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Health benefits of Lactobacillus GG

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Bacteria Maintain the Well-Being of the Body

The concentration of bacteria in different parts of the gastrointestinal tract varies considerably (Figure 1). Oral mucosa and tooth surfaces are rich in bacteria, which along with saliva and chewed food get transported down the oesophagus into the stomach.

In the stomach, food is mixed with gastric juice whose acidity effectively kills the majority of incoming bacteria. Food stays in the stomach for approximately 4 hours and passes in small doses into the small intestine.

The proximal small intestine is acidic because of the incoming gastric acid. Bile acids, which hydrolyse fats, are secreted there. The bacterial content in the proximal small intestine is relatively low. As the acidity decreases and the bile acids become diluted, the bacterial content towards the terminal small intestine increases.

The length of the small intestine is several meters and it is extensively folded to form intestinal villi. This increases the surface area of the mucous membrane so much that if flattened out, it would cover a whole tennis court (Figure 2). This large surface area enables an effective

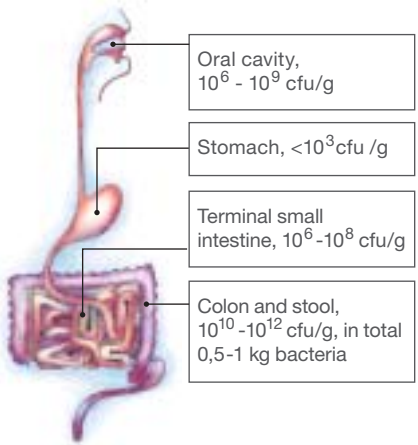


Figure 1. Bacterial contents in various parts of the gastrointestinal tract.

breakdown of foodstuffs and a more efficient absorption of nutrients into the bloodstream via the intestinal mucosa. Intestinal epithelial cells are joined together by tight junctions and covered by a mucus layer.

Powerful peristalsis in the gastrointestinal tract pushes the chyme forward. Moving on from the small intestine to the large intestine, the peristalsis becomes slower, fluid is absorbed into the bloodstream and the bowel content becomes more solid. At the same time, the bacterial content increases dramatically. The bacteria split the remaining poorly digestible nutrients, such as fibre. Approximately half of the faecal volume is bacterial mass.

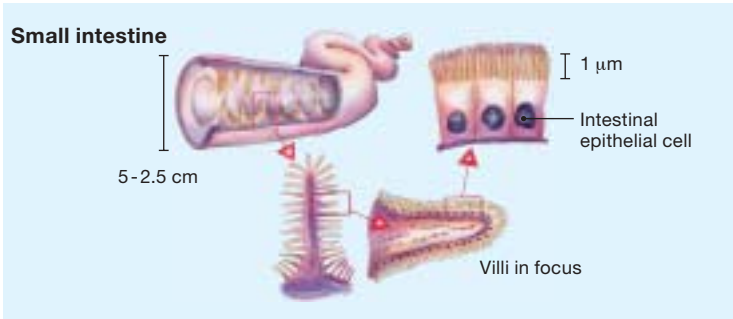


Figure 2. The wall of the small intestine is folded and forms intestinal villi.

Intestinal bacteria

Approximately 400 to 500 species of intestinal bacteria have been identified. However, not all bacterial species can be identified as yet. The majority of intestinal bacteria are beneficial. The dominant bacterial species in the large intestine are *Bacteroides, Bifidobacterium, Eubacterium* and *Peptostreptococcus*. Less dominant, but still significant are e.g. bacteria of the *Streptococcus, Lactobacillus, Enterococcus*, and *Clostridium* species and the *Enterobacteriaceae* family. The intestines also contain bacteria which, in excess, can become harmful. These conditionally harmful species include *Veillonellae, Clostridium, Staphylococcus, Proteus* and *Pseudomonas*. They produce harmful metabolic end products, e.g. ammonium, hydrogen sulphide, amines, phenols, indoles and secondary biliary acids. These substances may have a harmful effect directly on the intestinal mucosa or when absorbed into the bloodstream.

