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## *Aloe vera* and its biological activities

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### Abstract

*Aloe vera* is used for medicinal purposes since ancient times. The botanical name is *Aloe barbadensis miller*. It belongs to the Liliaceae family. It is also called the healing plant or the silent healer, because of its wound and burn healing properties. Latex and gel are the two basic products of *Aloe* leaves. The latex and gel contain biologically active components. Polysaccharides contained in the gel of the leaf attribute most of the health benefits associated with *Aloe Vera*. *Aloe* was available as pills, ointments, jellies, sprays, drinks, etc. The important application *aloe vera* was wound healing, treating burns, anti-inflammatory, antidiabetic, anti-cancer, anti-ulcer, protection against skin damage from x-rays, lung cancer, intestinal problems, increasing HDL, reducing LDL, reducing blood glucose in diabetics, fighting against acquired immune deficiency (AIDS), allergies, etc. The *aloe vera* plant, its biological properties are briefly reviewed in this article.

### Key words:

*Aloe vera*, Immunomodulatory effect, Liliaceae family, HDL, LDL, Anti inflammatory effect.

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### Introduction

The burn plant (*Aloe Vera*) has been known and used for its beauty, health, medicinal, and skincare properties. *Aloe vera* is famous for its considerable medicinal properties. The *Aloe vera* plant contains mostly water, and 75 ingredients including minerals, vitamins, glyconutrients, glycoproteins, polysaccharides amino acids, enzymes, and phytonutrients. The chemistry of the plant discloses the presence of quite 200 different biologically active substances. The inner gel of the *Aloe vera* leaf is associated with many biological properties. Many kinds of research have been consolidated on the biological activities of the various species of *Aloe*, such as antibacterial and antimicrobial activities. *Aloe vera* has important medicinal properties such as anti-rheumatoid, anticancer, antitumor, antiarthritic, and antidiabetic properties. *Aloe vera* has also been promoted for gastrointestinal disorders, constipation, and immune system deficiencies and used externally to treat various skin conditions such as cuts, burns, and eczema.

### Immunomodulatory effect

*Aloe vera* gel has the strongest immunomodulatory activity, which is mainly due to components such as aloctin A and acemannan. A study of the mouse macrophage cell line RAW 264.7 was made to explore the consequences of acemannan and it had been noticed that acemannan stimulates macrophage cytokine production, gas release, surface molecule expression, and cell morphologic changes [1]. Halder S et al was conducted a study to explore the effect of the aqueous

extract of burn plant on parameters of humoral and cell-mediated immunity, and it had been found that *Aloe vera* (400 mg/kg, orally) crucially enhanced the secondary humoral immune response [2]. The recent trial proved that oral treatment with *aloe vera* extract reduces pyrogallol-induced suppression of humoral and cell-mediated immune response. The 100-mg/kg dose was found to suppress delayed-type hypersensitivity reactions during a mouse model study [3]. Stimulation of both cellular and humoral immune responses after immunization may occur when *Aloe vera* is taken orally by affecting the effects on the composition of lymphocyte subsets and serum immunoglobulins. Burn plant administration leads to the rise in phagocytic and proliferative activity of the RES [4].

### Anti-inflammatory effect

Inflammation is the body's response to wounds and healing. burn plant is natural, gentle, and effective, without the tough side effects of anti-inflammatory drugs burn plant may be a good selection as an anti-inflammatory due to its versatility. It not only is often used internally and externally, but it also reduces inflammation by inhibiting different aspects of the inflammation process, and by promoting tissue regeneration. Burn plant is the best remedy for reducing swelling and redness. mannose-6-phosphate and acemannan produce the anti-inflammatory effect of the burn plant. Acemannan was proved to accelerate tissue regeneration, activate macrophages, stimulate the system, and have antibacterial and

