 DOI: **10.21608/adjalexu.2021.55192.1146**

ADJUNCTIVE TREATMENT WITH LOCALLY DELIVERED ALOE VERA GEL IN PATIENTS WITH CHRONIC PERIODONTITIS (A RANDOMIZED, CONTROLLED TRIAL)

Fatma E. Tayeb[1*] BDS, Mohy El Din A. El Rashidy[2] PhD, Rania A. Fahmy[3] PhD, Mohamed S. Abdel Gaffar[4] PhD

ABSTRACT:

INTRODUCTION: Aloe Vera (AV), is a plant widely used in pharmaceutical, medical, and cosmetic applications. It is known for its therapeutic benefits. The biological active components of AV include antibacterials and antioxidants. Aloe Vera also has anti-inflammatory and immunomodulatory effects which promote tissue regeneration. Aloe Vera gel have been demonstrated as an adjunctive treatment for several inflammatory diseases including periodontitis.

OBJECTIVE: To evaluate the effect of AV gel as an adjunctive treatment to SRP in management of chronic periodontitis.

MATERIALS AND METHODS: In a randomized, single-blinded study. Patients were divided into two groups, each included fifteen patients with mild to moderate chronic periodontitis having 1-4 mm attachment loss. Group 1 (test): treated with scaling and root planning followed by subgingival application of AV gel at day 1 and after 1 and 2 weeks, and group 2 (control): treated with scaling and root planning only. Probing depth, clinical attachment level and gingival index were measured at baseline and after 3, 6 and 9 months.

RESULTS: Compared to baseline, the two groups showed an improvement in all parameters at 9 months follow up. In AV gel group changes from baseline to 9 months were significantly greater compared to control group regarding reduction of PD, GI and CAL gain, moreover, intergroup differences were statistically significant in favor of AV group.

CONCLUSION: according to this study results, adjunctive use of AV gel might add advantages to SRP alone in management of chronic periodontitis.

KEY WORDS: Chronic Periodontitis, Aloe Vera Gel, Natural Treatment, Topical Treatment, Locally Delivered Treatment.

---

1 Dentist at Ministry of Health, BDS 2011 Alexandria Egypt
2 Professor, Department of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Alexandria University
3 Assistant Professor, Department of Oral Medicine, Periodontology, Oral Diagnosis and Radiology, Faculty of Dentistry, Alexandria University
4 Professor, Department of Pharmaceutics, Faculty of Pharmacy, Alexandria University

Corresponding author

Email: fatmaislam2011@yahoo.com

INTRODUCTION

Periodontitis is an inflammatory disease which is initiated by pathogenic bacteria which causes periodontal destruction. It is one of the common diseases affecting teeth and can cause tooth loss. Periodontitis starts as an inflammation of gingival tissues which if neglected could result in progression of the inflammation to deeper tissues causing disruption of bone homeostasis. (1)

Bacterial biofilm is the main perpetrator identified in periodontitis, which is thriving on tooth surfaces. It is thought that there are about 800 species of bacteria identified in the mouth(2). Host response decides the propagation of the disease alongside other factors such as genetics, dental biofilm and calculus, environmental variables, systemic conditions of the individual, and lifestyle habits. (2, 3)

Improving and preserving the gingival heath and remaining periodontal tissues are the main focus of periodontal therapy. It starts with reduction of bacterial load and correcting the local factors, alongside the modification of behavioral factors like quitting smoking and improving oral hygiene. Then it is followed by non-surgical periodontal therapy, including scaling and root planning, mouth rinses, using local drug delivery agents and prescribing the appropriate antimicrobial agents. (4)

Pharmacological ingredients extracted from plants and natural microbials have been utilized since old

times, for treatment of different diseases, for example cancers , diabetes mellitus and atherosclerosis. Usage of phytotherapeutic agents in dentifrices, mouthwashs, locally delivered drugs have been utilized effectively in preventing and treating periodontal disease ages ago (5) .Polyphenols derived from herbs and other Herbal derivatives contain an assortment of ingredients which have anti-microbial, anti-inflammatory and anti-oxidative properties (6). These days there have been an interest in alternative natural remedies; especially to avoid the adverse effects that are caused by synthetic antimicrobials (7). Herbal drugs with its extended usage experience enjoy good patient tolerance and acceptance. They are a renewable source, thus ensuring sustainable supply of cheaper medicines which are more readily available in developing countries. (8)

