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Application of Aloe Vera in Dentistry

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Application of Aloe Vera in Dentistry

Aniket U. Vaidya [α] & Manisha M. Khorate [σ]

Abstract- Research since ancient times have claimed the therapeutic benefits of Aloe Vera in medical field. The role of Aloe Vera in reducing inflammation is already established. The recent research has thrown light on the immunomodulatory properties of Aloe Vera gel. The immunomodulatory property of Aloe Vera is attributed to the various polysaccharides present in the gel, primarily Acemannans. In this review the possible use and applications of Aloe Vera in dentistry is elaborated.

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I. Introduction

Alternative medicine is described as 'Any of various systems of healing or treating disease (such as chiropractic, homeopathy or faith healing) not included in the traditional medical curricula of the United States and Britain' (Mandala, 2017). This term is loosely used for almost all the forms of medicine except Allopathy. Alternative medicine practice exists in all the cultures worldwide and terms such as traditional medicine, indigenous medicine or folk medicine etc. are used to describe such practices. Every country or region has its own traditional system of health and medical care such as the Chinese created acupuncture, the French practice magnetic healing, the Germans widely use Heilpraxis, the English use Herbalism, the Indians believe and practice Ayurveda with Siddha, the Japanese are known for Shiatsu etc (Newcomer, 2017).

In India, Ayurveda is being practiced for more than 5000 years. Ayurvedic philosophy is such that illness is a state of imbalance among the body's systems that can be detected through such diagnostic procedures as reading the pulse and observing the tongue. Nutrition counselling, massage, natural medications like various herbs, meditation and many other modalities are used to address a broad spectrum of ailments (Newcomer, 2017; Indian Board of Alternative Medicines, 2014). Presently, herbal medicines are gaining more attention due to their lesser side effects. Recently the popular interest and use of Aloe Vera (AV) gel has increased dramatically. It is one of the most widely used ingredients in healthcare and cosmetic products and is readily available all over the country. This review throws light upon the various uses and applications of AV in dentistry.

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II. Aloe Vera (AV)

AV is perennialsucculent xerophyte, several species of which have been identified namely Aloe Vera, Aloe barbadensis, Aloe ferox, Aloe chinensis, Aloe indica, Aloe peyrii, etc. Amongst these *Aloe barbadensis Miller* is accepted unanimously as the correct botanical source of aloe (IARC Monographs, 2015). This plant is commercially cultivated in India, Haiti, Aruba, the United States of America, Bonaire, South Africa and Venezuela (IARC Monographs, 2015). In India, it is seen plenty in the coastal areas of Maharashtra, Gujarat and South India (Reddy et al., 2012).

Historical Perspective: In Mesopotamia, clay tablets dated 1750 B.C. showed that AV was being used in a pharmaceutical manner. In 74 A. D., a Greek physician, Discordes wrote a book titled, '*De Materia Medica'* in which he stated that AV can treat wounds, heal infections of the skin, cure chapping, decrease hair loss and eliminate haemorrhoids (Shelton R M 1991). Now a days it is used very much in cosmetic industry whereas the original commercial use of the AV plant was in the production of a latex substance called Aloin which is a yellow sap used for many years as a laxative ingredient (IARC Monographs, 2015). *The Ayurvedic Pharmacopoeia ofIndia* recommends the use of driedjuice of leaves in dysmenorrhoea and diseases of the liver (Rajeswari R et al., 2012).

AV extracts shows antimicrobial activity and hence it is used the treatment of pimples, acne and mouth ulcers. It has also been used to control bleeding, itching of piles and relief from arthritic pain. Historically the Chinese used the aloe vera juice as a mild laxative wash for piles, abscesses and scabies. In the Philippines, it was used to treat dysentery and pain in the kidneys. It was also used as aperients, anthelmintic, carminative, deobstruent, stomachic and diuretic (Kumbhar PS et al., 2015). Juice is also used in skin care medicine, amenorrhea, dyspepsia, burns, colic, hepatopathy, splenopathy, constipation, span menorrhea, abdominal tumors, carbuncles, sciatica, lumbago and flatulence (Kumbhar P S et al., 2015).

