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PHYTOCHEMICAL CONSTITUENTS OF *ALOE VERA* AND THEIR MULTIFUNCTIONAL PROPERTIES: A COMPREHENSIVE REVIEW

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ABSTRACT: *Aloe vera* belongs to the family Liliaceae commonly known as Ghrit Kumari, is the ever known oldest and the most applied medicinal plant worldwide. *Aloe Vera* is used for vigor, wellness and medicinal purposes since rigvedic times. Health benefits of *Aloe vera* include its application in wound healing, treating burns, minimizing frost bite damage, protection against skin damage from x-rays, lung cancer, intestinal problems, increasing high density lipoprotein (HDL), reducing low density lipoprotein (LDL), reducing blood sugar in diabetics, fighting against acquired immuno deficiency syndrome (AIDS), allergies and improving immune system. Phytochemistry of *Aloe vera* gel has revealed the presence of more than 200 bioactive chemicals. Commercially, aloe can be found in pills, sprays, ointments, lotions, liquids, drinks, jellies, and creams, to name a few of the thousands of products available. In the present scenario, the aloe industry is blooming but the consumers are misguided leading to unfavorable outcome due to reasons like unawareness about its proper and adequate medicinal and health value, improper marketing and unavailability of processing units at farmer's level, misleading hyped advertisement in cosmetic and health products. So, there is a burning need to educate about the importance of *Aloe vera* for human race and popularize it for greater interest.

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." Today, the *Aloe vera* plant has been used for various purposes in dermatology¹.

There are over 550 species of aloe grown around the world. However, only two species are grown today commercially, with *Aloe barbadensis* Miller and *Aloe aborescens* Miller being the most popular.

Aloe can be found in Mexico, the Pacific Rim countries, India, South America, Central America, the Caribbean, Australia and Africa². The leaves of the Aloe plant grow from the base in the rosette pattern. Mature plants can grow as tall as 2 and a half inches to 4 feet with the average being around 28 to 36 inches in length. Each plant usually has 12 - 16 leaves that, when mature, may weigh up to three pounds. Each leaf is composed of three layers: An inner clear gel that contains 99% water and rest is made of glucomannans, amino acids, lipids, sterols and Vitamins.

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The middle layer of latex which is the bitter yellow sap and contains anthraquinones and glycosides. The outer thick layer of 15 - 20 cells called as rind which has protective function and synthesizes carbohydrates and proteins^{3, 4}. The plants can be harvested every 6 to 8 weeks by removing 3 to 4 leaves per plant.

Taxonomical Position of *Aloe vera*:

Kingdom : Plantae

Order : Asparagales

Division : Spermatophyta

Subdivision : Angiospermae

Class : Monocotyledoneae

Family : Liliaceae

Genus : Aloe

Species : *barbadensis* Mill⁵



FIG. 1: *ALOE BARBADENSIS* MILL

Active Constitutes of *Aloe vera*: The *Aloe vera* leaf gel contains about 98% water⁶. The total solid content of *Aloe vera* gel is 0.66% and soluble solids are 0.56% with some seasonal fluctuation. On dry matter basis aloe gel consists of polysaccharides (53%), sugars (17%), minerals (16%), proteins (7%), lipids (5%) and phenolic compounds (2%) (Fig. 2). *Aloe vera* contains 200 potentially active constituents: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids, which are responsible for the multifunctional activity of Aloe⁷⁻⁹.

Vitamins: It contains Vitamins A (beta-carotene), C and E, which are antioxidants. It also contains Vitamin B₁₂, folic acid, and choline. Antioxidant neutralizes free radicals.

Enzymes: It contains 8 enzymes: aliase, alkaline phosphatase, amylase, bradykinase, carboxypeptidase, catalase, cellulase, lipase, and peroxidase. Bradykinase helps to reduce excessive inflammation when applied to the skin topically, while others help in the breakdown of sugars and fats.

Minerals: It provides calcium, chromium, copper, selenium, magnesium, manganese, potassium, sodium and zinc. They are essential for the proper functioning of various enzyme systems in different metabolic pathways and few are antioxidants.

Sugars: It provides monosaccharides (glucose and fructose) and polysaccharides: (glucomannans / polymannose). These are derived from the mucilage layer of the plant and are known as mucopolysaccharides. Recently, a glycoprotein with anti-allergic properties, called alprogen and novel anti-inflammatory compound, C-glucosyl chromone, has been isolated from *Aloe vera*.

