Vol: 9 Issue: 1

EDJ

# Effects of Low-Level Laser Therapy on Histological Changes of Lingual Papillae in Streptozotocin-Induced Diabetes Mellitus in Rats: An Experimental Study

**Bayar Taher Saeed[(1)] , Shukrya Mohammed Hussain[(1)] , Tuqa Yousif Sherif[(1)]**

**ABSTRACT**

**Background and Objectives:** Diabetes mellitus (DM) is associated with structural alterations in oral tissues, including the lingual papillae, where epithelial atrophy, fibrosis, and degeneration of taste buds may occur. Low-level laser therapy (LLLT) has been suggested as a non-invasive therapeutic approach that may enhance tissue repair and regeneration.

**Aim:** This study evaluated STZ-induced diabetic changes in rat lingual papillae and the therapeutic effect of low-level diode laser therapy.

**Methods:** 21 Wistar albino rats were used. 3 Rats served as healthy controls, while diabetes was induced in 18 rats by a single intraperitoneal injection of STZ at 50 mg/kg. After confirmation of hyperglycemia (blood glucose level >= 300 mg/dL), diabetic rats were divided into two equal subgroups: untreated diabetic rats and LLLT-treated diabetic rats. Untreated diabetic rats were examined histologically at 2, 3, and 4 weeks after diabetes induction. The treated subgroup received diode laser therapy three times weekly starting 4 weeks after diabetes induction and was evaluated at 6, 7, and 8 weeks. Body weight and blood glucose levels were monitored throughout the study. Tongue specimens were collected for histological and semi-quantitative evaluation.

**Results:** Untreated diabetic rats showed progressive histological deterioration, including epithelial atrophy, fibrosis, and reduced taste bud density. These changes became more pronounced with longer diabetes duration. In contrast, LLLT-treated rats demonstrated improved epithelial thickness, better preservation of taste buds, and reduced fibrosis.

**Conclusion:** STZ-induced DM caused progressive degenerative changes in the lingual papillae. LLLT promoted histological improvement and may support tissue repair in diabetic lingual tissues.

**Keywords:** Photo biomodulation Therapy; Hyperglycemia; Tongue; Streptozotocin; Tissue Regeneration

**Article Information**

Submission Date: 1/7/2025
Revision date: 18/8/2025
Acceptance date: 31/8/2025
Publishing date: June 2026

**Affiliation Info**

[(1)]College of Dentistry, Hawler Medical University, Kurdistan Region, Iraq.
Corresponding Author: Bayar Taher Saeed
Email: bayar.saeed@den.hmu.edu.krd
ORCID iD: https://orcid.org/0009-0009-0664-3772



DOI: doi.org/10.15218/edj.2026.6

## INTRODUCTION

Low-level laser therapy (LLLT), also referred to as photobiomodulation, was introduced as a non-invasive method for supporting tissue repair in the early 1960s.[1] Since then, LLLT has been studied for several medical applications, mainly pain reduction, inflammation control, and acceleration of wound healing.[2] Therapeutic wavelengths used in LLLT are usually within the visible red and near-infrared spectrum, commonly ranging from 600 to 1,100 nm.[3] Although the precise cellular and molecular mechanisms remain under investigation, LLLT is generally considered to reduce inflammation, promote tissue regeneration, increase mitochondrial activity, and relieve pain without causing irreversible thermal damage to tissues.[4]

Several clinical and experimental studies have reported that LLLT may accelerate healing of cutaneous and mucosal wounds.[5-14] Diode lasers, including wavelengths around 915 nm, have shown promising effects on tissue repair and regeneration.[6] Postoperative oral mucosal wounds may be susceptible to infection and inflammation because of the bacterial environment of the oral cavity.[7] Previous investigations have suggested that diode laser irradiation may accelerate epithelial repair, reduce postoperative pain and edema, and improve wound healing in animal and clinical models.[8-9]

Diabetes mellitus (DM) is a common chronic disease and a major global health concern. It is characterized by hyperglycemia resulting from insulin deficiency, insulin resistance, or both.[10-11] DM is associated with systemic complications, including peripheral vascular disease, retinopathy, nephropathy, and neuropathy, and it increases the burden of medical care.[12]

In the oral cavity, DM has been associated with delayed wound healing, infection, halitosis, fissured tongue, burning mouth, recurrent aphthous ulceration, traumatic ulceration, lichen planus, and other mucosal alterations.[13-14]

The present study investigated the effect of STZ-induced DM on the tongue and lingual papillae of male albino rats, as well as the possible effect of LLLT on diabetes-related histological alterations. Histological and semi-quantitative assessments were used to evaluate the extent of tissue damage and the degree of tissue repair after laser treatment.

