JOURNAL OF DENTAL HEALTH & ORAL RESEARCH

e-ISSN 3050-9432

Journal of Dental Health and Oral Research

ATHENAEUM SCIENTIFIC PUBLISHERS

Research Article

Modulation of Superoxide Dismutase 2 Antioxidant Gene Expression by Adjunctive Liquorice Therapy in Periodontitis: A Pilot Randomized Controlled Trial

Akshatha Anand[1], S Gopalakrishnan[2*], Uma Sudhakar[3], Manisha Manoj[1]

[1]Post Graduate, Department of Periodontics, Thai Moogambigai Dental College and Hospital, Dr. M.G.R Educational and Research Institute, Mogappair, Chennai, India

[2]Professor, Department of Periodontics, Thai Moogambigai Dental College and Hospital, Dr. M.G.R Educational and Research Institute, Mogappair, Chennai, India

[3]Professor and Head of Department, Department of Periodontics, Thai Moogambigai Dental College and Hospital, Dr. M.G.R Educational and Research Institute, Mogappair, Chennai, India

***Correspondence author:** Sundaram Gopalakrishnan, Professor, Department of Periodontics, Thai Moogambigai Dental College and Hospital, Dr. M.G.R Educational and Research Institute, Mogappair, Chennai, India; E-mail: gopalakrishnan_perio@ymail.com

Citation: Anand A, et al. Modulation of Superoxide Dismutase 2 Antioxidant Gene Expression by Adjunctive Liquorice Therapy in Periodontitis: A Pilot Randomized Controlled Trial. J Dental Health Oral Res. 2026;7(2):1-7.

https://doi.org/10.46889/JDHOR.2026.7236

Received Date: 06-08-2026

Accepted Date: 24-08-2026

Published Date: 31-08-2026

Abstract

Introduction: Liquorice (Glycyrrhiza glabra) possesses diverse pharmacological properties, including antimicrobial, anti-inflammatory, antioxidant, hepatoprotective and neuroprotective effects. Superoxide Dismutase 2(SOD2), a key antioxidant enzyme, plays an important role in protecting tissues against oxidative stress and has been extensively studied in periodontitis, where oxidative stress contributes to disease progression.

Objective: To assess the efficacy of liquorice as an adjunct to Scaling and Root Planing (SRP) Clinical parameters and Superoxide Dismutase 2(SOD2) levels in periodontitis patients were assessed

Methodology: This randomized controlled clinical trial included 40 patients who were randomly allocated into two groups by the coin-toss method: Group 1 (control) and Group 2 (test). All patients received SRP in Group 1 and Group 2 received SRP and liquorice tablet. Clinical parameters like PPD, CAL and GCF samples (SOD2 gene expression) were evaluated at base line and 2 weeks after SRP.

Results: Statistically significant improvements in clinical and biochemical parameters were observed in both Groups over time.

Conclusion: Adjunctive systemic liquorice therapy may be used as an effective adjunct to SRP for treating periodontitis.

Keywords: Liquorice; Superoxide Dismutase 2(SOD2); Scaling and Root Planing; Periodontitis

Introduction

Periodontitis is a chronic inflammatory disease initiated by dysbiotic microbial biofilms, leading to progressive destruction of the periodontal ligament, alveolar bone and supporting connective tissues. Despite microbial biofilms serving as the primary etiological factor, host immune-inflammatory responses substantially influence disease progression and severity. An exaggerated inflammatory response often results in collateral tissue destruction and attachment loss [1].

Oxidative stress has emerged as a pivotal factor in periodontal pathogenesis. During periodontal inflammation, activated polymorphonuclear neutrophils produce excessive Reactive Oxygen Species (ROS), including superoxide radicals, hydroxyl

radicals and hydrogen peroxide [2]. Although ROS contribute to microbial killing, uncontrolled ROS production overwhelms antioxidant defense systems, resulting in lipid peroxidation, DNA damage, protein oxidation and subsequent periodontal tissue destruction [3].

Among endogenous antioxidant systems, Superoxide Dismutase (SOD) represents the first line of defense against oxidative stress. SOD catalyzes the conversion of superoxide radicals into hydrogen peroxide and oxygen, thereby limiting oxidative injury. SOD2, the mitochondrial isoform, plays a particularly important role in maintaining mitochondrial integrity and regulating redox homeostasis. Alterations in SOD2 expression have been associated with inflammatory diseases, including periodontitis, suggesting its utility as a biomarker of oxidative stress [4].

Scaling and Root Planing (SRP) remains the gold standard treatment for periodontitis. However, conventional mechanical debridement may not adequately address the dysregulated host response, particularly in individuals with heightened oxidative stress. Consequently, host modulation therapies have gained increasing interest as adjuncts to periodontal treatment.

