

# References relevant for probiotic use of *Lactobacillus reuteri*

This clinical study summary document prepared specifically for Dental Professionals

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## References relevant for probiotic use of *Lactobacillus reuteri*

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*Lactobacillus reuteri* Protectis is the human *Lactobacillus reuteri* strain used in BioGaia Probiotics for gut and immune health. BioGaia Probiotics for oral health contains *L. reuteri* Prodentis, which is a blend of two *L. reuteri* strains. Their benefits and safety in use for all ages is supported by the clinical studies summarized below.

To date 55 clinical studies on more than 4,100 individuals have been conducted, and the results are published in 28 articles in scientific journals. Another 13 studies are published as abstracts of presentations at scientific conferences.

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# Oral health

## Short-term effect of chewing gums containing probiotic *Lactobacillus reuteri* on the levels of inflammatory mediators in gingival crevicular fluid.

Twetman S, Derawi B, Keller M, Ekstrand K, Yucel-Lindberg T, Stecksén-Blicks C. (2008) Acta Odontol Scand 67:19-24.

42 healthy adults with moderate gingival inflammation were recruited into a double blind, placebo-controlled randomised study. The aim was to assess the dose-effects of a probiotic chewing gum containing *Lactobacillus reuteri* Prodentis (ATCC 55730 and ATCC PTA 5289,  $1 \times 10^8$  CFU of each strain). Group A/P (n=13) received one active and one placebo chewing gum daily, group A/A received 2 active chewing gums daily and group P/P received 2 placebo chewing gums daily. Study treatment was administered for 2 weeks. The degree of inflammation was assessed both as Bleeding on Probing (BOP) and amount of gingival crevicular fluid (GCF). The GCF was also assessed for concentration of the inflammatory mediators IL-1, TNF- $\alpha$ , IL-6, IL-8 and IL-10. All assessments were carried out on day 0 before treatment, and after 1 and 2 weeks. Follow-up assessment was made at 4 weeks (i.e. 2 weeks after treatment was stopped). The BOP was improved and the GCF volume was decreased in all study groups, but the results were statistically significant only in the two groups (A/P and A/A) receiving *Lactobacillus reuteri* Prodentis. IL-6 and IL-10 remained unaffected during the 2-week treatment period in all groups. However, in the group receiving 2 active chewing gums per day, TNF- $\alpha$  and IL-8 decreased significantly and at 4-week follow up, IL-6 was also significantly decreased.

**Conclusion:** The study provides the first indication of a significant dose-dependent effect of *Lactobacillus reuteri* Prodentis on the oral immune response and the results support previous beneficial clinical results on gingival health.

## Decreased gum bleeding and reduced gingivitis by the probiotic *Lactobacillus reuteri*.

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Krasse P, Carlsson B, Dahl C, Paulsson A, Nilsson Å, Sinkiewicz G. (2006) Swed Dent J. 30:55-60.

A prospective, randomised, placebo-controlled trial to study the effect on gingivitis and dental plaque of a probiotic chewing gum and the occurrence of the probiotic in saliva. The 59 subjects suffering from moderate to severe gingivitis were randomly assigned to one of three different chewing gums, containing one of two *L. reuteri* strains, LR-1 and LR-2, respectively, or a placebo gum. On Day 0 the dentist cleaned all surfaces and the patients were instructed regarding daily oral hygiene and to use the chewing gum twice daily after brushing their teeth. After 14 days the subjects visited the dentist for outcome assessments. Gingival index fell significantly in all groups. *L. reuteri* group 1, but not group 2, improved significantly more than placebo ( $p < 0.0001$ ). Plaque index fell significantly in both *L. reuteri* groups between day 0 and 14 while there was no significant change in the placebo group. Both probiotic strains colonized the saliva, LR-1 in 65% of the patients and LR-2 in 95% of the subjects.

**Conclusion:** *L. reuteri* was efficacious in reducing both gingivitis and dental plaque in patients with moderate to severe gingivitis.

## A probiotic lozenge administered medical device and its effect on salivary mutans streptococci and lactobacilli.

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Çaglar E, Kuscu OO, Kavaloglu SC, Kuvvetli SS, Sandalli N. (2008) Int J Pediatr Dent. 18:35-39.

This was a randomised, double blind placebo-controlled clinical study involving 20 women with high counts of salivary mutans streptococci, but otherwise healthy. During the study course over 10 days, the subjects either received one lozenge daily containing either  $10^8$  CFU of *Lactobacillus reuteri* Prodentis (n=10) or the corresponding placebo lozenge (n=10). Both study treatments were administered via a medical device, which released the contents of the lozenge over a 15-minute period. Salivary samples were collected immediately before treatment and then again after 10 days. The samples were analysed for load of mutans streptococci and lactobacilli. Counts of lactobacilli remained unchanged in both groups during the study period. However, mutans streptococci load was significantly decreased in the group receiving *Lactobacillus reuteri* Prodentis but not in the placebo group. The decrease was significant both versus the initial load and against the placebo group.