## METHODS

Twenty-one healthy adult male albino rats were used in this study. The animals were approximately three months old and weighed 180-200 g. All rats were kept in plastic cages with separate ventilation for two weeks for acclimatization at the College of Pharmacy, Hawler Medical University, Erbil, Iraq. The animals were maintained under standard laboratory conditions, including a 12-hour light/12-hour dark cycle, unrestricted access to food and water, and a controlled temperature of 21-24 °C.[15]

The study was approved by the Research Ethics Committee of the College of Dentistry, Hawler Medical University, on January 12, 2025, under protocol number HMUD,2425081.

### Animal Grouping and Experimental Timeline

The study included 21 male Wistar albino rats. Three rats were assigned to the healthy control group and did not receive STZ. The remaining 18 rats were used for diabetes induction. After confirmation of hyperglycemia (blood glucose level >= 300 mg/dL), the diabetic rats were divided into two equal subgroups: untreated diabetic group (n = 9) and LLLT-treated diabetic group (n = 9). In the untreated diabetic group, three rats were sacrificed at each time point: 2, 3, and 4 weeks after diabetes induction. In the LLLT-treated group, laser therapy started 4 weeks after diabetes induction, and three rats were sacrificed at each time point: 6, 7, and 8 weeks after diabetes induction.

**Table 1.** Animal Grouping, Treatment Allocation, and Evaluation Time Points

| Group | Condition | Treatment | Number of rats | Evaluation time |
|---|---|---|---|---|
| Control | Healthy | No STZ, no laser | 3 | Baseline/control evaluation |
| Untreated diabetic | STZ-induced DM | No laser | 9 | 2, 3, and 4 weeks; 3 rats/time point |
| LLLT-treated diabetic | STZ-induced DM | Diode laser therapy | 9 | 6, 7, and 8 weeks; 3 rats/time point |

**Induction of Diabetes**

After overnight fasting, rats received a single intraperitoneal injection of streptozotocin (STZ) (Macklin Biochemical Co., Ltd., Shanghai, China) at a dose of 50 mg/kg to induce experimental DM.[16] This dose was selected to induce hyperglycemia while maintaining animal survival. After STZ administration, rats had unrestricted access to food and water. DM was allowed to develop and stabilize over four days.

Blood samples were obtained from the tail tip after overnight fasting, and blood glucose levels were measured using a glucometer (VivaChek Ino, VivaChek Laboratories, China). Blood glucose levels of 300 mg/dL or higher were considered indicative of diabetes.[17]

**Laser Treatment Procedure**

Laser therapy began 4 weeks after diabetes induction and continued during the 6-, 7-, and 8-week evaluation periods. Before each laser therapy session, diabetic rats were anesthetized by inhalation of ethyl ether (Chem-Lab Diagnostics, Belgium). A cotton ball soaked in ethyl ether was placed inside a closed plastic box, and rats were introduced individually. After 4-5 minutes, when the rat was fully unconscious, sterile tweezers were used to gently hold and expose the tongue.

A low-level diode laser (Doctor Smile Diode Laser, Italy) was used to irradiate the anterior, middle, and posterior regions of the tongue with wavelength 980nm, power 1W, energy density 10 J/cm2, exposure time 120s, distance from tissue 3-5mm. After irradiation, each rat was monitored until full recovery from anesthesia and then returned to its cage.

**Table 2.** The Laser Irradiation Parameters Used in this Study to Allow Reproducibility of the Treatment Protocol

| Laser parameter | Value |
|---|---|
| Laser type | Low-level diode laser |
| Device | Doctor Smile Diode Laser, Italy |
| Wavelength | 980 nm |
| Output power | 1 W |
| Energy density | 10 J/cm² |
| Exposure time | 120 seconds |
| Application site | Anterior, middle, and posterior regions of the tongue |
| Distance from tissue | 3–5 mm |
| Frequency | Three sessions per week |
| Start of treatment | 4 weeks after diabetes induction |
| Treatment duration | Until evaluation at 6, 7, and 8 weeks |

**Histopathological and Histomorphometric Analysis**

The LLLT-treated diabetic animals were euthanized by intraperitoneal injection of xylazine (10-20 mg/kg) and ketamine (80-100 mg/kg) at the end of weeks 6, 7, and 8, whereas the control and untreated diabetic groups were sacrificed at the end of weeks 2, 3, and 4.[18-19] Tongues were carefully removed, sectioned longitudinally, and fixed in 10% formalin for 24 hours. After fixation, specimens were processed for routine histological preparation. Tissues were dehydrated, cleared, infiltrated, embedded in paraffin wax, sectioned at 5 µm thickness, mounted on slides, and stained with hematoxylin and eosin (H&E).

**Microscopic Scoring Criteria**

Histological evaluation was performed using the zigzag technique.[20] This systematic microscopic scanning method allows standardized and unbiased assessment of entire histological sections. Instead of selecting fields randomly, the observer examined the tissue by moving the microscope stage in a zigzag or serpentine pattern across the entire section.

