Original Article

DOI: 10.7860/JCDR/2024/70809.19620

Dentistry Section

Additive Effect of Brown Flaxseed Extract Gel on Postsurgical Periodontal Therapy in Periodontitis Patients: A Randomised Controlled Trial

P SWARNA MEENAKSHI[1], SANKARI MALAIAPPAN[2]

ABSTRACT

Introduction: Flaxseed is known for its anti-inflammatory and antioxidant properties, which could be attributed to periodontal wound healing. Early wound healing contributes to favourable treatment outcomes. Glutathione peroxidase is a ubiquitous antioxidant biomarker known for its scavenging action of free radicals, thereby maintaining the health of periodontal tissues.

Aim: To evaluate the additive effect of brown flaxseed gel following surgical periodontal therapy.

Materials and Methods: This randomised controlled trial was conducted at the Department of Periodontics, Saveetha Dental College in Chennai, Tamil Nadu, India from November 2023 to February 2024. Total of 30 patients were included in the study, with 15 patients in the control group and the other 15 patients (test group) were administered brown flaxseed gel following flap surgery. The included patients were allocated into test and control groups through simple randomisation. Postoperative flap surgery, the Early Healing Index (EHI), and healing scores were evaluated at the 1st and 2nd weeks. Salivary glutathione peroxidase levels were also assessed at the 1st and 2nd weeks following periodontal therapy. An Independent t-test was used to compare the mean values between the test group and the control group.

Results: The mean age of the eligible participants was 35.6±4.57 years. Better healing was observed in the test group compared to the control group in the 1st postoperative week, as recorded by the EHI with a mean of 2.96±0.90 in the test group and 2.06±0.70 in the statistically significant control group. Salivary glutathione levels were significantly increased in the test group with a mean concentration of 14.1±.78 mu/mL and 10.5±0.42 mu/mL in the control group at the end of the 2nd week, respectively.

Conclusion: Brown flaxseed gel is an efficacious therapeutic agent in improving periodontal wound healing and also has prudent antioxidant activity.

Keywords: Anti-inflammatory, Antioxidant properties, Flap surgery, Linoleic acid, Omega-3 fatty acids, Wound healing

INTRODUCTION

Periodontitis is a persistent inflammatory disease that results in the degradation of the periodontal attachment structure and the potential loss of teeth [1]. Its onset is triggered by the interplay between supragingival and subgingival biofilms, in conjunction with the host's inflammatory response. The treatment approach employed varies, ranging from non surgical to surgical interventions, depending on the disease's severity. The patient's comprehension of and adherence to postoperative care instructions are pivotal factors influencing the recovery process following any surgical procedure. During the postoperative phase, three primary considerations are patient comfort, wound stability, and effective plaque control [2]. Common complications that may arise following periodontal surgery encompass postoperative pain, bleeding, swelling, delayed healing, trismus (limited mouth opening), and alterations in taste perception [3].

Wound healing in a periodontal defect after flap surgery is a multifaceted process that initiates with the formation of a blood clot within the closed flap following suturing [4]. This flap is positioned adjacent to another vascularised wound margin, encompassing gingival connective tissue and the alveolar process. Several factors impede the healing process, sustaining inflammation and triggering necrotic or hyperplastic reactions. Reactive Oxygen Species (ROS) are by-products produced during the regular metabolism of oxygen and serve crucial functions in cell signaling [5]. ROS have been linked to mechanisms that cause tissue harm, such as protein degradation, lipid peroxidation, Deoxyribonucleic Acid (DNA) impairment, oxidation of critical enzymes, and the triggering of proinflammatory cytokine release [6]. These processes collectively contribute to the retardation of the healing process and the acceleration of disease progression.

Antioxidants (AOs) are substances that, when present in relatively low concentrations compared to oxidisable substances, effectively impede or delay the oxidation of those molecules [7]. One prominent and widespread antioxidant is glutathione, a small-molecule thiol found in both eukaryotic and prokaryotic cells, present in every human cell. Glutathione serves as a potent antioxidant, safeguarding vital cellular components against damage caused by ROS, and it also plays a pivotal role as a coenzyme for enzymes involved in ROS neutralisation [8]. Oxidative Stress (OS) results from an imbalance between ROS and AO, disrupting redox signaling and control and leading to molecular damage.

