

References for *Lactobacillus reuteri* ATCC 55730

Other names for this *L. reuteri* strain in the scientific literature are SD2112, ING1 and MM53. The commercial name is *L. reuteri* *Protectis*.

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***Lactobacillus reuteri*: natural colonisation in humans**

Occurrence of *Lactobacillus reuteri*, lactobacilli and bifidobacteria in human breast milk.

Sinkiewicz G, Nordström EA. (2005) Presented at the Annual Meeting of the ESPR, European Society for Pediatric Research, Siena, Italy, 31 Aug.–3 Sep., 2005. *Pediatr Res* **58**:415, abstract 353.

This study investigated the occurrence of lactobacilli, *Lactobacillus reuteri* and bifidobacteria in milk from lactating mothers in different countries. Samples were collected from 226 women living in urban or rural areas in Sweden, Denmark, Israel, South Africa, South Korea, Japan and Peru. The isolation rates varied from 50% *L. reuteri* positive samples from rural areas in Japan and Sweden to negative samples from urban areas in Peru, Denmark and Israel. Overall, 12% of the mothers had detectable counts of *L. reuteri*. 50% of samples from rural areas in Israel, Japan and Korea had positive total lactobacilli levels. Urban samples from Israel, Peru and Denmark contained about 20% positive total lactobacilli counts. Bifidobacteria were detected in 100% of the samples from rural areas in Japan and 79% of rural samples in Korea, whilst mothers from rural areas in Denmark, Peru and Sweden had low or non-detectable levels. **Conclusion:** breast milk microbiota varies between different countries and parts of the world. Breast milk from rural areas contains more lactic acid bacteria than milk from urban areas.

The *Lactobacillus* and *Bifidobacterium* microflora of the human intestine: composition and succession. Reuter G. (2001) *Curr Issues Intest Microbiol* **2**:43-53.

An article describing how *L. reuteri* has been isolated in living form from every part of the digestive tract: the oral cavity, the stomach, the small intestine and the colon and from stool samples. *L. reuteri* has also been isolated from the vagina. Professor Reuter also puts forward evidence that *L. reuteri* is a bacterium that belongs to the indigenous intestinal flora, i.e. has the digestive tract as its natural ecological niche and

establishes itself naturally in the newborn child. Only a few other probiotic bacteria can be described as belonging to the natural, indigenous intestinal flora.

Clinical studies in children: colonisation in infants

Intestinal microbiota in infants supplemented with the probiotic bacterium *Lactobacillus reuteri*. Abrahamsson T, Jakobsson T, Sinkiewicz G, Fredriksson M, Björkstén B (2005) Presented at the 38th ESPGHAN Annual Meeting, 1-5 June, 2005 in Porto, Portugal. Abstract PN1-17. J Ped Gastroenterol Nutr 40(5):692.

As part of a prospective study of decreasing the risk of allergy during the first years of life, the colonisation rate of *Lactobacillus reuteri* ATCC 55730 in the enrolled infants was also investigated. 232 mothers and their infants were recruited to the main study. The mothers were randomised to take *Lactobacillus reuteri* (1×10^8 CFU, in an oil suspension) or placebo during 4 weeks before delivery. After delivery their babies continued taking the supplement in the same dose up to 12 months of age. At day 5-6 80% of the infants were colonised in the *L. reuteri* group compared to 19% in the placebo group, measured as live cells in the stools. At 12 months of age 63% and 23% of the infants, reuteri vs. placebo, respectively, were colonised. *L. reuteri* was found in 12% and 2% of the

L. reuteri vs. placebo group, respectively, of the samples of the first expressed breast milk (colostrum).

Conclusion: the gastrointestinal tracts of infants from birth up to one year of age, were colonised in a high degree by *Lactobacillus reuteri* ATCC 55730 after long term supplementation with Reuteri Drops.

