

***Aloe vera* - A Herbal Panacea for Periodontal Disease?**

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Abstract

The increasing interest and research in the field of alternative and ayurvedic medicine has paved way for various herbal and natural products for their multiple uses in the field of dentistry and periodontology in particular. Among the various currently available herbal agents *Aloe vera* is attracting scientific attention. The pharmacological attributes of *Aloe vera* have been revalidated and have shown it to be a promising herb for various clinical applications in the field of periodontology. The current review article is an attempt to highlight the properties and possibilities of utilizing *Aloe vera* for benefits of patients with periodontal diseases.

Keywords: *Aloe vera*; Herbal; Gingivitis; Periodontal Disease

Introduction

Long before the advent of modern medicine, herbs were the mainstream remedies for nearly all ailments [1]. According to World Health Organisation, medicinal plants would be the best source for obtaining a variety of drugs [2]. The increasing interest and research in the field of alternative and ayurvedic medicine has paved way for various herbal and natural products for their multiple uses in the field of dentistry [3]. This interest to unlock the secrets of traditional herbal remedies has provided a wide scope for use of natural products in the prevention and treatment of oral conditions. This could also be of benefit to low socioeconomic level in urban and rural communities [4,5]. Over the last decade, herbal and Ayurvedic drugs have become a subject of world importance, with both medicinal and canonical implications [6]. Plant extracts represent a continuous effort to find new compound against pathogens. Approximately 20% of the plants found in the world have been submitted to pharmacological or biological test [7].

Among the various herbal agents, *Aloe vera*, belonging to the family Liliaceae, is currently receiving a lot of scientific attention. The word *Aloe* is derived from the Arabic word "Alloeh" which means "a shining bitter substance," while the word "vera" in Latin means "true". It is also known as "the wand of heaven," "heaven's blessing," and "the silent healer". The role of *Aloe* plant and its derivative products in the field of medicine dates as far back as the 4th century B.C [8]. It is a perennial succulent xerophyte, which stores water in the tissues of its leaves to survive in dry areas of low or uneven rainfall. More than 250 species of *Aloe* are grown around the world. Only two species are grown commercially: *Aloe barbadensis* Miller and *Aloe arborescens*, of which *Aloe barbadensis* Miller (Figure 1), is most biologically active among 400 species [9-12].



Figure 1: *Aloe vera* plant.

Parts of *Aloe vera*

The *Aloe vera* plant has stiff grey-green lance-shaped leaves containing clear gel in a central mucilaginous pulp (Figure 2) [13]. The leaves consist of three layers - outer protective layer of 15 - 20 cells thick, middle layer and inner colourless layer. The outer layer is attributed to synthesis of carbohydrates and proteins (Figure 3). The bitter yellow latex containing anthraquinones and glycosides is contributed by the middle layer. The inner layer consists of a gel made up of water (99%), with glucomannans, amino acids, lipids, sterols and vitamins [14,15].



Figure 2: *Aloe vera* gel.

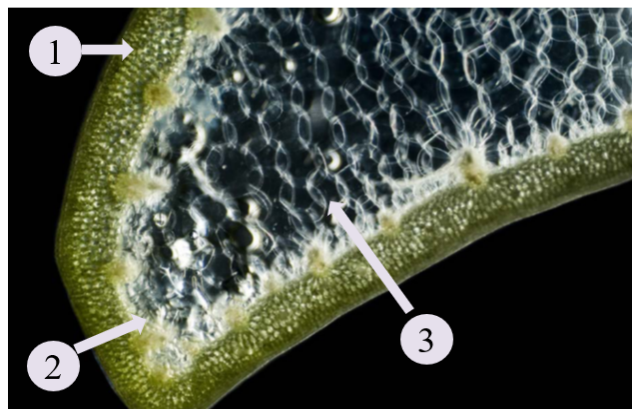


Figure 3: Transverse section of a leaf of *Aloe vera* depicting the three layers. 1- Outer layer, 2 – middle layer and 3 – inner layer.

