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Wound healing effect of a one-week Aloe Vera mouthwash: a pilot study

Efeito de reparação tecidual de uma semana de enxaguante bucal de Aloe Vera: um estudo piloto

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ABSTRACT

Aloe Vera, a perennial Liliaceae plant, has medical, cosmetic, and wound-healing properties. Aloe vera has antioxidant, anti-cancer, anti-diabetic, and regenerative effects. Glucommannan increases collagen synthesis and aids healing after ginivectomy treatment. Natural mouthwashes may offer gingival wound healing efficacy with reduced side-effects when compared to Chlorhexidine. **Objective:** the objective of this clinical study was to compare the effects on wound healing of a one-week Aloe vera mouthwash with chlorhexidine mouthwash before gingivectomy surgical therapy. **Material and Methods:** a total of 45 individuals experiencing inflammatory gingival enlargement were included in the study. They underwent professional mechanical plaque removal and were then randomly divided into three groups. In group I, comprising 15 patients, participants were advised to utilize 100% Aloe vera juice as a mouthwash twice daily. Group II, also consisting of 15 patients, was instructed to use Chlorhexidine (0.2%) mouthwash twice daily. The Control group, which consisted of 15 patients, was recommended to use a placebo mouth rinse in addition to mechanical plaque removal. During the second visit, which occurred one week after the initial visit, the enlarged gingival tissue was surgically removed through scalpel gingivectomy. Immunohistochemical (IHC) analysis was performed on the excised tissue to measure the levels of fibroblast growth factor-2. **Results:** when compared to the control group, Aloe vera showed significant differences regarding the expression of fibroblast growth factor-2(FGF-2), and highly significant differences in angiogenesis. At the same time, there were substantial differences in angiogenesis with no significant differences in the expression of FGF2 between Chlorhexidine and control groups. **Conclusion:** aloe vera has exhibited potential wound-healing effects as it significantly affected the IHC expression of FGF2 and angiogenesis when used as an adjunct to plaque control before gingivectomy surgical therapy.

KEYWORDS

Aloe-vera; Fibroblast growth factor-2; Gingival overgrowth; Chlorhexidine; Mouthwash.

RESUMO

Aloe Vera, uma planta perene de Liliaceae, tem propriedades médicas, cosméticas e cicatrizantes. Aloe vera tem efeitos antioxidantes, anticancerígenos, antidiabéticos e regenerativos. O glucomanano aumenta a síntese de colágeno e auxilia na cicatrização após o tratamento de gengivectomia. Enxaguatórios bucais naturais podem oferecer eficácia na reparação de feridas gengivais com efeitos colaterais reduzidos quando comparados à clorexidina. **Objetivo:** O objetivo deste estudo clínico foi comparar os efeitos na cicatrização de feridas de uma semana de enxaguatório bucal de Aloe vera com clorexidina antes da terapia cirúrgica de gengivectomia. **Material e Métodos:** um total de 45 indivíduos com aumento gengival inflamatório foram incluídos no estudo. Eles foram submetidos à remoção mecânica profissional da placa e foram divididos aleatoriamente em três grupos. No grupo I, composto por 15 pacientes, os participantes foram orientados a utilizar 100% de suco de Aloe vera como enxaguante bucal duas vezes ao dia. O grupo II, também composto por 15 pacientes, foi instruído a usar enxaguante bucal com clorexidina (0,2%) duas vezes ao dia. O grupo controle, composto por 15 pacientes, foi recomendado o uso de enxaguatório bucal placebo além da remoção mecânica da placa.

Durante a segunda visita, que ocorreu uma semana após a visita inicial, o tecido gengival aumentado foi removido cirurgicamente por meio de gengivectomia com bisturi. A análise imuno-histoquímica (IHC) foi realizada no tecido excisado para medir os níveis do fator de crescimento de fibroblastos-2 (FGF-2). **Resultados:** quando comparado ao grupo controle, o Aloe vera apresentou diferenças significativas em relação à expressão do FGF-2, e diferenças altamente significativas na angiogênese. Ao mesmo tempo, houve diferenças substanciais na angiogênese, sem diferenças significativas na expressão de FGF-2 entre a clorexidina e os grupos controle. **Conclusão:** Aloe vera exibiu potenciais efeitos de cicatrização de feridas, pois afetou significativamente a expressão IHC de FGF-2 e a angiogênese quando usada como adjuvante no controle de placa antes da terapia cirúrgica de gengivectomia.

PALAVRAS-CHAVE

Aloe Vera; Fator 2 de crescimento de fibroblastos; Crescimento excessivo da gengiva; Clorexidina; Antissépticos Bucais.

INTRODUCTION

Regardless of gender, age, or ethnicity, over 90% of individuals experience gingivitis caused by plaque, making it one of the most prevalent periodontal conditions [1]. Gingivitis is initiated by the noxious substances resulting from the deposition of microbial plaque at or close to the gingival sulcus [2].