Flaxseed (Linum usitatissimum) is gaining prominence as a valuable functional food ingredient due to its high levels of α-linolenic acid (ALA, an omega-3 fatty acid), lignans, and dietary fiber [9]. Flaxseeds are available in two varieties: yellow/golden seeds and brown seeds. Notably, brown flaxseeds possess a distinct oil profile, rich in omega-3 fatty acids compared to golden flaxseeds. They are also abundant in essential amino acids, particularly glutamic acid, glycine, and cysteine [10,11]. Brown flaxseeds exhibit anti-inflammatory properties by soothing inflammation, stimulating collagen production, and enhancing cell turnover, thereby boosting their anti-inflammatory and antioxidant attributes [12]. In the realm of dentistry, flaxseeds offer multiple benefits, proving highly effective in managing gum diseases like gingivitis and periodontitis. They have even found utility as a local drug delivery agent in periodontal treatments, reducing gum bleeding, inflammation, and swelling

[13]. Additionally, flaxseeds exhibit antimicrobial properties effective against both Gram negative and Gram-positive organisms [14].

To the author's best knowledge, present study is the first study to evaluate the additive effect of brown flaxseeds in postsurgical periodontal therapy. Therefore, the primary objective of the study was to evaluate the efficacy of brown flaxseeds on wound healing following periodontal flap surgery in chronic periodontitis patients. And the secondary objective was to assess the salivary levels of glutathione peroxidase following periodontal flap surgery in chronic periodontitis patients.

MATERIALS AND METHODS

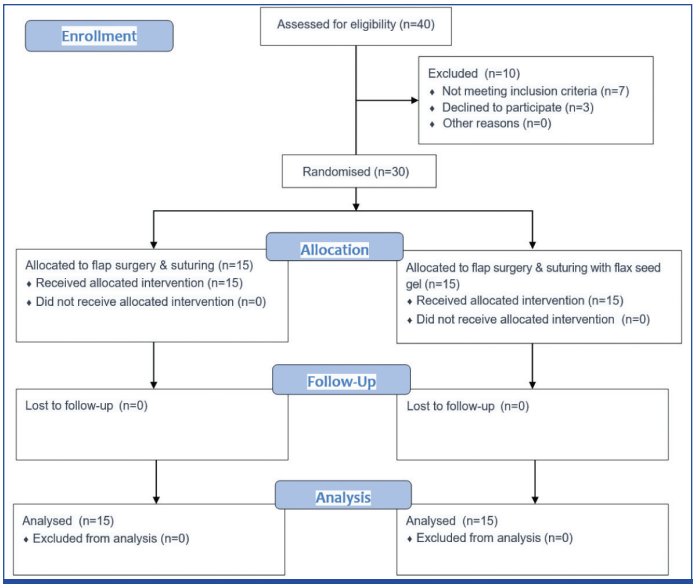
The randomised controlled trial was conducted at the Department of Periodontics, Saveetha Dental College in Chennai, Tamil Nadu, India from November 2023 to February 2024. The study protocol received approval from the Institutional Ethical Committee at Saveetha Dental College in Chennai, Tamil Nadu, India with the ethical clearance number (IHEC/SDC/PERIO-2102/23/125). The study was registered in Clinical Trail Registry India (CTRI) with the number CTRI/2024/05/067413.

Inclusion criteria:

- Patients aged between 30 and 55 years with moderate-to-severe chronic periodontitis;
- Infrabony pockets measuring >6 mm;
- Systemically healthy patients who are advised for periodontal surgery.

Exclusion criteria:

- Immunocompromised patients;
- Patients with present or past systemic diseases known to interfere with the outcomes of periodontal therapy;
- Patients who are under medications that may interfere with periodontal therapy;
- Patients who are chain smokers;
- Individuals who have tobacco-related habits;
- Partially edentulous individuals [Table/Fig-1].



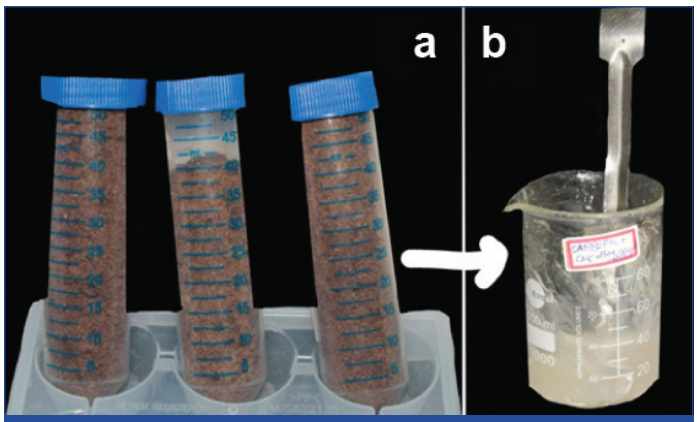
[Table/Fig-1]: Patient selection flowchart.
Consodilated Standards of Reporting Trails (CONSORT) 2010 flow diagram

Sample size calculation: The sample size was calculated using G* Power, with a power level of 0.80 (80%), equivalent to 1-β, and by setting the significance level to 0.05 (5%), denoted as α. The sample size was estimated to be 30 patients.

