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ORIGINAL RESEARCH

Efficacy of *Aloe vera* Gel delivered locally as an Adjunct to Scaling and Root Planing in the Treatment of Chronic Periodontitis: A Pilot Study

[1]Ajay Chouksey, [2]Hitesh Dilliwal, [3]Richa Agrawal, [4]Himanshu Khashu

ABSTRACT

Introduction: *Aloe vera* has been shown to have various biological and pharmacological effects like wound healing, anti-inflammatory effects, antibacterial and antiviral property, immunomodulating effects, and antioxidant property.

Aim: The study was conducted to evaluate the efficacy of *Aloe vera* gel as local drug delivery agent for treatment of pockets in chronic periodontitis through clinical assessment.

Materials and methods: A split-mouth designed study was conducted in 15 patients with total 30 sites, having bilateral mild to moderate periodontal pockets (5–7 mm). Following clinical parameters were recorded: probing pocket depth, gingival bleeding index, plaque index, and clinical attachment level for test group in which scaling and root planing (SRP) was done followed by placement of *Aloe vera* gel on day 0, 7, and 14 and in control group where only SRP was done.

Results: All the clinical parameters showed significant difference on 30th day in both intragroup and intergroup.

Conclusion: The use of *Aloe vera* gel resulted in more clinical improvements when compared with control group. Thus, it can be stated that *Aloe vera* shows promising future as local drug delivery in both preventive and therapeutic treatments available for chronic periodontitis.

Keywords: *Aloe vera*, Chronic periodontitis, Local drug delivery, Periodontal pockets.

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INTRODUCTION

Periodontitis is an inflammatory disease that causes destruction of tooth-supporting tissues and is characterized by multifactorial etiology with pathogenic bacteria being the primary etiologic agents that inhabit the subgingival area.[1] These pathogenic bacteria induce infections causing inflammation and destruction of the attachment apparatus, often leading to tooth loss.[2] Ignorance among population about oral care is the most prompting factor for deposition of plaque thus leading to increased prevalence of periodontal disease.[3] Periodontal pockets are well-disposed area within the gums for periodontopathic pathogens where access to routine cleaning is also difficult. Thus, microorganisms reside in large numbers within these pockets and start releasing toxic substances harmful to host resulting in destruction of soft tissues supporting teeth and loss of clinical attachment. In response to above, the host as a part of immune response antagonize by releasing inflammatory mediators like cytokines, prostaglandins, matrix metalloproteinase (MMP), which are initially meant for defense and in later stages are responsible for destruction of periodontal tissue.[4] Treatment strategy for the periodontal diseases must include the glide paths that will target the microorganisms as well as regulate the destructive host response.[5] Mechanical plaque control is the most effective method of curbing plaque and gingivitis.[6] But even though mechanical debridement removes plaque which contains microorganisms, it is impossible to entirely eradicate all virulence factors, due to tissue incursive nature of some periodontal pathogens, thus rendering mechanical therapy alone ineffectual, therefore antibacterial therapy is recommended as an adjunct to mechanical debridement. When antimicrobials are administered systemically it exposes the body to large dose causing antibiotic resistance, adverse drug reaction, and side-effects.[7] Moreover, less concentration of drug is attained in gingival crevicular fluid due to loss of drug during circulation to other parts of the body.[8] Since periodontal pockets form the primary source of infections with respect to periodontal infections, local drug delivery in the form of intrapocket administration of drugs will prove to be more advantageous than systemic administration, as the drug reaches the base of the pocket and is maintained there by some means like reservoir for an adequate time for the antimicrobial effect to occur.[9] Second, the drug is delivered at higher concentrations directly into diseased sites reducing the microbial load, requirement of less

[1]Senior Lecturer, [2]Postgraduate Student, [3]Reader, [4]Professor and Head

[1-4]Department of Periodontics, Mansarovar Dental College Bhopal, Madhya Pradesh, India

