albicans and through which normal gastrointestinal function is re-established. Assisted by the anthraquinones, acemannan also stimulates intestinal motility, helping to remove allergenic proteins from the small intestine into the colon for elimination. All these reactions have a normalizing effect on the function and structure of the gastrointestinal walls and, therefore, stop the vicious circle of damage to the immune system. Acemannan also has a powerful and immediate effect, activating and stimulating macrophages, antibodies and T-cells. Acemannan acts as a bridge between foreign proteins like virus and macrophage particles, facilitating the ingestion of the proteins by the macrophages in a process known as phagocytosis. The activation of this receptor site is a key component of cell-mediated immunity, which is deficient in HIV infections. The Aloe component, acemannan, increases the number and activity of macrophages, killer T-cells, and monocytes.19-21

Antioxidant Properties
There are many substances in Aloe that exhibit the antioxidant effects. Monovalent or singlet oxygen occurs by secondary reactions which are responsible for the destruction of intercellular tissues and the insurgence of precancerous activity is interrupted to some degree. The acting substances are the minerals, Manganese and Copper, vitamins B2, B6, C, and E and the amino acid cysteine. Manganese is a powerful
antioxidant that slows down the aging process and makes cells stronger in the fight against the negative effects of oxygen and broad spectrum radiation, to which we are exposed daily. It constitutes a part of the enzyme superoxide dismutase, an allied anti-free radical of the pancreas, liver and kidneys. Copper is an oligoelement essential to health. Also a strong antioxidant, Copper greatly limits the damaging effects of free radicals, mainly through the protein ceruloplasmin, which oxidizes the reduced form of iron responsible for the formation of free radicals. Through the enzyme superoxide dismutase, the copper element, which is one of its constituents, prevents rancidity of polyunsaturated fatty acids and keeps the cellular membranes strong. Similarly, it also produces an anti-cancer property. Vitamin B12 actively takes part in complex cellular metabolic processes by being an indispensable regulator together with the enzyme glutathione reductase, as part of the process of maintaining stable levels of glutathione, a highly active anti-free radical. Riboflavin limits and inhibits, in part, the toxic by-products of cellular respiration, a natural metabolic process which is highly oxidative. Vitamin B6 plays a role in the metabolism of the important essential amino acid, tryptophan, which is involved in protein synthesis and is a strong antioxidant. Vitamin C, another strong antioxidant, limits the damage caused by the oxidation of free radicals to the white blood cells. It is known that white blood cells are responsible for our immune defence, by which sickness or disease is overcome more easily. Vitamin E interacts in cellular energy production processes and is truly important to our health, especially during nervous system and immune system illnesses. Cysteine is also a member of Aloe’s antioxidant team. This non-essential amino acid is considered a guarantee to our health and longevity, by de-activating free radicals through its sulphurous function group, a good antioxidant, and, secondly, by protecting and strengthening cellular membranes from external attacks. Recent studies have demonstrated that cysteine, together with the B group of vitamins, can bind toxic molecules formed by disease processes and create nontensive and harmless compounds.13,22

Healing Properties
Glucominan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interacts with growth factor receptors on the fibroblast, thereby stimulating its activity and proliferation, which in turn significantly increases collagen synthesis after topical and oral Aloe vera.23 Aloe gel not only increased collagen content of the wound but also changed collagen composition (more type III) and increased the degree of collagen cross linking. Due to this, it accelerated wound contraction and increased the breaking strength of resulting scar tissue.24 An increased synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound following oral or topical treatment has been reported.25

Skin and Body Anti-aging Properties
The invaluable oligoelements present in Aloe juice, manganese and selenium, constitute the enzymes superoxide dismutase and glutathione peroxidase, recognized as powerful antioxidants and cellular anti-aging agents. Their high antioxidant properties slow down the aging process. This helps cells to become stronger in combating the negative effects caused by oxygen and the broad spectrum radiation we are exposed to daily. The non-essential amino acid, proline, is instead a constituant of collagen, whose role is to ensure the perfect holding capacity and elasticity of epithelial tissues. It naturally follows that the intake of the vitamins and minerals present in Aloe stimulates proper blood saturation, thus guaranteeing better oxygenation and faster expulsion of toxins. Skin becomes smoother, hydrated and more elastic, protected from free radicals and their degenerative activity, resulting in impressive / substantial antiaging effects.26

Antiviral and Antitumor Activity
These actions may be due to indirect or direct effects. Indirect effect is due to stimulation of the immune system and direct effect is due to anthraquinones. The anthraquinone aloin inactivates various enveloped viruses such as herpes simplex, varicella zoster and influenza. In recent studies, a polysaccharide fraction has shown to inhibit the binding of benzoyprene to primary rat hepatocytes, thereby preventing the formation of potentially cancer initiating benzopyrene-DNA adducts.27

Anti-inflammatory Action
Aloe vera inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid. Recently, the novel anti-inflammatory compound called C-glucosyl chromone was isolated from gel extracts.28

Anti-diabetic Effect
In a study on streptozotocin-induced diabetic rats, oral administration of Aloe vera gel (alcohol insoluble residue extract) significantly reduced the fasting blood glucose, hepatic transaminases, plasma and tissue cholesterol, triglycerides, free fatty acids and phospholipids and in addition also significantly increased plasma insulin levels. The decreased plasma levels of high density lipoprotein cholesterol and increased levels of low density lipoprotein cholesterol in the streptozotocin-induced rats were restored to normal after treatment with gel extract.29

Side Effects
Topical
It may cause redness, burning, stinging sensation and rarely generalized dermatitis in sensitive individuals. Allergic reactions are mostly due to anthraquinones, such as aloin and Barbaloin.

Oral
Abdominal cramps, diarrhoea, red urine, dependency or worsening of constipation. Prolonged use has been reported to increase the risk of colorectal cancer. Laxative effect may cause electrolyte imbalances (low potassium levels)15.

Contraindications
As with other stimulant laxatives, products containing Aloe should not be used in patients with intestinal obstruction or stenosis, atony, severe dehydration with electrolyte depletion, or chronic constipation. Aloe should not be administered to patients with inflammatory intestinal diseases, such as appendicitis, Crohn disease, ulcerative colitis, irritable bowel syndrome, or diverticulitis or to children less than 10 years of age. Aloe should not be used during pregnancy or lactation except under medical supervision after evaluating benefits and risks. Aloe is also contraindicated in patients with cramps, colic, haemorrhoids, nephritis, or any undiagnosed abdominal symptoms such as pain, nausea, or vomiting.30
Drug-Herb Interactions
Increase the actions of cardiac glycosides and Antiarrhythmic drugs, thiazide diuretics, loop diuretics, liquorice and corticosteroids. Aloe gel, when taken orally, can reduce the absorption of many medications. Thus, it should be taken two hours apart from all medications. A study reported that Aloe vera preparations improved the absorption of both vitamins C and E.

CONCLUSION
Aloe and its preparations have been widely used as a medicine since ancient times. Now, various researches have been conducted to prove the efficacy of Aloe vera in various health problems. In spite of the reporting of these positive benefits of the plant, most of the Aloe vera research studies are of small scale in nature. So, more and better trial data are needed to define the clinical effectiveness of this popular herbal remedy more precisely.

REFERENCES


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