

# Bacterial therapy to help eradicate *Helicobacter pylori* and to reduce the gastrointestinal side effects of antibiotics: a possible treatment scheme?

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*Helicobacter pylori* (Fig. 1), previously called *Campylobacter pylori*, is a gram-negative, microaerophilic bacterium found usually in the stomach. It was identified in 1982 by two Australian who found it in a patient with chronic gastritis and gastric ulcers, conditions not previously thought to have a bacterial aetiology. *H. pylori* is also linked to the development of duodenal ulcers and stomach cancer. It is present in the stomach of 50% of the world's population and asymptomatic in over 80% of those infected. The standard first-line therapy to eradicate *H. pylori*, is the so-called *triple therapy* consisting of proton pump inhibitors (PPI), mainly omeprazole, along with the antibiotics clarithromycin and amoxicillin. Variations on the triple therapy have been developed over the years, using a different PPI, or replacing amoxicillin with metronidazole for those with an allergy to penicillin. Due to antibiotic-resistant bacteria, an additional round of antibiotic therapy, the quadruple therapy, consisting of a PPI, a bismuth colloid, metronidazole and tetracyclines, has been developed. Triple therapy is ineffective in 15%–30% of cases and quadruple therapy in 10%–25% of cases [1]. Therapy also often causes side effects such as anti-

biotic-induced diarrhoea [2]. Recently meta-analysis involving a pediatric population including 29 trials (3122 participants) and involving 17 probiotic regimens was published. Compared with placebo, probiotic-supplemented PPI and antibiotic therapy significantly increased *H. pylori* eradication rates and reduced the incidence of side effects [3].

Similarly, 13 randomized controlled trials involving 2306 of adult patients were recently included in another meta-analysis. These authors also reported that probiotic supplementation during *H. pylori* treatment may be effective for improving eradication rates, minimizing the incidence of therapy-related adverse events and alleviating most disease-related clinical symptoms [4].

One of the most investigated probiotics is *Bifidobacterium animalis* subspecies *lactis* BB12 (DSM 15954, hereafter referred to as BB12). Reported to reduce episodes of antibiotic-induced diarrhoea during anti-*Helicobacter* treatment by 60% [5], BB12 increased the eradication rate of *H. pylori* by 13% in the case of triple therapy, and by 14% in case of quadruple therapy [6,7], and decreased *H. pylori* urease activity after 6 weeks of therapy [8].

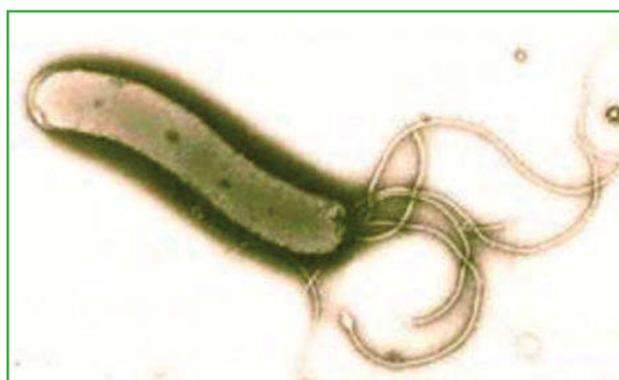
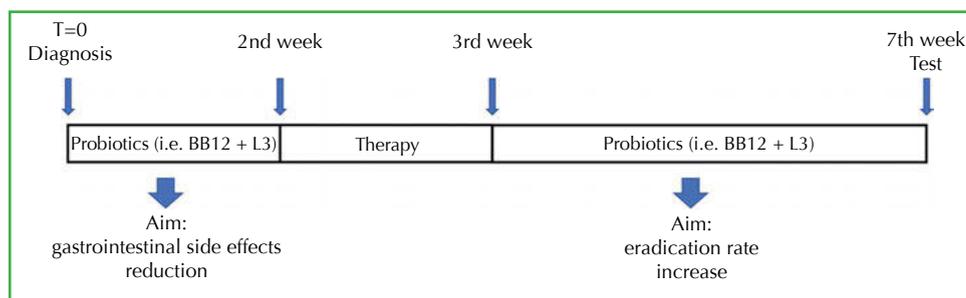


Figure 1 - *Helicobacter pylori*



Figure 2 - *Helicobacter pylori* growth inhibition zones after L3 enterococin activity



**Figure 3** - Suggested treatment scheme to increase *Helicobacter pylori* eradication rates and to reduce the side effects of antibiotics

*Helicobacter pylori* uses molecular hydrogen as a respiratory substrate when grown in the laboratory. It is also known that hydrogen is available in the gastric mucosa and that its use greatly increases stomach colonization by *H. pylori*. Therefore, hydrogen present in animals as a consequence of normal colonic flora activity can facilitate the maintenance of a pathogenic bacterium [9].

The strongest hydrogen-producing organisms, are thought to be *Escherichia coli*, *Clostridium*, and *Enterobacter* species [10]; BB12 increased the numbers of stool bifidobacteria and suppressed coliform bacteria (*Escherichia*, *Clostridium*, *Enterobacter*) [11]. Therefore, since colonic bifidobacteria decrease colonic hydrogen production, BB12 might alter

hydrogen production and can lessen the severity of *H. pylori* infection. Another strain has recently been shown to preserve the growth of bifidobacteria thus reducing of the number of opportunistic microorganisms: *Enterococcus faecium* L3 (LMG P-27496, hereafter referred to as L3) [12], which inhibits *H. pylori* growth in vitro (Fig. 2). On this basis, BB12 and L3 might be able to be used to better eradicate the gastric pathogen while reducing the number of side effects. The pre-antibiotic use of probiotics likely reduces the severity and/or the length of antibiotic-induced diarrhoea (by increasing the bacterial load), while their use following antibiotic administration likely increases the eradication rate (as they act on a pathogen already reduced in terms of vitality and strength). Thus, a possible treatment approach could be to use probiotics as add-on therapy in order to achieve better eradication of *H. pylori* while minimizing the gastrointestinal side effects of antibiotic use (Fig. 3).

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