Corresponding Author: Richa Agrawal, Reader, Department of Periodontics, Mansarovar Dental College, Bhopal, Madhya Pradesh, India, e-mail: dr.richa.agrawal12@gmail.com

applications, reduction in systemic dosing, high potential acceptability, and minor side-effects.[10] Several chemical agents are commercially available which can alter oral microbiota but are proposed to have many undesirable side-effects, such as tooth staining, drug resistance, vomiting, diarrhea, etc.[11] Hence, the search for more desirable substitute products continues and natural phytochemicals quarantined from plants used in traditional medicine are weighed as good alternatives to synthetic chemicals.[12] Herbal products of medicine have been used for centuries throughout the world. As it was best aforesaid by Hippocrates "Let food be your medicine and let medicine be your food." It is still rightful today that "you are what you eat."[13] Among the various traditional medicinal plant extracts, *Aloe vera* has shown to be a promising herb for abridging the growth of oral pathogens, thus reducing the development of dental plaque and the symptoms of oral diseases.[14]

The plant *Aloe vera* has a history dating back to scriptural times. The name *Aloe vera* is derived from the Arabic word "Alloeh" meaning "shining bitter substance," while "vera" in Latin means "true." There are over 250 species of Aloe grown around the world, of which only two species are grown commercially: *Aloe barbadensis* Miller and *Aloe arborescens*. The Aloe plant is cropped in warm, tropical areas. Over the years, this plant has been known by a number of names, such as "heaven's blessing," "the wand of heaven," and "the silent healer."

Aloe barbadensis plant consists of two different parts, each of which produces substances with completely different compositions and therapeutic properties. The parenchymal tissue makes up the inner portion of the Aloe leaves and produces the *Aloe vera* gel (or mucilage): a clear, thin, tasteless, jelly-like material. This tissue is recovered from the leaf by separating the gel from the inner cellular debris. The other part of the plant is a group of specialized cells known as the pericyclic tubules, which occur just below the outer green ring of the leaf. These cells produce an exudate that consists of bitter yellow latex with powerful laxative-like actions. *Aloe vera* has been shown to have various biological and pharmacological effects like wound healing, anti-inflammatory effects, antibacterial and antiviral property, immunomodulating effects, and antioxidant property.[15] These properties are attributed to 75 potentially active constituents contained in *Aloe vera* which are vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids.[16]

- *Enzymes*: It contains eight enzymes: 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.
- *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.
- *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. The most prominent monosaccharide is mannose-6-phosphate, and the most common polysaccharides are called glucomannans [beta-(1,4)-acetylated mannan]. Acemannan, a prominent glucomannan, has also been found. Recently, a glycoprotein with antiallergic properties, called alprogen and novel anti-inflammatory compound, C-glucosyl chromone, has been isolated from *Aloe vera* gel.
- *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.[17]
- *Anthraquinones:* It provides 12 anthraquinones, which are phenolic compounds traditionally known as laxatives. Aloin and emodin act as analgesics, antibacterials, and antivirals.
- *Hormones:* Auxins and gibberellins are present that help in wound healing and have anti-inflammatory action.
- *Fatty acids:* It provides four plant steroids: cholesterol, campesterol, β-sitosterol, and lupeol. All these have anti-inflammatory action, and lupeol also possesses antiseptic and analgesic properties.
- *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 properties.[18]

Aloe vera is extremely helpful in the treatment of gum diseases like gingivitis and periodontitis. It acts by reducing bleeding, swelling, and inflammation of the gums. It acts as powerful antiseptic in pockets where normal cleaning is difficult. Thus, it yields a potent natural soothing healer for periodontal diseases.[19]

In previous studies, the effect of *Aloe vera* were studied mostly in the form of toothpastes, mouthwashes, and topical gel, but there is less of literature on the use of *Aloe vera* as local drug delivery for treatment of periodontal pockets. The purpose of this study was to evaluate the efficacy of *Aloe vera* gel as an adjunct to SRP when used as a local drug delivery in patients with chronic periodontitis.

