

Probiotics in oral health and disease: a systematic review

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Table S5 - Characteristics of clinical trials of probiotics in periodontal diseases

Reference Oral condition	Parameters evaluated - Evaluation time	Study design - Groups of study	Sample size (at the end of the study)- Age or age group	Vehicle - Administration time	Probiotic strain(s) used (Dose)
Butera <i>et al.</i>, 2021 Periodontitis	Clinical: PD, CAL, BOP, GI, PI, AG, RG / Microbiological (subgingival samples) - baseline, 3 and 6 months	RCT parallel, controlled, single-blind Group 1 (control): SRP + Chlorhexidine-based toothpaste Group 2: SRP + probiotics-based toothpaste Group 3: SRP + probiotics-based toothpaste and chewing-gum	60 patients with periodontitis stage II-III - 18-70 years	Chewing-gum (20 min per day, the last 10 days of each month) and toothpaste – 6 months (twice a day)	<i>Bifidobacterium</i> and <i>Lactobacillus</i> in toothpaste ; <i>L. reuteri</i> (SGL 01), <i>L. salivarius</i> (SGL 03), <i>L. plantarum</i> (SGL 07) in chewing-gum
Laleman <i>et al.</i>, 2020 Chronic periodontitis	Clinical: PD, CAL, BOP, PI, RG /Microbiological (saliva, dental plaque, tongue, subgingival samples) - baseline, 12, 24 weeks	RCT placebo-controlled, double-blind 1 st step: SRP + 5 Probiotic drop - Probiotic group and Placebo group	39 patients treated for chronic periodontitis, with residuals pockets - media 58+/-12-13 years	Drop (5) and lozenges - 12 weeks (twice a day)	<i>Lactobacillus reuteri</i> ATCC PTA 5289 and DSM 17938 (2 x 10 ⁸ CFU)
Ikram <i>et al.</i>, 2019 Chronic periodontitis	Clinical: PI, BOP, CAL, PD - baseline, 6 and 12 weeks	RCT - Group A: SRP + ATB (amoxicillin 500mg + metronidazole 400mg 3 times a day for 7 days) / Group B: SRP + Probiotic	30 healthy patients with generalized chronic periodontitis – mean age> 30 years	Brushing with powder mixed with water - 3 months (twice a day)	<i>Lactobacillus reuteri</i> (1.2 x 10 ⁹ CFU)
Yuki <i>et al.</i>, 2019 Periodontitis	Clinical: PD, GI, PMA - baseline, 45, 90, 120 days	RCT placebo controlled, double-blind - Probiotic group: <i>L. rhamnosus L8020</i> (+ <i>S. thermophilus</i>); pH 4.35 and Placebo group: <i>L. bulgaricus</i> (+ <i>S. thermophilus</i>) (1.5 × 10 ⁹ acid lactic bacteria); pH 4.37	23 patients with intellectual disability - 20-45 years	Yogurt 80g (once a day) - 90 days	<i>Lactobacillus rhamnosus L8020</i> (+ <i>Streptococcus thermophilus</i>) (1.5 × 10 ⁹ acid lactic bacteria + 2.0 × 10 ⁷ CFU L8020/gr)
Boyeena <i>et al.</i>, 2019 Chronic periodontitis	Clinical: PI, BOP, PD - baseline, day 45	RCT parallel - Group A: SRP + probiotics/Group B: SRP + tetracycline fibers (10mg mixed with 0.2mL of saline)/Group C: SRP + tetracycline fibers (10mg) + probiotics (0.04mg)	30 patients with chronic periodontitis - 20-50 years	Subgingival – 1time application	<i>Lactobacillus acidophilus</i> , <i>Lactobacillus rhamnosus</i> 0.6 x 10 ⁹ CFU each, <i>Bifidobacterium bifidus</i> , <i>Bifidobacterium longum</i> 0.60 x 10 ⁶ CFU mixed with tragacanth gum (TG) powder (0.04 mg of probiotic powder* mixed with 0.02 mg of TG powder + 0.2 ml of saline)
Grusovin <i>et al.</i>, 2019 Periodontitis stages III and IV, grade C (TPS)	Clinical: PD, BOP, CAL - baseline, 3, 6, 9 and 12 months	RCT placebo-controlled, double-blind 3 months of probiotics/ 3 months of wash- out/3months of probiotics/3 months of wash-out (12 months) - Probiotic group and Placebo group + SRP	20 patients with periodontitis stages III-IV, grade C, treated - 31-70 years	Lozenges – 3 months (twice a day)	<i>Lactibacillus. reuteri</i> DSM 17938 and PTA 5389
Murugesan <i>et al.</i>, 2018 Aggressive periodontitis	Clinical: OHI-S, GI, BOP, PD, CAL - baseline, 4, 8, 12 weeks	RCT placebo-controlled, double-blind - Test group: SRP + ATB + symbiotic / Control group: SRP + ATB + placebo Note: ATB = doxycycline 100mg 2x / day on the 1st day followed by 100mg 1x / day for 1 week	60 patients with aggressive periodontitis - 18-30 years	Lozenges - 8 weeks (twice a day)	<i>Clostridium butiricum</i> TO-A (2 x 10 ⁶), <i>Bacillus mesentericus</i> TO-A JPC (1 x 10 ⁶), <i>Lactobacillus sporogenes</i> (50 x 10 ⁶), prebiotic <i>Streptococcus faecalis</i> T-110 JPC (30x10 ⁶ CFU)
Invernici <i>et al.</i>, 2018 Chronic periodontitis	Clinical: PI, BOP, PD, CAL, RG/ Immunological: IL-1, IL-10, IL-8 levels in GCF/Microbiological (subgingival plaque samples in moderate 4-6mm and deep pockets >7mm: evaluation of 40 subgingival bacterial species) - baseline, 30, 90 days	RCT placebo-controlled - Test group: SRP + probiotic / Control group: SRP + placebo	41 healthy patients with generalized chronic periodontitis - > 30 years	Lozenges - 30 days (twice a day)	<i>Bifidobacterium animalis subsp. lactis</i> HN019 (10 ⁹ CFU)
Sajedinejad <i>et al.</i>, 2018 Chronic periodontitis	Clinical: PI, GI, BOP, PD - baseline, 14, 28 days	RCT placebo-controlled, double-blind - Test group: SRP + probiotic / Control group: SRP + placebo	40 healthy patients with moderate to severe chronic periodontitis (PD ≥4 mm, CAL ≥3 mm, bone loss ≥3 mm) - 24-52 years	Mouthwash 20mL - 28 days (twice a day)	<i>Lactobacillus salivarius</i> NK02 (10 ⁸ CFU)