Aloe Vera (AV), a succulent, drought resisting plant, is notable for its therapeutic usages. It contains approximately 75 potentially active ingredients including: nutrients, vitamins, sugars, anti-inflammatory substances, minerals, lignin, sterols, saponins, salicylic acids, amino acids and enzymes (9). AV have various beneficial effects which is accounted for, such as immune-modulatory, wound healing, hypoglycemic effect ,anticancer, gastro protective, anti-microbial and anti-inflammatory properties (10, 11). These properties, make AV a great contender for plaque control, thereby helps in management of gingivitis and periodontitis alongside the ease of accessibility, no common adverse effects, and its cost effectiveness. (12)

AV extracts have exhibited the ability to inhibit cyclooxygenase pathway and reduce prostaglandin synthesis from arachidonic acid, thus reducing inflammation. Those extracts contain many vitamins such as vitamin A, C and E. Vitamin A maintains the integrity of epithelial cells. Vitamin C is thought to be involved in collagen synthesis, thus helps in connective tissue regeneration and plays an important role as it increases the oxygen concentration at the wound site by dilating the blood vessels. Vitamin E acts as an antioxidant which positively influence the immune system (13). Acemannan, which is a polysaccharide from AV, has been found to improve osteogenesis, minerals deposition and capable of increasing the mRNA expression of bone morphogenetic protein 2 (14). In his study Kudalkar et al. (15), concluded that AV decreased the Matrix metalloproteinase (MMP-2 and MMP-9) in the gingival tissue samples; thus inhibiting tissue destruction related to periodontitis. So those AV components can be attributed for the clinical parameters improvement of chronic periodontitis.

This study aimed to assess the clinical effects of AV as an adjunctive treatment to scaling and root planning in patients with chronic periodontitis.

The null hypothesis assumed that there is no difference in the improvement of periodontal clinical parameters between the test group and the control group.

MATERIALS AND METHODS

Ethical Approval

Appropriate ethical clearance was obtained from the Research Ethics Committee of the Faculty of Dentistry, Alexandria University (IRB NO: 00010556 -IORG0008839) where the study was carried out. Also, an informed consent was signed by the patients participating in the study.

Sample Size Estimation

A sample size of 15 patients per group (number of groups = 2) (total sample size = 30 patients) was the required sample as statistically significant with 80% power and at a significance level of 95% (accepted α error = 0.05) (16). G. power software was used to calculate the sample size. (17)

Forty two patients were screened, thirty of them (23 females, 7 males) were enrolled in this randomized, controlled, clinical trial, started at January 2018. Patients were recruited from the outpatient clinic at the department of Oral Medicine, Periodontology, Oral Diagnosis, and Oral Radiology, Faculty of Dentistry, Alexandria University. Patients were randomized into two groups: test and control, the first group (test) included 15 patients treated with full mouth supra-and-subgingival scaling and root planning (18, 19) followed by subgingival application of AV gel, and the second group (control): included 15 patients treated only with full mouth supra-and-subgingival scaling and root planning (18, 19). Allocation of cases to either treatment approach was conducted randomly using simple randomization procedures (computerized random numbers). (17)

This study was written following the CONSORT 2010 guidelines for clinical trials and the CONSORT flow diagram was showed in figure 1. (20)

Inclusion Criteria

Patients age from 30 to 55 years.

Both sexes was included.

Systemically healthy individuals.

Patients with mild to moderate chronic periodontitis (CAL 1-4mm) according to the American Academy of Periodontology classification (1999). (21)

Exclusion Criteria

Smoking and alcoholism.

Patients with systemic illnesses (i.e., diabetes mellitus, cancer, human immunodeficiency syndrome, bone metabolic diseases, or disorders that compromise wound healing, radiation, or immunosuppressive therapy, conditions leads to xerostomia).

Patients on any medication affecting the periodontium.

Lactating, pregnant or menopausal females.

Patients with parafunctional habits.

Patients with poor oral hygiene.

Patients were selected after careful clinical examination, including probing depth (22), clinical attachment level (22) and gingival index (23). Clinical parameters were measured at baseline first then 3, 6 and 9 months postoperatively. Orthopantograms (OPG) was performed at the first visit to exclude any pathology.