**Procedure**

After staining, histological slides were examined under a light microscope at predetermined magnifications (e.g., ×10 for general assessment and ×40 for cellular details). The microscopic field was scanned from one corner of the section to the op-


DOI: doi.org/10.15218/edj.2026.6

posite side in a continuous zigzag pattern to ensure that all regions were evaluated without overlap or omission. Scoring was performed using a semi-quantitative ordinal scale. Histological evaluation was performed by a blinded examiner to reduce observer bias.

1. **Fibrosis (lamina propria)**
   - −: No fibrosis (normal connective tissue)
   - -+: Minimal fibrosis (very focal collagen increase)
   - +: Mild fibrosis
   - ++: Moderate fibrosis
   - +++: Severe fibrosis
2. **Epithelial atrophy / epithelial thickness**
   - −: Normal epithelial thickness (no atrophy)
   - − +: Minimal epithelial thinning
   - +: Mild epithelial atrophy (mild thinning)
   - ++: Moderate epithelial atrophy
   - +++: Severe epithelial atrophy (marked thinning/disorganization)
3. **Taste bud density**
   - −: Very low or markedly reduced taste bud density
   - − +: Minimal density (slight improvement compared with -)
   - +: Low density
   - ++: Moderate density
   - +++: High or near-normal taste bud density

For statistical purposes, the semi-quantitative scoring system was converted into numerical values ranging from 0 to 4.

**Statistical Analysis**

Statistical analysis was performed using a semi-quantitative scoring system for histological parameters. Fibrosis, epithelial atrophy, and taste bud density were graded on an ordinal scale from 0 to 4 (− = 0, − + = 1, + = 2, ++ = 3, +++ = 4).

Data were expressed as median and interquartile range (IQR). Because the data were ordinal and the sample size was small, non-parametric tests were applied. The Kruskal-Wallis test was used to compare differences among multiple groups, followed by the Mann-Whitney U test for pairwise comparisons. Post hoc comparisons were adjusted using Bonferroni correction.

Due to the small number of animals at each time point and the semi-quantitative nature of the histological scoring, the findings were mainly interpreted descriptively. Scores for fibrosis, epithelial atrophy, and taste bud density were summarized using an ordinal scale.

Statistical significance was considered at $p < 0.05$; however, exact p-values were interpreted cautiously because of the limited sample size.

## RESULTS

**Body Weight Monitoring and Trends**

Body weight was measured using a digital electronic scale (Fujian, China) at baseline and weekly for two months. After STZ-induced diabetes, body weight decreased from 180-200 g to 160-180 g in the second week. By the third and fourth weeks, body weight stabilized at approximately 175-185 g, suggesting partial metabolic adaptation. During the laser therapy period, body weight remained approximately 175-190 g during the first week of treatment and gradually increased to 180-195 g during the second and third weeks. This may indicate a possible improvement in general condition.

Histological analysis of the tongue in the control group revealed normal architecture (Figure 1). Filiform papillae (FFP) were well defined and covered by a uniform layer of keratinized stratified squamous epithelium (EP). Fungiform papillae (FGP) showed distinct taste buds within the epithelial layer, indicating intact structural morphology. In contrast, untreated diabetic groups showed progressive deterioration over time (Figures 2-4).

At 2 weeks after diabetes induction, FFP appeared atrophied and flattened (Figure 2a,b), although the surface epithelium remained largely intact. At 3 weeks, taste bud density was reduced and subepithelial collagen deposition was increased (Figure 3a,b), indicating compromised tissue integrity. At 4 weeks, fibrosis and epithelial atrophy became more evident (Figure 4a,b). LLLT-treated diabetic groups showed histological improvement over time (Figures 2-4).

After 2 weeks of LLLT, taste buds were moderately preserved, and only mild epithelial atrophy and subepithelial fibrosis were observed (Figure 2c,d), suggesting early tissue repair. After 3 weeks of LLLT, the tissue showed moderate taste bud density and improved epithelial morphology (Figure 3c,d). Fibrotic changes appeared reduced, suggesting ongoing regeneration. After 4 weeks of treatment, fibrosis was minimal and epithelial thickness appeared closer to normal (Figure 4c,d). However, taste bud density remained reduced, suggesting that neuroepithelial recovery may require a longer period than epithelial and connective tissue repair.