Clinical studies in children: decreased risk of common infections

Effect of a probiotic infant formula on infections in child care centers: Comparison of two probiotic agents. Weizman Z, Asli G, Alsheikh A. (2005) Pediatrics 115:5-9.

This is a prospective, randomized, double blind, placebo-controlled study, aimed at investigating whether probiotics affect the occurrence of infections in infants in day care. 194 healthy children, aged 4–10 months, were studied for 12 weeks in three different groups: They were given formula with *L. reuteri* ATCC 55730 or *Bifidobacterium lactis* Bb-12, or formula without probiotics (placebo control). Probiotics resulted in significantly fewer infections compared with placebo, as measured by the number of febrile episodes and episodes of gastrointestinal infection. *L. reuteri*, however, had a superior effect compared with *B. lactis*. Only the children receiving *L. reuteri* needed significantly fewer doctors' visits, less antibiotics, and spent fewer days away from day care.

Feeding of a probiotic for the prevention of community-acquired diarrhea in young Mexican children. Ruiz-Palacios G, Guerrero ML, Hilty M. (1996) Pediatr Res 39(4) part 2:184A, abstract 1089.

A prospective, randomized, double blind and placebo-controlled study of 258 healthy children aged 12–36 months living in Mexico City. The aim was to study the preventive effect of probiotics in relation to diarrhoeal disease of different causes. For 4 months the children took a daily drink of a probiotic mixture containing 5×10^7 CFU (colony forming units) of *L. reuteri* per day, or a placebo drink. In the *L. reuteri*-group, 90/119 children (76%) were entirely free of diarrhoeal disease, which differed significantly from the control group, in which 77/120 children (64%) escaped diarrhoeal disease.

Effect of probiotic-containing beverages on incidence of diarrhoea. Guerrero M, Dohnalek M, Newton P, Kuznetsova O, Ruiz-Palacios G, Murphy T, Calva J, Hilty M, Costigan T. 1st World Congress of Pediatric Infectious Diseases, Dec. 1996, abstract no. 610:45-2.

A prospective, double blind, randomised, placebo-controlled study investigating the effect of the daily intake of two different drinks with probiotics on the incidence of diarrhoea in healthy children. They were 12–32 months old, and living in Mexico City. The daily intake for 16 weeks of either drink containing probiotics reduced the number of diarrhoeal episodes compared with the effect of a placebo drink: in the *L. reuteri* group 92/129 children (71%) were completely free of diarrhoea, in the group with the other probiotic drink 88/129 (68%) were free of diarrhoea, while the result for the control group was 80/130 children (61%). The number of diarrhoeal episodes was significantly lower in the *L. reuteri* group (44 episodes, $p=0.04$ compared with placebo) than in the group taking other probiotics (47 episodes, $p=0.135$ compared with placebo) and the placebo group, which had 62 episodes.

Clinical studies in children: gastrointestinal disorders

***Lactobacillus reuteri* ATCC 55730 versus simeticone in the treatment of infantile colic: a prospective randomised study.** Savino F, Palumeri E, Pelle E, Castagno E, Oggero R, Miniero R. (2005) Presented at the Annual Meeting of the ESPR European Society for Pediatric Research, Siena, Italy, 31 Aug.–3 Sep., 2005. *Ped Res* **58**:411, abstract 328.

Prospective, randomised study with the objective to investigate the efficacy and side effects profile of the probiotic *Lactobacillus reuteri* ATCC 55730 in the treatment of infantile colic. 49 breastfed infants, aged 21 to 90 days, and with confirmed infantile colic, were randomly assigned to two treatments: P – *Lactobacillus reuteri*, 10^8 CFU daily and administered in an oil suspension, or S – simeticone, 6 mg/kg daily. 46 infants completed the study. Baseline average daily crying time was the same in the two groups: 210 minutes for the P group and 208 minutes for the S group. After 7 days crying time was significantly reduced in the P group, 140 min/day, vs 172 min/day in the S group ($P=0.025$). By day 28 the crying time in the Reuteri group was reduced to only 20 min/day vs 156 min/day in the simeticone group ($P < 0.005$). No side effects were observed in either group. Conclusion: The intake of *L. reuteri* resulted in significantly less crying time within one week of treatment compared to standard therapy in these infants. This effect was even more pronounced at the end of this 4-week study.