MATERIALS AND METHODS

The study population comprised 15 patients (7 females, 8 males), aged 25 to 50 years, each with two sites (hence 30 sites), who were selected from the outpatient department of the Department of Periodontics, Mansarover Dental College, Bhopal, India. All patients exhibited the clinical signs of moderate–advanced periodontitis with probing depth of >5 mm present bilaterally at least at one site. A randomized, split-mouth, single-blind study was planned to reduce the error variance of the experiment. Patients with poor oral hygiene maintenance, current smokers, pregnant or lactating mothers, systemically compromised or on any medication, or who had undergone periodontal therapy in past 6 months were excluded from the study. All the screened participants were informed about the nature of the study design and procedure for local drug delivery, and a written consent was obtained. Group I consisted of periodontal pockets on one side of the jaw in which SRP was done followed by application of *Aloe vera* gel. Group II consisted of periodontal pockets on the contralateral side, in which only SRP were done. Full mouth SRP were done with hand instruments. Only two contralateral sites in the posterior teeth were selected per volunteer for the study. After SRP, in Group I, *Aloe vera* gel was applied by a syringe inserted up to the base of the pocket. It is the pure *Aloe vera* extract obtained from the center of the leaf, processed to eliminate the toxins and having 2% sodium benzoate as a preservative. *Aloe vera* gel was reapplied on 7th day and 15th day on the selected site just at the entrance of the periodontal pocket. The syringe was not inserted up to the base while reapplication so as not to disturb healing. After the placement of *Aloe vera* gel, the treated areas were given periodontal pack to isolate the area. All treatments were performed by an experienced periodontal specialist. The patient was instructed not to use any other antiplaque agents other than brushing and rinsing, not to floss or probe the area with tongue, finger, or toothpick, no dietary restrictions were imposed during or after the treatment. Patients were instructed to report immediately to the clinic if the periodontal pack was dislodged before the scheduled recall visit or if any pain, swelling, or irritation occurred.

Data analysis after completion of the clinical trial was done. Data obtained from the sites were computed and put to statistical analysis. Site-based analysis was performed using parameter tests for the comparison between groups I and II for outcome variables under study. For each treatment group, the mean values for the probing pocket depth (U.N.C. 15 probe), gingival index, plaque index, and clinical attachment level were calculated at baseline, 7th day, and 15th day. Statistical analysis was obtained on these values. For statistical data analysis, Friedman test followed by Wilcoxon and Mann–Whitney U-test were applied.

RESULTS

Data were entered in Microsoft Excel 2007, which was transferred to Statistical Package for the Social Sciences software, version 19.0, which is used to apply statistical tests. Kolmogorov–Smirnov test was applied to know the normality of the data, and the data were found to be non-normal, hence nonparametric tests were applied. For plaque index and gingival index, there were three intervals for which Friedman test was applied followed by Wilcoxon signed rank test between each time interval. For pocket depth and clinical attachment level, there were only two time intervals, hence Wilcoxon signed rank test was applied directly. Mann–Whitney U-test was applied for comparison between two different treatment regimes. The level of significance was set at 0.05 and was considered to be statistically significant.

The study result shows that for groups I and II for plaque index all the intervals are highly significant with each other, which means that the plaque index in each interval is affected significantly. In case of gingival index for both the groups, there was no significant difference between 0 day and 15th day, but it changes significantly on 30 days (Table 1). We can conclude by saying that both the treatments are effective in short term for plaque index but only long-term effect is seen for gingival index. For pocket depth and clinical attachment level in intragroups (for both groups I and II) result shows highly significant difference between both the intervals (Table 2). On comparing all the variables between groups I and II, the results were found to be significantly different on