**Control Group**

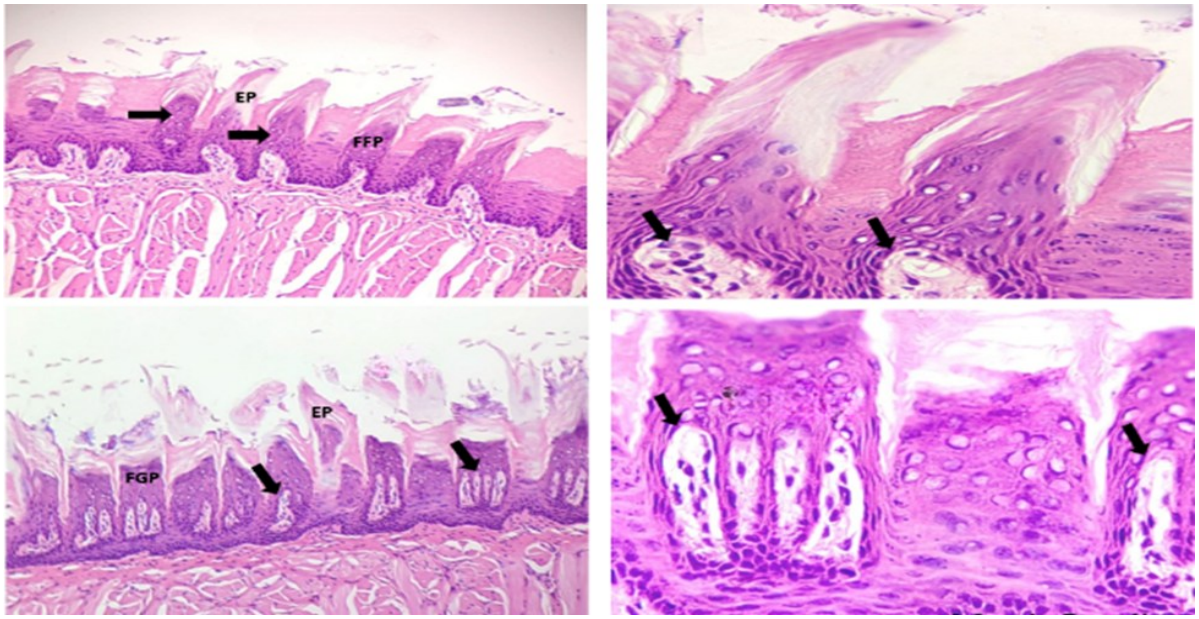


**Figure 1.** Histological features of normal lingual papillae in the control group. In (a,b), filiform papillae (FFP) appear as long conical structures covered by keratinized stratified squamous epithelium (EP). In (c,d), fungiform papillae (FGP) show dome-shaped morphology with taste buds embedded in the surface epithelium (black arrows). Sections were stained with hematoxylin and eosin (H&E) and examined at ×100 and ×400 magnification.