Oral hygiene adjuncts, such as mouth rinses, are commonly utilized as anti-plaque agents [3], and also act as vehicles to deliver active agents to the teeth and gingiva [1]. According to a review, there is strong evidence supporting the effectiveness of chlorhexidine (CHX) mouthwash in reducing gingivitis and plaque levels among patients with mild to moderate disease. However, there is moderate evidence suggesting that prolonged use of CHX mouthwash can lead to external staining of teeth. Furthermore, the prolonged usage of chlorhexidine (CHX) mouthwash is discouraged due to several side effects, such as brown staining of teeth and tongue, altered taste sensation, and increased calculus formation [4]. Hence, there is a need to develop natural products and domestic and economic oral hygiene aid. Aloe vera extract could be one such plaque control aid [1].

Aloe vera, belonging to the Liliaceae family, is a cactus-like plant known for its gel-like mucilaginous tissue. This gel has been traditionally used as a laxative and for the treatment of various conditions, including sunburn, wounds, and digestive tract disorders [5]. Pharmacological attributes of Aloe vera show that it acts as an antibacterial, antiviral, antifungal, antioxidant, and anti-inflammatory [6]. Upon oral or topical administration, a specific active ingredient found in Aloe vera stimulates the proliferation and activity of fibroblasts. This stimulation, in turn, affects the composition of collagen, particularly an increase in type III collagen. Additionally, there is an enhancement in collagen synthesis and cross-linking, which contributes to the process of wound contraction [7]. A study done by Abed and Al-Hijazi in 2016 used Aloe vera gel in periodontal defects related to its ability to accelerate wound healing as it increases syndecan 1 expression in epithelial cells, precursor progenitor cells and in the early stage of cell proliferation of the mesenchymal cell, inflammatory cells, and cementoblast [8].

Aloe vera contains approximately 75 potentially active components, including water, sugars, enzymes, lignin, vitamins, amino acids, and minerals [9]. One of these compounds is glucomannan, a growth hormone and mannose-rich polysaccharide; it interacts with growth factor receptors on the fibroblast to activate proliferation and increase collagen synthesis [10]. Aloe vera may change collagen composition (increasing type III collagen), improve collagen cross-linking [11] and increase the amount of collagen in wounds thereby promote wound healing [12]. Prior studies on aloe vera gel have indicated that it has the potential to decrease skin fragility and enhance skin flexibility [13]. In a study that was done on rats; following oral and topical treatment with aloe-vera, an increase in the synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound has been seen [14].

Growth factors are natural biological mediators responsible for regulating important events in the cell, including the tissue-repairing process by binding to a specific receptor on the cell's surface [15].

Fibroblast growth factors (FGFs) are a group of growth factors known for their involvement in angiogenesis, wound healing, and embryonic development. Specifically, FGF-2 plays a crucial role by promoting the proliferation of fibroblasts and osteoblasts, as well as enhancing angiogenesis.

These activities have a direct association with the regeneration of periodontal tissues [16]. Some efficacy can be expected from FGF- 2 in stimulating the regeneration of periodontal tissue in patients having periodontitis [17].

Only a few studies have been conducted to assess and compare the effects of Aloe vera and chlorhexidine on the expression of fibroblast growth factor-2 (FGF-2) [18,19], so it was eventually needed to carry out this study to study and compare the effects on wound healing between Aloe-vera and chlorhexidine mouthwashes when used one-week before gingivectomy.

MATERIALS, METHODS AND SUBJECTS

Sample/study design

This pilot study adhered to the guidelines outlined in the 1975 Helsinki Declaration, revised in 2013, and received approval from the ethical committee of the University of Baghdad. Prior to participation, each subject provided informed consent, acknowledging their understanding of the study's objectives and their freedom to withdraw at any time. The study was conducted at the teaching hospital of the College of Dentistry, University of Baghdad, spanning from September 2019 to July 2020.

Inclusion criteria

To be included in the study, patients had to meet the following criteria:

- Being systemically healthy, with an age range between 15 and 30 years old;
- Not having used any medication within the past three months;
- Having inflammatory gingival enlargement;
- Not having any known allergy to chlorhexidine or aloe vera.

Exclusion criteria

Exclusion criteria for the study are as follows:

- Patients with systemic conditions such as liver and/or kidney dysfunction, inflammatory bowel disease (e.g., Crohn's disease), diabetes mellitus, a history of organ transplant or cancer treatment, or cardiovascular disease;
- Patients who have undergone extensive periodontal therapy in the past or are currently undergoing active periodontal therapy;
- Patients who have taken immunosuppressive drugs or antibiotics within the previous three months;
- Patients who have gingival enlargements not caused by inflammation;
- Patients with a known allergy to aloe vera or chlorhexidine.

