Periodontitis-Mediated TMD Pathology Associated with Increased Cytokine Expression in the TMJ and the Therapeutic Effect of Nisin

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Introduction

- Temporomandibular joint disorders (TMD) and periodontitis are prevalent inflammatory diseases with shared immunological mechanisms.
- Evidence supports an oral-systemic connection, where periodontal inflammation contributes to pathology in distant organs.[1]
- Key cytokines (TNF-α, IL-6) mediate tissue destruction and pain in both periodontitis and TMD.[1,2]
- In periodontal disease, red complex bacteria, particularly *Treponema denticola*, are major drivers of cytokine upregulation.[3]
- Nisin has shown antimicrobial and anti-inflammatory effects in periodontitis.
- **Hypothesis**: *T. denticola*-induced periodontitis promotes TMJ inflammation, and nisin attenuates this cytokine-mediated response.

Methods

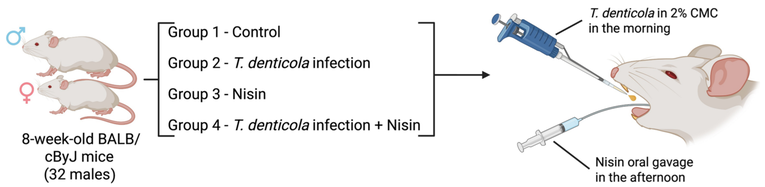

Figure 1. Experimental design for BALB/cByJ male mice (n = 32) randomized to four groups (control, *T. denticola*, nisin, *T. denticola* + nisin). Mice received oral lavage with *T. denticola* (1 × 10^9 CFU in 0.2 mL 2% CMC) or sterile 2% CMC (control) 4 consecutive days/week for 8 weeks, and nisin by daily oral gavage (800 mg/kg; 0.1 mL) for 8 weeks. At study end, mice TMJs were harvested.

- Periodontal disease was assessed by micro-computed tomography (Micro-CT) scans, alveolar bone density, and periodontal ligament (PDL) distance.
- Inflammatory cytokine expression (IL-1β, IL-6, IL-17, TNF-α) was measured by RT-qPCR.
- Bacterial DNA was assessed by qPCR using *F. nucleatum*, *P. gingivalis*, *T. denticola*, and universal bacterial primers.

Results

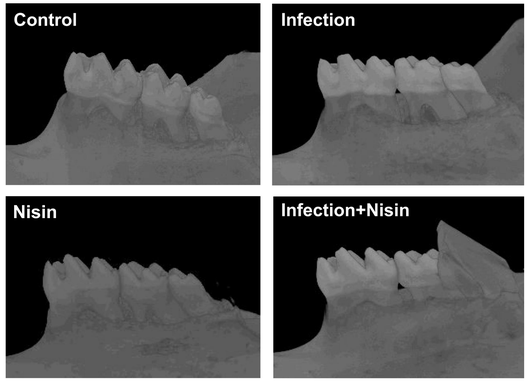

Figure 2. Micro-CT of mouse mandibles showed periodontal disease after infection with *T. denticola* and reversal with nisin. Scans were acquired on a SkyScan 1272 (Bruker) at 70 kV with 3.6 µm resolution over 360° (0.2° steps; 6-frame averaging; 1800 images/mandible), reconstructed in NRecon and visualized in CTvox.

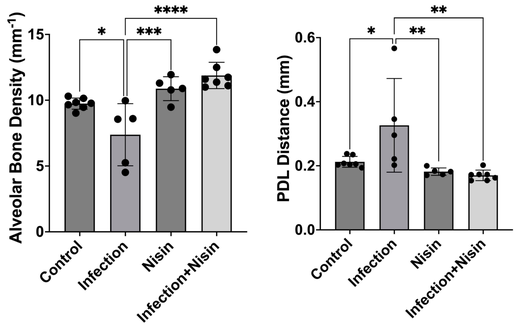

Figure 3. *T. denticola* infection reduced alveolar bone density and increased PDL width versus controls, while nisin significantly restored both to control levels. Reconstructed 3D mandible images were trimmed in DataViewer and analyzed in CTan (Bruker).

Results

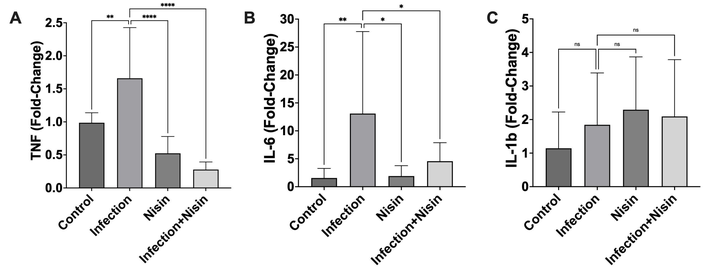

Figure 4. Periodontal disease increases TMJ inflammatory cytokine expression, which is attenuated by nisin. (A) TNF-α and (B) IL-6 expression were higher in *T. denticola*-infected mice vs. controls (TNF-α: 1.6-fold, $p < 0.01$; IL-6: 13-fold, $p < 0.01$) and lower with nisin treatment (TNF-α: 6-fold vs. untreated infection, $p < 0.0001$; IL-6: 2.9-fold vs. untreated infection, $p < 0.05$). IL-1β expression did not differ between groups ($p>0.05$).

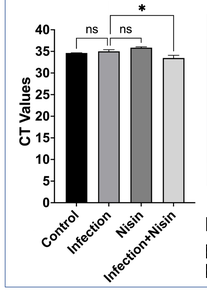

Table 1. No bacterial DNA was detected in TMJs on qPCR.

	F. nucleatum	*P. gingivalis*	*T. Denticola*
Control	ND	ND	ND
Infection	ND	ND	ND
Nisin	ND	ND	ND
Infection + Nisin	ND	ND	ND

ND: Not Detected (C_T >35 on qPCR)

Figure 5. qPCR of TMJ bacterial DNA using universal bacterial primers showed high C_T across groups, indicating minimal bacterial DNA; ns: not significant, * $p < 0.05$.

Conclusions

- Periodontal disease promotes pro-inflammatory cytokines (IL-6, TNF-α) expression in the TMJ.
- Nisin attenuates this inflammatory cascade, supporting its therapeutic potential in TMD secondary to periodontitis.
- Periodontal bacterial DNA was not detected in TMJ tissues, suggesting an inflammation-driven, non-infectious mechanism in periodontitis-induced TMD.

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References

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