antiviral effects. Burn plant constituents are thought to scale back inflammation caused by a rise in prostaglandin synthesis and a rise within the infiltration of leukocytes. Vazquez B et al perform a study to look at the consequences of various sorts of the extract on carrageenan-induced edema in rat paws; it that the aqueous and chloroform extracts reduced the edema within the hind paw which the aqueous extract inhibited prostaglandin E2 production from [14C] arachidonic acid [5]. Hanley DC et al reported that the burn plant extract decreased inflammation by 48% during a rat adjuvant-induced arthritic inflammatory model [6]. Another study was performed on streptozotocin (STZ)-induced diabetic mice, during which the anti-inflammatory activities of both *A. vera* and gibberellin were measured, and it had been found that both equally inhibited inflammation during a dose-response manner [7]. When *Aloe vera* is given topically will hinder inflammation induced by a moderate amount of irritant. generally, the decolorized *Aloe* was effectual than the colorized *Aloe* (with anthraquinone).

*Aloe vera* directly inhibits the cyclooxygenase pathway and lower prostaglandin E2 production, which plays an important role in inflammation [8]. Langmead L et al demonstrated that the inner gel of *Aloe* contains anthraquinones and chromone, which possess a strong anti-inflammatory effect. *Aloe* gel has a pharmacological activity to reduce inflammatory reactions in inflammatory bowel disease [9]. The *A. vera* gel tested here might be useful in the topical treatment of inflammatory skin conditions such as UV-induced erythema oral *aloe vera* gel is widely used by patients with inflammatory bowel disease.

An important study is carried out in streptozotocin (STZ)-induced diabetic mice, in which the anti-inflammatory activities of *Aloe vera* were measured, and it was found that it inhibited inflammation in a dose-response manner. *Aloe vera* contains the enzyme Brady kinase, which breaks bradykinin which is responsible for pain, allergies, and chronic and acute inflammation. *Aloe vera* contains salicylic acid, which reduces inflammation.

### Anti-diabetic effect

*Aloe vera* plays a crucial role in the anti-diabetic effect. Burn plant act as an antihyperglycemic agent and hypercholesterolemic agent for type 2 diabetic patients. *Aloe* gel increases the tolerance in diabetic rats and it also found that *Aloe* contains a hypoglycaemic agent which decreases blood sugar level. Burn plant gel has an antidiabetic and cardioprotective property which reduces oxidative stress in streptozocin-induced diabetic rats. Tanaka et al reported reductions in both fasting and random blood sugar levels of db/db diabetic mice chronically treated with equivalent phytosterols from *A. vera* gel [10]. Shin E et al manifest that dietary *Aloe* formula also inhibits obesity-induced glucose tolerance by suppressing inflammatory responses and also by inducing anti-inflammatory cytokines within the white fat and liver, both of which are important peripheral tissues suffering from insulin resistance [11]. In vivo and In vitro studies strongly indicate that the water-soluble fraction of *Aloe* spp. possesses glucose-lowering activities and its components modulate glucose transporter-4 mRNA expression [12].

The gel improves carbohydrate metabolism and improves metabolism in prediabetes patients by reducing weight, body fat mass, fasting blood sugar [13]. Rajasekaran S et al have shown a notable increase within the blood sugar level and food and water intake in STZ-induced diabetic rats compared to regulated group rats, and therefore the administration of *Aloe vera* juice extract to diabetic rats showed a bent to bring these changes back to the normal level [14].