Anthraquinones: It provides 12 anthraquinones, which are phenolic compounds traditionally known as laxatives. Aloin and emodin act as analgesics, anti-bacterials and anti-virals.

Fatty acids: It provides 4 plant steroids; cholesterol, campesterol, β -sisosterol and lupeol. All these have anti-inflammatory action and lupeol also possesses antiseptic and analgesic properties.

Hormones: Auxins and gibberellins that help in wound healing and have anti-inflammatory action.

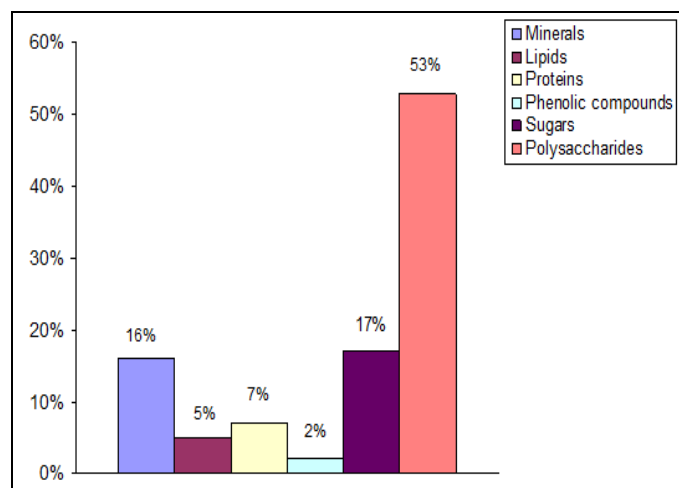


FIG. 2: CHEMICALS COMPOSITION OF *ALOE VERA* GEL

Others: It provides 20 of the 22 human required amino acids and 7 of the 8 essential amino acids. It also contains salicylic acid that possesses anti-inflammatory and antibacterial properties. Lignin, an inert substance, when included in topical preparations, enhances penetrative effect of the other ingredients into the skin. Saponins that are the soapy substances form about 3% of the gel and have cleansing and antiseptic properties¹⁰.

Therapeutic Uses:

Wound Healing Properties: Wound healing is a dynamic process, occurring in 3 phases. The first phase is inflammation, hyperaemia and leukocyte infiltration. The second phase consists of removal of dead tissue. The third phase of proliferation consisting of epithelial regeneration and formation of fibrous tissue¹¹. Various researchers reported that the effective components for wound healing may be tannic acid and a type of polysaccharide¹². Other researcher have also reported that glucomannan, a mannose rich polysaccharide and gibberellin a growth hormone interacts with growth factor receptors on the fibroblast their by stimulating its activity and proliferation which in turn significantly increase collagen synthesis after topical and oral *Aloe vera*.

Aloe vera gel not only increased collagen content of the wound but also changed collagen composition and increased the degree of collagen cross linking. Acemannan is also considered the main functional component of *Aloe vera*, is composed of a long chain of acetylated mannose (mucopolysaccharides)^{13, 14}. This complex carbohydrate accelerates wound healing and reduces radiation induced skin reactions. Macrophage - activating potential acemannan may stimulate the release of fibrogenic cytokines. Direct binding of acemannan to growth factors and their stabilization may lead to promotion of prolong stimulation of granulation tissue^{14, 15}.

Beauty care properties: Aloin and its gel are used as skin tonic against pimples. *Aloe vera* is also used for soothing the skin, and keeping the skin moist to help avoid flaky scalp and skin in harsh and dry weather. *Aloe vera* may also be used as a moisturizer for oily skin. Studies show that *Aloe vera* improves the skin's ability to hydrate itself, aids in the removal of dead skin cells and has an

effective penetrating ability that helps transport healthy substances through the skin¹⁶. Each of these factors makes *Aloe vera* an ideal ingredient in cosmetic and dermatological products. In fact, *Aloe vera* is currently one of the most important ingredients in the cosmetics industry, being utilized in over 95 per cent of the dermatologically valuable extracts manufactured worldwide. The aloe sugars are also used in moisturizing preparations. Mixed with selected essential oils, it makes an excellent skin smoothening moisturizer, sun block lotion plus a whole range of beauty products. Due to its soothing and cooling qualities, Maharishi ayurveda recommends *Aloe vera* for a number of skin problems^{17, 18}.

Skin and Body Anti - Aging Properties: The invaluable oligo-elements present in aloe juice, manganese and selenium, constitute the enzymes superoxide dismutase and glutathione peroxidase, recognized as powerful antioxidants and cellular anti-aging agents¹⁶. Their high antioxidants 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 vera* 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 anti-aging effects¹⁹.

