

# Lactobacilli in the normal microbiota and probiotic effects of *Lactobacillus plantarum*

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien,  
Göteborgs Universitet, kommer att offentligen försvaras i föreläsningssalen (plan 3),  
Guldhedsgatan 10A, Göteborg

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av

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Avhandlingen baseras på följande arbeten:

- I. Siv Ahrné, Elisabet Lönnermark, Agnes E. Wold, Nils Åberg, Bill Hesselmar, Robert Saalman, Inga-Lisa Strannegård, Göran Molin, Ingegerd Adlerberth. Lactobacilli in the intestinal microbiota of Swedish infants. *Microbes and Infection* 2005;7:1256-1262
- II. Elisabet Lönnermark, Forough Nowrouzian, Ingegerd Adlerberth, Siv Ahrné, Agnes E. Wold, Vanda Friman. Oral and faecal lactobacilli and their expression of mannose-specific adhesins in individuals with and without IgA deficiency. *In manuscript*.
- III. Elisabet Lönnermark, Vanda Friman, Georg Lappas, Torsten Sandberg, Anna Berggren, Ingegerd Adlerberth. Intake of *Lactobacillus plantarum* reduces certain gastrointestinal symptoms during treatment with antibiotics. *Journal of Clinical Gastroenterology* 2009 [Epub ahead of print]
- IV. Elisabet Lönnermark, Georg Lappas, Vanda Friman, Agnes E. Wold, Erik Backhaus, Ingegerd Adlerberth. Effects of probiotic intake and gender on non-typhoid *Salmonella* infection. *In manuscript*.



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## ABSTRACT

Lactobacilli colonise most adult individuals and are also frequently used as probiotics, i.e. bacteria which possibly have health promoting effects when ingested. In this thesis, the intestinal *Lactobacillus* microbiota was studied in longitudinally followed infants. The oral and intestinal *Lactobacillus* microbiota of adults with and without IgA deficiency was examined to investigate the influence of secretory-IgA (S-IgA) on mucosal lactobacilli. Probiotic effects of the strain *L. plantarum* 299v were studied in antibiotic-treated patients and in patients with salmonellosis.

In infants, colonisation by lactobacilli increased until six months of age, when 45 % were colonised, most often by *L. rhamnosus* or *L. gasseri*. Colonisation dropped and reached its lowest point by one year, to increase again by 18 months. By that time, *L. paracasei* and other food-related *Lactobacillus* species were most common. Only 30% of the infants harboured the same strain on at least two sampling occasions, indicating that stable colonisation by lactobacilli is quite uncommon in infants. Colonisation by *L. rhamnosus* was more common in breastfed than in weaned infants at six months, suggesting that breastfeeding favours this species. *Lactobacillus* colonisation was not significantly related to delivery mode, or to contact with siblings or pets.

The influence of S-IgA on the oral and faecal *Lactobacillus* microbiota was studied by comparing IgA-deficient and healthy adult individuals. Expression of mannose-specific (MS) adhesins by lactobacilli was studied since such adhesins could possibly interact with mannose-containing polysaccharide chains of S-IgA. Lactobacilli were isolated from the oral cavity and faeces of the majority of both IgA-deficient and healthy individuals. *L. paracasei* and *L. gasseri* dominated in oral samples, and *L. paracasei* was the most common species in faecal samples from both groups. The only significant difference in species distribution was a lower colonisation by *L. fermentum* in the oral cavity of IgA-deficient individuals. Thus, the presence of S-IgA seems to have little influence on the *Lactobacillus* species distribution. The expression of MS adhesins was more common in oral than in faecal lactobacilli, indicating that these adhesins may be of advantage for oral colonisation. Faecal isolates from IgA-deficient individuals more often expressed MS adhesins than faecal isolates from controls. Possibly, expression of MS adhesins is less advantageous for lactobacilli in the presence of S-IgA in the gut.

In two double-blind placebo-controlled studies we explored if intake of *L. plantarum* 299v could counteract gastrointestinal side-effects during treatment with antibiotics, and reduce time to clearance and symptoms of *Salmonella* in patients with non-typhoid salmonellosis, respectively. Intake of *L. plantarum* reduced the risk of experiencing loose stools or nausea in antibiotic-treated patients. The risk of diarrhoea, i.e. at least three loose stools a day for at least two days, was not reduced, and there was no effect on colonisation by toxin-producing *C. difficile*. In patients with salmonellosis, intake of *L. plantarum* 299v did not reduce time to clearance of *Salmonella*, or time to resolution of diarrhoea and other symptoms. After clearance of *Salmonella*, patients receiving *L. plantarum* less frequently had hard stools, but tended to have more loose stools than patients on placebo. The differences regarding effects of *L. plantarum* 299v in the two studies could relate to e.g. differences between the studies regarding doses and formulas of the probiotic strain.

Gender seemed to influence the course of salmonellosis. Women tended to clear *Salmonella* more quickly than men, but had diarrhoea for a longer period. After *Salmonella* clearance, women had more loose stools, nausea and flatulence than men. Also, effects of *L. plantarum* after clearance of *Salmonella* were influenced by gender. Women receiving *L. plantarum* had more abdominal pain than those on placebo, whereas men in the *L. plantarum* group had less hard stools, but more diarrhoea than men on placebo. The gender-related differences regarding salmonellosis and probiotic effects need to be further explored.

**Key words:** *Lactobacillus*, oral microbiota, gut microbiota, infants, adults, secretory IgA, IgA-deficiency, adherence, *Lactobacillus plantarum*, probiotics, antibiotics, salmonellosis, diarrhoea