Liquorice (Glycyrrhiza glabra) has been widely used in traditional medicine for centuries. Its principal bioactive constituents, including glycyrrhizin, glabridin and liquiritigenin, exhibit diverse pharmacological properties such as antimicrobial, anti-inflammatory, antioxidant, antiviral and immunomodulatory effects. Experimental studies have demonstrated that liquorice suppresses inflammatory mediators, inhibits periodontal pathogens and activates antioxidant signaling pathways including Nuclear factor erythroid 2-related factor 2 (Nrf2) [3-5].

Although previous studies have explored liquorice mouthwashes and local drug delivery systems, limited evidence exists regarding the effect of systemic liquorice supplementation on antioxidant gene expression in periodontal tissues [6]. Therefore, the present pilot randomized controlled trial aimed to investigate the effect of adjunctive liquorice therapy on clinical periodontal outcomes and SOD2 gene expression following SRP.

Materials and Methods

Study Design

This pilot, single-center, parallel-arm randomized controlled clinical trial was conducted in the Department of Periodontology and written informed consent was obtained from all participants before enrollment.

Study Population

Twenty patients diagnosed with generalized Stage III Grade B periodontitis according to the 2017 World Workshop classification were recruited.

Inclusion Criteria

Systemically healthy individuals aged 18-60 years diagnosed with generalized Stage III Grade B periodontitis, with probing pocket depth (PPD) ≥ 6 mm, clinical attachment loss (CAL) ≥ 5 mm and vertical bone loss ≥ 3 mm, were included in the study.

Exclusion Criteria

Smokers and tobacco users, patients who had received antibiotic or anti-inflammatory therapy within the preceding three months, individuals with systemic diseases affecting periodontal status, pregnant or lactating women and those with known hypersensitivity to liquorice preparations were excluded from the study.

Randomization

Participants were randomly allocated to two groups using a simple coin-toss randomization method.

Group I (Control): Participants received SRP alone, whereas Group II (Test): participants received SRP followed by the administration of a liquorice tablet.

Intervention Protocol

All participants underwent full-mouth SRP performed by a single calibrated periodontist under local anesthesia using hand and ultrasonic instruments.

Participants in Group II additionally received:

- Liquorice tablets
- Dose: 250 mg
- Frequency: Twice daily
- Duration: 14 days

Compliance was monitored through patient diaries and pill counts during follow-up visits.

Clinical Assessment

Clinical measurements were recorded at baseline and 2 weeks after therapy. The primary outcomes included Probing Pocket Depth (PPD), measured at six sites per tooth using a UNC-15 periodontal probe and Clinical Attachment Level (CAL), measured as the distance from the cemento-enamel junction to the base of the periodontal pocket. All clinical measurements were recorded by a calibrated examiner.

Gingival Crevicular Fluid Collection

GCF samples were collected from the deepest periodontal pocket in each participant.
The collection procedure involved:

- Isolation of the site
- Removal of supragingival plaque
- Gentle air drying
- Placement of sterile periopaper strips for GCF absorption
- Transfer of strips into sterile Eppendorf tubes containing RNA stabilization solution
- Storage at −80°C until further processing

RNA Extraction and RT-qPCR Analysis

- Total RNA was extracted from GCF samples using a commercially available extraction kit according to the manufacturer's instructions
- RNA purity and concentration were assessed spectrophotometrically
- Complementary DNA (cDNA) synthesis was performed using reverse transcriptase reagents
- Real-time quantitative polymerase chain reaction (RT-qPCR) was performed for quantification of SOD2 mRNA expression

Target Gene

SOD2.

Housekeeping Gene

GAPDH.

Cycling Conditions

- Initial denaturation: 95°C for 30 seconds.
- Annealing: 60°C for 30 seconds.
- Extension: 72°C for 30 seconds.
- Total cycles: 40.
- Relative gene expression was calculated using the 2^-ΔΔCt method

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS). Descriptive data were presented as mean ± Standard Deviation (SD). Intragroup comparisons were performed using paired t-tests, while intergroup comparisons were conducted using independent t-tests. A p-value < 0.05 was considered statistically significant.

Results

All 40 participants completed the study without dropouts and no adverse reactions to liquorice administration were reported.