Table 1: Plaque index and gingival index

Groups	*Variable*	*Interval*	*Mean rank*	*p-value*
Group I	Plaque index	0 day	3.00^{a}	0.001*
		15th day	1.90^{b}	
		30th day	1.10^{c}	
	Gingival index	0 day	2.60^{a}	0.001*
		15th day	2.33^{a}	
		30th day	1.07^{b}	
Group II	Plaque index	0 day	3.00^{a}	0.001*
		15th day	1.00^{b}	
		30th day	2.00^{c}	
	Gingival index	0 day	2.47^{a}	0.001*
		15th day	2.30^{a}	
		30th day	1.23^{b}	

Test applied: Friedman test between different intervals followed by Wilcoxon signed rank test for pairwise comparison; *p ≤ 0.001 (highly significant); dissimilar alphabets in the superscript of mean rank show significant difference

Table 2: Pocket depth and clinical attachment level

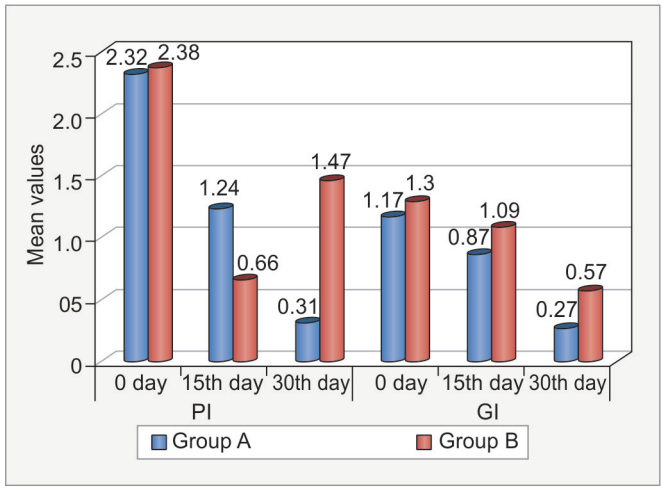
Groups	*Variable*	*Interval*	*Z value*	*p-value*
Group I	Pocket depth	0 day 30th day	−3.690	0.001*
	Clinical attachment level	0 day 30th day	−3.384	0.001*
Group II	Pocket depth	0 day 30th day	−3.571	0.001*
	Clinical attachment level	0 day 30th day	−3.493	0.001*

Test applied: Wilcoxon signed rank test for between-interval comparison; *p ≤ 0.001 (highly significant)