Beneficial bacteria, however, predominate over harmful bacteria in quantitative terms. The balance of this quantitative ratio may be disturbed e.g. due to antibiotic therapy or dietary changes and results in abdominal complaints or stomach upset.

Beneficial bacteria maintain the equilibrium by suppressing the growth of harmful bacteria. The proportion of beneficial bacteria can be increased by supplementing the diet with fermented milk products which contain scientifically documented probiotics.

Diverse functions of intestinal bacteria

The intestinal bacteria have many important functions. Together with the intestinal mucosa they protect against external microorganisms, and they participate in breaking down nutrients, controlling regeneration of intestinal mucosa and supporting immune defence.

The composition of bacteria on the intestinal mucosa depends on various characteristics of the host organism. This composition results from many factors, including human immune defences, antimicrobial compounds produced by polymorphonuclear white blood cells and epithelial cells, composition of the intestinal mucus and the regeneration rate of epithelial cells. A bacterial community operates in terms of both competition and cooperation. The bacteria compete with each other for adherence sites in the intestinal mucosa (Figure 3) and for available nutrients. They also produce compounds that impair the growth of other bacteria. Only bacteria capable of adhering to the intestinal mucus and the epithelial cell surface are able to stay on the intestinal mucosa. In addition, they are in a position to best effect the organism through the mucosa because of their close contact.

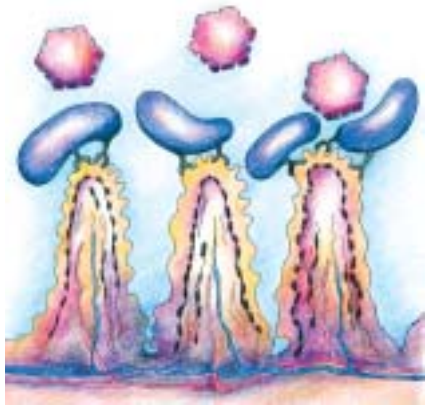


Figure 3. Lactobacillus GG adheres to the surface of the intestinal mucosa and inhibits the adherence of harmful bacteria.

Bacteria can be incorporated into the diet to promote health and physical well-being. They are considered "functional" if they have been shown in clinical studies to have health-promoting effects – when ingested in sufficient amounts. Health-promoting bacteria, i.e. probiotics, mostly are similar to the bacterial flora of the healthy intestines, e.g. lactobacilli and bifidobacteria. These are used, along with other fermenting bacteria or starter cultures, in normal product manufacturing processes.

Intestinal mucosa gives protection

There is an interaction between bacteria and the body. The intestinal mucosa acts as a protective barrier against the outside world. Furthermore, the mucosa and the gut-associated lymphoid tissue collectively represent the most important immunological organ and contribute to the formation of the immune defence. Intestinal bacteria play a role in both innate (non-specific) and acquired (specific) immunity. The role of the immune response is to distinguish between familiar and foreign or harmful bacteria and to react, when necessary, by producing antibodies and other chemical agents to act as messengers to the body about intruders. Endogenous immune cells and the compounds (e.g. antibodies) they produce inactivate harmful bacteria and viruses (Figure 4).

The cells of the intestinal mucosa are covered by a mucus layer that they produce to protect themselves. The antibodies maintaining the local immune response are also secreted in the intestinal mucus. The intestinal mucus and epithelial cells are in a constant state of regeneration, and the bacteria use the degenerating cells and intestinal mucus for their growth. Intestinal bacteria contribute to the permeability of the gut mucosal barrier. Harmful bacteria may increase the permeability, thus enabling passage through the mucosal wall for bacteria and dietary macromolecules [1]. A well-known probiotic, *Lactobacillus* GG, is able to prevent and repair such mucosal lesions whether caused by food antigens[2,3] or medicinal substances[4]. It has been shown to increase the "density" of the intestinal mucus[5,6] and to protect from tight junction damage to epithelial cells caused by inflammatory *E. coli* bacteria [7].