**Study Groups**
**6 weeks after diabetes induction and 2 weeks after LLLT**

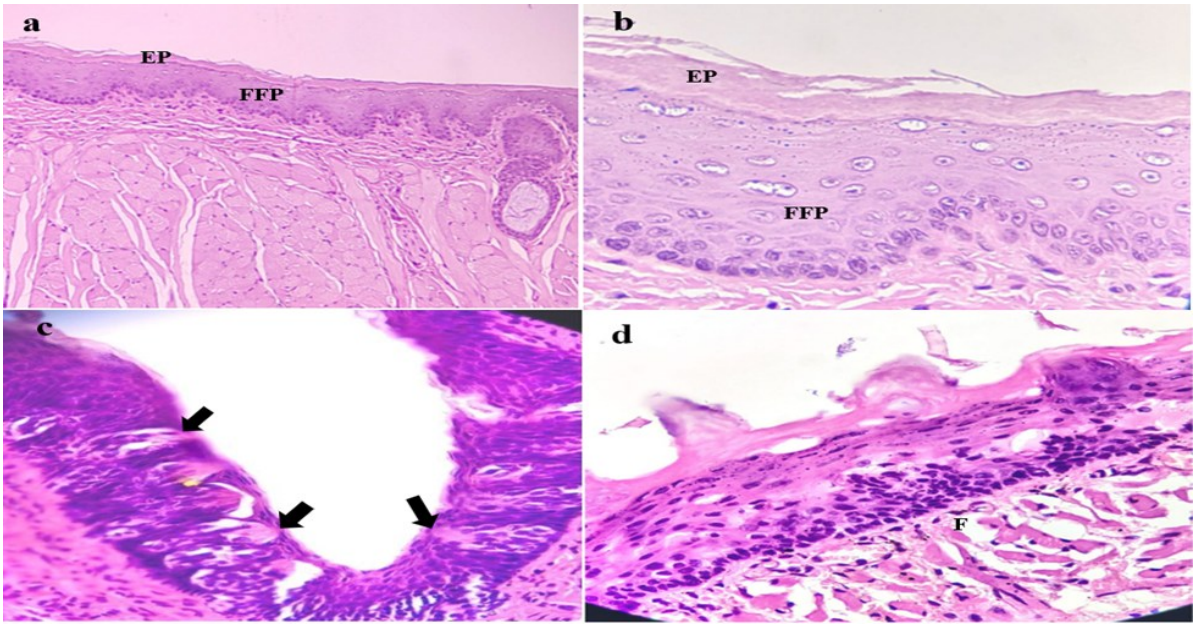


**Figure 2.** Histological changes in lingual papillae 6 weeks after diabetes induction and 2 weeks after LLLT. In the untreated diabetic group (a,b), filiform papillae (FFP) appear flattened, and epithelial details are visible. In the LLLT-treated diabetic group (c,d), moderate taste bud density is observed in the surface epithelium (black arrows), with mild epithelial atrophy and mild subepithelial fibrosis (F). Sections were stained with H&E and examined at ×100 and ×400 magnification.


DOI: doi.org/10.15218/edj.2026.6

**7 weeks after diabetes induction and 3 weeks after LLLT**

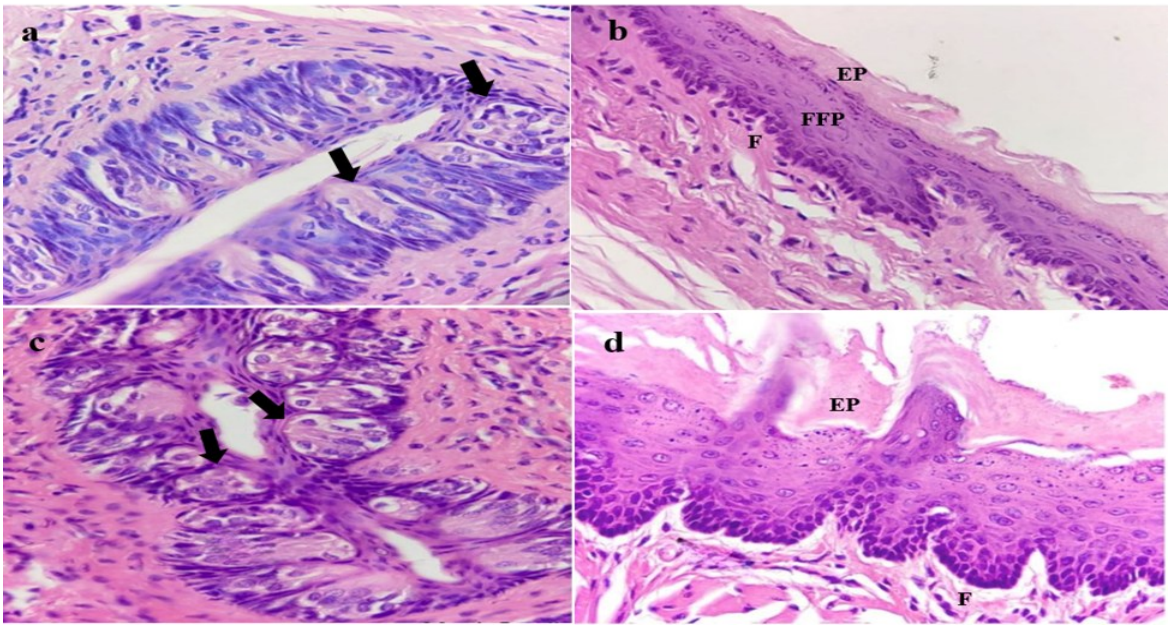


**Figure 3.** Histological features of lingual papillae 7 weeks after diabetes induction and 3 weeks after LLLT. In the untreated diabetic group (a,b), moderate taste bud density and subepithelial collagen deposition (F) are observed. In the LLLT-treated diabetic group (c,d), moderate taste bud density is maintained, with mild subepithelial collagen deposition and slight epithelial atrophy. Sections were stained with H&E and examined at ×400 magnification