Study Procedure

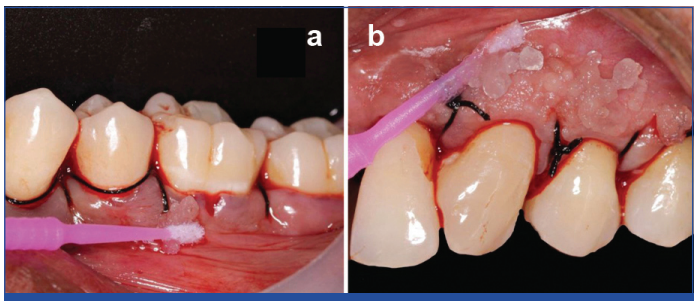
The study enrolled 30 patients who needed periodontal flap surgery on a minimum of two interproximal sites, located on either side of the maxillary or mandibular arch. Patients were presented with a comprehensive explanation of the study, and their informed consent was duly obtained. After completion of non surgical periodontal therapy, which included providing oral hygiene instructions and performing scaling and root planing, a re-evaluation was conducted four weeks later. A simple randomisation method with single blinding was used to allocate candidates into two groups. Group A, constituting the control group, comprised fifteen patients who were subjected to surgical periodontal therapy and were advised to follow the postoperative instructions. On the other hand, group B, which was categorised as the test group, consisted of 15 patients who were subjected to topical application of brown flaxseed gel as an adjunct to surgical periodontal therapy.

The triogel was formulated using freshly obtained brown flaxseeds. A total of 2 grams of brown flaxseed powder was mixed with 100 milliliters of distilled water, followed by thorough blending and weighing. The resulting mixture was then subjected to heating and subsequent filtration. The filtered flaxseed extract was concentrated by boiling it in a centrifuge using supercritical fluid. Concurrently, 0.5 grams of carboxymethyl cellulose was dissolved in 10 milliliters of distilled water, while another 0.5 grams of carbopol was dissolved in a separate 10-milliliter portion of distilled water. These two solutions were then combined and incorporated into the concentrated brown flaxseed extract [Table/Fig-2a,b] [14]. The facts about the superior qualities of flaxseed gel were not informed to the patients to avoid its psychological effect and to avoid the placebo effect.



[Table/Fig-2a,b]: Flaxseed gel containing flaxseed extract. CMC and carbopol.

Clinical protocol: Both groups underwent periodontal flap surgery, and the flaps were positioned back together using 3-0 non absorbable black silk sutures. Only the patients in the test group were instructed to apply the provided flaxseed gel topically to the surgical site where the sutures were positioned three times a day for one week. They were explicitly advised against massaging the area and were instructed to gently apply the gel to the surgical site for 10 minutes [Table/Fig-3a,b].



[Table/Fig-3a,b]: Application of flaxseed gel on the sutured site after periodontal flap surgery.

Postoperative instructions: After the surgical procedures, each patient received postoperative care, which included a prescription for amoxicillin, 500 mg, to be taken every eight hours for five days, as well as ibuprofen 400 mg + paracetamol 325 mg to be taken

twice daily for three days, which are non steroidal anti-inflammatory drugs. The sutures were removed a week after the periodontal flap surgery, and during this time, the surgical sites were gently rinsed with a solution of normal saline and betadine.

Clinical assessment:

- **Wound healing:** Postoperative healing of the surgical site was evaluated using the EHI [15] after the 1st week and the Healing Index (HI) [16] after the 1st and 2nd weeks following periodontal therapy.

Assessment of glutathione peroxidase marker:

- **Saliva collection:** Informed consent was obtained from all patients who participated in the study. Before saliva collection, subjects rinsed their mouths with water and observed a 15-minute waiting period before pooling saliva. Saliva samples were obtained by instructing patients to spit into prelabelled sterile containers positioned beneath the lower lip, resulting in the collection of approximately 5 mL of saliva. Following collection, salivary samples underwent centrifugation at 10,000 xg for 5 minutes to eliminate cellular debris and reduce saliva turbidity. Subsequently, the samples were divided into 1.5 mL Eppendorf tubes and stored at -80 °C until the biochemical analysis was performed. The salivary glutathione levels were evaluated after one week and two weeks following the flap surgery. The levels were assessed by conducting an Enzyme-linked Immunosorbent Assay (ELISA) test.

