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

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ABSTRACT

Aloe vera has been used for over five thousand years. Throughout history, it has been considered a magical plant, almost a panacea, capable of remedying many of mankind's ailments. It is only in the last 20 years, after a series of proven research, that we can highlight the characteristics of this plant, whose secrets have been hidden behind a blanket of botanical and pharmacological puzzles that only today begin to yield some answers. The *Aloe vera* plant and its clinical uses are briefly reviewed in this article.

Keywords: *Aloe vera*, Antioxidant, Unani Medicine

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, Emenagogue 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* Mill^{3,4}

Vernacular Names^{5,6}

Arabic - Sibr
Persian - Sibr
Urdu - Ailwa
Hindi - Kumari
Sanskrit - Ghritra kumari
Kannada - Karilola
Telugu - Kalabanda
Tamil - Kattalai
Gujarati - Eliyo
Kashmiri - Musabbar
Marathi - Korphad
Oriya - Musaboro
Punjabi - Musabbar
Assamese - Musabhar

Chinese - Lu Hui
Cuba - Sabilla
Dutch - Aloe
French - Aloes
German - Aloe
Greek - Aloï
Haiti - Laloï
Italian - Aloe
Japanese - Rokai
Korian - Nohwa
Russian - Aloe, Aloï, 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.¹²⁻¹⁵

Unani Description

Mizaj	Hot and Dry (2 ⁰) ⁷
Part used	Fresh and dried juice of leaves pulp ⁷
Actions	Mushil, Mudir-e-haiz, Mohallil-e-warm, Muharrik-e-kabid ^{8,9,10}
Therapeutic Uses	Qabz, Deedan-e-Ama, Warm-e-Kabid, Waja-ul- Mafasil, Izm-e-Tihal, Ehtebas-e-Tams ^{8,9,10}
Muzir (adverse effects)	Excessive use causes dysentery, irritation in the intestines, Tenesmus ⁷
Musleh (correctives)	kateera, mastagi and rose ⁸
Contraindications	During Lactation and pregnancy ^{7,8}
Dose	1-4 gm ⁸
Compound formulations	Zimad-e-jalinoos, Majoon-e-antaki, Kohal-e-bayaz, Habb-e- Muntinakbar, Habb-e-mudir, Habb-e-Ghafis, Iyarji-e-laghaziya, Tiryag-e-wabai ⁵
Detoxification process	Prepare the decoction of Balchad, Charaita, Tagar, Taj, Jawitri, Izkhar, Jaifal, Darchini, Ood-e- balsan, Filfil, Mastagi 10gm each in 1 ser water. Add ½ ser aloe vera gel in this decoction and keep the mixture for some time. Decant it and use the precipitate for medicinal purpose ¹¹ .

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 peristalsis and, hence, a laxative action). This strong purging 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 aloe-emodin, aloetic acid, anthranol, chrysophanic acid, an ester of cinnamic acid and resistannol. 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 lack of colon tone. Excessive doses cause diarrhoea 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 polynuclear 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.

Aloetic Acid

The specific properties of aloetic acid are not yet fully known, but it seems to act as a natural antibiotic, especially if synergistically combined with Barbaloin, isobarbaloin, and aloe-emodin. This hydroxymethylanthraquinone comes from the division of aloe-emodin in acid and a simple sugar.

Cinnamic Acid

The cinnamic 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 an organic acid which, like cinnamic acid, has an anthraquinone radical. 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 fungicidal, especially in the intestine.

Salicylic Acid

Salicylic acid forms part of the organic chemical composites called hydroxyl acids because they possess both a hydroxyl and a carboxyl component, similar to lactic acid and malic acid. Salicylic acid is the principal component of aspirin and its salts, the salicylates, are used as analgesics and anti-rheumatics in the pharmaceutical industry. In *Aloe* juice, salicylic acid functions as an antiseptic, anti-bacterial, and an anti-inflammatory.

Aloe-emodin

Aloe-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-tumoral effect, especially in pre-cancerous and cancerous cells of ectodermic tissues, as is being demonstrated in some of the recent research. Aloe-emodin's chemical description is that of a methoxyanthraquinone 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, Antimutagenic, Antileishmanial, Radioprotective and Wound healing.^{2,15,16}

Analgesic Properties

The analgesic action of *Aloe* is dominated by three different molecules, all of which collaborate with the beneficial action of anthracenes and anthraquinones on the cell. To these, an enzyme is added. They are the ester of cinnamic acid, isobarbaloin, 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 anaesthetic 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.¹⁸⁻²¹

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 inoffensive and harmless compounds.^{13,22}

Healing Properties

Glucomannan, 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 tissue²⁴. 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 constituent 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 benzopyrene 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 extract²⁹.

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 vomiting¹⁵.

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 E¹⁵.

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.

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