

Probiotics in oral health and disease: a systematic review

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Table S10 - Characteristics of clinical trials of probiotics in oral wound healing and treatment of oral mucositis related to cancer treatment

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)
Twetman <i>et al.</i>, 2018 Biopsy oral wound	Clinical: healing, pain, VAS scores, need other medication/Immunological (through wound exudate, saliva) - 2, 5 and 8 days	RCT, placebo-controlled, double-blind (pilot study) Run-in (1 week)/ biopsy (standardized wound)/ intervention (8 days)/ washout 4 weeks/ run-in (1 week)/ biopsy (standardized wound)/ intervention (8 days) - Probiotic group and Placebo group	10 healthy adults with normal mucosa - 21-66 years	Lozenge + oil topic drop 2mL - 1 week (twice a day + once a day) before the wound and 8 days after	<i>Lactobacillus reuteri</i> DSM 17938 and ATCC PTA 5289 (5 x 10 ⁸ live bacteria in each lozenge and 2 x 10 ⁸ CFU/mL in each drop)
Twetman <i>et al.</i>, 2018 Biopsy oral wound and MMPs, IFNs	Immunological: levels of MMPs, IFNs in wound exudate - 2, 5 and 8 days	RCT, placebo-controlled, double-blind (pilot study) Run-in (1 week)/ biopsy (standardized wound)/ intervention (8 days)/ washout 4 weeks/ run-in (1 week)/ biopsy (standardized wound)/ intervention (8 days) - Probiotic group and Placebo group	10 healthy adults with normal mucosa - 21-66 years	Lozenge: 1 week (twice a day) before the wound and 8 days after Oil topic drop: 8 days after wound (once a day)	<i>Lactobacillus reuteri</i> DSM 17938 and ATCC PTA 5289 (5 x 10 ⁸ live bacteria in each lozenge and 2 x 10 ⁸ CFU/mL in each drop)
Wälivaara <i>et al.</i>, 2019 Surgical removal of third mandibular molars	<i>Staphylococcus aureus</i> and <i>S.β-hemolytic</i> in wound exudate, pain, swelling, oxytocin salivary - 1, 2 weeks	RCT, placebo controlled, double-blind, parallel - Probiotic group and Placebo group	61 patients - 18-34 years	Lozenges – 2 weeks (3 times a day)	<i>Lactobacillus reuteri</i> DSM 17938 and ATCC PTA 5289 (2 x 10 ⁸ CFU/ml in each drop)
Jiang <i>et al.</i>, 2018 Oral mucositis induced by chemo-radiotherapy	Oral mucositis - baseline, 7 weeks	RCT placebo-controlled, double-blind - Probiotic group and Placebo (starch) group	93 patients with nasopharyngeal carcinoma treated by chemoradiotherapy (70 Gy in 32 fractions: 2,19 Gy/day, 5days/week; with the gross tumor volume and the clinical target volume receiving 60 Gy in 32 fractions for 45 days (total, 6-7 weeks) + cisplatin intravenous 100mg/m ² day 1, 22, 43 - 18-70 years	Capsule – 7 weeks (three times a day)	<i>Bifidobacterium longum</i> , <i>Lactobacillus lactis</i> and others <i>Enterococcus faecium</i>
Limaye <i>et al.</i>, 2013 Oral mucositis induced by chemotherapy	Oral mucositis, vital signs, bacterial and hTFF1 levels in saliva and mucosa, delivery vehicle - cycle 1: every day cycle 2: baseline, day 2, 7 and 14, up to 1 year	RCT placebo-controlled, single blind Cycle 1: QT appearance of oral mucositis (25 subjects) Cycle 2: intervention (22 subjects at the end) - Test group: AG013 once a day/Test group: AG013 times a day/Test group: AG013 6times a day/Control group: placebo	22 patients with newly diagnosed squamous cell LAHNC (QT: cisplatin, 5-FU, with or without docetaxel (PTF or PF) with oral mucositis - mean age 54 years	Mouthwash 15mL – 14 days (1 or 3 or 6 times a day)	<i>Lactococcus lactis</i> (AG013) [2 x 10 ¹¹ CFU / 15mL (<i>i.e.</i> 2 x 10 ¹¹ or 6 x 10 ¹¹ or 1.2 x 10 ¹² CFU / day for each frequency of administration respectively)]
Sharma <i>et al.</i>, 2012 Oral mucositis induced by chemotherapy and radiotherapy	Parameters evaluated: mucositis grade, quality of life, body weight, nutrition - N/A	RCT double-blind - Probiotic group and Placebo group (sugars and salts)	188 patients with radical RT at the dose of 70 Gy (35 fractions) for 7 weeks (5 fractions / week) per linear accelerator / parallel / parallel fields and medullary shield at 44 Gy; QT concomitant with cisplatin (DDP) 40 mg / m ² weekly (7 doses: days 1, 8, 15, 22, 29, 36, 43) from day 1 of the RT treatment - mean age 51 years	Lozenge - During QT/RT and up to 1 week after (6 lozenges per day)	<i>Lactobacillus brevis</i> CD2 (2 x 10 ⁹ CFU)