Inter and intra examiner reliability: all the clinical measurements were taken by the same examiner and intra examiner reliability was calculated for probing depth and attachment loss with Intraclass correlation coefficient >0.82 indicating very good reliability. (24)

Formulation of AV gel

AV gel was prepared in the laboratories of the Faculty of Pharmacy, Alexandria University, guided by the procedures described by Velam et al (25).

The central parenchymatous pulp was collected from AV leaves and the pulp was flushed repeatedly with water then washed with 0.1N sodium hydroxide (NaOH) solution, then mixed in the blender to obtain a juice. Using a cotton bed the obtained juice was pre-filtered to remove the leftover peel particles. Then the juice was subjected to repeated vacuum filtration until a clear liquid was obtained. 1% w/w carbopol 934 was dissolved uniformly till no lumps of carbopol were left. While dispersing the carbopol 0.5% w/w methyl paraben was added. A solution of 0.5 N NaOH was added dropwise until a gel was formed. The final gel was weighed and filled in dark air tight containers to avoid photo-oxidation. (25)

Interventions

Phase I therapy was performed for both groups and patients were instructed to follow oral hygiene measures _including tooth brushing 3 times daily_, then scaling and root planing was performed. Coronoplasty was performed if needed. For test group the targeted area was flushed with saline to remove debris. Using atraumatic needle, 1cc AV gel was applied subgingivally. Instructions were given to patients not to eat, drink, rinse for an hour. Gel was applied at base line and after 1 and 2 weeks. (26)

Statistical analysis

Data analysis was performed using SPSS for windows version 23.0 and significance was set at p value < 0.05. Means and standard deviations (SD) were calculated, and parametric tests were used for normally distributed variables (age, probing depth and gingival index). Medians and interquartile range (IQR) and non-parametric tests were calculated for non-normally distributed variables (attachment loss). Percent change was calculate using the following equation: $\frac{value\ at\ 9\ months - value\ at\ baseline}{value\ at\ baseline} \times 100$. ANOVA and t-test, or Mann-Whitney U test and Friedman tests were used to analyze the data statistically according to the variable normality, both followed with Bonferroni adjustment for multiple comparisons.

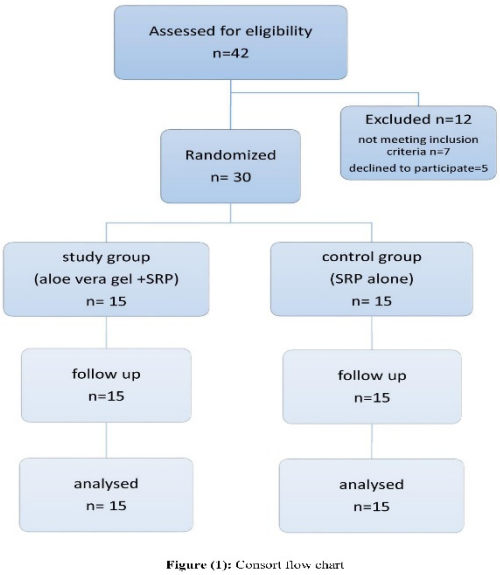

Figure (1): Consort flow chart

RESULTS

All of thirty patients, split into two groups (fifteen each), completed the study, none of them complained any adverse effects or discomfort. The mean age of the test group was (37.0) and the control group was (39.58) with no significant difference between groups (P =0.30). 73.3% of the test group participants were females and 26.7% were males, while 80% of control group were females and 20% were males. At baseline, intergroup parameters values were not significantly different ($P < 0.05$).

A statistically significant reduction in probing depth (PD) were found from baseline to 9 months in both groups. Moreover, AV group showed more reduction in PD than control group with a statistically significant difference at 3, 6 and 9 months ($p < 0.05$). (Table 1/ Figure 2)

For clinical attachment level (CAL), a statistically significant reduction were found in both groups from baseline to 9 months postoperatively. On intergroup comparison, CAL gain showed more improvement in AV group versus control group at 3, 6 and 9 months which was statistically significant. (Table 2/ Figure 3)