STATISTICAL ANALYSIS

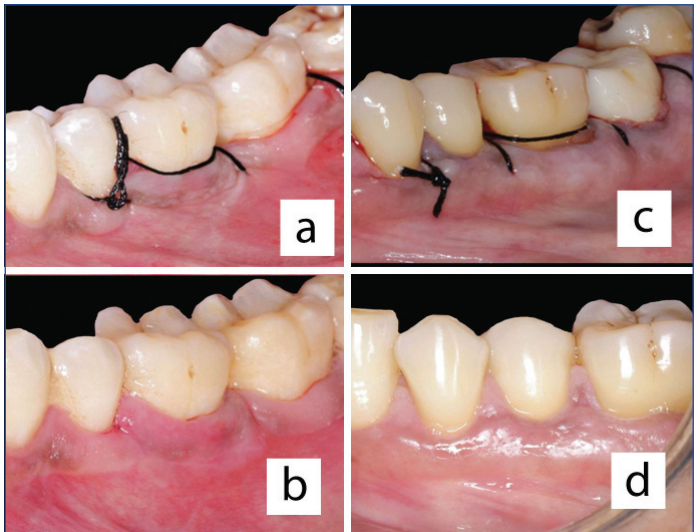
Statistical analysis was conducted using Statistical Package for Social Sciences (SPSS) software version 23.0, and p-value≤0.05 was considered statistically significant. To compare the mean values between the test and control groups, an Independent t-test was performed.

RESULTS

The mean age of the eligible participants was 35.6±4.57 years. Total 15 (50%) patients were males and 15 (50%) patients were females.

Better postoperative healing was detected in the test group compared to the control group. In the 1st postoperative week, as evaluated by the EHI, statistically significant results were seen in the test group with a mean value of 2.96±0.90, compared to 2.06±0.70 in the control group (p-value=0.02*).

The outcomes of HI by Landry RG et al., indicated that the results were not statistically significant in the 1st postoperative week, with a mean value of 3.01±0.7 in the control group and 3.3±0.6 in the test group, respectively (p-value=0.66) [16]. The results of the 2nd postoperative week showed a mean value of 3.4±0.62 in the control group and 4.41±0.40 in the test group, indicating a significant difference between the two groups (p-value=0.03) [Table/Fig-4a-d,5].



[Table/Fig-4]: (a) Immediate postoperative picture in control group; (b) Healing after two weeks in control group; (c) Immediate postoperative picture in test group; (d) Healing after two weeks in test group.

Groups	Test group	Control group	p-value
Healing Index (HI) score in 1st postoperative week	3.3±0.6	3.01±0.7	0.66
Healing Index (HI) score in 2nd postoperative week	4.41±0.40	3.4±0.62	0.03*

[Table/Fig-5]: Depicts the Healing Index (HI) score between test and the control group in the 1st and 2nd postoperative week.

Glutathione peroxidase levels: Evaluation of salivary glutathione peroxidase levels revealed that the mean concentration of glutathione was 8.23±0.62 mu/mL in the control group and 12.56±0.72 mu/mL in the test group by the end of the 1st week, respectively. In the 2nd postoperative week, the mean concentration was significantly higher in the test group with p-value=0.02, indicating superior antioxidant activity in the test group [Table/Fig-6].

Groups	Test group	Control group	p-value
Mean concentration of glutathione peroxidase in 1st week (mu/mL)	12.56±0.72 mu/mL	8.23±0.62 mu/mL	0.78
Mean concentration of glutathione peroxidase in 2nd week (mu/mL)	14.1±0.78 mu/mL	10.5±0.40 mu/mL	0.02*

[Table/Fig-6]: Mean concentration of glutathione peroxidase between test group and control group in 1st and 2nd postoperative week.

DISCUSSION

The objective of present investigation was to evaluate the supplementary impact of utilising brown flaxseed gel on the postoperative healing of wounds following periodontal flap surgery in individuals diagnosed with chronic periodontitis. The findings of the study demonstrated that the administration of brown flaxseed gel proved to be effective in achieving enhanced wound healing after one week compared to the control group. Additionally, the levels of the glutathione peroxidase marker were elevated in the flaxseed gel group two weeks following the periodontal therapy, indicating the discernible presence of antioxidant activity.