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 extracts²⁰. Fresh *Aloe vera* gel significantly reduced acute inflammation in rats (carrageenin-induced paw oedema), but not in chronic inflammation. In croton oil-induced oedema in mice, three *Aloe vera* gel sterols were able to reduce inflammation by up to 37%. Lupeol, the most active anti-inflammatory sterol, reduced inflammation in a dose dependent manner²¹.

The aloe sterol includes campesterol, β -sitosterol, lupeol, and cholesterol which are anti-inflammatory in nature, helps in reducing the inflammation pain and act as a natural analgesic. Other aspirin-like compound present in Aloe is responsible for anti-inflammatory and antimicrobial properties²¹. Even, *Aloe vera* extract (5.0% leaf homogenate) decreased inflammation by 48% in a rat adjuvant-induced arthritic inflammatory model^{20, 22}.

Antiseptic Effects: The antiseptic property of *Aloe vera* is due to presence of six antiseptic agents namely lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols and sulphur. These compounds have inhibitory action on fungi, bacteria and viruses. Though most of these uses are interesting controlled trials are essential to determine its effectiveness in all diseases²³.

Laxative Effects: Anthraquinones present in latex are a potent laxative. It increases intestinal water content, stimulates mucus secretion and increases intestinal peristalsis^{9, 22}. The anthraquinones decrease in stool specific gravity indicating a greater water-holding characteristic of the stool and improved gastrointestinal motility with reduced bowel transit time. This would indicate that the *Aloe vera* supplementation had a tonic effect on the intestinal tract, thereby promoting a reduced transit

time with decreased residence of fecal material in the colon.

***Aloe vera* Fights Stress:** In the modern scenario many people suffer from stress. Today's fast stressful life causes some bio-chemical and physiological changes in the body, making us susceptible to diseases and dysfunction of organ systems. Aloe juice is helpful in smooth functioning of the body machinery²⁴. It reduces cell-damaging process during stress condition and minimizes bio-chemical and physiological changes in the body. Oxidative stress refers to chemical reactions in which compounds have their oxidative state changed. Some antioxidants are part of the body's natural regulating machinery while other dietary antioxidants are derived from diet sources. *Aloe vera* is an excellent example of a functional food that plays a significant role in protection from oxidative stress^{8, 25}.

Medicinal Uses: *Aloe vera* has been used for medicinal purposes in several cultures for millennia: Greece, Egypt, India, Mexico, Japan, and China. The Egyptians used the *Aloe vera* to make papyrus like scrolls as well as for treatment of tuberculosis. Various preparation of *Aloe barbadensis* like confection, lotion and juice are useful remedies for curing various disease (Fig. 3)^{26, 27}.