The effect of oral administration of *Lactobacillus reuteri* on antibiotic-associated gastrointestinal side-effects during *Helicobacter pylori* eradication therapy. Lionetti E et al. (2005) Proceedings of the 3rd Conference on Probiotics, Prebiotics & New Foods, 4-6 Sep. 2005, Rome, Italy and of the 12th National Congress of Italian Society of Paediatric Gastroenterology, 22-24 Sep. 2005, Milan, Italy.

A double blind, randomised and placebo-controlled study investigating the effect of *Lactobacillus reuteri* ATCC 55730 on gastrointestinal side-effects during and after anti-*Helicobacter pylori* treatment. Twentyfive dyspeptic children, aged 3-16 years, with confirmed *H. pylori* infection were enrolled. They were treated with 10-day sequential antibiotic treatment and randomised to receive either *L. reuteri* (10^8 CFU/day) or placebo for 20 days, starting from the first day of treatment. The severity of side effects was measured using a validated scoring system (GSRS score). At entry, children in both groups had similar GSRS scores but during eradication therapy and follow-up, the *L. reuteri*-supplemented children had significantly improved gastrointestinal health compared to the placebo group. The rates of *H. pylori* eradication were the same in the two groups. Conclusion: *L. reuteri* supplementation during and after *H. pylori* eradication therapy significantly reduced the frequency and intensity of antibiotic-associated side effects.

***Lactobacillus reuteri* as a therapeutic agent in acute diarrhea in young children.** Shornikova AV, Casas IA, Isolauri E, Mykkänen N, Vesikari T. (1997) *J Pediatr Gastroenterol Nutr* 24:399-404.

A prospective, randomized and placebo-controlled study of 40 children, aged 6–36 months, who were hospitalised due to acute diarrhoea (caused by rotavirus in 75%). The children receiving active treatment were given *L. reuteri* in a daily dose of 10^{10} – 10^{11} CFU for up to 5 days. A significant effect was apparent from the second day of treatment, when 74% of the children in the active group were free of watery diarrhoea, as opposed to only 19% of the children in the control group.

Bacteriotherapy with *Lactobacillus reuteri* in rotavirus gastroenteritis.

Shornikova AV, Casas IA, Mykkänen N, Salo E, Vesikari T. (1997) *Pediatr Infect Dis J* 16:1103-1107.

A prospective, randomized and placebo-controlled study of 66 children, aged 6–36 months, who were hospitalised due to acute diarrhoea caused by rotavirus. The children were divided into three groups: placebo or *L. reuteri* in a daily dose of 10^7 or 10^{10} CFU for up to five days. From the second day of treatment, 30% of the children given the lower *L. reuteri* dose were free of watery diarrhoea, compared with 52% of the children given the higher dose. The difference was significant for the high-dose *L. reuteri* group compared with the control group, in which 20% of the children no longer had watery diarrhoea. The high-dose group also had a significantly shorter period of watery diarrhoea: 1.5 days on average compared with the 2.5 days of the control group. For the low dose group the mean duration of watery diarrhoea was 1.9 days.

Clinical studies in children: effects on the immune system

Effectiveness of *L. reuteri* in patients with atopic dermatitis and cow milk intolerance. Preliminary study. Cirillo Al., Boccia E, Cirillo Ar., Scotto G, Maiella D, De Crescenzo G, Leone G, Grimaldi S, Cirillo Ag. (2005, abstract). Presented at the Italian Society for Clinical Allergy and Immunology (SIAIC) Congress, Rome, Italy, 4-7 May 2005. Abstract P-08.