Table 3 showed gingival index (GI), for test and control groups, with reduction in mean GI from baseline to 9 months follow up which was statistically significant at $p \leq 0.05$, the intergroup difference of mean GI index was not statistically significant at 3 months follow up (p=0.06), but the reduction in GI was higher in test group with statistically significant difference at 6 and 9 months follow up ($p \leq 0.001$). (Table 3/ Figure 4)

DISCUSSION

Periodontitis is a multi-factorial disturbance in the homeostasis between dental bacterial biofilm and susceptible host (27, 28). The established treatment strategy of scaling and root planning is considered to be the "gold standard" for non-surgical treatment of chronic periodontitis (29).Various studies have evaluated the efficacy of some of chemical and non-chemical agents like antibiotics and herbals as an adjunctive treatment in periodontitis management. (30, 31)

The pharmacological action of AV and its usage in periodontal diseases have been well documented in literature. The subgingival delivery of AV gel as well as usage of mouthwashes that contains AV showed promising improvement in periodontal condition. (32, 33)

Our study goal was to evaluate AV gel clinical effectiveness as an adjunct to SRP for treatment of patients with chronic periodontitis. AV gel exhibited considerable improvement in clinical parameters of PD, CAL gain and GI compared to SRP alone.

In our study based on the PD and CAL gain the AV group showed a considerably better improvement than the control group with statistically significant difference at all time points. Bhat et al. (34) with similar findings in patients whom had chronic periodontitis, reported a considerable decrease in pocket depth in areas of AV gel treatment combined with SRP, which was statistically significant. Verdi et al. (26) had also published similar results on the effectiveness of AV gel in patients with chronic periodontitis. Another study by Kurian et al. (35) assessed locally-delivered AV gel effect on periodontitis, the adjunct subgingival application of AV gained superior results that mechanical periodontal therapy alone.

AV, also was shown to be of a great effect in the management of gingivitis (36). Gingival index was used to consider the periodontal tissue status, based on the inflammation symptoms including swelling, redness, and bleeding (37). In the current study despite gingival index showed that there was no statistically significant difference between both groups at 3 months (P=0.06) but the improvement in GI in AV group was statistically significant compared to controls at 6 and 9 months ($p \leq 0.001$).

Ajmera et al. (37) showed that AV, as an auxiliary treatment with mechanical cleaning can be a beneficiary treatment for gingivitis, although, AV alone showed no effect in management of gingivitis. Chandrahas et al. (38) made a comparison between the AV mouthwash and chlorhexidine 0.2% mouthwash which showed to be similar in recovery of gingivitis. Also compared to control group (using distilled water), it greatly decreased modified gingival index and bleeding index. Pradeep et al. (39) showed healing effects of AV toothpaste on gingivitis and observed a reduction in gingival inflammation. They reported higher therapeutic effects compared to toothpastes without such compounds and similar to the ones with fluoride and triclosan. (39) Pradeep et al. studied type II diabetics with chronic periodontitis and in his study he assessed the adjunctive local delivery effects of AV gel, there was an improvement in clinical parameters. Our present study results are also consistent with his results (40)

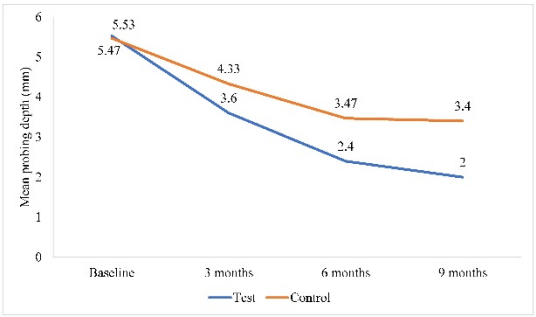

Figure (2): Probing depth at different time points in the two study groups.

Figure (2): Probing depth at different time points in the two study groups.

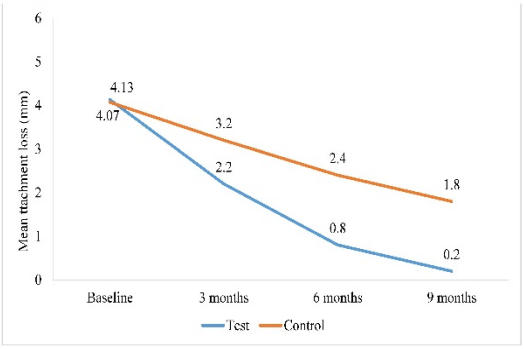

Figure (3): Attachment loss at different time points in the two study groups.