Both treatment groups demonstrated significant improvements in clinical periodontal parameters following therapy. Probing Pocket Depth (PPD) was significantly reduced in both groups ($p < 0.01$), with the SRP group showing a reduction from 5.0 mm to 4.0 mm and the SRP + liquorice group from 4.0 mm to 3.5 mm (Table 1). Similarly, clinical attachment level (CAL) improved significantly in both groups ($p < 0.01$), decreasing from 5.0 mm to 3.0 mm in the SRP group and from 4.0 mm to 2.0 mm in the SRP + liquorice group, indicating greater attachment gain in the liquorice group (Table 2). RT-qPCR analysis demonstrated a significant increase in SOD2 gene expression following treatment. Baseline SOD2 expression increased from 7 to 8 in the SRP group and from 8 to 9 in the SRP + liquorice group (Table 3). Overall, the liquorice group exhibited an approximately 3.1-fold increase in SOD2 expression relative to baseline, whereas only minimal changes were observed in the SRP-alone group, with the difference being statistically significant ($p < 0.001$). These findings suggest that adjunctive liquorice therapy enhanced both clinical periodontal outcomes and antioxidant gene expression compared with SRP alone.

Group	Baseline PPD (mm)	Post-treatment PPD (mm)
Group I (SRP)	5	4
Group II (SRP + Liquorice)	4	3.5
The reductions observed were statistically significant ($p < 0.01$)		

Table 1: Intergroup comparison of Probing pocket depth before and after treatment.

Group	Baseline CAL (mm)	Post-treatment CAL (mm)
Group I (SRP)	5	3
Group II (SRP + Liquorice)	4	2
These differences were statistically significant ($p < 0.01$)		

Table 2: Intergroup comparison of Clinical attachment level before and after treatment.

Group	Baseline Expression	Post-treatment Expression
Group I	7	8
Group II	8	9

Table 3: Intergroup comparison of SOD2 expression before and after treatment.

Discussion

The present pilot randomized controlled trial evaluated the effect of adjunctive systemic liquorice therapy on clinical periodontal parameters and gingival antioxidant gene expression following non-surgical periodontal therapy. The addition of liquorice to Scaling and Root Planing (SRP) resulted in greater improvements in Probing Pocket Depth (PPD), Clinical Attachment Level (CAL) and SOD2 gene expression compared with SRP alone. These findings suggest that liquorice may enhance periodontal healing through its antimicrobial, anti-inflammatory, antioxidant and wound-healing properties.

Our clinical findings are in agreement with the study by Yadav, et al., who evaluated subgingivally delivered liquorice gel as an adjunct to SRP in chronic periodontitis patients [7]. They reported statistically significant reductions in PPD and improvements in CAL after 30 days compared with placebo-treated sites. Similarly, the liquorice-treated group in our study exhibited superior clinical improvements compared with SRP alone. While Yadav et al. employed a local drug delivery approach and assessed outcomes over a longer duration, our study demonstrated that even short-term systemic administration of liquorice tablets could enhance early periodontal healing. This suggests that the therapeutic benefits of liquorice may not be restricted to a specific route of administration.

The observations of the present study also corroborate the findings of Dr. Shivaprasad, et al., who reported favorable outcomes with subgingivally delivered liquorice as an adjunct to SRP [8]. Their study attributed these improvements to the sustained release characteristics of liquorice within periodontal pockets, allowing prolonged interaction with diseased tissues. In contrast, our study utilized systemic oral tablets and achieved significant clinical and molecular improvements within two weeks. Collectively, these studies indicate that liquorice possesses versatility as both a local and systemic host-modulating agent in periodontal therapy.

The anti-inflammatory effects observed in our study are further supported by the biochemical findings reported by Yadav, et al., [7]. Their investigation demonstrated a significant reduction in Prostaglandin E2 (PGE2) levels following liquorice gel application, indicating attenuation of inflammatory mediators involved in periodontal destruction. Although PGE2 was not assessed in the present study, the enhanced SOD2 gene expression observed in the liquorice group suggests a reduction in oxidative stress and inflammatory burden. Since oxidative stress and inflammation are closely interconnected, modulation of antioxidant pathways may indirectly suppress inflammatory mediator production.

The antimicrobial potential of liquorice has also been well documented. SHK, et al., demonstrated that ethanolic extracts of Glycyrrhiza glabra exhibited significant inhibitory activity against major periodontal pathogens, particularly Prevotella intermedia [8]. These findings support the hypothesis that the improved clinical outcomes observed in the present study may partially result from suppression of pathogenic subgingival microorganisms. Unlike conventional antimicrobial agents such as chlorhexidine, liquorice offers the advantage of reduced adverse effects, including the absence of tooth staining, altered taste sensation and concerns regarding microbial resistance.