A prospective pilot study of children with mild atopic dermatitis aggravated by the intake of cow's milk. Fifteen children, 3-5 years old, were enrolled. They all had a clinical history of atopic dermatitis improvement after removal of cow's milk from the diet. The existence of allergy to cow's milk proteins was excluded by analyses of specific IgE against milk proteins and skin prick test. The children were re-challenged with cow's milk whilst also receiving *L. reuteri* ATCC 55730 (2 tablets daily = 2×10^8 CFU), or no probiotic. During the first two weeks after challenge, where antihistamines and steroids were used, all patients had ameliorated eczema. However, in the follow up period of 3 months, during which *L. reuteri* was given, all children in the *L. reuteri* group (n=8) showed no relapse to eczema despite continued intake of milk. In the control group (n = 7), all children showed a relapse to eczema. These children also used more antihistamines and steroids than the *L. reuteri* group. Conclusion: The daily intake of *L. reuteri* during concomitant intake of cow's milk for three months could prevent the relapse of atopic eczema and itching in children where cow's milk previously had been shown to worsen their atopic eczema.

Clinical studies in children: safety aspects

Safety of D(-)-lactic acid producing bacteria in the human infant. Connolly E, Abrahamsson T, Björkstén B. (2005) *J Pediatr Gastroenterol Nutr* 41:489-492.

Lactobacillus reuteri ATCC 55730 is one of many species of *Lactobacillus* known to produce both L(+)-lactic acid and D(-)-lactic acid through normal sugar fermentation. As part of a prospective study of decreasing the risk of allergy during the first years of life, a safety investigation was performed of the levels of D(-)-lactic acid in the blood at the age of 6 and 12 months. A sample group of 24 infants were randomly chosen from the total study population of 232 infants. They had been supplemented with this probiotic, or placebo, from birth and up to the age of 12 months. The daily dose of *L. reuteri* was 10^8 CFU, suspended in oil. 14 infants were supple-

mented with *L. reuteri* and 10 with placebo. All 24 infants had very low levels of D(-) lactic acid (range 0.020 – 0.130 mmol/L), and there was no difference between the infants who had ingested *L. reuteri* and those who received the placebo. The highest level observed was well within the normal range seen in humans (0.020 – 0.250 mmol/L) and far below levels associated with D-lactic acidosis in humans (over 3 mmol/L). No symptoms were reported that would normally be associated with acidosis, and there were no safety problems in any of the participating children. Conclusion: The daily supplementation of *L. reuteri* ATCC 55730 to healthy newborns during their first 12 months was safe, also in regard to the levels of D(-)-lactic acid in the blood.

Safety of infant formula supplemented with probiotics in early infancy.

Alsheikh A, Weizman Z. (2003) *Pediatric Research* **53**:abstract 174A.

50 full-term, healthy children, aged 3–65 days, were studied with the aim of investigating the safety of two different probiotics: *Lactobacillus reuteri* (ATCC 55730) and *Bifidobacterium lactis* (BB-12). The children were divided into three groups, which were given either of the probiotics in infant formula or ordinary formula only. Once a week for a total of 60 days the children were followed up in regard to growth, food intake, stools and behaviour. The three groups did not differ from each other in any of the parameters and no side effects could be observed. Conclusion: Both probiotics are safe to use in infant formula for infants of this age.

Safety and possible antidiarrhoeal effect of the probiotic *Lactobacillus reuteri* after oral administration to neonates. Karvonen A, Casas I, Vesikari T. (2001) *Clin Nutr* **20** (suppl 3):63: abstract 216.

A double blind, randomised, placebo-controlled study of healthy newborn, full-term children. The aim was to study safety aspects following the daily intake of *L. reuteri* ATCC 55730 given from the day of birth and the following 28 days. Four groups of children were studied: *L. reuteri* in the doses 10^5 CFU/day (n=12), 10^7 CFU/day (n=25) and 10^9 CFU/day (n=25), and placebo (n=28). All the doses of *L. reuteri* were well tolerated. The degree of *L. reuteri* colonisation, measured as the number of living cells in stool samples, was related to the given dose. The occurrence of watery diarrhoea was significantly lower in children given *L. reuteri*.