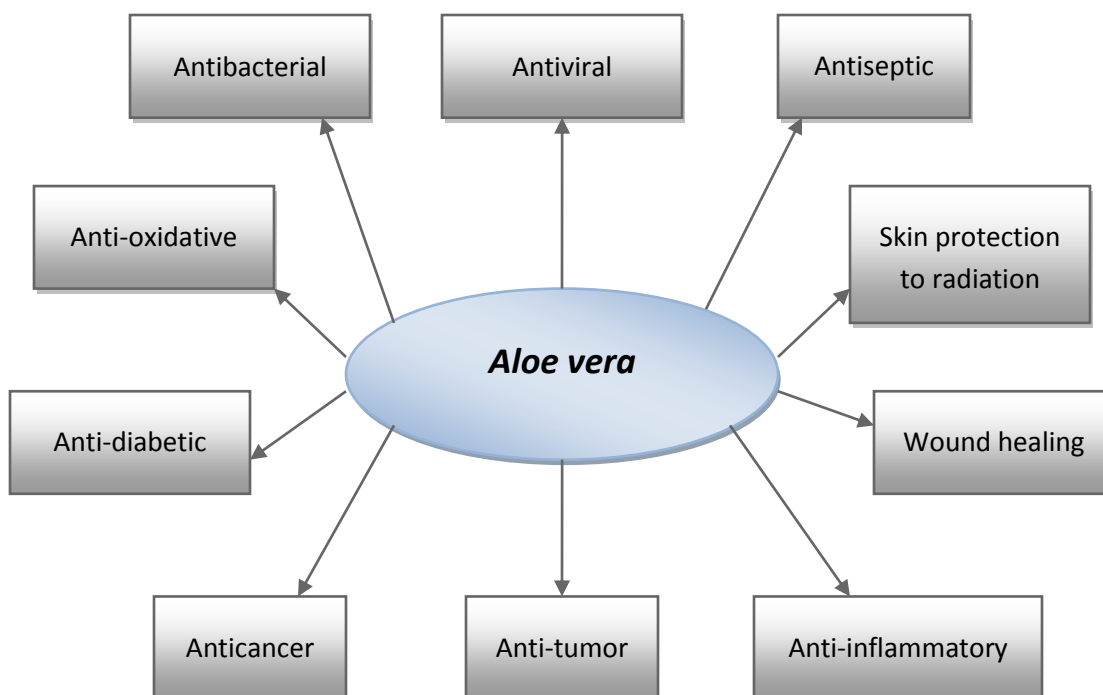


FIG. 3: THERAPEUTIC AND MEDICINAL UTILITIES OF ALOE VERA

Antidiabetic activity: Several pre-clinical (in animal) and clinical (in human) trials showed a blood glucose lowering effects for *Aloe vera* gel preparations in different forms (e.g. juice or as constituents in bread etc.). In a study on streptozotocin - induced diabetic rats oral administration of *Aloe vera* gel (alcohol insoluble residue extract) significantly reduced the fasting blood glucose (FBG), hepatic transaminases, total cholesterol (TC), triglycerides (TG), free fatty acids (FFA) and phospholipids and in addition also significantly increased plasma insulin levels. The decreased plasma levels of high density lipoprotein cholesterol (HDLc) and increased levels of low density lipoprotein cholesterol (LDLc) in the streptozotocin-induced rats were restored to normal levels after treatment with Aloe gel extract²⁸. It was further proposed that the glucose lowering effect could be explained by an antioxidant mechanism because it attenuated oxidative damage in the brains of streptozotocin-induced mice and reduced peroxidation levels in the kidneys of streptozotocin-induced diabetic rats²⁹.

Role of *Aloe vera* in Heart Disease: Coronary heart disease associated with the accumulation of blood fats (lipids) in the lining of the arteries is still one of the major causes of death in the Western world. Several studies in animal models as well as in human subjects have suggested that the ingestion of Aloe gel may have a beneficial effect by lowering serum cholesterol, serum triglycerides, and serum phospholipids, which, when elevated, seem to accelerate the deposition of fatty materials in the large and medium-sized arteries, including the coronary arteries of the heart^{22,30}. In one study, albino laboratory rats were fed high cholesterol diets with the experimental group fed the polysaccharide (Glucomanan) from Aloe. Compared with the control animals, the group fed the Aloe fraction showed significantly decreased in the levels of TC, TG, phospholipids and non-esterified fatty acid along with the elevation in the levels of HDL and HDL / TC ratio. The evidence suggests that the ingestion of Aloe gel may have a salubrious effect on fat (lipid) metabolism which, if active in human subjects, would tend to decrease the risk of coronary artery disease in people³¹.

Role of *Aloe vera* in Immune Modulation: The *Aloe vera* gel polysaccharide can boost the working

of the macrophages in the intestines allowing the immune system to improving the activity of T-Lymphocytes by up to 50 per cent for penetrate the bad bacteria, viruses, tumor cells and various pathogens^{32,33}. In a pilot study in HIV-infected persons acemannan increased the number of white blood cells and improved symptoms. In a study on mice that had previously been implanted with murine sarcoma cells, acemannan stimulates the synthesis and release of interleukin -1(IL-1) and tumor necrosis factor from macrophages in mice, which in turn initiated an immune attack that resulted in necrosis and regression of the cancerous cells^{13,34}.

Anti - Tumor Activity: A number of glycoproteins present in *Aloe vera* gel have been reported to have antitumor and antiulcer effects and to increase proliferation of normal human dermal cells^{25,35}. 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. An induction of glutathione S-transferase and an inhibition of the tumor-promoting effects of phorbol myristic acetate has also been reported which suggest a possible benefit of using aloe gel in cancer chemoprevention^{14,36}.