### Hepatoprotective effect

Liver disease is the common unhealthiest within planet-wide. Mainly anti-inflammatory drugs are used to reduce pain, fever and inflammation are the most offenders in liver damage. *Aloe* is involved in the inhibition of obesity-induced inflammatory reactions by acting on inflammatory cytokines. They reduce the levels PPAR $\gamma$ /liver X receptor  $\alpha$ , and 11 $\beta$ -hydroxysteroid dehydrogenase 1, and enhance the effect of anti-inflammatory cytokines in the white fat and liver. *Aloe vera* gel extract is involved in the mRNA expression of lipogenic genes in the liver. They act by suppression of these genes which alternatively prevents ethanol-induced disease. Saito et al proved that the extract can stop the ethanol-induced disease. He corroborated his study by subduing the mRNA expression of lipogenic genes. The study was also confirmed that *Aloe vera* gel along with the mixture of probiotic *Lactobacillus rhamnosus* GG will produce a therapeutic potential that results in the demotion levels of cholesterol. This study was important in analyzing the danger of cardiovascular complications [15]. Etim OE et al performed a study on the protective effects of fresh *Aloe vera* leaf extract on LD-induced hepatotoxicity and genotoxicity. The results indicate that pre-treatment of the extract at 1.0mL/kg weight reduced the serum levels of GPT, GGT, and ALP which elevated the levels by 100mg/kg weight of LD [16].

Madhav NV reported the hepatoprotective activity of the aqueous extract of *Aloe vera* against paracetamol-induced hepatotoxicity in albino rats; it had been observed that single-day treatment of aqueous extract of *Aloe vera* (doses of 250 mg/kg and 500 mg/kg) reduced aspartate transaminase (AST) and alanine transaminase (ALT) levels which the five hundred mg/kg dose especially reduced the ALP levels and restored the depleted liver thiol levels [17].

### Anticancer Activity

*Aloe vera* and its constituents have a significant effect on the control of cancer development, through the regulation of genetic pathways. Aloin, the important ingredient of *Aloe*, has been noted for its potential therapeutic options in cancer. Aloin treatment could hinder the secretion of VEGF in cancer cells. *Aloe-emodin* is an important drug that is used in the treatment of anticancer therapy that has been significantly involved in the biological system. A crucial study was performed by Saini MR et al to research the antitumor activity of burn plant against stage-2 skin carcinogenesis induced by 7,12-Dimethylbenz[a]anthracene (DMBA) and croton (croton) oil; the results showed that compared to 100% incidence of tumor development in group I (DMBA + oil only), the incidence of tumors decreased to 50%, 60%, and 40% in groups II (DMBA + oil + topical burn plant gel), III (DMBA + oil + oral burn plant extract), and IV (DMBA + oil + topical burn plant gel + oral burn plant extract)

respectively [18]. In human endothelial cells, aloin treatment is involved in the inhibition of in vitro VEGF-induced angiogenic response. It results in further inhibition of multiplication and migration of endothelial cells. AE (1,8-dihydroxy-3-hydroxymethyl-9,10-anthracenedione) is an herbal anthracene Dione derivative from *A. vera* leaves. AE has a vital role in the antiproliferative mechanism and subsequent effect in cancer cells, like lung, squamous, glioma, and neuroectodermal cancer cells [19,20]. AE induced apoptosis in the T24 human bladder was demonstrated recently by Lin et al [21]. To investigate the antiproliferative and cytotoxic potential of the anthracycline aloin, studies were conducted on human uterine carcinoma HeLa S3 cells and the results concluded that aloin showed a prominent antiproliferative effect on physiological concentration, caused cell cycle arrest within the S-phase, and noticeably increased HeLa S3 cell apoptosis [22]. Another study revealed that emodin and AE are capable of inhibiting carcinoma cell proliferation by downregulating estrogen receptor (ER) $\alpha$  protein levels and suppressing ER $\alpha$  transcriptional activation [23]. Lee HZ found that the decrease within the expression of protein kinase C- $\delta$  and protein kinase C- $\epsilon$  isoforms plays a critical role in AE-induced apoptosis [24].