Morales <i>et al.</i>, 2018 Chronic periodontitis	Clinical: CAL, BOP, PI/ Microbiological (subgingival plaque samples on 4 periodontal sites (1 in each quadrant) with CAL> 1mm, PD> 4mm and BOP) - baseline, 3, 6 and 9 months	RCT controlled, double-blind - Antibiotic group (azithromycin 500mg once a day for 5 days) / Placebo group / Probiotic group	47 healthy patients with chronic periodontitis - > 35 years	Tablet - 3 months (once a day)	<i>Lactobacillus rhamnosus</i> SP1 (2 x 10 ⁷ CFU)
Chandra <i>et al.</i>, 2016 Chronic periodontitis	Clinical: PD, CAL, PI, GI / Viability of probiotic in pocket (days 0, 2, 4, 7, 14) - baseline, 1 week, 3 and 6 months	RCT placebo-controlled - Test group: SRP + probiotic (1 st site) / Control group: SRP + placebo (2 nd site)	30 patients with chronic periodontitis at least 2 PD pockets> 5mm and at least 1 pocket in each quadrant - 25-50 years	Power 1g blend - N/A	<i>Saccharomyces boulardii</i> (5 x 10 ⁹ CFU) with fructooligosaccharide prebiotic
Penala <i>et al.</i>, 2016 Chronic periodontitis and halitosis	Clinical: halitosis (ORG), PI, GI, BOP, PD, CAL, CAG/ Microbiological (subgingival samples)/Biochemical: BANA – baseline, 1 and 3 months (PD, CAL only at baseline and 3 months)	RCT placebo-controlled, double-blind - Test group: SRP + probiotic / Control group: SRP + placebo	29 healthy patients with chronic periodontitis at least 4 teeth with PD ≥ 5 mm, CAL ≥ 4 mm, and clinically perceptible halitosis - 25-59 years	Subgingival (after SRP, weeks 1, 2, 4) and mouthwash (14 days, twice a day)	<i>Lactobacillus salivarius</i> , <i>Lactobacillus reuteri</i> (2 x 10 ⁹ CFU each)
Iwasaki <i>et al.</i>, 2016 Chronic periodontitis (SPT)	Clinical: PI, GI, BOP, PD - baseline, 4, 8, 12 weeks	RCT placebo-controlled, double-blind - Probiotic group and Placebo group	36 patients in the SPT phase after chronic periodontitis with one or more initial periodontal pockets≥ 4mm and have completed treatment - mean age 66.2 years	Capsule - 12 weeks (once a day)	<i>Lactobacillus plantarum</i> L-137
Imran <i>et al.</i>, 2015 Chronic periodontitis	Clinical: PI, GI/Microbiological: <i>P. gingivalis</i> , <i>P. intermedia</i> , <i>A. actinomycetacomitans</i> (subgingival samples) - baseline, 1 and 2 months	RCT - Probiotic group and Placebo group	42 healthy patients with chronic periodontitis generalized (slight-moderate) - 20-50 years	Milk - 1 month (once a day)	<i>Lactobacillus casei</i> (6.5 x 10 ⁹ -10 ⁸ CFU/mL)
Ince <i>et al.</i>, 2015 Chronic periodontitis	Clinical: PI, GI, BOP, PD, CAG/ Immunological: levels of MMP-8, TIMP-1 in GCF (in 2 teeth with 8 sites) - baseline, days 21, 90, 180, 360	RCT parallel, placebo-controlled, double-blind - Test group: SRP + probiotic / Control group: SRP + placebo	30 patients with chronic periodontitis, horizontal bone loss detected radiographically and with at least 2 teeth with proximal site, each with PD 5-7mm and GI> 2 in each quadrant - 35-50 years	Lozenges - 3 weeks (twice a day)	<i>Lactobacillus reuteri</i>
Laleman <i>et al.</i>, 2015 Periodontitis	Clinical: PD, BOP, CAL, GI, PI, REC/ Microbiological (supragingival plaque, subgingival, saliva and tongue samples) – baseline 12, 24 weeks	RCT placebo-controlled, double-blind - Test group: SRP + probiotic / Control group: SRP	48 healthy patients with moderate to severe periodontitis - 37-58 years	Tablet - 12 weeks (twice a day)	<i>Streptococcus oralis</i> KJ3, <i>Streptococcus uberis</i> KJ2, <i>Streptococcus rattus</i> JH145
Tekce <i>et al.</i>, 2015 Chronic periodontitis	Clinical: PI, GI, BOP, PD, CAL/ Microbiological (at least 2 teeth with a proximal site with a PD of 5-7 mm and an GI of ≥2 in each quadrant, total counts of viable cells and proportions of anaerobic bacteria) – baseline, days 2, 21, 90, 180, 360	RCT controlled, double-blind - Test group: SRP + probiotic / Control group: SRP + placebo	40 patients with chronic periodontitis with at least two teeth with a proximal site, each with PD 5-7 mm and GI≥2 in each quadrant and horizontal bone loss detected radiographically - 35-50 years	Lozenges - 3 weeks (twice a day)	<i>Lactobacillus reuteri</i>
Szkaradkiewicz <i>et al.</i>, 2014 Chronic periodontitis	Clinical: PI, GI, CAL, PD/ Immunological: levels of TNF-α, IL-1β, IL-17 in GCF – N/A	RCT - Probiotic group and Control group	38 healthy patients with moderate chronic periodontitis - 31-46 years	Tablet - (twice a day)	<i>Lactobacillus reuteri</i> ATCU PTA 5289 (10 ⁸ CFU)