Tolerance and fecal colonization with *Lactobacillus reuteri* in children fed a beverage with a mixture of *Lactobacillus* spp. Ruiz-Palacios G et al. (1996) *Pediatr Res* **39**(4) part 2:184A, abstract 1090.

A double blind, randomised and placebo-controlled pilot study of 72 healthy children, aged 12-36 months, living in Mexico City. *L. reuteri* ATCC 55730 was given in a drink, together with two other probiotics, to 72 children aged 12–36 months. Three groups were given the probiotic drink, which differed in the dose of *L. reuteri*: 10^6 , 10^8 and 10^{10} CFU, respectively, and the control group consumed a placebo drink. All dose levels of *L. reuteri* were well tolerated and no side effects were noted compared with the placebo group.

Clinical studies in adults: colonisation and effects on the immune system

The effect of oral supplementation of *Lactobacillus reuteri* on the immunological composition of breast milk. Jakobsson T, Abrahamsson T, Björkstén B, Fredrikson M, Böttcher M (2005) Presented at the 38th ESPGHAN Annual Meeting, 1-4 June, 2005, Porto, Portugal. Abstract OP4-05. *J Ped Gastroenterol Nutr* **40**(5):624.

As part of a prospective study of decreasing the risk of allergy during the first years of life, it was also investigated whether the intake of *Lactobacillus reuteri* ATCC 55730 could affect the immunologic composition of breast milk. 109 pregnant women received *L. reuteri* (10^8 CFU daily), or placebo, during the last 4 weeks of pregnancy. Samples of breast milk were taken within the first three days after delivery (colostrum) and after one month. The levels of the anti-inflammatory substance Interleukin-10 (IL-10) were significantly increased in the first delivered milk of mothers taking *L. reuteri* as compared to the milk of the control group mothers. The levels of Transforming Growth Factor beta 2 (TGF- β 2) were on the other hand decreased in the colostrum

milk in the *L. reuteri* group compared to the controls. A month later the content of immunoactive substances of the milk were the same in the two groups. Conclusion: The study shows that the oral intake of *Lactobacillus reuteri* ATCC 55730 can exert effects beyond the gut wall, i.e. on other parts of the body, in this case the mammary glands.

Colonization and immunomodulation by *Lactobacillus reuteri* ATCC 55730 in the human gastrointestinal tract. Valeur N, Engel P, Carbajal N, Connolly E, Ladefoged K. (2004) Appl Environ Microbiol **70**:1176-1181.

This was an open study with the objective to investigate the colonisation of *L. reuteri*, as detected by the gene-based so-called FISH method, as well as effects on the immune system. 10 healthy subjects and 9 with ileostomy took *L. reuteri* ATCC 55730 in tablet form (4×10^8 CFU daily) for 28 days. Tissue samples (biopsies) were taken from the gastric mucosa and from the first part of the small intestine (the duodenum) in 10 of the subjects and from the distal part of the small intestine (the ileum) in 9 of the subjects. The biopsies were taken prior to the start of *L. reuteri* intake and after 28 days' intake. At the end of the study period, all 10 healthy subjects were colonised in the stomach and/or duodenum. All the 6 subjects in whom a biopsy could be taken from the ileum (of 9 with ileostomy) were colonised. Stool samples also verified colonisation, up to 2 to 4 weeks after the end of *L. reuteri* intake. A significant effect on the immune system in the mucosa was shown in the form of an increase in the number of B lymphocytes (CD20-positive cells) in the duodenum and an increase in the number of T lymphocytes (CD4-positive cells) in the ileum.

Clinical studies in adults: decreased risk of common infections

Increasing work-place healthiness with the probiotic *Lactobacillus reuteri*: A randomised, double blind placebo-controlled study. Tubelius P, Stan V, Zachrisson A. (2005) Environmental Health **4**:25, Open Access e-publication 7 November 2005, <http://www.ehjournal.net/content/4/1/25>.