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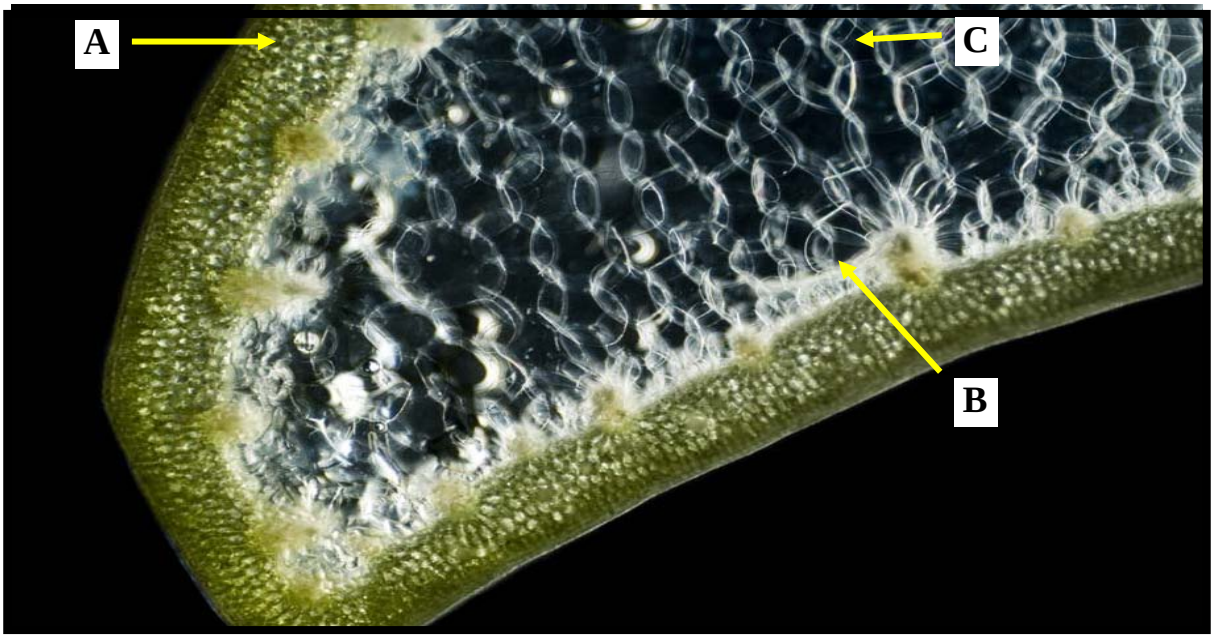


Fig. 1: The Transverse Section of the Leaf Exhibiting Three Cells Layers; A) The Protective Layer, B) Middle Layer and C) Colourless Inner Layer.

III. Parts of the Aloe Vera Leaf: (Fig. 1)

a) Outer Protective Layer of the Leaf

The bitter yellow latex of pericyclic tubules in the outer layer of the leaves contain derivatives of hydroxyanthracene, anthraquinone and glycosides aloin A and B in the percentage of 15– 40%. The other active principles of Aloeinclude hydroxyanthrone, aloe – emodin-anthrone 10-C-glucoside and chrones (Sahu PK et al., 2013).

b) Middle Layer of the Leaf

The middle layer of the leaf also contains bitter yellow latex containing anthraquinones and glycosides. The parenchymatous tissue or pulp contains proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds, small organic compounds and different polysaccharides (Sahu PK et al., 2013).

c) Inner Layer of the Leaf

The innermost layer of leaf gel contains water upto 99%, with glucomannans, amino acids, lipids, sterols and vitamins. The other potentially active ingredients include enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids. It has numerous monosaccharide's and polysaccharides; vitamins B1, B2, B6, and C and several inorganic ingredients, enzymes (acid and alkaline phosphatase, amylase, lactate dehydrogenase, lipase) and organic compounds (aloin, barbaloin, and emodin). The main functional component of AV is a long chain of acetylated mannose (Sahu PK et al., 2013).

