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Short Communication

Targeting the oral microbiome: Delivery of *Lactobacillus paracasei* through orodispersible tablets

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ABSTRACT

With increasing interest in probiotic-based strategies for oral health, *Lactobacillus paracasei* (*L. paracasei*) has emerged as a potent candidate for controlling oral dysbiosis. Recent pre-clinical and clinical evidences support the use of *L. paracasei*, particularly in the context of its delivery through orodispersible tablets (ODTs). Studies consistently report reductions in *Streptococcus mutans*, improvements in gingival health, and suppression of plaque regrowth with *L. paracasei*-based interventions. As a user-friendly and targeted delivery platform, ODTs ensure direct mucosal contact and improved patient compliance, especially in pediatric and geriatric populations. This short communication highlights the mechanisms, benefits, and prospects of ODT-based delivery of *L. paracasei* in oral care.

Keywords: Dysbiosis, Oral microbiome, Probiotic, Symbiosis

INTRODUCTION

The oral cavity is host to a dynamic microbiota comprising commensal and opportunistic species. Disruption of this microbial equilibrium, oral dysbiosis, is central to the etiology of common dental diseases such as caries and gingivitis. Conventional chemical agents such as fluoride and chlorhexidine have long served as preventive tools, but growing concern over side effects and microbial resistance has prompted interest in biologically compatible alternatives like probiotics.[1]

Among oral probiotics, *Lactobacillus paracasei* (*L. paracasei*) stands out due to its robust anti-cariogenic and anti-inflammatory properties.[2] Clinical studies suggest that it can reduce *Streptococcus mutans* levels, modulate plaque formation, and improve gingival outcomes.[2-6] Despite promising effects, the efficacy of probiotics in oral care is often limited by formulation stability and delivery efficiency.[7] Orodispersible tablets (ODTs) present a novel solution, ensuring immediate mucosal contact, stability without refrigeration, and ease of use across age groups.[8]

MECHANISM OF ACTION OF *L. PARACASEI* IN ORO-DENTAL CONDITIONS

L. paracasei is a lactic acid bacterium capable of surviving the oral environment and competitively inhibiting cariogenic pathogens.[2] The multifaceted mechanism of *L. paracasei* – including co-aggregation with pathogens, antimicrobial activity, and immunomodulatory effects – is illustrated in Figure 1.

Table 1: Clinical evidence supporting *Lactobacillus paracasei* efficacy in oro-dental conditions.

Study	Population studied	Intervention and duration of treatment	Key findings
Chuang *et al.*,[2] 2011	Healthy adult volunteers	*Lactobacillus paracasei* GMNL-33 for 2 weeks	• Decrease in *Streptococcus mutans* counts
Srinivasan *et al.*,[5] 2017	Pediatric subjects	*Lactobacillus paracasei* as one one-time application	• Inhibited plaque regrowth up to 45 min post-brushing
Maden *et al.*,[6] 2018	Children (6–12 years)	*Lactobacillus paracasei*+xylitol for 6 weeks	• Decrease in *Streptococcus mutans* from 75% to 20% • Decrease in gingival inflammation

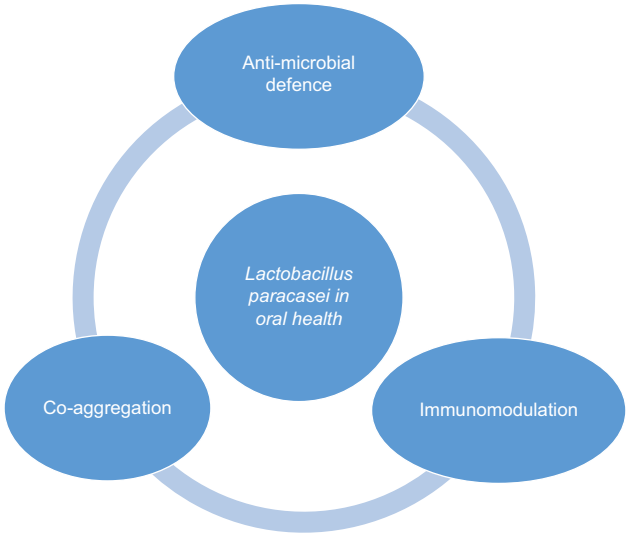

Figure 1: Mechanism of *Lactobacillus paracasei* in oral health.

- Co-aggregation: *L. paracasei* can coaggregate with oral pathogens such as *S. mutans*, disrupting their ability to adhere and form biofilms. This interaction promotes competitive exclusion, limiting pathogen colonization and supporting oral microbial balance.[5,9]
- Anti-microbial defense: *L. paracasei* contributes to microbial homeostasis by producing organic acids such as lactic acid and acetic acid, which would inhibit the growth of strains less tolerant of acid, and bacteriocins (antimicrobial agents) that target and inhibit competing pathogens. This dual action creates an unfavorable environment for aciduric and pathogenic bacteria, suppressing their growth and colonization.[5,10]
- Immunomodulation: *L. paracasei* plays a significant role in regulating host immune responses. It downregulates pro-inflammatory cytokines, thereby reducing local and systemic inflammation. Simultaneously, it promotes the production of secretory immunoglobulin A, a key component of mucosal immunity that helps neutralize pathogens and prevent their adhesion to epithelial surfaces.[5,11]

These properties suggest its utility not only for caries prevention but also for managing gingival and periodontal conditions.