Active ingredients

More than 75 active ingredients from inner gel have been identified. The active components of *Aloe* include anthraquinones, chromones, polysaccharides, and enzymes, the main functional component being the long chain of acetylated mannose [16-18]. The polysaccharides contained in the gel of the leaves contributes to its medicinal properties [13]. The anthraquinones and chromones are responsible for the anti-cancer activity, anti- inflammatory, and evacuating [19]. The other potentially active ingredients include vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids [20-23]. It has numerous monosaccharides and polysaccharides; vitamins B1, B2, B6, and C; niacinamide and choline, several inorganic ingredients, enzymes (acid and alkaline phosphatase, amylase, lactate dehydrogenase, lipase) and organic compounds (aloin, barbaloin, and emodin) [24]. Details of the components and their therapeutic properties are given in table 1.

Constituents	Therapeutic properties
Amino acids	Basic building blocks of proteins in the body and muscle tissues
Anthraquinones	Analgesic, antibacterial
Enzymes	Antifungal and antiviral activity but toxic at high concentrations
Hormones	Wound healing and anti-inflammatory
Minerals	Essential for good health
Salicylic acid	Analgesic
Saponins	Cleansing and antiseptic
Steroids	Anti-inflammatory agents, lupeol has Antiseptic and analgesic properties
Sugars	Anti-viral, immune modulating activity of acemannan
Vitamins	Antioxidant (A, C, E), neutralises free radicals

Table 1: Various constituents of *Aloe vera* and their therapeutic properties [25].

Various forms of *Aloe vera* in use

Researchers have investigated various forms of *Aloe vera* and the ones currently in use include [3,26]:

1. Toothpaste [27]
2. Mouthwash
3. Gel- protects the wound and promotes healing. It also keeps the wound moisturized.
4. *Aloe* activator topical spray - useful in throat infections, dental and joint pains
5. *Aloe vera* juice - useful as a strong detoxifying agent and an immune enhancer.

Therapeutic properties of *Aloe vera* as applicable for periodontal diseases

Role in wound healing

Aloe vera helps in wound healing in the following proposed ways [15]:

1. Keeps the wound moist
2. Increases migration of epithelial cells
3. Enhances collagen maturation
4. Reduces inflammation

The wound healing property of *Aloe vera* gel is attributed to Mannose-6-phosphate [28]. When administered orally or topically, glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, stimulate the proliferation and activity of fibroblasts by interacting with the growth factor receptor on its surface. This influences the collagen composition especially of type III collagen. Also, there is increase in collagen synthesis and cross linking for wound contraction and improving breaking strength [29]. It also increases synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound [15,30].

In a study by Yagi, *et al.* it was reported that the glycoprotein present in *Aloe vera* gel promoted cell proliferation, while Davis, *et al.* noted that *Aloe vera* gel improved wound healing by increasing blood supply (angiogenesis), which in turn increased oxygenation [9,31]. Another polysaccharide called acemannan is reported to activate macrophages that improved wound healing in a rat model [32,33]. It also enhances the production and release of fibrogenic cytokines. Direct binding of acemannan to growth factors and their stabilization is shown to promote and prolong stimulation of granulation tissue [34-36].

Effects on immune system

Aloe vera is a well-known adaptogen that has the capability to boost body's natural immunity. It balances the body's system by stimulating body's defense and adaptive mechanisms. It contains 90% rhodium and iridium (trace minerals) in the acemannan which is one of the polysaccharides. It acts as a great stimulant and dramatically increases the white blood cells or macrophages and T cells. Thus, immunomodulating effects occur via activation of macrophage cells to generate nitric oxide, secrete cytokines (e.g. tumor necrosis factor, interleukin-1, interleukin-6, and interferon- γ), and present cell surface markers [23,24]. It helps the thymus gland to enlarge in size by 40% and thereby increase the production of T cells [6].