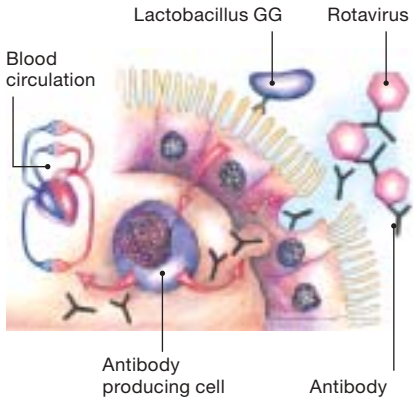
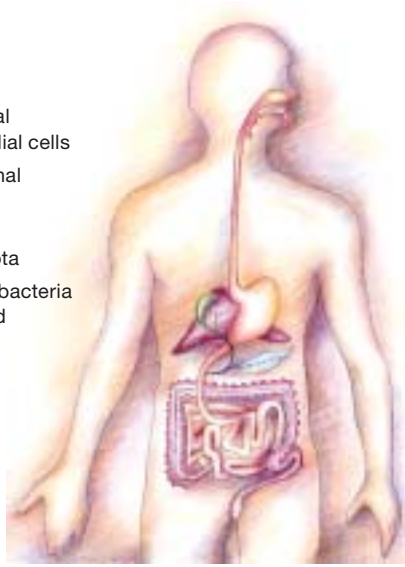


Figure 4. Lactobacillus GG adheres to the intestinal mucus and intestinal epithelial cell, thus boosting local immune response and antibody formation. Antibodies inactivate the viruses.

- Adhers to intestinal mucus and epithelial cells
- Survives in intestinal conditions
- Adapts to healthy intestinal microbiota
- Boosts beneficial bacteria (bifidobacteria and lactobacilli)



- Supresses the adhesion and growth of potentially harmful bacteria
- Supresses the formation of harmful enzymes and other compounds
- Binds toxins
- Enhances the defence systems against harmful bacteria and viruses

Figure 5. The main functions of Lactobacillus GG in the gastrointestinal ecosystem.

Probiotics – individual as humans

Since the effects of lactobacilli may vary from one strain to another, the properties of each probiotic strain should be evaluated separately. The best known probiotic whose effects have been most extensively studied is *Lactobacillus* GG (*L. rhamnosus* ATCC 53103). It survives the intestinal conditions, adheres to the intestinal mucosa and boosts the natural defence mechanisms of the body via the intestines. When used on a regular basis, *Lactobacillus* GG adapts to the normal bacterial flora. It increases the proportion of not only lactobacilli but also of beneficial bifidobacteria in the intestinal microbiota. *Lactobacillus* GG has positive effects on gastrointestinal metabolism, since it suppresses the formation of harmful compounds in the large intestine (Figure 5).

Lactobacillus GG is probiotic

1. Regular intake of *Lactobacillus* GG decreases illnesses among children

Illness-related absences among day care children decreased by 16% when day care centres in Helsinki, Finland started consuming milk enriched with *Lactobacillus* GG on a regular basis. At the same time, children's complicated respiratory tract infections decreased by 17% and required fewer antibiotics (Figure 6)[8] .

A Brazilian day care centre study yielded similar reports[9]. Daily intake of a probiotic fermented milk drink enriched with *Lactobacillus* GG decreased the content of potentially harmful bacteria (*Staphylococcus aureus, Streptococcus pneumoniae*, β–haemolytic streptococci) present in the nasal mucosa of adult subjects [10].

2. *Lactobacillus* GG decreases the risk of caries

In day care centres in Helsinki, daily consumption of milk enriched with *Lactobacillus* GG compared to regular milk decreased the risk of caries in children (Figure 7)[11]. The intake of milk or other dairy products alone decreases caries, because they provide calcium and phosphorus, building material for teeth. There was a 47% difference in the caries risk between children receiving