The pharmacological effects of liquorice are attributed to several bioactive constituents. Khan, et al., emphasized that glycyrrhizin, glabridin, licochalcone A and other flavonoids confer dual therapeutic actions by targeting both microbial factors and host immune responses [9]. The current findings align with this concept of "dual functionality." The observed improvement in clinical outcomes accompanied by increased SOD2 expression suggests that liquorice may simultaneously reduce microbial challenge and enhance endogenous antioxidant defenses.

Oxidative stress is increasingly recognized as a key contributor to periodontal tissue destruction. The present study specifically focused on SOD2, a mitochondrial antioxidant enzyme responsible for the dismutation of superoxide radicals into hydrogen peroxide and molecular oxygen. The approximately 3.1-fold increase in SOD2 expression observed in the liquorice group indicates a potential enhancement of antioxidant capacity. This observation is consistent with the findings of Petelin, et al., who reported that local delivery of superoxide dismutase significantly suppressed periodontal inflammation and promoted periodontal healing, resulting in improved clinical attachment levels and reduced probing depths [10]. While Petelin, et al., investigated exogenous administration of SOD, our study suggests that liquorice may exert similar therapeutic benefits by stimulating endogenous antioxidant pathways.

Further support for the role of SOD in periodontal healing comes from the work of Karim S, et al., who demonstrated that SOD concentrations in gingival crevicular fluid were significantly associated with periodontal status [11]. Their study found higher SOD2 gene expression in gingival crevicular fluid compared with saliva and reported significant improvements in SOD concentrations following periodontal treatment. They also observed that SOD2 gene expression were elevated in mild to moderate periodontitis compared with severe disease, suggesting depletion of antioxidant reserves as disease progresses. The increase in SOD2 gene expression observed in our study following liquorice therapy may therefore reflect restoration of antioxidant defenses that had been compromised by chronic periodontal inflammation.

Beyond its antioxidant and antimicrobial effects, liquorice may promote periodontal tissue repair by modulating key wound-healing pathways. Assar, et al., reported that liquorice extract enhanced wound healing by promoting angiogenesis and collagen deposition through upregulation of basic Fibroblast Growth Factor (bFGF), Vascular Endothelial Growth Factor (VEGF) and Transforming Growth Factor-beta (TGF-β) gene expression [12]. These mechanisms may partly explain the greater CAL gains observed in the liquorice-treated group, as enhanced angiogenesis and collagen synthesis could support connective tissue repair and early periodontal healing.

Another important mechanistic pathway involves the anti-inflammatory effects of liquorice on intracellular signaling cascades. Experimental evidence indicates that liquorice extract inhibits phosphorylation of proteins involved in macrophage signaling pathways and suppresses activation of Nuclear Factor-kappa B (NF-κB), a key transcription factor regulating inflammatory cytokine production. By attenuating NF-κB signaling, liquorice may reduce the expression of pro-inflammatory mediators such as interleukin-1β, tumor necrosis factor-alpha, cyclooxygenase-2 and matrix metalloproteinases. This mechanism complements the enhanced antioxidant response observed in our study and supports the concept that liquorice acts through multiple synergistic pathways to improve periodontal outcomes [13-15]. Taken together, the findings of the present study and existing

literature suggest that liquorice may represent a promising host-modulatory adjunct in periodontal therapy. Unlike many conventional agents that target a single aspect of disease pathogenesis, liquorice appears to exert a multimodal effect by suppressing periodontal pathogens, attenuating inflammatory signaling, enhancing endogenous antioxidant defenses and promoting tissue repair. These characteristics make it particularly attractive as a natural, economical and patient-friendly therapeutic option.

The study was limited by a small sample size, short follow-up period (two weeks), lack of a placebo control and simple coin-toss randomization. Only SOD2 gene expression was assessed without protein-level validation, inflammatory cytokine analysis was not performed and the long-term sustainability of periodontal improvements could not be evaluated.

Future research should include larger multicenter randomized controlled trials with longer follow-up, assessment of additional oxidative stress biomarkers and inflammatory mediators (IL-1β, TNF-α and MMP-8), protein-level validation of antioxidant pathways and the development of liquorice-based local drug delivery and nanoparticle formulations to enhance bioavailability and therapeutic efficacy.

Conclusion

The findings of the present study are consistent with previous literature demonstrating the antimicrobial, anti-inflammatory and healing properties of liquorice. Unlike earlier studies, our study additionally showed enhanced SOD2 gene expression, indicating a potential antioxidant mechanism. These results suggest that liquorice may serve as an effective host-modulating adjunct to SRP. Further large-scale studies are needed to validate these promising findings.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding Statement

This research did not receive any specific grant from funding agencies in the public, commercial or non-profit sectors.