CLINICAL EVIDENCE SUPPORTING *L. PARACASEI* EFFICACY IN ORO-DENTAL CONDITIONS

Chuang *et al.*[2] reported a significant reduction in salivary *S. mutans* levels after 2 weeks of administering *L. paracasei* GMNL-33 in adult volunteers. Notably, the total aerobic flora remained unchanged, indicating a selective antibacterial effect of the probiotic.[2]

In another study, Maden *et al.*[6] evaluated *L. paracasei* and observed a marked decrease in *S. mutans* prevalence – from 75% to 20% – over a 6-week period. A clinical trial by the same group assessed a combination of *L. paracasei* and xylitol in 48 adolescents and found that the probiotic group demonstrated a statistically significant reduction in plaque ($P = 0.001$) and gingival inflammation ($P = 0.001$), compared to xylitol alone and fluoride-only formulations.[6]

Supporting these results, Srinivasan *et al.* demonstrated that *L. paracasei* inhibited plaque regrowth for up to 45 min following use, as measured by spectrophotometric analysis.[5]

To provide a comparative overview, [Table 1] compiles studies focusing on *L. paracasei* and its clinical impact on oral microbiome modulation across diverse populations.

INTRODUCTION OF ODT

While traditional delivery formats such as toothpastes have been explored for administering probiotics in the oral cavity,[12] these approaches face notable limitations, including imprecise dosing and limited residence time.[13] In contrast, ODTs offer a promising formulation strategy for delivering probiotic bacteria directly to the oral cavity. ODTs are well accepted by patients and rapidly disperse upon contact with saliva, typically within seconds, before being swallowed. This delivery method not only improves patient compliance but also prolongs the adhesion of probiotics to the oral mucosa.[14]

RATIONALE OF ODTs FOR DELIVERY OF ORAL PROBIOTICS

1. Improved stability and shelf-life: ODTs can be engineered to enhance the viability of probiotic strains by protecting them from moisture, heat, and lingual lipases.[15]
2. Convenient administration: ODTs rapidly disintegrate in the mouth without the need for water, enhancing ease of use among children and elderly individuals.[16]
3. Targeted oral effects: By dissolving in the oral cavity, ODTs allow for localized probiotic action – especially beneficial in preventing or managing oral dysbiosis, halitosis, gingivitis, and dental caries.[12]
4. Dairy-free and allergen-free alternative: Unlike fermented dairy products (e.g., yogurts), ODTs provide a lactose-free and allergen-minimized platform, making them suitable for individuals with lactose intolerance or milk protein allergies.[15]
5. Precise and standardized dosing: ODTs enable accurate dosing of specific probiotic strains, which are more difficult to ensure with food-based delivery vehicles due to batch variability and storage conditions.[17]

LIMITATIONS AND CONSIDERATIONS IN THE DEVELOPMENT OF ODTs FOR ORAL PROBIOTIC DELIVERY

Despite their advantages, ODTs present formulation challenges:

1. Survival of viable strains: Exposure to heat and moisture during processing must be controlled.[18]
2. Taste masking: The characteristic taste of probiotic lysates or supernatants may necessitate flavoring agents.[16,19]
3. Moisture sensitivity and packaging constraints: Probiotic ODTs are highly sensitive to humidity, requiring specialized packaging (e.g., alu-alu blisters, desiccants) to maintain stability and viability over shelf life.[19]

POTENTIAL SAFETY CONSIDERATIONS IN LONG-TERM USE

While *L. paracasei* is generally safe and well-tolerated, long-term use of probiotic ODTs may require consideration in specific populations.[7] Potential concerns – though uncommon – include minor shifts in oral microbiota, acid exposure to enamel, and hypersensitivity to excipients.[2,7,13] These are mostly theoretical and rare, with current evidence supporting a favorable safety profile. Nonetheless, long-term studies are warranted to validate sustained use across broader demographics.[12]

An emerging solution is the use of postbiotics – non-viable microbial products with retained functionality. These offer improved shelf-life and regulatory acceptance for functional oral products.[20]

FUTURE PERSPECTIVES AND DIRECTIONS

The integration of *L. paracasei* into ODTs represents a promising innovation in managing oral dysbiosis.

Potential future directions include:

1. Multi-strain formulations
   - Combining *L. paracasei* with other complementary probiotics to enhance synergistic effects on oral microbial balance.
2. Time-release ODTs
   - Developing sustained or controlled-release ODTs that extend probiotic contact time with the oral mucosa for prolonged action.
3. Personalized oral probiotics
   - Customizing probiotic combinations based on individual oral microbiome profiles, potentially identified through saliva testing, to offer targeted therapy.
4. Postbiotic integration
   - Exploring non-viable microbial metabolites (Postbiotics) as an alternative or supplement to live strains for improved shelf stability and regulatory ease.
5. Robust clinical validation
   - Conducting long-term, well-powered clinical trials to determine:
     - Optimal dosage and frequency
     - Long-term colonization potential
     - Effectiveness in diverse populations (children, the elderly, and immunocompromised)
     - Comparative effectiveness against conventional oral care agents.

CONCLUSION

L. paracasei has demonstrated consistent efficacy in reducing *S. mutans* levels, controlling plaque regrowth, and improving gingival health. When delivered through ODTs, it combines targeted action with convenience and compliance. This format holds great promise as an adjunct to conventional oral hygiene regimens, especially in populations with limited brushing efficacy or high caries risk. The development of *L. paracasei*-based ODTs is thus a significant step toward oral dysbiosis.

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