Figure (3): Attachment loss at different time points in the two study groups.

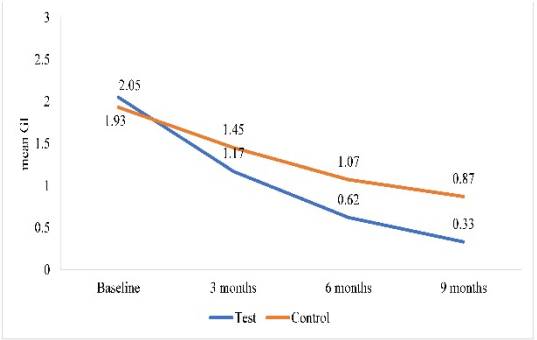

Figure (4): Gingival index (GI) at different time points in the two study group.

Figure (4): Gingival index (GI) at different time points in the two study group.

Table (1): Probing depth (mm) at different time points in the two study groups.

	Test (n=15)	Control (n=15)	Difference	95% CI	T-test P value
	Mean ± SD				
Baseline	5.53 ± 1.06 [a]	5.47 ± 0.92 [a]	0.07 ± 1.49	-0.67, 0.81	0.86
3 months	3.60 ± 0.83 [b]	4.33 ± 0.72 [b]	-0.73 ± 1.03	-1.32, -0.15	0.02*
6 months	2.40 ± 0.63 [b,c]	3.47 ± 0.64 [b,c]	-1.07 ± 0.88	-1.54, -0.59	<0.001*
9 months	2.00 ± 0.38 [c]	3.40 ± 1.18 [c]	-1.40 ± 1.24	-2.08, -0.72	<0.001*
Percent change	-63.32 ± 6.81	-38.38 ± 16.21	-24.94 ± 19.48	-34.23, -15.64	<0.001*
Repeated measures ANOVA p value	<0.001*	<0.001*			

SD: Standard deviation, CI: Confidence interval, *statistically significant at p value <0.05

[a,b,c] different superscripted letters denote statistically significant differences between different time points in each group using Bonferroni adjustment for multiple pairwise comparisons

Table (2): Attachment loss at different time points in the two study groups.

	Test (n=15)	Control (n=15)	difference	95% CI	Mann-Whitney P value
	Mean ± SD				
Baseline	4.13 ± 0.92 [a]	4.07 ± 0.70 [a]	0.07 ± 1.16	-0.54, 0.68	0.68
3 months	2.20 ± 0.77 [a,b]	3.20 ± 0.68 [a,b]	-1.00 ± 0.93	-1.54, -0.46	0.003*
6 months	0.80 ± 0.56 [b,c]	2.40 ± 0.63 [b,c]	-1.60 ± 0.74	-2.05, -1.15	<0.001*
9 months	0.20 ± 0.41 [c]	1.80 ± 1.01 [c]	-1.60 ± 0.99	-2.19, -1.01	<0.001*
Percent change	-95.11 ± 10.53	-57.56 ± 20.53	-37.56 ± 20.14	-49.95, -25.16	<0.001*
Friedman test p value	<0.001*	<0.001*			

SD: Standard deviation, IQR: Interquartile range, CI: Confidence interval, *statistically significant at p value <0.05

[a,b,c] different superscripted letters denote statistically significant differences between different time points in each group using Bonferroni adjustment for multiple pairwise comparisons

Table (3): Gingival index at different time points in the two study groups.

	Test (n=15)	Control (n=15)	Difference	95% CI	T-test P value
	Mean ± SD				
Baseline	2.05 ± 0.54 [a]	1.93 ± 0.59 [a]	0.12 ± 1.00	-0.30, 0.54	0.57
3 months	1.17 ± 0.28 [b]	1.45 ± 0.48 [b]	-0.28 ± 0.67	-0.58, 0.02	0.06
6 months	0.62 ± 0.23 [c]	1.07 ± 0.39 [c]	-0.45 ± 0.54	-0.69, -0.21	0.001*
9 months	0.33 ± 0.12 [d]	0.87 ± 0.39 [c]	-0.53 ± 0.41	-0.76, -0.31	<0.001*
Percent change	-82.83 ± 7.69	-53.84 ± 24.19	-28.99 ± 25.80	-42.83, -1515	<0.001*
Repeated measures ANOVA p value	<0.001*	<0.001*			

SD: Standard deviation, CI: Confidence interval, *statistically significant at p value <0.05
[a,b,c,d] different superscripted letters denote statistically significant differences between different time points in each group using Bonferroni adjustment for multiple pairwise comparisons

CONCLUSION

According to this study, Usage of AV combined with SRP as adjunctive therapy significantly improved the clinical parameters of PD, CAL and GI, indicating possible effectiveness of AV gel in management of chronic periodontitis.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding statement

The authors received no specific funding for this work.