The results of the present study showed better postoperative healing in the test group compared to the control group, as evaluated by the EHI. The outcomes of the current study align with the findings of McDaniel JC et al., who assessed the effects of marine-derived ω-3 eicosapentaenoic acid and docosahexaenoic acid on proinflammatory cytokines in wound serum to evaluate wound healing on human skin [17]. The results demonstrated significant wound healing. This can be correlated with present study, as flaxseed is also rich in eicosapentaenoic acid, serving as a rich source of diverse biologically active compounds known to influence various stages of wound healing. Flaxseed's high content of flavonoids is particularly noteworthy for its role in promoting wound repair. These flavonoids are linked to improved collagen fibril viability, leading to enhanced strength of collagen fibers and a reduction in cellular damage through facilitated DNA synthesis.

In-vitro and in-vivo studies conducted by various authors indicated that linseed stimulates the proliferation of fibroblast cells and their differentiation into specialised myofibroblasts [18-20]. In another study, Merkher Y et al., demonstrated that flavonoids play a crucial role in reducing lipid peroxidation, thereby preventing or slowing the onset of cell necrosis [21]. Consistent findings were reported by Hudwekar A et al., who found that the application of aloe vera extract significantly improved healing scores after surgical periodontal therapy. This improvement was attributed to the presence of carboxypeptidase and lignin in aloe vera, which inactivates bradykinin. These carboxypeptidases are also present in brown flaxseed, which helps to alleviate pain and thereby enhances wound healing [22].

Linseed contains a diverse array of bioactive compounds, including tocopherols (a type of vitamin E), β-carotene, and an assortment of phenolic compounds, encompassing lignans, flavonoids, and

phenolic acids. Moreover, tocopherol, a variant of vitamin E, not only stimulates protein synthesis but also augments cellular proliferation and facilitates migration within the wound tissue [23]. It additionally exerts antiphlogistic effects by mitigating the production of proinflammatory cytokines and chemokines. Moreover, flaxseed is rich in magnesium and calcium, both of which play significant roles in wound healing. Calcium, in particular, is recognised for its ability to regulate the infiltration of inflammatory cells, promote the multiplication of fibroblasts, and facilitate the proliferation, differentiation, and migration of keratinocytes [24]. Elevated levels of calcium also contribute to the improvement of wound healing by enhancing blood clotting and the aggregation of platelets at the wound site, especially during the hemostatic phase of the healing process [25].

In another study by Pappu R et al., both in-vitro and in-vivo studies were performed using flaxseed gel as a local drug delivery agent in chronic periodontitis patients [26]. It was observed that there was a significant improvement in gingival health, which appeared to be linked to the anti-inflammatory attributes of omega-3 fatty acids. The mechanism behind this improvement involves omega-3 fatty acids inhibiting the cyclooxygenase and lipoxygenase pathways, consequently reducing the generation of proinflammatory molecules.

Huang CB et al., noted the effect of various omega fatty acids, especially omega-3 fatty acids, to have an antimicrobial effect against certain microbes (*S. mutans, S. gordonii, S. sanguis, C. albicans, AAA, F. nucleatum, and P. gingivalis*) [27]. Owing to the antibacterial effect, omega fatty acids are also furnished with anti-inflammatory properties, which may be linked to the therapeutic outcomes, thereby maintaining the harmony of gingival as well as periodontal health. This makes flaxseed gel a promising local drug delivery agent as an adjunct to non surgical periodontal therapy.

Flax proteins boast a wealth of essential amino acids, including glutamic acid, glutamine, arginine, as well as branched-chain amino acids such as valine and leucine, and aromatic amino acids like tyrosine and phenylalanine [28]. Arginine and glutamine play crucial roles in promoting the rejuvenation of dermal collagen protein synthesis and bolstering the process of wound healing [28,29].

Many research studies have provided evidence that Oxidative Stress (OS) serves as one of the fundamental pathophysiological mechanisms in the development of periodontitis [30,31]. Consequently, it becomes pertinent to assess the byproducts of Reactive Oxygen Species (ROS)-induced damage and the performance of both enzymatic and non enzymatic antioxidants, as they emerge as valuable candidates for understanding the implications of OS-related events in the progression of chronic periodontitis [32]. Glutathione is a ubiquitous protagonist in cellular regulation. In its capacity as an antioxidant, glutathione functions as a co-factor for enzymes like glutathione peroxidase and other defenders within the cell's arsenal, which collectively work to safeguard the cell against pro-oxidants [33].