A prospective study investigating if a daily supplementation with the probiotic *Lactobacillus reuteri* ATCC 55730 could reduce the incidence of common infections and thereby reduce short-term sick leave at a major Swedish workplace. 262 healthy employees, 18-65 years old, were enrolled and in a double blind manner randomised to use a probiotic drinking straw containing 10^8 CFU of *L. reuteri* (BioGaia LifeTop™ Straw) or an identical placebo drinking straw, together with at least 100 ml liquid. 181 subjects completed the study, i.e. used one drinking straw daily for 80 days and completed a diary on symptoms of gastrointestinal infection or upper respiratory tract infection (common cold), duration of symptoms and number of days away from work due to such symptoms. In the placebo group 26.4% (23/87) reported sick leave during the study period. In the *L. reuteri* group 10.6% (10/94) reported sick leave ($p < 0.01$). The frequency of sick-days of ordinary workdays decreased from 0.9% in the placebo group to 0.4% in the *L. reuteri* group ($p < 0.01$). The effect on sick leave was even more pronounced in the 53 shift-workers in the study: 33% in the placebo group (9/27) were on sick leave compared with none (0/26) in the *L. reuteri* group ($p < 0.005$). Conclusion: The daily intake of *Lactobacillus reuteri* ATCC 55730 significantly reduced the number of reported sick days of ordinary workdays due to common infections, and this effect was even more pronounced in the shift-workers.

Clinical studies in adults: gastrointestinal disorders

***Helicobacter pylori* eradication with *Lactobacillus reuteri*. A double blind placebo-controlled study.** Saggioro A et al. (2005) Presented at SIGE (Italian Society of Gastroenterology and Endoscopy) congress, March, 2005. Dig Liver Dis **37**(suppl 1): S88, abstr. PO1.49.

This was a prospective, randomised, double blind and placebo-controlled study that investigated the effect of *L. reuteri* ATCC 55730 on the eradication of *Helicobacter pylori*. Thirty patients were enrolled, aged 25-56, and suffering from dyspepsia (indigestion) caused by a confirmed infection with *H. pylori*. 15 patients were given

omeprazole (20 mg/day) plus *L. reuteri* (10^8 CFU, twice daily) and 15 received omeprazole plus placebo, for 30 days. The extent of *H. pylori* infection was controlled 4 weeks after the end of the therapy. In 60% (9/15) of the patients supplemented with *L. reuteri*, *H. pylori* was totally eradicated, while no eradication occurred in the group that received omeprazole plus placebo ($p < 0.0001$). **Conclusion:** From this study it seems that probiotic supplementation with *L. reuteri* ATCC 55730 has a beneficial effect on *H. pylori* infection in humans, being by itself able to eradicate the bacteria.

The efficacy of *Lactobacillus reuteri* ATCC 55730 in the treatment of patients with irritable bowel syndrome – a double blind, placebo-controlled, randomized study. Niv E et al. (2005) Clin Nutr. (E-publication ahead of print: 27 July 2005.)

This prospective, randomised, double blind and placebo-controlled study investigated the short- and long-term effects of *Lactobacillus reuteri* ATCC 55730 on clinical symptoms of irritable bowel syndrome (IBS). 54 patients, mean age 46 years, were randomised to take either a tablet with 10^8 CFU of *L. reuteri*, twice daily, or a similar placebo tablet. The participating subjects were of all IBS symptom types: constipation or diarrhoea dominant, or mixed types of symptoms, respectively. Both the probiotic and the placebo group subjects significantly improved in their symptoms during the study period of six months. There were no statistical differences between groups, although there was a tendency of lowered frequency of constipation and passing of gases, with time, in the *L. reuteri* group ($P = 0.0714$ and $P = 0.0971$, respectively). **Conclusion:** the strong placebo effect and the lack of uniformity in type of IBS in these patients may contribute to the results not reaching higher levels of statistical significance.