Blinding and randomized

For the intervention assignment in this study, a computer random number generator (such as the one available in Microsoft Excel) was used. Each participant had an equal chance of being assigned to one of the interventions. The study involved three different compounds: aloe vera juice (test group), 0.2% chlorhexidine (control group), and distilled water with flavors (placebo group).

To ensure blinding and allocation concealment, an independent dentist who was not involved in the study assigned sequential number codes (1, 2, and 3) to identical, opaque bottles containing the mouthwashes. This process ensured that neither the examiner nor the participants could identify the interventions contained in the opaque bottles. After the study concluded, the decoding of the interventions took place.

The examiner received the blinded interventions according to a predetermined sequence list of interventions identified by numbers. This methodology ensured a double-blinded trial, where both the examiner and the participants were unaware of which interventions were being administered until the decoding process occurred.

Study sample and grouping

In this study, a total of 45 subjects (13 males, 32 females) with inflammatory gingival enlargement and an age range of 15 to 30 years participated. During the first phase of periodontal treatment, which included motivation, oral hygiene instructions, scaling, and polishing, the patients underwent the necessary procedures. Plaque index (PI) and gingival index (GI) were measured for the patients to ensure that plaque control was satisfactory to proceed to the surgical phase. For gingivectomy, a plaque index of less than 0.5 was deemed suitable. Afterward, the participants were randomly assigned one of the mouthwash bottles labeled as

No. 1, No. 2, or No. 3. These 45 participants were examined and assisted by the same professional dental examiner who underwent intra and inter examiner calibrations to ensure taking the right measurements of the parameters. The assessment of inter- and intra-examiner calibration for (PI) and (GI) was conducted by the utilization of the kappa-coefficient assay. A kappa value of ≥75% was established as the threshold for determining the presence of a satisfactory level of agreement.

The subjects were instructed to rinse their mouths with the assigned mouthwash for one minute, twice daily, over a period of seven days.

Grouping

The participants in the study were divided into three groups as follows:

Study Group I (Aloe vera group): Consisting of 15 patients who used aloe vera mouthwash. The mouthwash used in this group was made of 100% pure aloe vera juice.

The subjects were instructed to rinse their mouths with 10 ml of it for one minute, twice daily, over a period of seven days.

Study Group II (CHX group): Comprising of 15 patients who used chlorhexidine mouthwash (0.2%) and rinse with 10 ml of it for 1 minute, twice daily for seven days. This group served as the positive control.

Control Group: Including 15 patients who used a mouthwash made of distilled water with flavors. The same instructions were given to this group too. This group served as the placebo or negative control in the study.

All the participants were instructed to rinse after 30 minutes from brushing and to restrain from eating and drinking for another 30 minutes after rinsing.

During the second visit, after a period of 7 days, the gingival tissue of patients who underwent conventional gingivectomy was carefully excised using a surgical scalpel. Following the excision, a periodontal dressing was applied to cover the surgical area for protection. The excised gingival tissue was then washed with normal saline to remove any debris or contaminants. Subsequently, the tissue samples were fixed using a 10% formalin solution to preserve their structure for subsequent histological evaluation. In addition to histological evaluation, immunohistochemical analysis of the basic fibroblast growth factor (FGF-2) was performed on the fixed gingival tissue samples. This analysis aimed to study the presence and distribution of FGF-2 in the excised gingival tissue samples.

Tissue preparation and staining

Sections: From each of these paraffin-embedded tissue blocks; serialized sections of 4μm were cut as follows:

- Sections were mounted on standard glass slides, stained with Hematoxylin and Eosin (H&E), and histopathologically re-evaluated by an experienced pathologist;
- One section for each case was cut and mounted on positively charged slides for Immunohistochemistry (IHC) staining with fibroblast growth factor-2 (FGF-2) polyclonal antibodies;
- For each immunohistochemistry run, one slide of positive controls (Figure 1) and one negative control slide were included.

Histomorphometric analysis

After the tissue sections were prepared on slides, the following steps were taken for immunohistochemical analysis:

1. Slide baking: The slides were baked at 60°C overnight to ensure proper adhesion of the tissue sections to the slides;
2. Deparaffinization: The slides were deparaffinized by immersing them in three changes of xylene for 10 minutes each. This step removes the paraffin wax from the tissue sections;

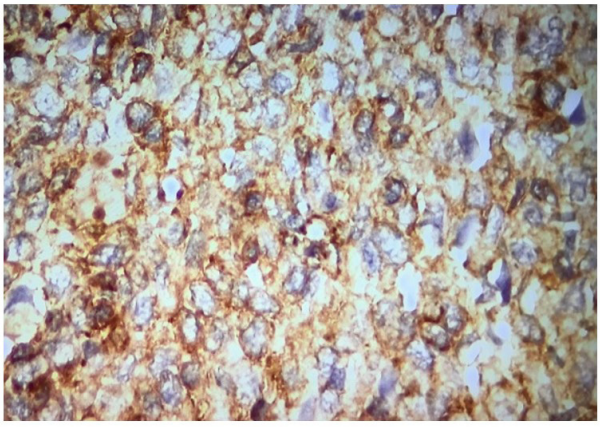

Figure 1 - IHC staining of hepatocellular carcinoma (40X).