IV. Chemical Composition of Aloe Vera

The AV plant contains 98 - 98.5 % water, with an average pH of 4.5, refractive index of 1.3340 - 1.3355 and specific gravity of 1.0030 - 1.0070. The remaining solid material contains over 75 different components (Kumbhar PS et al., 2015). (Table 1)

Table 1: Composition of Aloe Vera Gel (IARC Monographs, 2015; Kumbhar PS et al., 2015; Mangaiyarkarasi SP, 2015; Nair GR et al. 2016; Naroor N et al., 2014;Pol JS et al., 2016)

1. The principal ingredient	Water 98.5%
2. Other ingredients	Aloin, Barbaloin, Etheral oil, Cinnamic acid, Isobarbaloin, Emodin, Emoding lucosides of d – Arabinose, Ester of cinnamic acid, Resitannol
3. Inorganic ingredient	Calcium (30mg/dl), Potassium (13.4meq/l), Chlorine (3meq/l), Sodium (8.7meq/l), Manganese, Zinc (31mg/dl), Copper, Iron (15mg/dl), Magnesium (3.9mg/dl)
4. Amino acids	Lysine (5-6ppm), Histidine (2.8-3.3ppm), Arginine (4.5-5.5ppm), Hydroxyproline, Aspartic Acid (13-15ppm), Threonine(5-6ppm), Serine (6-7ppm), Glutamic acid (13.5-15.5ppm), Proline (8-9ppm),

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	Glycine (7-8ppm), Alanine (1-1.3ppm), Valine (6.5-7ppm), Methione (1.5-2ppm), Isoleucine (3.5-4ppm), Leucine (8.5-9ppm), Tyrosine (2.8-3.3ppm), Phenylalanine (4.3-4.7ppm)
5. Monosaccharides & polysaccharides	Glucose (77.8mg/dl), Mannose, Acemannan, Uronic acid
6. Enzymes	Amylase, Carboxypeptidase, Catalase, Cycloxegenase
7. Vitamins	Vitamin A, Vitamin E, Vitamin B_1(6-7mg/100ml), Niacinamide(30-37mg/100ml), Vitamin B_2(6-7mg/100ml), Vitamin B_6(3-3.7mg/100ml), Vitamin C(47-61mg/100ml), Choline (9.5-11.2mg/100ml), Folic Acid (13.2ng/ml), Alpha-Tocopherol, Beta Carotene.
8. Miscellaneous	Cholesterol (8mg/dl), Triglycerides (2.4mg/dl), Steroids, beta-Sitsterol, Lignins, Uric Acid (1mg/dl), Gibberellin, Salicyclic acid, Arachiodonic acid

V. Medicinal Properties and Therapeutic Potential of Aloe Vera

a) Burns and Wounds

AV gel has been tested for its efficacy on inflammation many times. The earliest experiments were carried out in 1930 which involved use of AV gel on skin burns. It was believed that the aloe or its components are useful for wound healing and in burns (Kumbhar PS et al., 2015).

b) Tissue Oedema

In an experiment, a swelling was produced caused by fluid accumulation in a tissue (Oedema) initiated by irritating compounds and it was used as an inflammatory model in the mouse ear or rat hind paw as subjects. Croton oil, a powerful irritant, was applied to the right ear with the left remaining as control. Inflammation was measured by weighing a tissue punch sample and it was shown to decrease after topical application of aloe gel. A subsequent trial demonstrated an even greater decrease when the gel was combined with a corticosteroid (Kumbhar P S et al., 2015).

c) Digestion

The Anthroquinones present in the outer leaf acts as a laxative and stimulates the bowels to move and helps with elimination if a person is constipated (Kumbhar P S et al., 2015; Reddy L et al., 2012).

d) Rheumatoid Arthritis

AV helps to strengthen joint flexibility and helps in the regeneration of body cells. It strengthens joint muscles which is beneficial to reduce pain and inflammation in weakened or aged joints (Kumbhar P S et al., 2015).