**8 weeks after diabetes induction and 4 weeks after LLLT**

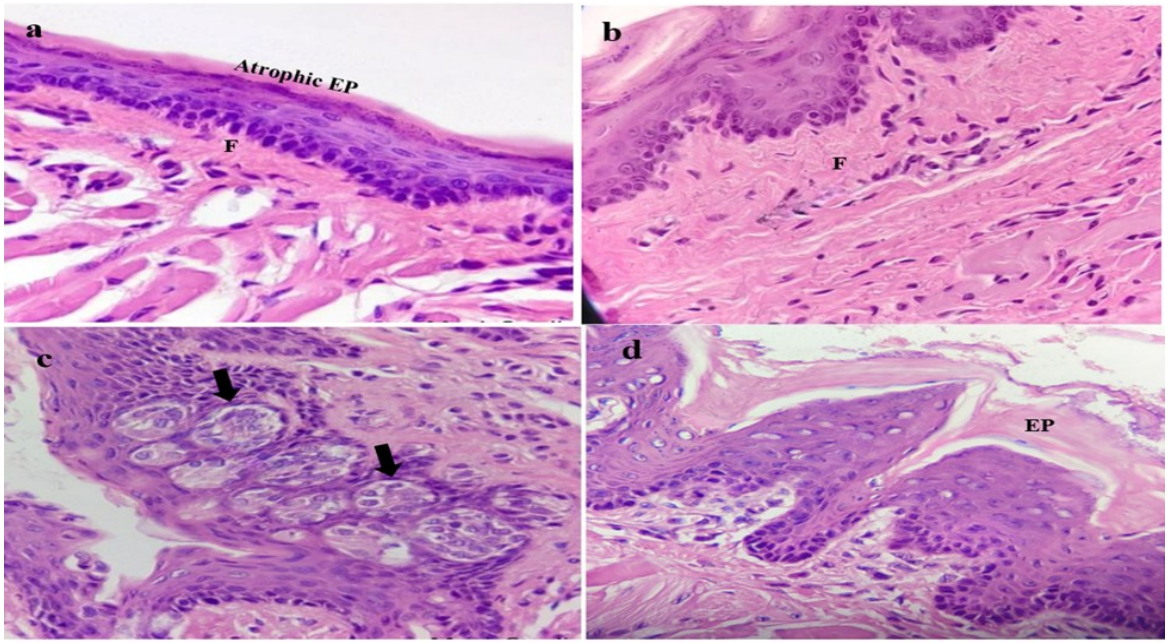


**Figure 4.** Histological changes in lingual papillae 8 weeks after diabetes induction and 4 weeks after LLLT. In the untreated diabetic group (a,b), moderate subepithelial fibrosis and epithelial atrophy are observed. In the LLLT-treated diabetic group (c,d), taste bud density remains reduced, whereas epithelial thickness appears more stable. Sections were stained with H&E and examined at ×400 magnification

DOI: doi.org/10.15218/edj.2026.6

Histological analysis of the tongue in the control group revealed normal architecture (Figure 1). Filiform papillae (FFP) were well defined and covered by a uniform layer of keratinized stratified squamous epithelium (EP). Fungiform papillae (FGP) showed distinct taste buds within the epithelial layer, indicating intact structural morphology. In contrast, untreated diabetic groups showed progressive deterioration over time (Figures 2-4).

At 2 weeks after diabetes induction, FFP appeared atrophied and flattened (Figure 2a,b), although the surface epithelium remained largely intact. At 3 weeks, taste bud density was reduced and subepithelial collagen deposition was increased (Figure 3a,b), indicating compromised tissue integrity. At 4 weeks, fibrosis and epithelial atrophy became more evident (Figure 4a,b). LLLT-treated diabetic groups showed histological improvement over time (Figures 2-4).

After 2 weeks of LLLT, taste buds were moderately preserved, and only mild epithelial atrophy and subepithelial fibrosis were observed (Figure 2c,d), suggesting early tissue repair. After 3 weeks of LLLT, the tissue showed moderate taste bud density and improved epithelial morphology (Figure 3c,d). Fibrotic changes appeared reduced, suggesting ongoing regeneration. After 4 weeks of treatment, fibrosis was minimal and epithelial thickness appeared closer to normal (Figure 4c,d). However, taste bud density remained reduced, suggesting that neuroepithelial recovery may require a longer period than epithelial and connective tissue repair.

**Semi-quantitative Histological Analysis**

Semi-quantitative analysis showed a progressive increase in fibrosis and epithelial atrophy scores in untreated diabetic groups over time, accompanied by a reduction in taste bud density.

Compared with the control group, untreated diabetic rats at weeks 2, 3, and 4 showed higher fibrosis and epithelial atrophy scores, whereas taste bud density scores were lower.

In contrast, LLLT-treated diabetic groups showed lower fibrosis and epithelial atrophy scores compared with untreated diabetic groups. Taste bud density showed partial improvement following LLLT, although complete recovery was not observed within the study period (Table 1).

Histological improvement appeared greater at 8 weeks, although confirmation in a larger sample is required.

**Table 3.** Semi-Quantitative Histological Scoring of Lingual Papillae

| Group | Fibrosis Score | Epithelial Atrophy Score | Taste Bud Density Score |
|---|---|---|---|
| Control | 0 | 0 | 4 |
| DM – 2 weeks | 1 | 1 | 2 |
| DM – 3 weeks | 3 | 2 | 1 |
| DM – 4 weeks | 3 | 3 | 1 |
| LLLT – 6 weeks | 1 | 1 | 2 |
| LLLT – 7 weeks | 1 | 1 | 2 |
| LLLT – 8 weeks | 0 | 0 | 2 |

Note: Scores were assigned using an ordinal scale: 0 = none/normal, 1 = minimal, 2 = mild/low, 3 = moderate, and 4 = severe/high.