3. Hydration: The slides were then hydrated by sequentially immersing them in a series of alcohol solutions and distilled water. Each immersion lasted for 5 minutes. This process gradually removes the alcohol and rehydrates the tissue sections;
4. Heat-induced epitope retrieval (HIER): The tissue sections underwent heat-induced epitope retrieval by subjecting them to heat at a temperature of 95-99°C for 20 minutes. This step helps to unmask the epitopes, making them more accessible for antibody binding;
5. Cooling: After HIER, the slides were allowed to cool down at room temperature for a minimum of 20 minutes;
6. Blocking endogenous peroxidase activity: The slides were treated with a peroxidase-blocking reagent for 10 minutes. This step prevents endogenous peroxidase activity, which can interfere with the immunohistochemical staining;
7. Washing: The slides were rinsed with a washing buffer to remove any residual reagents or debris;
8. Primary antibody incubation: The primary antibody (or washing buffer for a negative control) was added to the slides and incubated for 30 minutes at 37°C. This step allows the primary antibody to bind to the target antigen in the tissue sections;
9. Washing: The slides were rinsed again with the washing buffer to remove unbound primary antibody;
10. Enhancer treatment: An enhancer solution was added to the slides and incubated for 20 minutes. This step enhances the immunohistochemical staining signal;
11. Washing: The slides were rinsed once more with the washing buffer;
12. DAB incubation: The prepared DAB (3,3'-diaminobenzidine) solution, which produces a brown color when reacting with the peroxidase enzyme, was added to the slides and incubated for 10 minutes;
13. Washing: The slides were rinsed again with the washing buffer to remove excess DAB;
14. Counterstaining: The slides were counterstained with hematoxylin for 10 seconds. Hematoxylin imparts a blue color to the cell nuclei;
15. Washing: The slides were rinsed with tap water to remove excess counterstain;
16. Dehydration: The slides were dehydrated by immersing them in a series of alcohol solutions and two changes of xylene. This step removes water and ensures proper mounting;
17. Mounting: The final step involved mounting the slides with DPX, a mounting medium, and covering them with coverslips. DPX helps to preserve the stained tissue sections and provides optical clarity.

Once the mounting is complete, the slides are ready for examination under a microscope.

Immunohistochemical signal specificity was demonstrated by the absence of immunostaining in the negative control slides and its presence in recommending positive controls. For FGF-2, cells with clear brown cytoplasmic staining patterns were considered positive. The extent of staining was scored using the following scale:

Score 0 = 0-10% of cells (negative), Score I = staining 10-25% of cells (weak positive), Score II = staining 25-50% of cells (moderate positive), and Score III = staining up to 50% of cells (strong positive) [20].

Also, the number of newly formed blood vessels (angiogenesis) was calculated and compared between the groups [21].

Statistical analysis: the statistical analysis was done by SPSS by the use of Descriptive and inferential statistic and Multiple Mann-Whitney U test (Bonferroni method) with the P value <0.05.

RESULTS

Tables I and II show descriptive and statistical analysis of matrix FGF2 at the second visit. The median in Aloe-vera and CHX groups was 2, whereas, in the control group, it was 1, with significant differences among groups as the p-value (0.021). The intergroup comparison in matrix FGF2 at second visits shows a significant difference between Aloe-vera and control groups. At the same time, there was no significant difference between CHX and control groups and between CHX and Aloe-vera groups (Figures 2, 3, 4, 5, 6 and 7).

Regarding the angiogenesis; The Aloe-vera group had the highest median value of angiogenesis at 24, followed by the CHX group with a median of 22. The control group had the lowest mean value of

angiogenesis at 15 indicating less angiogenesis compared to the other two groups (Table III). When comparing the angiogenesis levels between the groups at the second visits, there was a highly significant difference between the Aloe-vera group and the control group. There was also a significant difference observed between the CHX group and the control group. However, no significant difference was found between the CHX group and the Aloe-vera group (Table IV).

These findings are summarized in Table III. Additionally, Figures 2, 3, 4, 5, 6, and 7 may provide visual representations of the data or further analysis related to angiogenesis in the different groups.