e) Anti-Cancer Activity

Acemannan is a molecule in AV gel. It was seen that growth of a murine sarcoma implanted in mice, showed regression after Acemannan treatment, probably due to an immune attack. Injection of mice with Acemannan inhibited the growth of murine sarcoma cells implanted subsequently and decreased mortality by about 40%. Aloe polysaccharides show evidence of anticancer effects by modifying and accentuating the immune response during activation of macrophages. Aloe-emodin induces apoptosis in T - 24 human bladder cancer cells (Joeng H Y et al., 1994; Kumbhar P S et al., 2015; Merriam E A et al., 1996).

f) Anti-Diabetic Activity

Historically, dried aloe exudates have been used in Arabia in diabetes treatment. In an experimental study, in normal mice, both Glibenclamide (10 mg/kg twice daily) and aloe (500 mg/kg twice daily) induced hypoglycaemia after 5 days. In the diabetic mice, fasting plasma glucose was significantly reduced by Glibenclamide and AV after 3 days (Ghannam N et al., 1986). Thus it can be conclude that AV contains a hypoglycaemic agent which lowers the blood glucose, the mechanism of which is yet known.

g) Antimicrobial Activity

The comparative antimicrobial activities of the gel and leaf of AV were tested against Staphylococcus Aureus, Pseudomonas Aeruginosa, Trichophyton Mentagra- phytes, Trichophyton Schoeleinii, Microspo-rium Canis and Candida Albicans. Ethanol was used for the extraction of the leaf after obtaining the gel from it. Antimicrobial effect was measured by the appearance of zones of inhibition. It was found that Anthraquinone inactivates various viruses such as herpes simplex, varicella zoster and influenza (Kumbhar PS et al., 2015).

In an in vitro experiment, theantimicrobial activity of an AV tooth gel (forever bright tooth gel) and commercially popular tooth pastes (Colgate Palmolive) was evaluated. It was concluded that AV tooth gel was effective than the commercially popular toothpastes in controlling all the oral organisms like Streptococcus Mutans, Candida Albicans, Lactobacillus Acidophilus, Streptococcus Mitis, Enterococcus Faecalis, Prevotella Intermedia, and Peptostreptococcus Anaerobius (George D et al., 2009).

h) Immunomodulatory Property

The immunomodulatory activity of Processed Aloe Vera gel (PAG) was evaluated *in vivo* in mice. Oral administration of PAG significantly reduced the growth of *C. Albicans* in the spleen and kidney following intravenous injection of *C. Albicans* in normal mice. PAG

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administration also reduced the growth of *C. Albicans* instreptozotocin-induced diabetic mice. PAG administration did not increase ovalbumin (OVA)-specific cytotoxic T lymphocyte (CTL) generation in normal mice, but did increase it in high fat-diet induced diabetic mice. These findings provide the first clear evidence for the immunomodulatory activity of orally administered AV gel (Im S A et al., 2010).

i) Periodontitis

Bhat G et al. (2011) evaluated the clinical effects of subgingival application of AV gel in periodontal pockets of adult periodontitis patients after mechanical debridement. In this study, 15 subjects were evaluated for clinical parameters such as plaque index, gingival index, probing pocket depth at baseline, followed by scaling and root planning. Test site comprised of scaling procedures followed by intra-pocket placement of AV gel which was compared with the control site in which only scaling and root planning was done and clinical parameters were compared between the two site sat 1month and 3 months from baseline. Results of this study exhibited encouraging findings in clinical parameters of the role of AV gel as a drug for local delivery and it was concluded that subgingival administration of AV gel results in improvement of periodontal condition and hence AV gel can be used as a local drugdelivery system in periodontal pockets.

j) Alveolar Osteitis (Dry Socket)