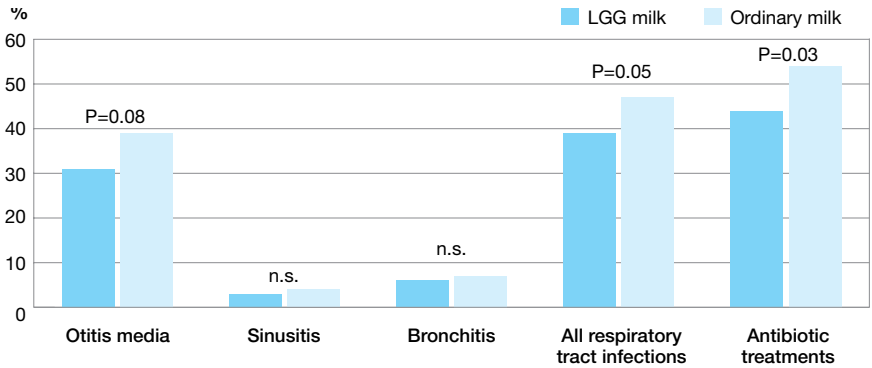


Figure 6. The effect of Lactobacillus GG on the incidence of children's respiratory tract infections and the number of prescribed antibiotic treatments. The children drank either normal milk or Lactobacillus GG-enriched milk with their meals in day care centres during a period of 7 months.

milk enriched with *Lactobacillus* GG and children receiving regular milk, which indicates that *Lactobacillus* GG enhances the protective effect of milk. Because *Lactobacillus* GG does not ferment sugar, it will not promote acid production. On the contrary, it decreases the concentration of *Streptococcus mutans* and prevents them from adhering to the teeth (Figure 8)[12-15]. Also cheese is known to be beneficial to teeth, and it is an ideal carrier product for *Lactobacillus* GG[16].

Figure 8. Lactobacillus GG decreases the number of caries bacteria and inhibits their adherence to the surface of the teeth.

3. *Lactobacillus* GG decreases the risk of stomach upset

Among children admitted to hospital for reasons other than stomach upset, the risk of getting acute diarrhoea was 80% lower for those receiving *Lactobacillus* GG than for those receiving placebo (Figure 9). Although the proportion of children infected by rotavirus in the hospital was equal in both groups, children receiving *Lactobacillus* GG actually got ill due to rotavirus less often[17].

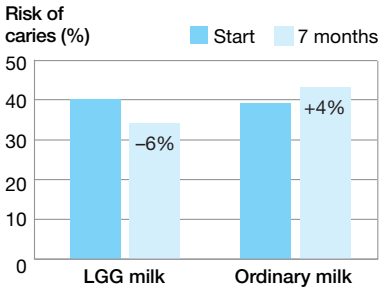


Figure 7. The effect of Lactobacillus GG on caries risk. The children drank either normal milk or Lactobacillus GG-enriched milk at their meals in day care centres during a period of 7 months.

Diarrhoea is less common in adults than in children. However, the risk of stomach upset increases e.g. when travelling to countries with warmer climate and poorer sanitary conditions. When travelling, one should pay special attention to hand hygiene and choose carefully what and where to eat. It is often wise to consume bottled water and cooked meals. *Lactobacillus* GG may provide additional protection, since it has been found to decrease the risk of tourist diarrhoea in adults [18,19].

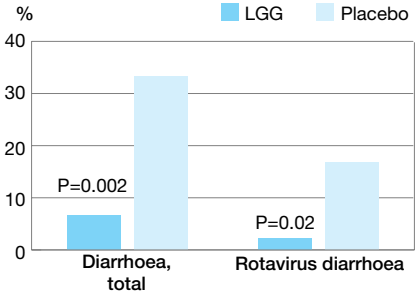


Figure 9. The effect of Lactobacillus GG on the duration of acute diarrhoea. Children admitted to hospital for reasons other than stomach upset received Lactobacillus GG or placebo during their stay in the hospital.

Lactobacillus GG also decreases the risk of antibiotic-induced abdominal complaints, especially diarrhoea and loose stools. This has been shown especially in children, among whom diarrhoea induced by antibiotics was 70% less frequent in those who received *Lactobacillus* GG than in those who received placebo [20,21]. In addition, the tolerability of treatments administered in combination with eradication of *Helicobacter pylori* was significantly better in the *Lactobacillus* GG group than in the placebo group [22-24]. The most common symptoms associated with the eradication therapy were nausea, diarrhoea, bloating and taste disturbances; those being 50 to 90% less frequent in the *Lactobacillus* GG group than in the control group.