Table I - Descriptive and inferential statistic of matrix FGF2 at 2nd visit for all groups

Statistics		Control	CHX	Aloe-vera
Descriptive	N	15	15	15
	Minimum	1.000	1.000	1.000
	Maximum	3.000	3.000	3.000
	Median	1	2	2
	Mean rank	16.96	21.30	28.87
Kruskal-Wallis	Chi-square		7.714	
	df		2	
	P-value		0.021(Sig.)	

Sig. = Significant at P<0.05; df = degree of freedom.

Table II - Multiple Comparisons of Matrix FGF2 at the second visit

(I) Groups	(J) Groups	Multiple Mann-Whitney U test (Bonferroni method)	
		Z	Sig.
Control	CHX	-0.996	0.957 NS
	Aloe-vera	2.734	0.018 Sig.
CHX	Aloe-vera	1.769	0.231 NS

Sig. = Significant at P<0.05; NS = Non-significant; Z: z-score

Table III - Descriptive and inferential statistic angiogenesis at 2nd visit for all groups

Statistics		Control	CHX	Aloe-vera
Descriptive	N	15	15	15
	Minimum	7.000	11.000	18.000
	Maximum	30.000	36.000	37.000
	Median	15	22	24
	Mean rank	13.39	24.83	28.67
Kruskal-Wallis	Chi-square		11.034	
	df		2	
	P-value		0.004 (HS)	

HS = High Significant at P<0.01; df = degree of freedom.

Table IV - Multiple Comparisons of angiogenesis at the 2nd visit

(I) Groups	(J) Groups	Multiple Mann-Whitney U test (Bonferroni method) Descriptive and inferential statistic	
		Z	Sig.
Control	CHX	2.402	0.048 Sig.
	Aloe-vera	3.206	0.003 HS
CHX	Aloe-vera	0.819	1.00 NS

HS = High Significant at P<0.01; Sig. = Significant at P<0.05; NS = Non-significant. EZ = t/√N, 0.2 = small, 0.5 medium, 0.8 Large; Z: z-score.

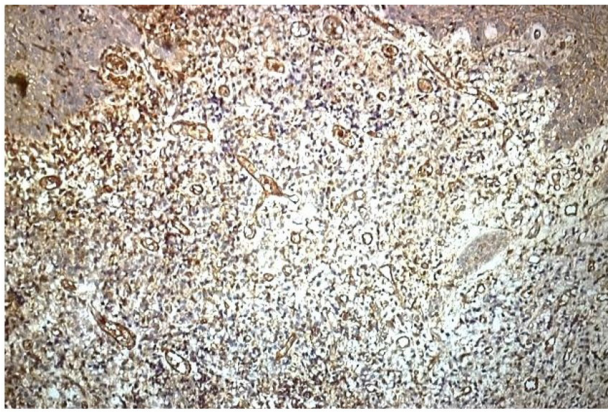

Figure 2 - IHC staining for Aloe-vera case (20X).

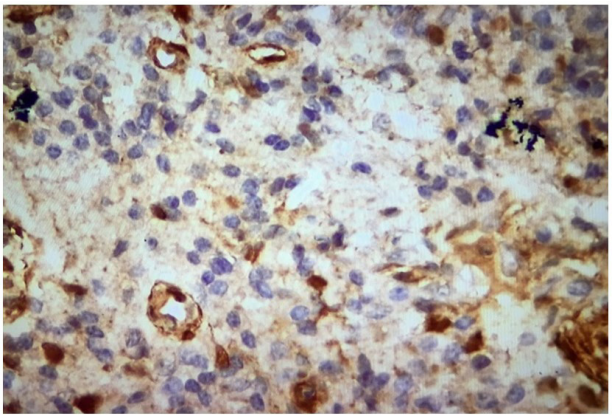

Figure 5 - IHC staining for CHX case (40X).

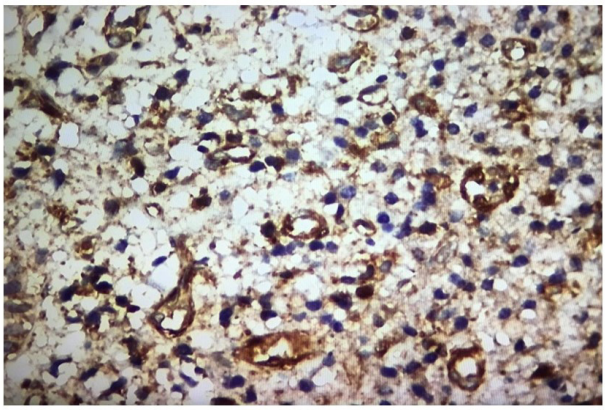

Figure 3 - IHC staining for Aloe-vera case (40X).