Anti-inflammatory action

Many *in vitro* and *in vivo* studies have revealed that anti-inflammatory action of *Aloe vera* gel which is exerted through bradykinase activity [37,38]. Bradykinase is a peptidase that can be isolated from *Aloe* and breaks down the bradykinin, an inflammatory substance that induces pain [39]. The cyclo-oxygenase pathway is inhibited by *Aloe vera* which in turn reduces prostaglandin E2 production from arachidonic acid. The *Aloe* sterol which include campesterol, β -sitosterol, lupeol, and cholesterol, possess anti-inflammatory property. They help in reducing the pain during inflammation by acting as a natural analgesic. Other aspirin-like compound that have been isolated from *Aloe* is attributed to exert anti-inflammatory and antimicrobial properties [40]. In a rat adjuvant-induced arthritic inflammatory model, *Aloe vera* extract (5.0% leaf homogenate) was shown to decrease inflammation by around 48% [41,42].

Anti-oxidant property

Aloe vera is rich in antioxidant nutrients. It is carried out via Glutathione peroxidase activity. The anti-oxidant effects are due to superoxide dismutase enzymes and a phenolic antioxidant. Also, vitamins like A, C, and E, present in *Aloe vera*, act as a free radical scavenger and get rid of the toxins and carcinogenic substances that may enter our body through the skin and food [28].

Antimicrobial properties

Various constituents of *Aloe vera* like sulphur, salicylic acid, cinnamic acid, urea nitrogen and phenol act as a team to prevent the growth of disease-causing microorganisms and thus exhibit antimicrobial activity. The help to eliminate many internal and external infections which may be of bacterial, fungal or viral in origin [6].

Antibacterial property

Aloe vera gel has a broad spectrum activity and is shown to be effective against both Gram-positive and Gram-negative bacteria [43]. The antibacterial effect is suggested to enhance the wound healing process by eliminating the bacteria which are responsible for producing inflammation [44]. The inner-leaf gel from *Aloe vera* was shown to be effective inhibiting the growth of *Streptococcus* and *Shigella* species *in vitro* [45]. Studies conducted with *Aloe vera* in toothpastes have suggested that *Aloe vera* in gel and toothpaste forms were equally effective against many species like *Candida albicans*, *Streptococcus mutans*, *Lactobacillus acidophilus*, *Enterococcus faecalis*, *Prevotella intermedia* and *Peptostreptococcus anaerobius*. Enhanced antibacterial effect against *S. mitis* by *Aloe vera* gel was also demonstrated in some studies [46].

Antifungal property

Aloe vera gel is reported to inhibit the growth of *Candida albicans* [47]. Agarry, *et al.* also reported similar result about the inhibitory action of the *Aloe* leaf on *Candida albicans* [48].

Antiviral property

Several ingredients in *Aloe vera* gel have been shown to be effective antiviral agent [49]. It was reported that the anthraquinones extracted from the inner leaf of *Aloe* are responsible for exhibiting the antiviral property. This action may be direct due to *Aloe* emodin and indirect due to stimulation of immune system [50]. It prevents virus adsorption and replication. A purified sample of *Aloe* emodin is reported to be virucidal to *Herpes simplex* virus type 1 and type 2, *Varicella zoster* virus, *Pseudorabies* virus, and *Influenza* virus [51]. It directly affects both DNA- and RNA- containing enveloped viruses but has no effect on naked (unenveloped) viruses. Acemannan also has a reducing effect in herpes simplex infection as was shown in a study with two cultured target cell lines. Lectins, fractions of *Aloe vera* gel, have the potential to directly inhibit the cytomegalovirus proliferation in cell culture, possibly by interfering with its protein synthesis [52,53].

Applications of Aloe vera in periodontology

Aloe vera has following applications:

1. *Aloe vera* is effective in decreasing plaque accumulation [54].
2. It is extremely helpful in the treating gingivitis and periodontitis.
 - a. *Aloe vera* greatly reduces the occurrence of gingival bleeding due to its soothing and healing properties,
 - b. Reduces swelling and soft tissue oedema
3. *Aloe vera* mouthwash is effective in reducing plaque. It has the potential to be an affordable herbal alternative to chlorhexidine. Through its wound healing and anti-inflammatory mechanism, it prevents radiation-induced mucositis. It is also helpful for patients with oral candidal infection.
4. Administration of *Aloe vera* gel subgingivally, has shown improvement in periodontal condition.
5. *Aloe vera* tooth gel tends to be less harsh on teeth, as it does not contain the abrasive elements typically found in commercial toothpaste; it is a great alternative for people with sensitive teeth or gums.
6. Direct application to the sites of periodontal surgery along with periodontal dressing has been suggested especially when the tissues have been traumatized by toothbrush-dentifrice abrasion, sharp foods, dental floss and toothpick injuries.
7. Also useful as local drug delivery agent.