## DISCUSSION

The present study showed that body weight in diabetic rats initially decreased after STZ induction and then partially stabilized. This pattern may reflect metabolic adaptation after the catabolic effects of insulin deficiency. Similar findings have been described in experimental models of diabetes, including STZ-induced models, in which body weight may decrease initially before stabilizing as animals adapt metabolically.[21-22]

Untreated diabetic rats showed progressive epithelial thinning, taste bud loss, papillary flattening, and increased fibrosis over the 4-week observation period. These findings are consistent with previous studies reporting harmful effects of chronic hyperglycemia on oral tissues, including delayed tissue repair, oxidative stress, and microvascular dysfunction.[23-24]

Between weeks 6 and 8 after diabetes induction, rats treated with LLLT showed improved histo-


DOI: doi.org/10.15218/edj.2026.6

logical features, including reduced fibrosis and better preservation of epithelial thickness. The beneficial effects of LLLT have been attributed to enhanced angiogenesis, increased adenosine triphosphate (ATP) synthesis, modulation of inflammation, and mitochondrial activation.[25-26]

These mechanisms have been supported by studies on diabetic wound healing, including reports of improved recovery of oral mucosal and skin wounds in STZ-induced diabetic animals treated with red or infrared laser irradiation.[27-28] In addition, meta-analyses have reported that LLLT may reduce ulcer size and accelerate healing in patients with diabetic foot ulcers.[29]

Despite structural improvement, taste bud density remained reduced after LLLT, suggesting that neuroepithelial regeneration may occur more slowly than epithelial and connective tissue repair. Similar observations have been reported in diabetic neuropathy research, where sensory recovery may require longer treatment periods or additional interventions.[30]

The semi-quantitative statistical analysis supported the histological observations and indicated differences among control, untreated diabetic, and LLLT-treated diabetic groups. The reduction in fibrosis and epithelial atrophy, together with partial recovery of taste bud density following LLLT, suggests a measurable therapeutic effect. However, these findings should be interpreted cautiously because the number of animals at each time point was small.

A limitation of this study is the small sample size, particularly the use of three animals per time point, which may limit the generalizability of the findings. In addition, the semi-quantitative scoring method may introduce observer variability.

Future studies should include larger sample sizes, detailed laser dosimetry, blinded scoring, and longer follow-up periods to confirm the regenerative effect of LLLT on lingual papillae in diabetic conditions.

## CONCLUSION

This study showed that STZ-induced DM caused histological alterations in the lingual papillae of the tongue, including collagen deposition, reduced taste bud density, epithelial atrophy, and structural tissue changes. These degenerative effects appeared time-dependent and increased with longer exposure to diabetes. LLLT was associated with improved histological features, reduced fibrosis, and partial restoration of the normal architecture of lingual papillae. The findings support the potential role of LLLT as a non-invasive adjunctive approach for reducing diabetes-related oral tissue damage and supporting healing.

## Acknowledgments

The authors would like to acknowledge the College of Dentistry and the College of Pharmacy, Hawler Medical University, Erbil, Iraq, for their support and for providing the facilities required to conduct this experimental study.

## Conflict of Interest

The authors declare no conflicts of interest.

## Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

### REFERENCES

1. Hamblin MR. Mechanisms and applications of the anti-inflammatory effects of photobiomodulation. APL Photonics. 2017;2(2):021101.
2. Anders JJ, Lanzafame RJ, Arany PR. Low level light/laser therapy versus photobiomodulation therapy. Photomed Laser Surg. 2015;33(4):183–4. doi:10.1089/pho.2015.9848
3. Migliaresi C, Ramakrishna S, editors. Laser therapy in wound healing. London: Academic Press; 2021.
4. de Freitas LF, Hamblin MR. Proposed mechanisms of photobiomodulation or low-level light therapy. IEEE J Sel Top Quantum Electron. 2016;22(3):7000417. doi:10.1109/JSTQE.2016.2561201
5. Mignon C, De Moor RJG, Meire MA, et al. Diode laser in soft tissue oral surgery: an effective approach. Photobiomodul Photomed Laser Surg. 2021;39(4):246–51.
6. Tsai SR, Hamblin MR. Biological effects and medical applications of infrared radiation. J Photochem Photobiol B. 2018;170:197–207. doi:10.1016/j.jphotobiol.2017.04.014
7. Zecha JAE, Raber-Durlacher JE, Nair RG, et al. Low-level laser therapy/photobiomodulation in the management of side effects of chemoradiation therapy in head and neck cancer. Support Care Cancer. 2016;24(6):2473–80.
8. Yoo YJ, Kang KW, Lee KH. Effect of low-level laser therapy on healing of surgically extracted molars in rats. J Periodontal Implant Sci. 2020;50(1):12–9.
9. Zupin L, Gratton R, Fontana F, et al. Diode laser therapy accelerates epithelial wound healing. J Biophotonics. 2022;15(4):e202100297.
10. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014;37(Suppl 1):S81–90. doi:10.2337/dc14-S081
11. World Health Organization. Report of the WHO Discussion Group for People Living with Diabetes: Virtual meeting, 30–31 March 2023. Geneva: WHO; 2023. ISBN: 978-92-4-008145-1.
12. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of

