In Vitro Inhibition of Oral Pathogens by Polyols: A Comparative Screening Study with Implications for the Oral–Systemic Axis

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Background

- Dental caries and periodontal diseases are driven by dysbiotic oral biofilms and the oral–systemic axis links these conditions to cardiovascular, metabolic, gastrointestinal, and neurodegenerative disease.
- Xylitol and erythritol are established non-cariogenic sweeteners, but head-to-head data comparing them with emerging compounds like allulose and D-mannose across clinically relevant oral taxa are lacking.

Objective

- To compare the concentration-dependent growth effects of four polyols—allulose, D-mannose, erythritol, and xylitol—against representative oral bacteria and yeast in a standardized in vitro screen.

Methods

- Four organisms—*Streptococcus mutans* (ATCC 25175), *Streptococcus anginosus* (ATCC 700231), *Candida albicans* (ATCC 18804), and *Fusobacterium nucleatum* (ATCC 23726)—were grown in species-appropriate media supplemented with each polyol at 0–20% w/v (0, 1, 2, 5, 10, 20%).
- Overnight cultures were diluted 1:100 into polyol-amended media, incubated under organism-specific conditions, and endpoint optical density (OD600) was recorded at ~24 h.
- One-way ANOVA was performed for each organism and concentration. Tukey's honestly significant difference (HSD) post hoc test was used to identify pairwise differences among polyols. A two-tailed significance threshold of $p < 0.05$ was used.

Disclosures

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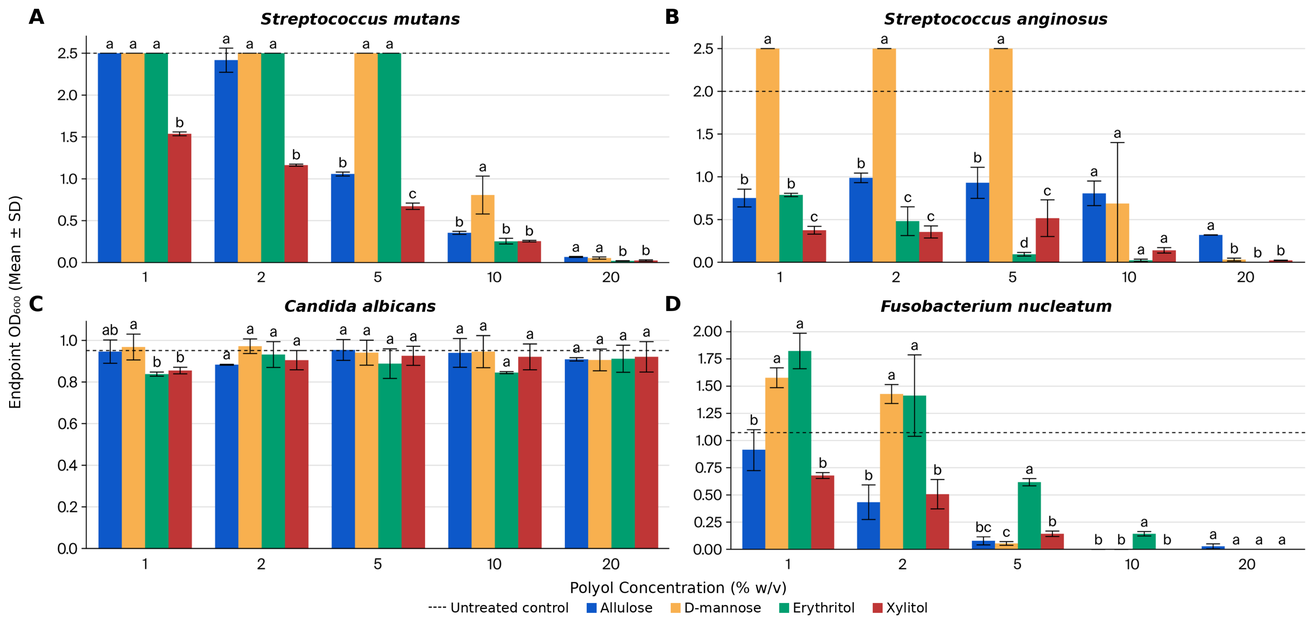
Results

Figure 1. Concentration–response profiles for four oral microorganisms exposed to polyols at 0–20% w/v



Different letters within a concentration indicate Tukey's HSD groupings ($p < 0.05$). Data are reported as mean ± SD (n = 3), normalized to untreated controls.