Acemannan hydro gel is used in the treatment of dry socket. Poor MR et al. (2002) carried out a comparative study of treatment of Alveolar Osteitis with Clindamycin soaked gel foam and freeze dried pledget that contains Acemannan Hydrogel obtained from inner gel of AV. A retrospective evaluation was done of records of 587 patients (1031 sockets) treated with Clindamycin soaked gel foam and a prospective trial was performed by treating 607 patients (1064 sockets) by placing Acemannan hydrogel into the sockets immediately after extraction. The results of the study showed that 78 of 975 sites (8.0%) in the Clindamycin Gelfoam group developed Alveolar Osteitis whereas only 11 of 958 sites (1.1%) in the Acemannan Hydrogel group developed Alveolar Osteitis ($P < 0.0001$).

k) Oral Submucous Fibrosis

Sudarshan R et al. (2012) carried out a preliminary study to compare the efficacy of AV with antioxidants in the treatment of oral submucous fibrosis (OSMF). In this study, 20 subjects with OSMF were included. Patients are divided into two groups, Group A received 5 mg of AV gel 3 times daily for 3 months and Group B received antioxidant capsules twice daily for 3 months. At the end of the study the authors concluded that AV group showed a better treatment response in reducing the burning sensation and enhanced mouth opening as compared to the antioxidants group. Hence it can be applied topically and effective in the treatment of OSMF.

l) Oral Lichen Planus (OLP)

Hayes S M (1999) was first to report the medical of use of AV for treating lichen planus. The patient was asked to drink 2 oz. of stabilized AV juice daily in addition to application of AV lip balm for lesions on the lip and 75% cutaneous AV cream. After one month there was complete healing of the oral lesions and the cutaneous lesions decreased gradually over a period of 4-5 months without any recurrence.

In a study done by Reynolds T and Dweck A C (1999), on various components of AV leaf gel they reported that polysaccharides of the inner gel of AV have a varied immunomodulatory activity. The polysaccharides from the AV gel contains multiple factors and components in the form of interleukin monotypes which directly acts on the immune system to reduce symptomatic inflammatory features which can prove effective in treatment of OLP.

A randomized controlled study was performed to compare the efficacy of AV and placebo in the topical management of OLP. The AV gel which they formulated consisted of 70% AV mucilage, sorbitol, potassium sorbate, sodium metabisulphite and hydroxyethyl-cellulose and the placebo gel contained the same ingredients except AV mucilage. The AV gel used in their studyproved to be statistically significantly more effective than placebo in inducing clinical and symptomatological improvement of OLP (Choonhakarn C et al., 2007)

Salazar Sanchez N et al. (2010) conducted a study on 64 patients to check the efficacy of topical AV in patients with OLP. In this study, patients were asked to apply 0.4 ml AV gel [70% with water, sorbitol, E-202 (potassium sorbate) and E-223 (sodium metabisulfite)] and 0.4 ml of placebo gel [water, sorbitol, E-202 (potassium sorbate) E-223 (sodium metabisulfite)] in the mouth three times a day, keeping it into the oral cavity for one minute for 12 weeks. The patients treated with AV showed a greater reduction in pain than the placebo group. After 12 weeks, 19patients in the AV group showed complete remission, whereas 9 patients presented partial remission and 3 patients failed to respond to the treatment. In ananother recent randomized controlled trial on 40 patients to test the efficacy of AV versus Triamcinolone Acetonide ointment in the treatment of OLP. The authors concluded that AV gel was safe and effective in reducing both clinical signs and burning sensations of the lesion when compared to triamcinolone acetonide (Reddy L et al., 2016).

m) Recurrent Aphthous Stomatitis

Bhalang K et al., 2013conducted a study to evaluate the effectiveness of Acemannan (polysaccharide) found in AV, in the treatment of oral

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aphthous ulcers. 180 subjects with recurrent aphthous ulceration randomly received one of three treatments; 0.1% Triamcinolone Acetonide, 0.5% Acemannan in Carbopol 934 and just pure Carbopol 934 (control). The authors observed that the effectiveness of Acemannan in reducing ulcer size and pain was superior to that of control but inferior to that of 0.1% triamcinolone acetonide.

n) Denture Cleanser and Adhesive

Acemannan was formulated into a denture adhesive and evaluated for adhesive strength in both wet and dry conditions; the adhesive also was used to evaluate cytotoxicity to human gingival fibroblasts. An optimal formula with a high and relatively stable adhesive bond strength and minimum cytotoxicity was observed (Mangaiyarkarasi SP et al., 2015).