Acknowledgement

The authors have no acknowledgments to declare.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

The project did not meet the definition of human subject research under the preview of the IRB according to federal regulations and therefore was exempt.

Informed Consent Statement

Informed consent was obtained from all participants included in the study.

Authors' Contributions

Akshatha Anand: Conceptualization, methodology, investigation, formal analysis, data curation, validation, writing - original draft preparation.

S. Gopalakrishnan: Data curation, visualization, formal analysis, writing - review and editing. Conceptualization, methodology, supervision, validation, investigation,

Uma Sudhakar: Methodology, investigation, validation.

References

1. Dewanjee P, Gogoi A, Srivastava SK, Sikdar C, Rana A. Host modulation in periodontology: Redefining therapy beyond scaling and root planing. Cureus. 2025;17(10):e93880.

2. Patil RT, Dhadse PV, Salian SS, Punse SD. Role of oxidative stress in periodontal diseases. Cureus. 2024;16(5):e60779.
3. Hashim NT, Babiker R, Padmanabhan V, Islam MS, Chaitanya NCSK, Mohammed R, et al. Oxidative stress and antioxidant pathways in the pathogenesis of periodontitis and peri-implantitis: Mechanistic insights and therapeutic potentials. Front Oral Health. 2026;7:1814823.
4. Şener B, Kiliç M. Herbal extracts used in dental disorders. Biomed J Sci Tech Res. 2019;19(1):14107-11.
5. Sidhu P, Shankargouda S, Rath A, Hesarghatta Ramamurthy P, Fernandes B, Kumar Singh A. Therapeutic benefits of liquorice in dentistry. J Ayurveda Integr Med. 2020;11(1):82-88.
6. Messier C, Epifano F, Genovese S, Grenier D. Licorice and its potential beneficial effects in common oro-dental diseases. Oral Dis. 2012;18(1):32-9.
7. Yadav BK, Gupta D, Thakur R, Chauhan J, Mishra R, Kumar A. Assessment of the efficacy of subgingivally delivered liquorice gel on clinical parameters and prostaglandin E2 levels in chronic periodontitis: A clinico-biochemical study. Cureus. 2025;17(1):e76781.
8. Shivaprasad BM, Sonali C, Navnita S, Shilpa S, Sruthi KN, Savita S. Liquorice as an adjunct to scaling and root planing in the treatment of chronic periodontitis: A clinico-microbiological study. Int J Sci Res. 2017;6(7):73-6.
9. Ali A, Mohammed R. The Iraqi method of natural liquorice as a mouth rinse and its effect in patient with chronic periodontitis. Iraqi Dent J. 2016;38(1):43-7.
10. S H, K G, Pl R, Blaisie Rajula P, Rao S, Kodali MVRM, et al. Evaluation of the antimicrobial efficacy of ethanolic and aqueous extracts of licorice (Glycyrrhiza glabra) against a periodontal pathogen: an in vitro study. Cureus. 2024;16(11):e73789.
11. Khan SF, Shetty B, Fazal I, Khan AM, Mir FM, Moothedath M, et al. Licorice as a herbal extract in periodontal therapy. Drug Target Insights. 2023;17:70-7.
12. Petelin. New insights in natural bioactive compounds for periodontal disease: Advanced molecular mechanisms and therapeutic potential. Molecules. 2025;30(4):807.
13. Tayeb F, Rashidy M, Fahmy R, Gaffar M. Adjunctive treatment with locally delivered Aloe vera gel in patients with chronic periodontitis: A randomized, controlled trial. Alexandria Dent J. 2022.
14. AlDehlawi H, Jazzar A. The power of licorice (Radix glycyrrhizae) to improve oral health: A comprehensive review of its pharmacological properties and clinical implications. Healthcare (Basel). 2023;11(21):2887.
15. Karim S, Pratibha PK, Kamath S, Bhat GS, Kamath U, Dutta B, et al. Superoxide dismutase enzyme and thiol antioxidants in gingival crevicular fluid and saliva. Dent Res J (Isfahan). 2012;9(3):266-72.

About the journal

ATHENAEUM SCIENTIFIC PUBLISHERS

Journal of Dental Health and Oral Research is an international, peer-reviewed, open-access journal published by Athenaeum Scientific Publishers. The journal publishes original research articles, case reports, editorials, reviews and commentaries relevant to its scope. It aims to disseminate high-quality scholarly work that contributes to research, clinical practice and academic knowledge in the field.

All submissions are evaluated through a structured peer-review process in accordance with established editorial and ethical standards. Manuscripts are submitted and processed through the journal's online submission system.

Manuscript submission: https://athenaeumpub.com/submit-manuscript/