Discussion

The clinical applications of *Aloe vera* in the field of periodontology can be attributed to its anti-inflammatory, antibacterial, wound-healing properties. The improvement in gingival index is attributed to the presence of sterols as anti-inflammatory agents and lupeol as an antiseptic analgesic. It was suggested from a study by Vazquez, *et al.* that *Aloe vera* has potential to decrease edema and also reduce the number and migration of neutrophils (PMNL) [55]. The potency of carboxypeptidase in *Aloe vera* gel to inactivate bradykinin by about 67% and relieves pain was studied by Fujita, *et al.* [56] Rocio Bautsta in 2004 showed that carboxypeptidase in *Aloe vera* had good anti-prostaglandin synthesis properties and compounds inhibiting oxidation of arachidonic acid, which might decrease inflammation [57,58].

A study was conducted by Ajmera N., *et al.* in 2013 to evaluate the anti-inflammatory property of *Aloe vera* mouthwash on plaque-induced gingivitis. It was concluded from the results that *Aloe vera* had a significant anti-inflammatory property and can be used as an adjunct to mechanical therapy for treating plaque-induced gingivitis [57]. Similar studies were conducted by Karim B., *et al.* [59], Chandras B., *et al.* [58] and Rezaei S., *et al.* [60] and it was concluded from these studies that *Aloe vera* mouthwash is effective as antiplaque and antigingivitis agent and can serve as an affordable herbal substitute for chlorhexidine.

A study conducted by Bhat G., *et al.* 2010 to evaluate the property of *Aloe vera* as a medicament in the periodontal pocket. The results of the study showed that there was improvement of periodontal condition upon subgingival administration of *Aloe vera* gel. Thus, it concluded that *Aloe vera* gel can be used as a local drug delivery system in periodontal pockets [3]. Pradeep AR., *et al.* carried out a randomized controlled trial in 2016 to investigate the clinical effectiveness of locally delivered AV gel when used as an adjunct to scaling and root planing in the treatment of patients with type 2 diabetes mellitus and chronic periodontitis. The data obtained from the study reflected significant reduction in clinical parameters and gain in attachment levels in patients [61]. Similar studies were conducted by Sethi S., *et al.* in 2015 where the efficacy of *Aloe vera* gel as an adjunct to scaling and root planing was shown [62].

Precautions

Use of *Aloe vera* is limited in cases of known allergy to plants in the Liliaceae family, pregnancy and breastfeeding. During pregnancy, theoretically it can cause stimulation of uterine contractions, and in breastfeeding mothers, it may sometime cause gastrointestinal distress in the nursing infant. Side effects may occur - topical like redness, burning, stinging sensation and allergic reactions and systemic like Abdominal cramps, diarrhea, red urine, hepatitis, dependency or worsening of constipation, colorectal cancer (upon prolonged use), low potassium levels (laxative effect), etc [63,64].

Conclusion

The therapeutic properties of *Aloe vera* have been explored and revalidated through various *in vivo* and *in vitro* studies. These scientific studies are good enough to conclude that *Aloe vera* is a promising herb and has immense potential for various clinical applications in dentistry especially in treating periodontal diseases. But standardization and quality assurance of *Aloe vera* products are the areas which require further attention. The studies currently available in literature are short-term studies. Thus, more clinical research needs to be undertaken especially to validate and explain the action of acemannan hydrogel in accelerating the healing of periodontal wound and to validate the efficacy of *Aloe* gel on plaque and gingivitis. Also, the potential long term side effects of *Aloe vera* need to be studied and evaluated. *Aloe vera* is undoubtedly a never-ending nature's gift to humanity provided we utilize the benefits.

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