**Health Benefits of Probiotics: Probiotics for Helicobacter pylori Infection**

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Probiotics have been defined as live microbial food supplements that have been shown to benefit human health. Probiotic products are marketed widely throughout the world. Until recently, probiotics were mainly selected on the basis of technological properties and resistance to acid and bile and were used in products aimed at promoting the well-being of consumers. However, now research efforts are focusing on the development of probiotics with special functional properties. *Lactobacillus gasseri* OLL2716 (LG21) was selected as a promising probiotic for *Helicobacter pylori* infection by *in vitro* and animal studies. The effects of yogurt containing LG21 on *H. pylori* infection in humans were examined. The ingestion of yogurt containing LG21 decreases the number of *H. pylori* and alleviates mucosal inflammation in the stomach. LG21 was shown to be effective as a probiotic for *H. pylori* infection.

Keywords: probiotics, *Lactobacillus gasseri*, *Helicobacter pylori*, LG21, mucosal inflammation

**Introduction**

It is empirically known that some kinds of lactic acid bacteria are good for health and it is thought that probiotics should be scientifically studied and assessed for their efficacy and safety. Recently, many clinical trials have been conducted to obtain scientifically convincing evidence that probiotics really influence health.

This review focuses on the health benefits of probiotics, especially a newly discovered probiotic for *Helicobacter pylori* infection.

**Definition and health benefits of probiotics**

Several definitions have been proposed to describe probiotics. Fuller (1993) defined a probiotic as a live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance. The intestinal microflora is a complex population of microorganisms that are known to exert numerous influences on the host. Probiotics have been shown to have health benefits such as relief of constipation (Ogata *et al.*, 1997), alleviation of diarrhea (Isolauri *et al.*, 1991; Colombel *et al.*, 1987) and suppression of some bacterial enzymatic activities (beta-glucuronidase, nitroreductase and azoreductase) (Goldin & Gorbach, 1984; Ling *et al.*, 1994) by improving the intestinal microbial balance. Probiotics have also been used as growth promoters of farm animals to replace antibiotics. Thus, the main desired effects of probiotics were to balance the intestinal microflora and promote the health of the consumer. However, some probiotic effects such as immune modulation (Schiffrin *et al.*, 1995), alleviation of lactose intolerance (Garvie *et al.*, 1984), prevention of infection of the stomach (Sakamoto *et al.*, 2001) and the urogenital tract (Reid *et al.*, 1987) may be achieved without changing the intestinal microbial balance. Therefore, a recent definition of probiotics is live microbial food supplements that have been shown to benefit human health (Salminen *et al.*, 1998). Extensive functional properties of probiotics including anti-inflammatory and anti-allergic effects (Kalliomäki *et al.*, 2001) have recently been reported from around the world.

**Probiotics for *Helicobacter pylori* infection**

*Helicobacter pylori* is a spiral, Gram-negative and flagellated bacterium (Fig. 1). This bacterium produces a strong urease which catalyzes urea in the stomach to ammonia and carbon dioxide. *H. pylori* can survive under strongly acidic conditions because of this ammonia production. This bacterium infects the human stomach and can cause chronic inflammation and ulcers of both the stomach and duodenum (Buck *et al.*, 1986; Warren & Marshall, 1983). *H. pylori* has also been identified as a risk factor for stomach cancer.

Probiotics for *H. pylori* infection After eradication of *H. pylori*, most of the symptoms disappear however, the eradication therapies using antibiotics are often accompanied by side effects. Moreover the number of antibiotic-resistant strains is increasing and eradication therapies are not always successful. Probiotics have been proposed as safe and simple alternatives to antibiotic therapy for *H. pylori* infection. It was demonstrated that lactic acid bacteria inhibit the growth of *H. pylori in vitro* (Bhatia *et al.*, 1989; Midolo *et al.*, 1995) and in a gnotobiotic murine model (Kabir *et al.*, 1997). Aiba *et al.* (1998) reported that orally administered lactobacilli eradicated *H. pylori* using a gnotobiotic murine model.

*Lactobacillus gasseri* OLL2716 (LG21) (Fig. 2) was selected as a promising probiotic for *H. pylori* infection by screening 203 Lactobacillus strains for the following properties: resistance to gastric juice, proliferation under acidic conditions, adherence to cultured gastric epithelial cells, suppression of *H. pylori* during co-fermentation, and suppression of *H. pylori* in mice infected...
with this bacterium. The suppressive effects of selected *Lactobacillus* strains on *H. pylori* during co-fermentation in the medium containing 5 mM of urea at pH 4 are shown in Fig. 3. Three *Lactobacillus* strains (LG21, *Lactobacillus salivarius* WB1004, and *Lactobacillus gasseri* No. 6) strongly inhibited the growth of *H. pylori*.

Fig. 1. *Helicobacter pylori.*

Fig. 2. *Lactobacillus gasseri* OLL2716 (LG21).