VI. Routes of Administration

It is currently available in the market as an external applicator like gel, oil, face powder, face wash and toothpaste (Kumbhar PS et al., 2015; Naroor N et al., 2014).

VII. Absorption, Distribution, Metabolism and Excretion of Aloe Vera

There are no reports of studies to determine the absorption, distribution, metabolism or excretion of topically applied AV gel or whole leaf extract in experimental animals or humans (IARC Monographs, 2015). AV gel contains non-starch polysaccharides of high molecular weight (Mostly Acemannan) that are composed of sugar moieties linked by β-1, 4-glycosyl bonds. In certain ex vivo experiments, it was observed that Acemannan labelled with Fluoresceinyl Isothiocyanate (FITC) in a suspension of fresh human faeces produced metabolites for 5 days which means that Acemannan is catabolized by human intestinal bacteria(IARC Monographs, 2015; Yagi A et al., 1999).

AV latex contains the Anthrone *C*-Glycosides Aloin A (Barbaloin) and Aloin B (Isobarbaloin) that are linked by β-Glycosyl bonds to D-Glucopyranose. Orally ingested Anthrone C-Glycosides (i.e. aloin A and aloin B) pass unchanged through the upper gastrointestinal tract and only in the lower gastrointestinal tract these molecules are cleaved to Aloe-Emodin-9-Anthrone by human Eubacterium sp. BAR, these results were obtained in germ-free rats (IARC Monographs, 2015; Akao T et al., 1996).

VIII. Adverse Effects of Aloe Vera

a) Topical Use

It may cause redness, burning, stinging sensation and rarely generalized dermatitis in sensitive individuals. Allergic reactions are mostly due to Anthraquinones (Aloin and Barbaloin). It is best to apply it to a small area first to test for possible allergic reaction (Rajeswari R et al., 2012).

b) Systemic Use

Diarrhea, red urine, abdominal cramps, hepatitis and dependency can lead to worsening of constipation. Laxative effect may sometimes cause electrolyte imbalances (Kavyashree G and Rosamma G, 2015). Verma A et al. in 2011conducted a study with an aim to evaluate the extent of cytogenetic toxicity of the crude leaf extract of AV using the onion root tip and murine bone marrow cells. The authors stated that when onion root tip cells were exposed to the AV extract, a highly significant increase in mitotic index (MI) was observed resulting from an increase in the number of cells in prophase. However there was no increase in chromosomal abnormalities.

The mice treated with AV extract also exhibited a marked increase in the number of dividing cells (metaphases) and thus the MI of bone marrow cells increased significantly. No significant increase was observed in structural abnormalities (break and break-related abnormalities) in chromosomes but the cells with variations in chromosome number were found to increase significantly.

IX. Contraindications of Aloe Vera

1. Contraindicated in cases of known allergy to plants in the Liliaceae family (Rajeswari R et al., 2012).
2. Oral aloe is not recommended during pregnancy due to theoretical stimulation of uterine contractions and in breastfeeding mothers, it may sometime causes gastrointestinal distress in the nursinginfant (Rajeswari R et al., 2012).
3. AV should not be used in patients with intestinal obstruction or stenosis, severe dehydration with electrolyte depletion (Sahu PK et al., 2013).
4. AV should not be administered to patients with inflammatory intestinal diseases, such as appendicitis, Crohn's disease, ulcerative colitis, irritable bowel syndrome or to children less than 10 years of age (Sahu PK et al., 2013).

X. Conclusion

The use of Aloe Vera looks very promising and must be explored further with long term studies to gain better insights. Advanced studies can be carried out to isolate individual compounds present in Aloe Vera using advanced techniques like High Pressure Liquid Chromatography. The emphasis is to find out the beneficial active constituents in Aloe Vera and their pharmacological actions in order to use them accurately in medical formulations.

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