### Antimicrobial Activity

*Aloe vera* act as antimicrobial agents. Burn plant leaf gel was isolated and thus the purified *Aloe* protein possesses a potent antifungal activity. *A. vera* has anthraquinones, the anthraquinones act like tetracycline that stops bacterial protein synthesis by blocking the ribosomal A site, so bacteria cannot grow on the media contain *Aloe vera* extract. Burn plant contains pyrocatechol a hydroxylated phenol, known to possess a toxic effect on microorganisms. Alemdar S et al figure out the antimicrobial activity of *Aloe vera* juice against Gram-positive bacteria and Gram-negative bacteria, and thus the results showed that the antibacterial activity of the tested plant juice was effective mainly against the Gram-positive bacteria [25]. Fani M et al conducted analysis was administered using pathogens isolated from patients with cavity and periodontal diseases; the inhibitory properties of plant gel on some cariogenic and periodontopathic pathogens and an opportunistic periodontal pathogen were investigated, and thus the results showed that *S. mutans* was the foremost sensitive species, with a minimum inhibitory concentration (MIC) of 12.5  $\mu$ g/mL, whereas *A. actinomycetemcomitans*, *P. gingivalis*, were less sensitive with a MIC of 25-50  $\mu$ g/mL [26]. The antimicrobial activity of burn plant juice was investigated using agar disk diffusion against bacteria, fungi, and yeast, and it had been observed that burn plant juice showed antibacterial activity against the Gram-negative bacteria *A. hydrophilia* and *E. coli* only [27]. Philip J performed a study on a plant, the serial dilution method revealed that a high concentration (1/10) inhibited the expansion of *Staphylococcus aureus*, while moderate concentrations were required to inhibit the expansion of *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi* [28].

### Burn wound healing effect

*Aloe* is additionally referred to as the healing plant. Burn plant has been used for medicinal purposes. burn plant features a direct effect on wound healing. Gel extracts resulted in faster

healing of wounds manifested by an increase in the rate of contraction of wound area and prove the effect of *A. vera* on increasing wound contraction and collagen synthesis. The wound healing property is attributed to the mannose-6-phosphate known to be present during *Aloe vera* gel [29,30]. Burn plants change the composition of collagen, increase collagen cross-linking, and thereby promote wound healing. Burn plant promotes wound healing by elevating the proliferation and migration of fibroblasts and keratinocytes. Shahzad MN et al conduct a clinical study, to see the efficacy of *A. vera* gel compared with 1% silver sulfadiazine cream as a burn dressing for the treatment of superficial and partial thickness burns, *Aloe vera* treated patients shows better healing of burn wounds earlier than those patients treated 1% silver sulfadiazine [31]. During the skin wound repair of rats, the study suggests that polysaccharides that are isolated from *aloe vera* induce a specific phenomenon, which is involved in the management of wound healing activity of *aloe vera* gel. The organic phenomenon associated with this is called metallopeptidase and metallopeptidase inhibitor-2 [32].

### Intestinal Absorption

Suboj P et al demonstrated that the Aloin, present within the gel, is metabolized by the colonic flora to reactive Aloe-emodin, which is liable for the purgative activity. Aloe-emodin isolated from *A. vera* inhibits carcinoma cell migration by downregulating MMP-2/9 and also inhibits ras a homolog loved one B and vascular endothelial protein (VEGF) via reducing DNA binding activity of nuclear factor  $\kappa$ -light-chain-enhancer of activated B cells [33]. Certain parts of the burn plant leaf have shown a possibility to reinforce drug permeation across the intestinal epithelial barrier. Chen W et al study has shown that *A. Vera* gel and whole leaf extract were ready to reduce significantly the transepithelial electric resistance of the Caco-2 cell monolayers and thereby showed the power to open tight junctions between adjacent cells. The transport of insulin across the Caco-2 cell monolayers was increased by *aloe vera* gel and leaf extract solutions [34].

### Antioxidative Activity

*Aloe vera* gel contains powerful antioxidants, which belong to an outsized family of drugs referred to as polyphenols. These polyphenols, alongside several other compounds in burn plants, can help inhibit the expansion of certain bacteria which will cause infections in humans. Azoxymethane induced oxidative stress in rats was tested to review the consequences of oral feeding with burn plant gel extract, and therefore the results showed that the hepatic glutathione and acid levels reduced by AOM were restored to normal levels with AGE feeding [35]. The antioxidative properties aged prepared in methanol, 95% ethanol, hexane (hexane extract of burn plant gel or HEAG), acetone (AEAG), and chloroform (chloroform extract of burn plant gel or CEAG) were tested by Saritha V et al, and it had been revealed that MEAG and AEAG possessed maximum 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical- and superoxide radical-scavenging activities [36]. There are various types of medicinal plants that consist of different types of constituents like vitamins, amino acids, carbohydrates, etc. These compounds control and neutralize ROS. Recent studies

also suggest that ROS is beneficial in cancer development, dietary antioxidants, and endogenous [37].