Effect of probiotics on constipation, fecal azoreductase activity and fecal mucin content in the elderly. Ouwehand AC, Lagström H, Suomalainen T, Salminen S. (2002) Ann Nutr Metabol **46**:159-162.

An open, parallel study of elderly persons (> 80 years) living in an institution and suffering from constipation. The aim was to investigate whether orange juice containing probiotics could reduce constipation problems. The control group ($n=6$) drank ordinary juice throughout the 10-week study period. Two groups were given probiotics, beginning with ordinary juice for 3 weeks, followed by 4 weeks with probiotics juice and 3 final weeks with ordinary juice. One group ($n=12$) was given juice containing *Lactobacillus reuteri* ATCC 55730 (Rela) and another group ($n=8$) juice containing the bacteria *Propionibacterium freudenreichii* and *Lactobacillus rhamnosus* (Bioprofit). Some effect in the form of a reduction in constipation was seen in both the probiotic groups.

Clinical studies in adults: oral health

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

Nikawa H, Makihiro S, Fukushima H, Nishimura H, Ozaki Y, Ishida K, Darmawan S, Hamada T, Hara K, Matsumoto A, Takemoto T, Aimi 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 investigation of probiotic bacteria isolated from 18 different Japanese fermented dairy products showed that *L. reuteri* ATCC 55730 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 took 95 g daily of yoghurt containing *L. reuteri* with their lunch, while half took the same amount of a placebo yoghurt. After 2 weeks the groups changed the study product and the subjects thus served as their own controls. Both the groups showed a significant decrease in the numbers of *S. mutans* in the saliva during the 2-week period when they took *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 they took placebo yoghurt.

Clinical studies in adults: safety aspects

Safety and tolerance of *Lactobacillus reuteri* supplementation to a population infected with the Human Immunodeficiency Virus. Wolf BW et al. (1998) *Food Chem Toxicol* **36**:1085-1094.

A prospective, double blind, placebo-controlled study in which 39 HIV-positive subjects (including 2 women), aged 23–50, consumed *L. reuteri* in a daily dose of 10^{10} CFU, or placebo, for 21 days. No significant differences could be seen in any of the parameters monitored (analyses of blood, serum and urine) or in regard to tolerance of *L. reuteri* intake. Colonisation of *L. reuteri* in the active group was verified.

Safety and tolerance of *Lactobacillus reuteri* in healthy adult male subjects.

Wolf BW et al. (1995) *Microb Ecol Health Dis* **8**:41-50.

A prospective, double blind, placebo-controlled study in which 30 healthy males, aged 18–75, consumed *L. reuteri* in a daily dose of 10^{11} CFU, or placebo, for 21 days. The subjects made a daily note of any symptoms from the gastrointestinal tract, and samples were taken on days 0, 7, 14, 21 and 28 for analysis of serum, blood, urine and stools. *L. reuteri* colonised the subjects in the active group within one week, as shown by a significantly higher amount of *L. reuteri* in their stools compared with the control group. The colonisation persisted for at least one week after intake had stopped, apart from in one individual, who remained colonised for up to 2 months after the end of the *L. reuteri* intake period. A tendency was observed for slightly increased, though transient, gas formation in a few subjects taking *L. reuteri*. No significant differences were shown in regard to blood and urine analyses or in regard to tolerance of bacterial intake.

L. reuteri: reviews

Enhancement of human health with *Lactobacillus reuteri* – A probiotic, immunobiotic and immunoprotective. Dobrogosz WJ. (2005) *Nutrafoods* **4**:15-28.