Fig. 3. Suppressive effects of *Lactobacillus* strains on *H. pylori* during co-fermentation in the medium containing 5 mM of urea at pH 4.

Fig. 4. Effects of administration of LG21 on *H. pylori* infected mice (8 weeks, *n*=5).
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During co-fermentation. In a study using mice infected with H. pylori, orally administered LG21 and Lactobacillus salivarius WB1004 eradicated H. pylori in mice and the anti-H. pylori IgG level of the LG21-administered mice was the lowest (Kimura et al., 2003; Fig. 4). LG21 was also found to act as a probiotic for clarithromycin-resistant H. pylori infection in mice (Ushiyama et al., 2003).

Effects of ingestion of yogurt containing LG21 on H. pylori infection in humans  The effects of yogurt containing LG21 on H. pylori infection in humans were examined (Sakamoto et al., 2001). Thirty-one subjects infected with H. pylori ingested 90 g of yogurt twice daily for 8 weeks. This 8 week period was followed by a 1 week period without yogurt ingestion. This was in turn followed by an 8 week period during which the subjects ingested 90 g of yogurt containing 10⁶ cfu of LG21 twice daily.

The urea breath test and assay of serum pepsinogen I/II ratios were performed to measure the population of H. pylori and to evaluate the degree of mucosal inflammation in the stomach respectively at three points: prior to ingestion of yogurt, 1 week following the first 8 week period, and 1 week following the second 8 week period. Moreover gastric biopsy specimens were taken from 6 subjects for quantitative culture both before and after ingestion of yogurt containing LG21. The Δ¹³C value for the urea breath test did not significantly change after yogurt ingestion, but did significantly decrease following the ingestion of yogurt containing LG21 (Fig. 5). The serum pepsinogen I/II ratio did not significantly change after ingestion of yogurt, but did significantly increase following ingestion of that containing LG21 (Fig. 6).

The number of H. pylori in the gastric biopsy specimens from all 6 volunteers decreased after ingestion of yogurt containing LG21 (Fig. 7). Similarly, the long-term ingestion of yogurt containing LG21 significantly decreased the Δ¹³C value in the urea breath test and significantly increased the serum pepsinogen I/II ratio.

![Graph showing effect of yogurt containing LG21 on Δ¹³C value of subjects infected with H. pylori (n=29).](image1)

![Graph showing effect of yogurt containing LG21 on serum pepsinogen I/II ratio of subjects infected with H. pylori (n=30).](image2)

![Graph showing the number of H. pylori in the stomach (cfu/g tissue) before and after ingestion of yogurt containing LG21.](image3)

![Graph showing effect of yogurt containing LG21 on Δ¹³C value of subjects infected with H. pylori (n=28).](image4)
Kimura et al., 2001; Figs. 8 and 9). These results suggest that the ingestion of yogurt containing LG21 decreases the number of H. pylori and alleviates the mucosal inflammation in the stomach.

The density of H. pylori colonization in the stomach is of importance in the pathogenesis of infection associated with this bacterium. It was reported that there was a correlation between H. pylori density and gastric inflammation or duodenal ulceration (Atherton et al., 1996), and that no duodenal ulceration was present in subjects with an antral H. pylori infection density of less than 10^5 cfu/mg biopsy protein (Khulusi et al., 1995). Since the ingestion of yogurt containing LG21 suppresses H. pylori in addition to alleviating inflammation in the stomach, LG21 may reduce the risk of the H. pylori-induced gastrointestinal diseases.

Mechanisms of therapeutic effect on H. pylori infection of LG21. LG21 displays high resistance to gastric juice, grows well under acidic conditions, and was found in the stomach of subjects who had ingested LG21 (unpublished data). LG21 also produced large amounts of lactic acid and inhibited the growth of H. pylori in vitro. Lactic acid exerted a stronger inhibitory effect on the growth of H. pylori than hydrochloric acid at the same pH (Aiba et al., 1998). On the other hand, LG21 inhibited gastric epithelial cells which were treated with H. pylori from producing IL-8 in vitro (Ushiyama et al., 2003). Considering these results, antimicrobial activity of lactic acid produced by LG21 and inhibition of H. pylori attachment to epithelial cells appear to be involved in the therapeutic effect on H. pylori infection of LG21. However, further experiments are required to elucidate the exact mechanism of the therapeutic effect on H. pylori infection of LG21.

Conclusion
H. pylori-positive peptic ulcer patients should receive eradication therapy. However, for many otherwise healthy people infected with H. pylori, probiotic therapy may be a safe and simple alternative to antibiotic therapy.

Probiotics have been shown to provide a wide range of health benefits. It is important for each probiotic strain to be adapted to a suitable carrier or fermentable substrate and for it to both remain viable in sufficiently high numbers and to retain its metabolic activity not only at the time of manufacture, but over the entire shelf life of the final product. Probiotic properties should be confirmed by clinical studies on the commercial products themselves.

References
Fig. 9. Effect of yogurt containing LG21 on serum pepsinogen I/II ratio of subjects infected with H. pylori (n=28).