### Antihyperlipidemic activity

*Aloe vera* acts as an Antihyperlipidemic agent. Huseini HF et al conducted a study on the evaluation and clinical effectiveness of *Aloe vera* in hyperlipidemic type 2 diabetic patients. The *Aloe vera* leaf gel efficacy was the parameter used for this study. To eliminate the power of suggestion, a double-blind placebo-controlled trial was accompanied. Reduction in total cholesterol and LDL levels were the beneficial result obtained [38]. In high-fat diet and fructose-induced hyperlipidemic rats, the effect of *aloe vera* was checked. For this purpose, the dried pulp of *Aloe succotrina* leaves was selected. Marked demotion levels of serum cholesterol, total triglycerides, LDL, VLDL, and HDL-cholesterol were shown by the study performed by Dhingra D et al [39]. Administration of some phytosterols isolated from *aloe vera* to Zucker diabetic fatty rats resulted in a reduction in visceral fat mass and a significant effect on hyperglycemia [40].

### Anti-ulcer property

Food ingredients, stress, smoking, NSAIDs, and drugs are factors responsible for gastric ulcers. Polysaccharides, anthraquinones, and other components of *Aloe vera* can act toward the inhibition of peptic ulcers by controlling gastric secretion. Another study in support of *Aloe vera* reported that sucralfate and *Aloe vera* treatment in the ulcer groups showed reduced gastric inflammation, enhanced epithelial cell proliferation, elongated gastric glands, and reduced ulcer sizes [41]. A clinical study reported that newly formulated aloe along with myrrh-based gels was found to be effective in minor recurrent aphthous stomatitis and also beneficial effect in decreasing ulcer size and exudation. In the double-blind controlled study, myrrh is effective in more pain reduction [42].

### Antiviral activity

Virus adsorption, attachment, or entry to the host cell were prevented by the *aloe vera* gel due to its antiviral activity. While analyzing an in vitro study of *Aloe vera* gel, the crude extract was found to possess antiviral activity against the herpes simplex virus of type 2 strain [43]. Olatunya OS et al proved that *Aloe vera* consumption shows some sort of relief in HIV - infected persons by enhancing the immunity of the body [44]. *Aloe-emodin*, *emodin*, and *chrysophanol*, the typical anthraquinone derivatives possess antiviral activity to a certain extent. It also indicates that the inhibitory mechanism against the influenza A virus is another important strategy to elucidate the statements [45]. *Aloe vera* also possesses many other properties like Skin protection and hydration activity, antiaging effect, laxative effect, and in the dental field.

### Conclusion

The plant possesses numerous pharmacological activities like antioxidant, antimicrobial, antiviral, anti-inflammatory, laxative, anti-diabetic, wound healing, anticancer, etc. Many uses also are like a burn injury, eczema, cosmetics, inflammation, and fever, which still be studied, and further research still has got to be one scientific evidence propose that

burn plant gel is safe for external use, allergies are rare and adverse reactions with other medications haven't been reported. The medicinal properties of *A. vera* are known for thousands of years, and modern science has established many of the biological activities. However, the potential use of *A. vera* gel and whole leaf extract in several applications of drug delivery has only been discovered relatively recently. Although *A. vera* leaves contain many various phytochemical compounds with a spread of biological activities, the polysaccharide-rich gel and whole leaf materials have specifically shown potential in drug delivery. Within the future, controlled studies are required to point out the effectiveness of *A. Vera*.

### Author Contribution

All authors Contributed Equally.

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