In the context of periodontal diseases, salivary glutathione levels are of particular interest as they indicate the neutralisation (scavenging) of ROS [34]. Research studies have consistently shown reduced amounts of salivary glutathione, GSH peroxides, and thiol levels in individuals with gingivitis and periodontitis when compared to periodontally healthy patients [35,36].

Studies have shown that periodontal therapy improves the salivary concentrations of glutathione and thiol levels in gingivitis and periodontitis patients, which was significant between the groups [37,38]. The current study's findings mirrored previous research, demonstrating an enhancement in salivary concentrations within the test group after surgical periodontal therapy compared to the control group. By the end of the second week, the mean glutathione concentration increased from 10.5±0.42 µm/mL in the control group to 14.1 µm/mL in the test group, indicating a statistically significant rise in glutathione levels. This increase can be attributed to the natural antioxidant brown flaxseed, which is rich in both omega-3 fatty acids and amino acids.

Simultaneously, glutathione peroxidase, enriched with glutamic acid, enhances antioxidant activity, leading to elevated glutathione levels following periodontal therapy. Diab R et al., also reported similar outcomes in their study, noting a rise in salivary glutathione concentrations from 3.12±0.21 µm/mL to 3.6±0.22 µm/mL. This change was observed in patients with periodontal disease who underwent a three-month treatment with a mouthwash containing extracts of Solanum melongena (eggplant) peduncles, as compared to a placebo group [39].

Limitation(s)

The limitation of the study is that flaxseed, being a natural product, poses difficulties such as standardisation and titration. Furthermore, incorporating larger sample sizes can make the results more reliable.

CONCLUSION(S)

Within the constraints of the study, it was found that brown flaxseed gel was effective in improving postoperative wound healing, as evidenced by the healing scores during the first and second weeks after application of the gel in periodontitis patients. Additionally, the salivary levels of glutathione peroxidase increased in patients who received the brown flaxseed gel, indicating enhanced antioxidant activity and maintenance of periodontal tissue harmony. Therefore, it can be concluded that brown flaxseed gel is a valuable therapeutic agent for enhancing the healing of periodontal tissues and exhibits significant antioxidant activity.

REFERENCES

[1] Petersen PE, Ogawa H. The global burden of periodontal disease: Towards integration with chronic disease prevention and control. Periodontol 2000. 2012;60(1):15-39.

[2] Matthews DC, McCulloch CA. Evaluating patient perceptions as short-term outcomes of periodontal treatment: A comparison of surgical and non-surgical therapy. J Periodontol. 1993;64(10):990-97. Available from: https://dx.doi.org/10.1902/jop.1993.64.10.990.

[3] Curtis JW, McLain JB, Hutchinson RA. The incidence and severity of complications and pain following periodontal surgery. J Periodontol. 1985;56(10):597-601.

[4] Listgarten MA, Rosenberg MM. Histological study of repair following new attachment procedures in human periodontal lesions. J Periodontol. 1979;50(7):333-44. Available from: https://dx.doi.org/10.1902/jop.1979.50.7.333.

[5] Chapple IL. Reactive oxygen species and antioxidants in inflammatory diseases. J Clin Periodontol. 1997;24(5):287-96. Available from: https://dx.doi.org/10.1111/j.1600-051x.1997.tb00760.x.

[6] Waddington RJ, Moseley R, Embery G. Reactive oxygen species: A potential role in the pathogenesis of periodontal diseases. Oral Dis. 2000;6(3):138-51. Available from: https://dx.doi.org/10.1111/j.1601-0825.2000.tb00325.x.

[7] D'Aiuto F, Nibali L, Parkar M, Patel K, Suvan J, Donos N. Oxidative stress, systemic inflammation, and severe periodontitis. J Dent Res. 2010;89(11):1241-46. Available from: https://dx.doi.org/10.1177/0022034510375830.

[8] Deneke SM, Fanburg BL. Regulation of cellular glutathione. Am J Physiol. 1989;257(4 Pt 1):L163-73. Available from: https://dx.doi.org/10.1152/ajplung.1989.257.4.L163.

[9] Mueed A, Shibli S, Korma SA, Madjirebaye P, Esatbeyoglu T, Deng Z. Flaxseed bioactive compounds: Chemical composition, functional properties, food applications and health benefits-related gut microbes. Foods. 2022;11(20):3307. Available from: https://dx.doi.org/10.3390/foods11203307.

[10] Goyal A, Sharma V, Upadhyay N, Gill S, Sihag M. Flax and flaxseed oil: An ancient medicine & modern functional food. J Food Sci Technol. 2014;51(9):1633-53. Available from: https://dx.doi.org/10.1007/s13197-013-1247-9.