4. *Lactobacillus* GG shortens the duration of diarrhoea

Numerous studies have shown that *Lactobacillus* GG shortens the duration of acute diarrhoea [25]. The most well known is its effect on the duration of rotavirus-related diarrhoea, but it also shortens diarrhoea caused by unknown aetiology. In hospital, the duration of diarrhoea was shortened by 1–2 days (Figure 10). In children treated at home, the duration of diarrhoea in the control group was 6 days, whereas in the *Lactobacillus* GG group it was only 3 days [26]. It is beneficial to start *Lactobacillus* GG therapy immediately at the onset of diarrhoea. If oral rehydration therapy is required to correct dehydration, *Lactobacillus* GG can be added to the treatment solution.

5. *Lactobacillus* GG decreases the incidence of atopic eczema and alleviates symptoms

The well-being of pregnant and lactating women is especially important for the child. A newborn infant's intestines contain no bacteria; the first exposure to bacteria occurs during birth, usually via the mother. The individual composition of intestinal microbiota is formed during the first years of life and the immunological defence systems mature. The body learns to recognise familiar

substances in food without reacting to them. Bacterial flora plays a significant role in the development and maintenance of defence systems and immune response. There has been discussion about the "hygiene hypothesis", according to which a developing baby should be exposed to a sufficient number of foreign micro-organisms in order to develop proper resistance. General hygiene has improved and children's diseases have decreased. This has decreased microbial exposure and the body does not get sufficient immunological stimuli. Consequently, the body learns an inappropriate way of reacting [28].

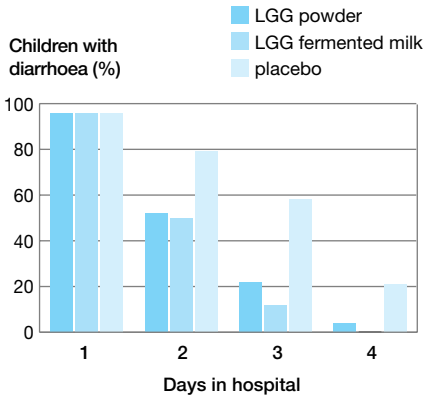


Figure 10. The effect of Lactobacillus GG on the duration of acute diarrhoea. Children admitted to hospital for acute diarrhoea received Lactobacillus GG in a powder form or in a Lactobacillus GG-fermented milk product twice-daily following oral rehydration therapy.

Lactobacillus GG was given to pregnant mothers whose children were in the risk group for allergies and to either the lactating mother or the infant after delivery. The children were followed up at age 2 and 4 years and results showed that *Lactobacillus* GG decreased the incidence of atopic eczema (Figure 11) [29,30]. At the age of three weeks children who later developed atopic eczema exhibited different intestinal bacterial flora compared to non-allergic children [31].

Important beneficial bacteria included bifidobacteria, which are proportionally increased by ingesting *Lactobacillus* GG [32]. In addition to the possibility of getting intestinal *Lactobacillus* GG at birth from the mother, an infant may also receive protection via breast milk. The concentration of a protective factor typical to mother's milk was higher in mothers who had received *Lactobacillus* GG than in mothers who had received placebo [33].

Lactobacillus GG, when combined with a milk-elimination diet, accelerated the recovery from atopic eczema in children [34,35]. The symptoms of eczema disappeared significantly faster in

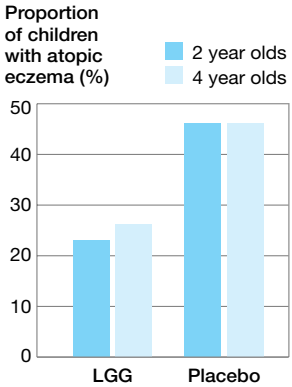


Figure 11. The effect of Lactobacillus GG on the incidence of acute eczema in early childhood. Pregnant women received Lactobacillus GG or placebo for 2–4 weeks before delivery. After delivery, it was administered either to the infant or to the breast-feeding mother for 6 months.

children receiving mother's milk substitute based on totally hydrolysed whey-protein containing *Lactobacillus* GG (Gefilus PeptidiTutteli) than from children receiving a corresponding placebo product (PeptidiTutteli). In addition, the content of intestinal inflammation markers in faeces decreased faster in the *Lactobacillus* GG group than in the control group [35].