Anti - Cancer Activity: The role of Aloe in carcinogenicity has not been evaluated well. The chronic abuse of anthranoid-containing laxatives has been hypothesized to play a role in colorectal cancer; however, no causal relationship between anthranoid laxative abuse and colorectal cancer has been demonstrated³⁷. *Aloe vera* juice enables the body to heal itself from cancer and also from the damage caused by radio and chemotherapy that destroys healthy immune cells crucial for the recovery. *Aloe vera* acts as radiation protectors and inhibits testicular damage from gamma radiation and reduces cancer. Acemannan is the major carbohydrate fraction obtained from *Aloe vera* leaf. This fraction promotes wound healing, has antiviral, anticancer and immune stimulation effect. Compounds extracted from *Aloe vera* have been used as an immuno-stimulant that aids in fighting cancers in cats and dogs²⁴. *Aloe vera* emodin, an anthraquinone, has the ability to suppress or inhibit the growth of malignant cancer cells making it to have anti-neoplastic properties³⁶.

Antimicrobial Activities:

Antibacterial Activity: *Aloe vera* gel was bactericidal against *Pseudomonas aeruginosa* and acemannan prevented it from adhering to human lung epithelial cells in a monolayer culture^{38, 39}. The aloe extract was potent against three strains of Mycobacterium (*M. fortuitum*, *M. smegmatis* and *M. kansasii*) and a strong anti-mycobacterial activity against *M. tuberculosis* as well as antibacterial activity against *P. aeruginosa*, *E. coli*, *S. aureus* and *S. typhi*. The preliminary phytochemistry revealed presence of terpenoids, flavonoids and tannins. Thus, *Aloe secundiflora* could be a rich source of antimicrobial agents and it can give scientific backing to its use by the local people of Lake Victoria region of Kenyas⁴⁰.

Antiviral Activity: Several ingredients in *Aloe vera* gel have been shown to be effective antiviral agent. Acemannan reduced herpes simplex infection in two cultured target cell lines⁴¹. Lectins, fractions of *Aloe vera* gel, directly inhibited the cytomegalo virus proliferation in cell culture, perhaps by interfering with protein synthesis. A purified sample of *Aloe emodin* was effective against infectivity of herpes simplex virus type I and type II and it was capable of inactivating all of the viruses, including varicella zoster virus, influenza virus, and pseudo-rabies virus⁴². The anthraquinone aloin also inactivates various enveloped viruses such as herpes simplex, varicella zoster and influenza⁴².

Antifungal Activity: *Aloe vera* was evaluated on the mycellium development of *Rhizoctonia solani*, *Fusarium oxysporum*, and *Colletotrichum coccodes*, that showed an inhibitory effect of the pulp of *A. vera* on *F. oxysporum* at 10^4 μL and the liquid fraction reduced the rate of colony growth at a concentration of 10^5 μL in *R. solani*, *F. oxysporum*, and *C. coccodes*^{43, 44}. The saponins substances from the gel that is capable of cleansing and having antiseptic properties. The saponins perform strongly as anti-microbial against bacteria, viruses, fungi and yeasts⁴⁵.

Safety Aspects of *Aloe vera* Products: Scientific community is divided into two groups regarding safety of *Aloe vera* products. One group advocates that the *Aloe vera* is quite safe for human consumption. While the other group warns to use it

with caution and utmost care to avoid contamination of aloin from the yellow exudates, as aloin is reported as DNA damaging and causes cancer⁴⁶. On the contrary scientists have reported that anthroquinones present in *Aloe vera* leaf, including aloin, are beneficial in a number of ways when used in small quantity, though the small quantity is not well defined. It is reported that *Aloe vera* gel is safe for external use, allergies are rare and adverse reactions with other medications have not been reported. Aloe should not be used internally during pregnancy, lactation or childhood and by persons suffering from abdominal pain, appendicitis or intestinal obstruction. Studies in mice revealed no acute toxicity in therapeutic doses but in high doses a decreased central nervous system (CNS) activity was noticed. In chronic treatment decrease in red cell count and significant sperm damage was noticed⁴⁷. However, no systematic investigation exists in humans on the effect of high doses of *Aloe vera* for longer periods on red cell count and sperm damage⁴⁸.

CONCLUSION: Hence there is no wonder in considering *Aloe vera* as the 'Wonder plant'. It's uses as multiple from like an antiseptic, anti-inflammatory agent, a curing agent for heart problems, helps in relieving the symptoms of severe illnesses like cancer and diabetes, being a beauty enhancer and improves health. This Ancient Indian herb has been known from centuries for its unique medicinal properties, but now it has been rediscovered and recognized as beneficial for the human beings. The active ingredients hidden in its succulent leaves have the power to smooth human life and health in a myriad ways. So, more and better trial data are needed to define the clinical effectiveness of this popular herbal remedy precisely. *Aloe vera* is undoubtedly, the nature's gift to humanity and it remains for us to introduce it to ourselves and thank the nature for its never-ending gift.

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