[11] Al-Madhagy S, Ashmawy NS, Mamdouh A, Eldahshan OA, Farag MA. A comprehensive review of the health benefits of flaxseed oil in relation to its chemical composition and comparison with other omega-3-rich oils. Eur J Med Res. 2023;28(1):240. Available from: https://dx.doi.org/10.1186/s40001-023-01203-6.

[12] Nowak W, Jeziorek M. The role of flaxseed in improving human health. Healthcare (Basel). 2023;11(3):395. Available from: https://dx.doi.org/10.3390/healthcare11030395.

[13] Zaidi SA, Quraishi F, Fatimee S, Farooq L, Masood H, Sultana T. Comparison of flax seeds extract and fenugreek seed extract rinse against streptococcus mutans colonies. Pak J Med Health Sci. 2022;16(04):280-80.

[14] Meenakshi PS, Sankari M, Rajeshkumar S. Formulation and evaluation of a novel herbal trio gel containing flax seed extract, carbopol and carboxymethyl cellulose. Bioinformation. 2023;19(5):540-45.

[15] Wachtel H, Schenk G, Böhm S, Weng D, Zuhr O, Hürzeler MB. Microsurgical access flap and enamel matrix derivative for the treatment of periodontal intrabony defects: A controlled clinical study. J Clin Periodontol. 2003;30(6):496-504. Available from: https://dx.doi.org/10.1034/j.1600-051x.2003.00013.x.
[16] Landry RG, Turnbull RS, Howley T. Effectiveness of benzydamyne HCl in the treatment of periodontal postsurgical patients. Res Clin Forums. 1988;10:105-18.
[17] McDaniel JC, Belury M, Ahijevych K, Blakely W. Omega-3 fatty acids effect on wound healing. Wound Repair Regen. 2008;16(3):337-45. Available from: https://doi/abs/10.1111/j.1524-475X.2008.00388.x.
[18] Chera EI, Pop RM, Pârvu M, Soriţău O, Uifălean A, Cătoi FA, et al. Flaxseed ethanol extracts' antitumor, antioxidant, and anti-inflammatory potential. Antioxidants (Basel). 2022;11(5):892. Available from: https://dx.doi.org/10.3390/antiox11050892.
[19] Czemplik M, Kulma A, Bazela K, Szopa J. The biomedical potential of genetically modified flax seeds overexpressing the glucosyltransferase gene. BMC Complement Altern Med. 2012;12:251. Available from: https://dx.doi.org/10.1186/1472-6882-12-251.
[20] Mekebo D, Chandravanshi BS. Levels of essential and non-essential metals in linseed (Linum usitatissimum) cultivated in Ethiopia. Bull Chem Soc Ethiop. 2014;28(3):349-62.
[21] Merkher Y, Kontareva E, Alexandrova A, Javaraiah R, Pustovalova M, Leonov S. Anti-cancer properties of flaxseed proteome. Proteomes. 2023;16;11(4). Available from: https://dx.doi.org/10.3390/proteomes11040037.
[22] Hudwekar A, Beldar A, Murkute S, Lendhey S, Thamke M. Aloe vera on wound healing after periodontal flap surgery in chronic periodontitis patient: A randomized control trial. J Oral Res Rev. 2019;11(2):72.
[23] Beroual K, Agabou A, Abdeldjelil MC, Boutaghane N, Haouam S, Hamdi-Pacha Y. Evaluation of crude flaxseed (linum usitatissimum l.) oil in burn wound healing in new zealand rabbits. Afr J Tradit Complement Altern Med. 2017;14(3):280-86.
[24] Bikle DD. Vitamin D regulated keratinocyte differentiation. J Cell Biochem. 2004;92(3):436-44. Available from: https://dx.doi.org/10.1002/jcb.20095.
[25] Lansdown ABG. Calcium: A potential central regulator in wound healing in the skin. Wound Repair Regen. 2002;10(5):271-85. Available from: https://doi/abs/10.1046/j.1524-475X.2002.10502.x.
[26] Pappu R, Varghese J, Koteshwara KB, Kamath V, Lobo R, Nimmy K. Evaluation of biodegradable gel containing flax seed extract (Linum usitatissimum) as a targeted drug delivery for management of chronic periodontitis. J Herb Med. 2019;15:100254. Available from: https://dx.doi.org/10.1016/j.hermed.2018.100254.
[27] Huang CB, George B, Ebersole JL. Antimicrobial activity of n-6, n-7 and n-9 fatty acids and their esters for oral microorganisms. Arch Oral Biol. 2010;55(8):555-60. Available from: https://dx.doi.org/10.1016/j.archoralbio.2010.05.009.