6. *Lactobacillus* GG is safe

Lactobacilli are considered safe food bacteria. They are extremely seldom isolated from clinical blood and pus samples. In Finland, *Lactobacillus* GG has already been on the market in Gefilus products for over 13 years. An extensive epidemiological study showed that it does not increase the incidence of lactobacilli in blood cultures and does not pose any greater risk to immunocompromised patients than do other intestinal lactobacilli [36]. In research studies, *Lactobacillus* GG has been administered to healthy and ill people from all age groups: elderly [37], adults [4,22], children [21,38], infants and premature infants [29,35,39], without any reported adverse effects.

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(Additional information on *Lactobacillus* GG studies is available on the internet at www.valio.com/licensing)

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Fresh dairy products and juices containing Lactobacillus GG.

Infant formulaes enriched with Lactobacillus GG.

Food supplements and oral rehydration solutions containing Lactobacillus GG.

Products containing *Lactobacillus* GG in the world, autumn 2003

1. Dairy products and fruit drinks

Country	Brand	Products
Europe		
Bosnia-Herzegovina	Dukat BioAktiv	Dairy products
Croatia	Dukat BioAktiv	Dairy products
Estonia	Valio Gefilus	Dairy products
Finland	Valio Gefilus	Dairy products, Juice drinks
Germany	Emmifit, Vollfit	Dairy products
Iceland and Greenland	LGG+, PLUS+	Dairy products
Ireland	Yoplait everybody Avonmore Milk plus	 Dairy products
Italy	Vivi Vivo	Dairy products
Latvia	Valio Gefilus	Dairy products
The Netherlands	Vifit Vitamel	Dairy products
Norway	Tine Biola	Dairy products
Northern Ireland	Yoplait everybody	Dairy products
Portugal	Emmifit	Dairy products
Russia	Valio Gefilus	Dairy products, juices
Serbia and Montenegro	Dukat BioAktiv	Dairy products
Slovenia	Dukat BioAktiv	Dairy products
Spain	Kaiku Actif	Dairy products
Sweden	Valio Gefilus	Juices
Switzerland	Aktifit Plus, 4Plus, Coop Lifestyle	 Dairy products
Middle East		
United Arab Emirates	Laban with Gefilac	Dairy products
Israel	Tnuva LGG1	Dairy products
Asia		
Indonesia	Vaalia	Dairy products
Japan	Onaka He GG!, LGG Plus	Dairy products
Korea Republic	Maeil GG	Dairy products
Papua-New Guinea	Vaalia	Dairy products
Taiwan	LGG	Dairy products
Oceania		
Australia	Vaalia	Dairy products
Latin America		
Ecuador	Toni	Dairy products
Uruguay	Vital+	Dairy products

2. Food Supplements

Country	Brand	Products
Europe		
Estonia	Valio Gefilus	Capsules
Finland	Valio Gefilus	Capsules
France	Ergyphilus plus	Capsules
Germany	Infectodiarrstop, LGG	Powders, capsules
Italy	Dicoflor, Floridral, Giflorex	Powders, capsules
Lithuania	Valio Gefilus	Capsules
North America		
USA	Culturelle	Capsules
Asia		
Malaysia	LactoGG	Capsules
Singapore	LactoGG	Capsules
Hong Kong	LactoGG	Capsules

3. Infant Foods

Country	Brand	Products
Europe		
Finland	Gefilus PeptidiTutteli, Gefilus Tutteli	Infant formula
Lithuania	Gefilus PeptidiTutteli, Gefilus Tutteli	Infant formula
Belgium	Nutramigen 2	Infant formula
Denmark	Nutramigen 2	Infant formula
Germany	Nutramigen 2	Infant formula
Italy	Nutramigen 2	Infant formula
The Netherlands	Nutramigen 2	Infant formula
Sweden	Nutramigen 2	Infant formula


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