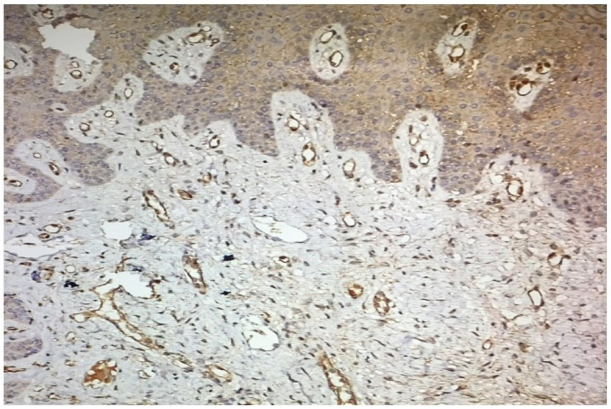

Figure 6 - IHC staining for control case (20X).

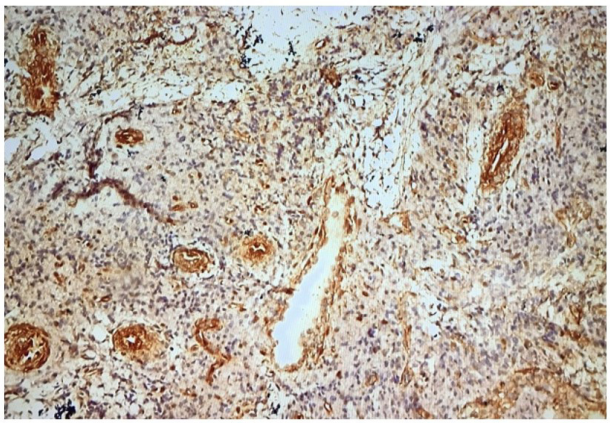

Figure 4 - IHC staining for CHX case (20X).

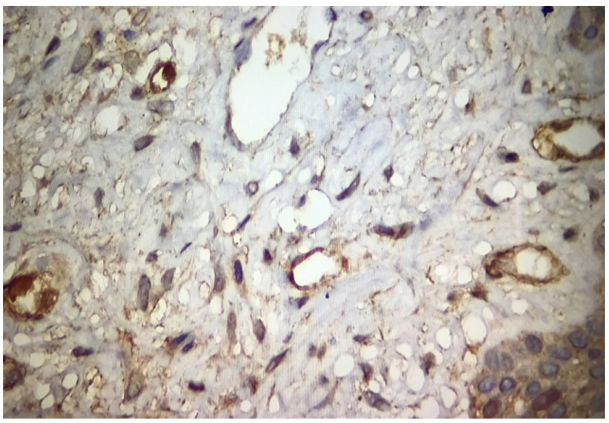

Figure 7 - IHC staining for control case (40X).

DISCUSSION

The findings of this study suggest that the wound-healing capacity of Aloe vera may contribute to these observed differences. Aloe vera has been studied for its wound healing properties in various research studies. For example, Davis et al. [22] conducted a study that highlighted the wound-healing ability of Aloe vera. Aloe-vera was found to increase oxygenation by promoting angiogenesis, which is the growth of new blood vessels. This increased blood flow to the wound, leading to improved oxygen supply. The study utilized a rat model and demonstrated that Aloe vera accelerated wound closure and enhanced the tensile strength of the wounds.

Overall, the significant differences observed in the study's results between the Aloe-vera group and the control group, as well as the observed angiogenesis, may be attributed to the wound-healing properties of Aloe vera [22].

In vitro and in vivo studies have demonstrated the positive effects of Aloe vera extract on fibroblast proliferation. Glucomannan, an active ingredient found in Aloe vera, has been shown to promote increased collagen synthesis by interacting with the fibroblast growth factor receptor (FGFR), thereby stimulating fibroblast activity. A study conducted by Zhi et al. [23] investigated the effects of glucomannan extract derived from Aloe vera on fibroblast proliferation and migration. The results of the study revealed that glucomannan extract increased the proliferation and migration of fibroblasts, which are critical cells involved in the process of wound healing. Based on their findings, the authors suggested that glucomannan may hold promise as a potential wound healing agent due to its ability to enhance fibroblast activity. These studies support the notion that Aloe vera, specifically its active component glucomannan, can positively influence fibroblast function and collagen synthesis, which are essential processes for effective wound healing [23]. Aloe vera gel polysaccharide acemannan has also been shown to have a significant role in wound healing. Acemannan activates macrophage proliferation, which is important for the body's immune response to injury. In a rodent model, the authors of the study discovered that acemannan promoted wound healing; these findings suggest that acemannan could be used as a potential healing agent [24]. In a study conducted by Sargowo et al. [25], the researchers investigated the effects of Aloe vera gel on angiogenesis in diabetic patients. The study revealed that Aloe vera gel played a significant role in promoting angiogenesis. Specifically, it enhanced the activity of endothelial progenitor cells (EPCs), reduced the levels of circulating endothelial cells (CECs), and increased the expression of vascular endothelial growth factor (VEGF) and endothelial nitric oxide synthesis (eNOS). The findings of the study suggested that Aloe vera gel has the potential to improve wound healing in diabetic patients by stimulating angiogenesis. Angiogenesis, the formation of new blood vessels, is crucial for delivering oxygen and nutrients to the wound site, as well as for removing waste products. By promoting angiogenesis and increasing blood flow to the wound, Aloe vera gel may facilitate the healing process in individuals with diabetes. These results support the use of Aloe vera gel as a potential therapeutic option for enhancing wound healing in diabetic patients, due to its ability to promote angiogenesis and improve blood circulation to the wound area [25].