Vicario <i>et al.</i>, 2013 Chronic periodontitis	Clinical: PI, GI, PD 4-5mm, PD> 6mm – baseline, 30 days	RCT placebo-controlled, double-blind - Probiotic group and Placebo group	19 healthy patients with chronic periodontitis slight to moderate - mean age 55 years	Tablet – 30 days (once a day)	<i>Lactobacillus reuteri</i> ATCC 55730 and ATCCPTA 5289 (2 x 10 ⁸ viable cells)
Teughels <i>et al.</i>, 2013 Chronic periodontitis	Clinical: PD, REC, BOP, GI, PI, CAL/ Microbiological (saliva, subgingival and supragingival plaques samples) – baseline, weeks 3, 6, 9, 12	RCT placebo-controlled, double-blind - Test group: SRP + probiotic /Control group: SRP + placebo	30 healthy patients with generalized moderate to severe chronic periodontitis - > 35 years	Lozenges - 12 weeks (once a day)	<i>Lactobacillus reuteri</i> DSM17938 and ATCC PTA5289 (9 x 10 ⁸ CFU each)
Shah <i>et al.</i>, 2013 Aggressive periodontitis	Clinical: PI, GI, PD, CAL/ Microbiological (saliva samples) - baseline, 2 weeks, 2months	RCT - Group A: probiotic /Group B: probiotic + doxycycline 100mg (1x/ day for 14 days) /Group C: doxycycline 100mg 1x / day for 14 days	30 patients with aggressive periodontitis - 14-35 years	Lozenges - 14 days (twice a day)	<i>Lactobacillus brevis</i> CD2 (10 ⁸ CFU)