REFERENCES

1. Raju Anarthe D, Mani A, Kale P, Maniyar S, Anuraga S. Herbal Approaches in Periodontics. Galore Int J Health Sci 2017;2:18-25.
2.Nazir MAJIjohs. Prevalence of periodontal disease, its association with systemic diseases and prevention. 2017;11(2):72.
3.Bartold PM, Van Dyke TEJP. Periodontitis: a host-mediated disruption of microbial homeostasis. Unlearning learned concepts. 2013;62(1):203-17.
4.Research S, Committee T, dentistry AAoPDJP. Treatment of plaque-induced gingivitis, chronic periodontitis, and other clinical conditions. 2005;27(7 Suppl):202-11.
5.Sanadi R, Kadri K, Sawarkar M, Benjamin A. Phytotherapeutic Agentsin Periodontal Therapy: A Review. IOSR JDMS. 2020;19:48-51.
6.Ohtani M, Nishimura TJE, medicine t. The preventive and therapeutic application of garlic and other plant ingredients in the treatment of periodontal diseases. 2020;19(2):1507-10.
7.Shah R, Gayathri G, Mehta DSJIJoOHS. Application of herbal products in management of periodontal diseases: a mini review. 2015;5(1):38.
8.Buggapati LJIJoPSI. Herbs in dentistry. 2016;5(6):07-12.
9.Sujatha G, Kumar GS, Muruganandan J, Prasad TS. Aloe vera in dentistry. Journal of clinical and diagnostic research : JCDR. 2014;8(10):ZI01-ZI2.
10.Kumar R, Singh AK, Gupta A, Bishayee A, Pandey AKJP. Therapeutic potential of Aloe vera—A miracle gift of nature. 2019;60:152996.
11.Maan A, Nazir A, Khan M, Ahmad T, Zia R, Murid M, et al. The therapeutic properties and applications of Aloe vera : A review. Journal of Herbal Medicine. 2018;12.
12.Sangur R, Bajwa W, Mahajan T, Banerjea A. Aloe Vera: An Ancient Option for Modern Day Dental Problems-A. Int J Contemp Med 2016.
13.B Aggarwal B, Prasad S, Reuter S, Kannappan R, R Yadav V, Park B, et al. Identification of novel anti-inflammatory agents from Ayurvedic medicine for prevention of chronic diseases:"reverse pharmacology" and "bedside to bench" approach. 2011;12(11):1595-653.
14.Sierra-García GD, Castro-Ríos R, González-Horta A, Lara-Arias J, Chávez-Montes AJNpc. Acemannan, an extracted polysaccharide from Aloe vera: A literature review. 2014;9(8):1934578X1400900836.
15.Kudalkar MD, Nayak A, Bhat KS, Nayak RNJA. Effect of Azadirachta indica (Neem) and Aloe vera as compared to subantimicrobial dose doxycycline on matrix metalloproteinases (MMP)-2 and MMP-9: An in-vitro study. 2014;35(1):85.
16.Pannucci CJ, Wilkins EGJP, surgery r. Identifying and avoiding bias in research. 2010;126(2):619.
17.Faul F, Erdfelder E, Lang A-G, Buchner AJBrm. G* Power 3: A flexible statistical power analysis