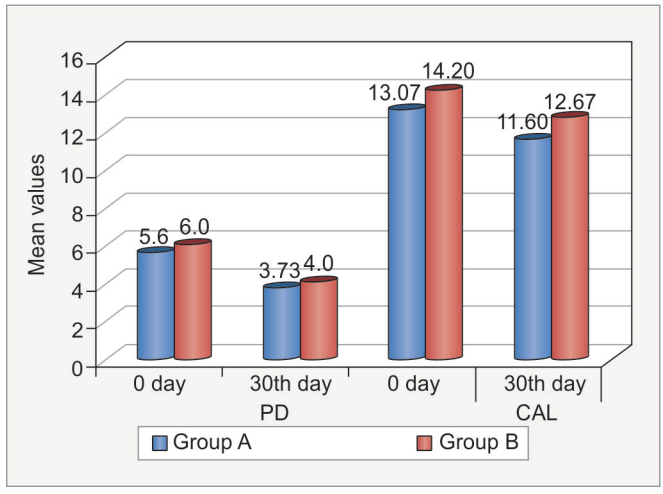
Table 3: Mann–Whitney U-test

Variables	*Intervals*	*Group I (mean ± SD)*	*Group II (mean ± SD)*	*p-value*
Plaque	0 day	2.32 ± 0.26	2.38 ± 0.26	0.512
	15th day	1.24 ± 0.52	0.66 ± 0.36	0.002*
	30th day	0.31 ± 0.12	1.47 ± 0.28	0.001**
Gingival index	0 day	1.17 ± 0.64	1.3 ± 0.45	0.567
	15th day	0.87 ± 0.4	1.09 ± 0.43	0.202
	30th day	0.27 ± 0.12	0.57 ± 0.45	0.041*
Pocket depth	0 day	5.6 ± 0.83	6.0 ± 1.13	0.436
	30th day	2.93 ± 0.70	4.0 ± 0.92	0.005*
Clinical attachment level	0 day	13.07 ± 1.53	14.2 ± 2.14	0.137
	30th day	11.13 ± 1.24	12.67 ± 2.09	0.029*

Mann–Whitney U-test for comparison between groups I and II; *p ≤ 0.05 (significant); **p ≤ 0.001 (highly significant); SD: Standard deviation



Graph 1: Comparison of plaque index and gingival index in both groups



Graph 2: Comparison of probing depth and clinical attachment level in both groups

15th and 30th day, with mean plaque index being highly significant, while mean gingival index, mean probing depth, and mean clinical attachment level significant at 30th day (Table 3; Graphs 1 and 2).

DISCUSSION

The primary objective of periodontal therapy is to reduce the microbial load, thereby leading to an improvement in the clinical parameters. Scaling and root planing remain the gold standard of periodontal therapy with numerous other agents being currently used as adjunctive therapeutic modalities. This study aimed at evaluating the effectiveness of *Aloe vera* gel when used along with SRP as a local drug delivery. The results of the present study showed statistically significant improvements in clinical parameters at 15th and 30th day of examination compared with those at baseline. *Aloe vera* applied in test site resulted in significant reduction in pocket depth and gingival index when compared with controls, due to its anti-inflammatory, antibacterial, wound healing properties[19] attributed to the substances found in *Aloe vera* like lignins, saponins, vitamins, minerals, enzymes, amino acids, anthroquinones, etc.[20] *Aloe vera* also has ingredients that act as anti-inflammatories. Bradykinase is an *Aloe vera* enzyme, which reduces skin inflammation. *Aloe vera* has 12 anthraquinones, also known as laxatives. It has fatty acids, salicylic acid, and hormones called auxins and gibberellins, all of which helps in subsiding inflammation.[21] Barrantes and Guinea in 2003 stated that *Aloe vera* suppresses the stimulated granulocyte MMPs, inhibiting cyclooxygenase (COX) and lipo-oxygenase pathways, and reduces the activity of prostaglandin E2.[22] These anti-inflammatories work most by stimulating immune system function and collagen growth or by blocking the paths of irritants.[21] Fujita et al stated that carboxypeptidase in *Aloe vera* inactivates bradykinin, an inflammatory substance, by about 67% and relieves pain. This study is in accordance with Payne et al, who also reported that *Aloe vera* gel used in wound site reduced inflammation along with relieving pain.[23] Bautista-Pérez et al[24] showed that carboxypeptidase in *Aloe vera* had good antiprostaglandin-synthesizing properties and compounds suppressing oxidation of arachidonic acid, which might decrease inflammation. *Aloe vera* contains salicylate magnesium lactate decarboxylase, which is known to inhibit histidine, thereby precluding the formation of histamine

from histidine within mast cells.[25] Heggers and Robson[26] showed that barbolin and aloe emodin in *Aloe vera* impede prostaglandin synthesis. Vázquez et al[27] stated that the decrease in gingival index is due to reduction in edema and number of neutrophils and also due to prevention of migration of polymorphonuclear leukocytes. *Aloe vera* is also shown to provide ease in swelling, bleeding gums, and is an antiseptic for pockets. Different mechanisms have been claimed for the wound healing effects of *Aloe vera* gel, which includes keeping the wound moist, more rapid maturation of collagen, increasing epithelial cell migration, and reduction in inflammation.[28] Glucomannan amannose-rich polysaccharide and gibberellin, a growth hormone, interact with receptors of growth factors on the fibroblast, thereby exhilarating its activity and proliferation, thus stimulating collagen synthesis after topical and oral application of *Aloe vera* gel.[29] Yagi et al[35] reported that *Aloe vera* gel contains a glycoprotein with cell proliferating activity, while Davis et al[30] noted that *Aloe vera* gel improved wound healing by increasing blood supply (angiogenesis), thus increasing the oxygenation to the tissues. The *Aloe vera* gel polysaccharide, acemannan, was shown to activate macrophages, an effect that ameliorated wound healing in a rat model.[31]