[28] Murakami H, Shimbo K, Inoue Y, Takino Y, Kobayashi H. Importance of amino acid composition to improve skin collagen protein synthesis rates in UV-irradiated mice. Amino Acids. 2011;42(6):2481-89.
[29] Murphy PS, Evans GRD. Advances in wound healing: A review of current wound healing products. Plast Surg Int. 2012; 2012:190436. Available from: https://doi.org/10.1155/2012/190436.
[30] Wang Y, Andrukhov O, Rausch-Fan X. Oxidative Stress and Antioxidant System in Periodontitis. Front Physiol [Internet]. 2017;8:295323. Available from: https://dx.doi.org/10.3389/fphys.2017.00910.
[31] Önder C, Kurgan Ş, Altıngöz SM, Bağış N, Uyanık M, Serdar MA, et al. Impact of non-surgical periodontal therapy on saliva and serum levels of markers of oxidative stress. Clin Oral Investig [Internet]. 2017;21(6):1961-69. Available from: https://dx.doi.org/10.1007/s00784-016-1984-z.
[32] Chen Y, Ji Y, Jin X, Sun X, Zhang X, Chen Y, et al. Mitochondrial abnormalities are involved in periodontal ligament fibroblast apoptosis induced by oxidative stress. Biochem Biophys Res Commun [Internet]. 2019;509(2):483-90. Available from: https://dx.doi.org/10.1016/j.bbrc.2018.12.143.
[33] Lubos E, Loscalzo J, Handy DE. Glutathione peroxidase-1 in health and disease: From molecular mechanisms to therapeutic opportunities. Antioxid Redox Signal. 2011;15(7):1957-97. Available from: https://dx.doi.org/10.1089/ars.2010.3586.
[34] Trivedi S, Lal N, Mahdi AA, Singh B, Pandey S. Association of salivary lipid peroxidation levels, antioxidant enzymes, and chronic periodontitis. Int J Periodontics Restorative Dent. 2015;35(2):e14-19. Available from: https://dx.doi.org/10.11607/prd.2079.
[35] Canakci CF, Cicek Y, Yildirim A, Sezer U, Canakci V. Increased levels of 8-hydroxydeoxyguanosine and malondialdehyde and its relationship with antioxidant enzymes in saliva of periodontitis patients. Eur J Dent. 2009;3(2):100-06.
[36] Novaković N, Čakić S, Todorović T, Anđelski-Raičević B, Dožić I, Petrović V, et al. Antioxidative status of saliva before and after non-surgical periodontal treatment. Srp Arh Celok Lek. 2013;141(3-4):163-68.
[37] Tsai CC, Chen HS, Chen SL, Ho YP, Ho KY, Wu YM, et al. Lipid peroxidation: A possible role in the induction and progression of chronic periodontitis. J Periodontal Res. 2005;40(5):378-84. Available from: https:///doi/abs/10.1111/j.1600-0765.2005.00818.x.
[38] Novakovic N, Todorovic T, Rakic M, Milinkovic I, Dozic I, Jankovic S, et al. Salivary antioxidants as periodontal biomarkers in evaluation of tissue status and treatment outcome. J Periodontal Res [Internet]. 2014;49(1):129-36. Available from: https://doi/abs/10.1111/jre.12088.
[39] Diab R, Mounayar A, Maalouf E, Chahine R. Beneficial effects of Solanum melongena (Solanaceae) peduncles extracts, in periodontal diseases. J Med Plant Res. 2011;5(11):2309-15.

PARTICULARS OF CONTRIBUTORS:
1. Postgraduate, Department of Periodontics, Saveetha Dental College and Hospitals,Saveetha Institute of Medical and Technical Sciences, Saveetha, Chennai, Tamil Nadu, India.
2. Professor and Head, Department of Periodontics, Saveetha Dental College and Hospitals,Saveetha Institute of Medical and Technical Sciences, Saveetha, Chennai, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Sankari Malaiappan,
162, Velapanchavadi, Poonamalle High Road, Chennai-600077, Tamil Nadu, India.
E-mail: sankari@saveetha.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 20, 2024
- Manual Googling: Apr 12, 2024
- iThenticate Software: Jun 01, 2024 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 19, 2024**
Date of Peer Review: **Apr 04, 2024**
Date of Acceptance: **Jun 03, 2024**
Date of Publishing: **Jul 01, 2024**