program for the social, behavioral, and biomedical sciences. 2007;39(2):175-91.
18.Armitage GCJAop. Development of a classification system for periodontal diseases and conditions. 1999;4(1):1-6.
19.Mariotti AJAop. Dental plaque-induced gingival diseases. 1999;4(1):7-17.
20.Schulz KF, Altman DG, Moher DJT. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. 2010;11(1):1-8.
21.Wiebe CB, Putnins EEJJ-cda. The periodontal disease classification system of the American Academy of Periodontology-an update. 2000;66(11):594-9.
22.Soeroso Y, Akase T, Sunarto H, Kemal Y, Salim R, Octavia M, et al. The risk reduction of recurrent periodontal pathogens of local application minocycline HCl 2% gel, used as an adjunct to scaling and root planing for chronic periodontitis treatment. 2017;13:307.
23.Kinney JS, Ramseier CA, Giannobile WVJAotNYAoS. Oral fluid-based biomarkers of alveolar bone loss in periodontitis. 2007;1098:230.
24.Liljequist D, Elfving B, Skavberg Roaldsen KJPo. Intraclass correlation–A discussion and demonstration of basic features. 2019;14(7):e0219854.
25.Velam V, Yalavarthi PR, Sundaresan C, Vandana K, Dudala TB, Kodavatikanti H, et al. In vitro and in vivo assessment of piroxicam incorporated Aloe vera transgel. 2013;3(4):212.
26.Virdi H, Jain S, Sharma SJIJoOS. Effect of locally delivered aloe vera gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A clinical study. 2012;3(2):84-.
27.Tariq M, Iqbal Z, Ali J, Baboota S, Talegaonkar S, Ahmad Z, et al. Treatment modalities and evaluation models for periodontitis. 2012;2(3):106.
28.Mohan R, Agrawal S, Gundappa MJCcd. Atomic force microscopy and scanning electron microscopy evaluation of efficacy of scaling and root planing using magnification: A randomized controlled clinical study. 2013;4(3):286.
29.Ehizele A, Akhionbare OJAom, research hs. Effect of Non‐Surgical Periodontal Therapy on the Concentration of Volatile Sulfur Compound in Mouth Air of a Group of Nigerian Young Adults. 2013;3(3):433-7.
30.Saglam M, Kantarci A, Dundar N, Hakki SSJLims. Clinical and biochemical effects of diode laser as an adjunct to nonsurgical treatment of chronic periodontitis: a randomized, controlled clinical trial. 2014;29(1):37-46.
31.Hrishi T, Kundapur P, Naha A, Thomas B, Kamath S, Bhat GJIjodh. Effect of adjunctive use of green tea dentifrice in periodontitis patients–A Randomized Controlled Pilot Study. 2016;14(3):178-83.
32.Kumar A, Sunkara MS, Pantareddy I, Sudhakar SJJoc, JCDR dr. Comparison of plaque inhibiting efficacies of Aloe vera and propolis tooth gels: A randomized PCR study. 2015;9(9):ZC01.
33.Moghaddam AA, Radafshar G, Jahandideh Y, Kakaei NJJoD. Clinical evaluation of effects of local application of Aloe vera gel as an adjunct to scaling and root planning in patients with chronic periodontitis. 2017;18(3):165.
34.Bhat G, Kudva P, Dodwad VJJoIsop. Aloe vera: Nature's soothing healer to periodontal disease. 2011;15(3):205.
35.Kurian IG, Dileep P, Ipshita S, Pradeep ARJJoi, dentistry c. Comparative evaluation of subgingivally-delivered 1% metformin and Aloe vera gel in the treatment of intrabony defects in chronic periodontitis patients: A randomized, controlled clinical trial. 2018;9(3):e12324.
36.Altincik A, Sönmez F, Yenisey Ç, Duman S, Can A, Akev N, et al. Effects of Aloe vera leaf gel extract on rat peritonitis model. 2014;46(3):322.
37.Ajmera N, Chatterjee A, Goyal VJJoISoP. Aloe vera: It's effect on gingivitis. 2013;17(4):435.
38.Chandrahas B, Jayakumar A, Naveen A, Butchibabu K, Reddy PK, Muralikrishna TJJoISoP. A randomized, double-blind clinical study to assess the antiplaque and antigingivitis efficacy of Aloe vera mouth rinse. 2012;16(4):543.
39.Pradeep A, Agarwal E, Naik SBJJop. Clinical and microbiologic effects of commercially available dentifrice containing aloe vera: a randomized controlled clinical trial. 2012;83(6):797-804.
40.Pradeep A, Garg V, Raju A, Singh PJJop. Adjunctive local delivery of Aloe vera gel in patients with type 2 diabetes and chronic periodontitis: a randomized, controlled clinical trial. 2016;87(3):268-74.