**Conclusion:** The probiotic lozenge containing *Lactobacillus reuteri* Prodentis significantly reduced salivary mutans streptococci.

## Effect of chewing gums containing xylitol or probiotic bacteria on salivary mutans streptococci and lactobacilli.

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Çaglar E, Kavaloglu SC, Kuscu OO, Sandalli N, Holgerson PL, Twetman S. (2007) Clin Oral Invest. 11:425-429.

This was a prospective, randomised placebo-controlled study aiming to evaluate the effect of xylitol and probiotics on salivary bacilli. 80 healthy young adults aged 21-24 years of age were included and divided into 4 groups (4x20). The study products were: One probiotic chewing gum containing  $1 \times 10^8$  CFU of *Lactobacillus reuteri* Prodentis per piece three times daily (Group A); 2 pieces of xylitol chewing gum three times daily (Group B); 2 xylitol gums in the morning + 2 probiotic chewing gums mid-day + 2 xylitol chewing gums in the evening (Group C) and; 3 placebo chewing gums per day. Dosing continued for three weeks and salivary samples for *Streptococcus mutans* and lactobacilli assessment were collected on day 0 before treatment start and again after three weeks. There were no differences between the groups before and after treatment regarding lactobacilli load. For Groups C and D there were no changes in strep mutans score before and after treatment. However, the strep mutans score was significantly improved in both Group A and B.

**Conclusion:** The results suggest that a three-week consumption of either 3 *L. reuteri* Prodentis chewing gums or 6 xylitol chewing gums can reduce the load of mutans streptococci.

## Salivary mutans streptococci and lactobacilli levels after ingestion of the probiotic bacterium *Lactobacillus reuteri* ATCC 55730 by straws or tablets.

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Caglar E, Cildir SK, Ergeneli S, Sandalli N, Twetman S. (2006) Acta Odontol Scand 64:314-318.

A prospective, randomised, placebo-controlled study with the aim to investigate the effect on mutans streptococci and lactobacilli of a probiotic delivered by two non-dairy delivery systems. The study included 120 young adults (21-24 years) with overall good health, including the oral cavity status. The study used parallel arms where the subjects were randomly assigned to four equally sized groups (n=30): group A drank 200 ml of water through a prepared straw containing *Lactobacillus reuteri* once daily for 3 weeks, while group B took 200 ml of water through a placebo straw during the same period. Group C was given one tablet containing the same probiotic once daily for 3 weeks, while group D received placebo tablets without bacteria. Salivary mutans streptococci and lactobacilli were enumerated with chair-side kits at baseline and 1 day after the final ingestion. A statistically significant reduction of the mutans streptococci levels was recorded after ingestion of the probiotic bacteria via the straw and the tablet, compared to the placebo controls. A similar but non-significant trend was seen for lactobacilli.

**Conclusion:** A short-term daily ingestion of *Lactobacillus reuteri* delivered by drinking straw or tablets reduced the levels of salivary mutans streptococci in young adults.

## Lactobacillus reuteri in fermented bovine milk decreases the oral carriage of mutans streptococci.

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Nikawa H, Makihira S, Fukushima H, Nishimura H, Ozaki Y, Ishida K, Darmawan S, Hamada T, Hara K, Matsumoto A, Takemoto T, Objectivei R. (2004) Int J Food Microbiol 95:219-223.

A study in several parts beginning with the effect of different probiotics on the growth of Streptococcus mutans (a bacterium correlated with the risk of caries). A laboratory screening of probiotic bacteria isolated from 18 different fermented dairy products available in Japan showed that L. reuteri was the only strain that inhibited the growth of S. mutans. A further laboratory study verified that L. reuteri had no harmful effect on dental enamel. A clinical study was also performed in which 40 subjects with healthy mouths took part. Half of them ingested 95 g daily of yoghurt containing L. reuteri with their lunch, while half ingested the same quantity of a placebo yoghurt. After 2 weeks the groups changed the study product and the subjects thus served as their own controls. Both groups showed a significant decrease in the number of S. mutans in the saliva during the 2-week period when ingesting L. reuteri. The group which started with L. reuteri yoghurt, also showed a significantly inhibiting effect on S. mutans in the two subsequent weeks when ingesting the placebo yoghurt.

**Conclusion:** The daily ingestion of yoghurt containing L. reuteri for a period of two weeks significantly reduced the number of Streptococcus mutans in the saliva of healthy subjects. This effect was consistent also for at least two weeks after ending the intake of the probiotic yoghurt. L. reuteri was the only bacterium in a laboratory screening test of probiotic bacteria from 18 fermented milk products that showed inhibition of S. mutans.