Bovik[32] used *Aloe vera* for the gingivectomy sites and showed that healing was improved. Davis has stated that wound healing with *Aloe vera* was due to increased blood supply, increased oxygenation, which stimulates fibroblast activity, and increased collagen proliferation.[33] It has a positive influence on the collagen content and constancy in a wound, therefore imposing a beneficial role in wound healing.[34] It also contains minerals that increase tensile strength of wound, thus facilitating early wound healing.[19] Yagi et al[35] found that three aloesin derivatives from aloe, namely, isorabaichromione, *p*-coumaroyl aloesin, and feruloyl aloesin, have potent-free radical and superoxide anion scavenging properties. It was found that aloesin compounds inhibited COX-2 and thromboxane A2 synthase, thus explaining the healing effects of *Aloe vera* gel.[27] The antibacterial property of *Aloe vera* has shown to be positive against both Gram-positive and Gram-negative bacteria.[36] George et al[37] conducted an *in vitro* evaluation regarding the antimicrobial activity of an *Aloe vera* tooth gel and concluded that *Aloe vera* tooth gel was highly beneficial in controlling all the organisms, i.e., *Streptococcus mutans*, *Lactobacillus acidophilus*, *Streptococcus mitis*, *Candida albicans*, *Prevotella intermedia*, *Enterococcus faecalis*, and *Peptostreptococcus anaerobius*. In addition, the *Aloe vera* gel showed superior antibacterial effect against *S. mitis* despite the absence of fluoride. *Aloe vera* has strong antioxidant nutrients. Glutathione peroxide, superoxide dismutase enzymes, and phenolic compounds were found to be present in *Aloe vera* gel, which may be responsible for these antioxidant effects.[38]

Aloe vera contains many vitamins including vitamins A, C, E, which also helps in antioxidant property by fighting against damaging free radicals and positively influences the immune system. Vitamin A helps in maintaining the integrity of epithelial cells. Vitamin E acts as an antioxidant and neutralizes the free radicals by donating one of their electrons, thus ending the electron-stealing reaction. Vitamin C in particular assists in wound healing by helping in connective tissue regeneration (collagen synthesis).[39] Thus, it can be speculated that *Aloe vera* extracts are beneficial in controlling and treating periodontal diseases by virtue of their antioxidant properties as well. Moore[40] used *Aloe vera* gel extensively in his patients and expressed that *Aloe vera* is not a malarkey, magic, or a myth but that it is truly a miraculous plant, which should be made a part of our medicines too.

CONCLUSION

The results presented in this study suggest that the *Aloe vera* gel is effective in the treatment of chronic periodontitis when used as an adjunct to SRP. *Aloe vera* can be used as a local drug delivery system because of its various benefits like easy availability, easy application with minimal equipments, affordability, and good biological acceptability by the oral tissues with no adverse effects. Oral *Aloe vera* is not recommended during pregnancy as it can stimulate uterine contractions, and in breastfeeding mothers, as it may sometimes cause gastrointestinal distress in the nursing infant.[40] To conclude, it can be stated that *Aloe vera* shows promising future in both preventive and therapeutic treatments available for the periodontal diseases if used cautiously. However, due to limited patient number and shorter time period in this study, a further research, based on long-term studies with larger patient number along with microbial analysis, is required in this field.

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