This review presents studies on a number of strains of the probiotic species *Lactobacillus reuteri* and their effect on the gut immune system (immunobiotic effect) as well as the local environment and microflora of the gut (immunoprotective effect). The studies show that members of the *Lactobacillus reuteri* species are able to communicate with and modify actions by important immune cells with regulatory functions, such as dendritic cells and other kinds of antigen-presenting cells, CD4⁺ T-cells, and the epithelial cells lining the gut wall. *L. reuteri* is also able to influence the gastrointestinal immune response to other beneficial bacteria in a direction towards a more balanced steady state. Thereby *L. reuteri* contributes to prevention of destructive inflammation and maintenance of intestinal integrity and normal function (homeostasis). These actions may explain the already proven clinical efficacy of *L. reuteri* strains in humans and animals.

***Lactobacillus reuteri* ATCC 55730 – A clinically proven probiotic.** Connolly E. (2004) *Nutrafoods* **3**:15-22.

This review covers 12 major clinical trials documenting the safety and efficacy of *L. reuteri* ATCC 55730 in 600 supplemented subjects in the age range of premature infants to adults. The clinical data show that the intake of *L. reuteri* ATCC 55730 significantly reduces the incidence and the severity of diarrhoea of different origins and reduces gastrointestinal illness and infections. The ability of *L. reuteri* ATCC 55730 to influence basic immune responses in the human gastrointestinal tract may be the basis for an improved protection against pathogen infection and further enhanced health of the host consuming this probiotic.

Validation of the probiotic concept: *Lactobacillus reuteri* confers broad-spectrum protection against disease in humans and animals.

Casas IA, Dobrogosz WJ. (2000) Microbial Ecology in Health and Disease **12**:247-285.

Review article about *Lactobacillus reuteri* and its occurrence, ecological niches and physiology, including antimicrobial substances formed. A description of the animal and human studies underlying the claim that *L. reuteri* fulfils all the criteria for a probiotic.

Product quality and delivery systems

***Lactobacillus reuteri* Drops – Novel delivery system.** Connolly E. (2005) Nutrafoods 4(2-3):65-68.

This article describes the rationale behind the development of a new type of probiotic product: an oil suspension with *Lactobacillus reuteri* ATCC 55730. *L. reuteri* Drops deliver the probiotic in a concentrated form, since five drops only (0.17 ml approx.) deliver the daily dose of 10^8 CFU of *L. reuteri*. The product has been tested in double blind, placebo-controlled clinical trials on full term and premature newborns with good colonisation results and without any adverse clinical events, in doses up to 10^9 CFU per day. It has also been used in clinical trials on somewhat older infants. The small delivery volume for a full dose makes the *L. reuteri* Drops suitable also for others, for example persons with chewing and swallowing difficulties or those where only a small volume is practical for delivery of a probiotic, such as enterally or parenterally fed patients. The *L. reuteri* Drops are sold in Europe and South Africa.

An evaluation of nine probiotics available in South Africa, August 2003. Elliot E, Teversham K. (2004) South African Medical Journal **94**:121-124.

The aim of the study was to test the quality of nine probiotic products sold as dietary supplements in South Africa. An independent laboratory was engaged to determine the species of bacterium/bacteria in each product and to analyse the number of living cells per gram of product. In only 3/9 products did the species of bacteria on the label correspond to the actual content, and five of the products contained sufficient bacteria to be able to produce an effect. Both LifeTop™ Straw and Reuteri™ Tablet, sold in South Africa under the brand names BioPro Reuteri Straws and BioPro Reuteri tablets, were among the few products that fully lived up to the quality criteria.

Identification and antibiotic susceptibility of bacterial isolates from probiotic products.

Temmerman R, Pot B, Huys G, Swings J. (2003) Int J Food Microbiol **81**:1-10.

A study on the quality of European probiotics. 30 dietary supplements and 25 dairy products were investigated in regard to the bacterial species and the amount of living cells they contained. The product information proved to be incorrect for 47 per cent of the supplements and 40 per cent of the dairy products. Only five of the dietary supplement products corresponded to their product information. The two products with *Lactobacillus reuteri* ATCC 55730, LifeTop™ Straw and Reuteri™ Tablet, belonged to the few products fulfilling the quality criteria.