type 2 diabetes mellitus and its complications. Nat Rev Endocrinol. 2018;14(2):88–98. doi:10.1038/nrendo.2017.151
13. Al Maskari AY, Al Maskari MY, Al Sudairy S. Oral manifestations and complications of diabetes mellitus: a review. Sultan Qaboos Univ Med J. 2011;11(2):179–86. PMID: 21969888. doi:10.18295/2075-0528.1261
14. López-Pintor RM, Casañas E, González-Serrano J, et al. Risk factors associated with xerostomia in patients with diabetes: a meta-analysis. Diabetes Metab Res Rev. 2016;32(6):707–17. doi:10.1155/2016/4372852
15. Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG. The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research. BMC Vet Res. 2020;16(1):242. doi:10.1186/s12917-020-02451-y
16. Sharma M, Chan HK, Lavilla CA Jr, Uy MM, Froemming GRA, Okechukwu PN. Induction of a single dose of streptozotocin (50 mg/kg) in rat model causes insulin resistance with type 2 diabetes mellitus. Fundam Clin Pharmacol. 2023;37(4):769–78. doi:10.1111/fcp.12892
17. Zhao X, Zhang L, Wang J, Liu Y. Establishment and evaluation of streptozotocin-induced diabetic rat models based on blood glucose thresholds. J Diabetes Res. 2022;2022:3492837. doi:10.1155/2022/3492837
18. Singh S, Shukla A, Bhattacharya S, Singh S. A review of anesthetic and analgesic agents in laboratory rodents: ketamine and xylazine use. Lab Anim Res. 2020;36(1):1–11. doi:10.1186/s42826-020-00040-x
19. Gopal S, Prabhu A, Kumar R, et al. The effects of low-level laser therapy on wound healing and pain management in skin wounds: A meta-analysis. J Wound Care. 2024;33(2):89–99. doi:10.1097/XX.me2024
20. Meyerholz DK, Beck AP. Principles and approaches for reproducible scoring of tissue stains in research. Lab Invest. 2018;98(7):844–855.
21. Reed MJ, Meszaros K, Entes LJ, et al. Differential effects of caloric restriction on tissue glucose metabolism in normal and diabetic rats. J Gerontol A Biol Sci Med Sci. 2000;55(1):B17–26.
22. Srinivasan K, Viswanad B, Asrat L, Kaul CL, Ramarao P. Animal models in type 2 diabetes research: an overview. Indian J Med Res. 2007;125(3):451–72.
23. Collaço LM, Lemos JC, Santos CF, Silva D. Histomorphometric analysis of tongue mucosa in diabetic rats. Acta Cir Bras. 2007;22(2):115–20.
24. Firat ET, Dağ A, Günay A, et al. Low-level laser therapy accelerates palatal wound healing and suppresses oxidative stress in diabetic rats. J Oral Pathol Med. 2014;43(2):103–10. doi:10.1111/jop.12106
25. Kim HR, Son K, Kim J, et al. A comparative immunohistochemical study of wound healing after dental diode laser treatment in the rat oral mucosa. Bioengineering. 2022;9(9):466. doi:10.3390/bioengineering9090466
26. Taha N, Daoud H, Malik T, et al. Effects of low-level laser therapy on wound healing and pain management in skin wounds: a meta-analysis. Cureus. 2024;16(10):e72542. doi:10.7759/cureus.72542
27. Ranjbar R, Takhtfooladi MA. Effects of low-level laser therapy on Staphylococcus aureus infected third-degree burns in diabetic rats. Acta Cir Bras. 2016;31(4):250–5. doi:10.1590/S0102-865020160040000005
28. Huang J, Chen J, Xiong S, et al. Effect of low-level laser therapy on diabetic foot ulcers: a meta-analysis of randomized controlled trials. Int Wound J. 2021;18(6):763–76. doi:10.1111/iwj.13577
29. Chen B, Lin Z, Zou S, et al. Intervention effects of low-level laser therapy on grade I–II diabetic foot ulcers: a meta-analysis. Wound Repair Regen. 2025;33(2). doi:10.1111/wrr.70021
30. Rojas DR, Tegeder I, Kuner R, Agarwal N. HIF-1α protects sensory neurons in diabetic neuropathy by limiting ROS. Transl Neurodegener. 2020;9:19. doi:10.1186/s40035-020-00197-z


DOI: doi.org/10.15218/edj.2026.6