For future studies, we suggest doing mechanistic studies to investigate the underlying mechanisms by which Aloe-vera affects FGF-2 expression and angiogenesis. This could involve in vitro studies using cell culture models or animal studies to explore the molecular pathways involved in the wound healing properties of Aloe vera.

Regarding the limitation of this study, this study had a relatively small sample size, which may limit the generalizability of the findings and also the study has a short duration of intervention. Longer intervention periods could provide a more comprehensive understanding of the sustained effects of Aloe-vera.

CONCLUSION

Aloe vera significantly has affected the immunohistochemical expression of FGF2 and angiogenesis in gingival tissue, which may explained the wound healing effects of Aloe vera. It can be used as might be considered a potential alternative to Chlorhexidine, especially in low socio-economic status populations. Further randomized controlled studies are necessary to investigate these findings.

Author's Contributions

BGA: Review & Editing, Supervision, Methodology. HMA: Review & Editing, Software, Writing. SAA: Conceptualization, Formal Analysis, Investigation, Resources, Data Curation, Writing – Original Draft Preparation, Writing – Review & Editing. FSR: Visualization, Supervision, Project Administration.

Conflict of Interest

There is no interest of confliction.

Funding

This study is self-funded.

Regulatory Statement

We certify that this study involving human subjects is by the Helsinki declaration of 1975, as revised in 2013 and that the relevant institutional ethics committee has approved it. The protocol number is 41 in 5-3-2019.

This clinical trial emphasizes on the wound healing effects of Aloe vera on gingival tissue so; it might

be considered a potential alternative to Chlorhexidine (CHX); and an alternative to CHX as an adjunct to mechanical plaque control before gingivectomy, especially in low socio-economic status population.