- *S. mutans* — All four polyols produced concentration-dependent inhibition. Xylitol was uniquely active at low concentrations, significantly separating from all other polyols at 1–2% (61% and 47% of control, respectively), while allulose, D-mannose, and erythritol remained at or near control levels. Allulose showed inhibition beginning at 5% (42% of control), occupying an intermediate position between the D-mannose/erythritol cluster and xylitol. At 10%, D-mannose remained significantly higher than the other three polyols (32% vs. 10–14% of control). By 20%, erythritol and xylitol achieved the lowest growth (≤1% of control), significantly below allulose and D-mannose.
- *S. anginosus* — Erythritol and xylitol were strongly inhibitory across the full range, with erythritol achieving complete suppression at 20% (0% of control). D-mannose displayed a biphasic response: growth above control at 1–5% (125%), followed by strong inhibition at ≥10%. Tukey's HSD confirmed that D-mannose was significantly higher than all other polyols at 1–5%. At 20%, allulose (16% of control) was significantly higher than D-mannose, erythritol, and xylitol, which converged near zero. No pairwise contrasts remained significant at 10% after correction.
- *C. albicans* — Minimal effects across all polyols and concentrations (88–102% of control). No consistent dose-response pattern. ANOVA was significant only at 1%, where Tukey's HSD identified differences between D-mannose and both erythritol and xylitol, but not among other pairs.
- *F. nucleatum* — The most sensitive organism. Allulose and xylitol were significantly more inhibitory than D-mannose and erythritol at 1–2%. At 5%, erythritol (58% of control) remained significantly higher than allulose, D-mannose, and xylitol, which dropped to ≤13%. At 10%, erythritol was the only polyol with measurable residual growth (13% of control); allulose, D-mannose, and xylitol were uniformly at 0%. Notably, low concentrations of D-mannose and erythritol enhanced growth (up to 170% of control), suggesting species-specific utilization or stress responses. The 5–20% range, which produced the strongest inhibition, overlaps with concentrations found in commercial oral care products (typically 3–25%, with ≥10% considered standard for efficacy).

Conclusion

- Polyols are not functionally interchangeable—growth effects are both polyol- and taxon-specific.
- The high sensitivity of *F. nucleatum*, a bridging periodontal pathogen with systemic disease associations, underscores the potential relevance of polyol-based interventions beyond caries prevention alone.
- D-mannose's biphasic behavior in *S. anginosus* and *F. nucleatum* warrants caution at low doses.
- *C. albicans* resistance suggests these polyols would not disrupt fungal commensals at tested concentrations.

Clinical Relevance

- The organisms tested here have documented systemic relevance: oral streptococci are leading causes of infective endocarditis, Cnm+ *S. mutans* strains have been linked to cerebral microbleeds, the *S. anginosus* group can seed deep-seated abscesses at distant sites, and *F. nucleatum*—the most polyol-sensitive organism in this screen—has been identified in colorectal cancer-associated microbiomes and linked to adverse pregnancy outcomes. These connections are mediated by periodontal inflammatory signaling, episodic bacteremia, and oral–gut microbial translocation.
- Reducing oral pathogen burden through targeted, swallow-safe polyol formulations could plausibly attenuate these pathways, though clinical validation with systemic biomarkers is needed.

Limitations

- This is a planktonic, single-species, endpoint OD screen—it does not capture biofilm architecture, viability, acid production, or in vivo exposure kinetics.
- Next steps include polymicrobial biofilm models, short-exposure time-kill assays, metabolic profiling, assessment of commensal impact, and clinical trials incorporating both oral endpoints and systemic biomarkers (CRP, HbA1c) in at-risk populations.

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