REFERENCES

1. Karim B, Bhaskar DJ, Agali C, Gupta D, Gupta RK, Jain A, et al. Effect of Aloe vera mouthwash on periodontal health: triple blind randomized control trial. Oral Health Dent Manag. 2014;13(1):14-9. PMid:24603910.
2. Nair AA, Malaiappan S. The comparison of the antiplaque effect of Aloe Vera, Chlorhexidine and placebo mouth washes on gingivitis patients. J Pharm Sci Res. 2016;8(11):1295-300.
3. Abed SA, Ali BG, Mohsin HJ. Comparison between the effects of Aloe vera and chlorhexidine on clinical periodontal parameters. J Baghdad Coll Dent. 2019;31(4):31-5. http://dx.doi.org/10.26477/jbcd.v31i4.2717.
4. James P, Worthington HV, Parnell C, Harding M, Lamont T, Cheung A, et al. Chlorhexidine mouthrinse as an adjunctive treatment for gingival health. Cochrane Database Syst Rev. 2017;2021(12):CD008676. http://dx.doi.org/10.1002/14651858.CD008676.pub2. PMid:28362061.
5. Dat AD, Poon F, Pham KB, Doust J. Aloe vera for treating acute and chronic wounds. Cochrane Database Syst Rev. 2012;2012(2):CD008762. http://dx.doi.org/10.1002/14651858.CD008762.pub2. PMid:22336851.
6. Chhina S, Singh A, Menon I, Singh R, Sharma A, Aggarwal V. A randomized clinical study for comparative evaluation of Aloe Vera and 0.2% chlorhexidine gluconate mouthwash efficacy on de-novo plaque formation. J Int Soc Prev Community Dent. 2016;6(3):251-5. http://dx.doi.org/10.4103/2231-0762.183109. PMid:27382543.
7. Chandrasekaran K, Salman M, Chavan SKD. *Aloe vera*: a herbal panacea for periodontal disease? EC Dental Science. 2018;17(10):1749-58.
8. Abed S, Al-Hijazi A. Expression of Syndecan 1 on Periodontium treated with Topical Application of Aloe-Vera. Journal of Baghdad College of Dentistry. 2016;28(3):82-6. http://dx.doi.org/10.12816/0031129.
9. Surjushe A, Vasani R, Saple DG. Aloe vera: a short review. Indian J Dermatol. 2008;53(4):163-6. http://dx.doi.org/10.4103/0019-5154.44785. PMid:19882025.
10. Chithra P, Sajithlal GB, Chandrakasan G. Influence of aloe vera on collagen characteristics in healing dermal wounds in rats. Mol Cell Biochem. 1998;181(1-2):71-6. http://dx.doi.org/10.1023/A:1006813510959. PMid:9562243.
11. Heggers JP, Kucukcelebi A, Listengarten D, Stabenau J, Ko F, Broemeling LD, et al. Beneficial effect of aloe on wound healing in an excisional wound model. J Altern Complement Med. 1996;2(2):271-7. http://dx.doi.org/10.1089/acm.1996.2.271. PMid:9395659.
12. Boudreau MD, Beland FA. An evaluation of the biological and toxicological properties of Aloe barbadensis (miller), Aloe vera. J Environ Sci Health Part C Environ Carcinog Ecotoxicol Rev. 2006;24(1):103-54. http://dx.doi.org/10.1080/10590500600614303. PMid:16690538.
13. Malek Hosseini A, Ghaffarzadegan R, Alizadeh SA, Ghaffarzadegan R, Haji Agaei R, Ahmadlou M. Effect of aloe vera gel, compared to 1% silver sulfadiazine cream on second-degree burn wound healing. Complementary Medicine Journal of Faculty of Nursing and Midwifery. 2013;3:418-28.
14. Chithra R, Sajithlal GB, Chandrakasan G. Influence of Aloe vera on the glycosaminoglycans in the matrix of healing dermal wounds in rats. J Ethnopharmacol. 1998;59(3):179-86. http://dx.doi.org/10.1016/S0378-8741(97)00112-8. PMid:9507902.
15. Anusaksathien O, Giannobile WV. Growth factor delivery to re-engineer periodontal tissues. Curr Pharm Biotechnol. 2002;3(2):129-39. http://dx.doi.org/10.2174/1389201023378391. PMid:12022256.
16. Takayama S, Yoshida J, Hirano H, Okada H, Murakami S. Effects of basic fibroblast growth factor on human gingival epithelial cells. J Periodontol. 2002;73(12):1467-73. http://dx.doi.org/10.1902/jop.2002.73.12.1467. PMid:12546097.
17. Kitamura M, Nakashima K, Kowashi Y, Fujii T, Shimauchi H, Sasano T, et al. Periodontal tissue regeneration using fibroblast growth factor -2: randomized controlled phase II clinical trial. PLoS One. 2008;3(7):e2611. http://dx.doi.org/10.1371/journal.pone.0002611. PMid:18596969.
18. Sánchez M, González-Burgos E, Iglesias I, Gómez-Serranillos MP. Pharmacological update properties of *Aloe vera* and its major active constituents. Molecules. 2020;25(6):1324. http://dx.doi.org/10.3390/molecules25061324. PMid:32183224.
19. Hormozi M, Assaei R, Boroujeni MB. The effect of Aloe vera on the expression of wound healing factors (TGFβ1 and bFGF) in mouse embryonic fibroblast cell: in vitro study. Biomed Pharmacother. 2017;88:610-6. http://dx.doi.org/10.1016/j.biopha.2017.01.095. PMid:28142117.
20. Miguita L, Martinez EF, Araújo NS, Araújo VC. FGF-2, TGFb-1, PDGF-A and respective receptors expression in pleomorphic adenoma myoepithelial cells: an in vivo and in vitro study. J Appl Oral Sci. 2010;18(1):83-91. http://dx.doi.org/10.1590/S1678-77572010000100014. PMid:20379686.
21. Pandiar D, Shameena PM. Immunohistochemical expression of CD34 and basic fibroblast growth factor (bFGF) in oral submucous fibrosis. J Oral Maxillofac Pathol. 2014;18(2):155-61. http://dx.doi.org/10.4103/0973-029X.140718. PMid:25328292.
22. Davis RH, Doner L, Paton A. Aloe vera gel dressing versus conventional dressing in burn wound healing: a prospective randomized controlled study. Burns. 2010;36(7):891-7.
23. Zhi L, Prabhakar S, Wang X. Aloe vera: a review of toxicity and adverse clinical effects. J Environ Sci Health Part C Environ Carcinog Ecotoxicol Rev. 2015;33(1):71-9.
24. Liu C, Cui Y, Pi F, Cheng Y, Guo Y, Qian H. Extraction, purification, structural characteristics, biological activities and pharmacological applications of acemannan, a polysaccharide from Aloe Vera: a review. Molecules. 2019;24(8):1554. http://dx.doi.org/10.3390/molecules24081554. PMid:31010204.
25. Sargowo D, Handaya AY, Widodo A, Lyrawati D, Tjokroprawiro A. Aloe-vera gel enhances angiogenesis in healing od diabetic wound. Indones Biomed J. 2011;3(3):204-15. http://dx.doi.org/10.18585/inabj.v3i3.152.

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