Nutrafoods (2018) 17:N76-N87
DOI 10.17470/NF-018-3003-4

Lactobacillus rhamnosus CRL1505

A probiotic for respiratory and digestive health

➢ by Sacco

Infections of the respiratory and gastrointestinal tracts remain serious healthcare problems worldwide. Acute respiratory infections including pneumonia, bronchitis, bronchiolitis, influenza and whooping cough are the primary cause of death during childhood [2].

Although mortality from these diseases is much lower in developed countries, acute respiratory infections are associated with almost 50% of hospitalizations in children. It is estimated that influenza viruses affect 20% of the global population every year and over 90% of deaths in the elderly are related to these infections. Diarrhoea also imposes a heavy burden on human health. Worldwide, one out of nine children under the age of 5 die from diarrhoeal disease, making it the second leading cause of death in this population [3].

In addition to the direct issues generated by infectious diseases, those with a bacterial aetiology often require antibiotic treatment. However, repeated or prolonged use of antibiotics can negatively affect the gastrointestinal microbiota with repercussions on the host's health, and can also contribute to antibiotic resistance, one of the biggest emerging problems in public health. The use of alternative therapies to relieve the burden of infectious diseases, including probiotics, is therefore of enormous interest.

Lactobacillus rhamnosus CRL1505 is a probiotic, originally isolated from goat's milk and produced by SACCO in Italy, that has been shown to increase resistance to intestinal, and especially respiratory, infections in several animal models of disease. In this article we summarize the main findings obtained in pre-clinical animal studies, the mechanisms involved in disease amelioration, and highlight a clinical trial with pre-school children that revealed a significant reduction in the number of infections in the study population when consuming *L. rhamnosus* CRL1505.

Technical information

- The *L. rhamnosus* CRL1505 genome has been sequenced and is publicly available [4].
- The *L. rhamnosus* CRL1505 strain is deposited in the German Collection of Microorganisms and Cell Cultures (deposit number DSM 29673).
- *L. rhamnosus* CRL1505 is stable when stored at –20°C for 24 months and when stored at 5°C for 12 months.

Mechanisms of action

L. rhamnosus CRL1505 has been shown to consistently immunomodulate an array of cytokines in different models [1, 4, 10]. Increased basal levels of interferon gamma (IFN-γ), a key activator of the innate and adaptive immune systems, and of the anti-inflammatory cytokine interleukin 10 (IL-10), were observed in the intestinal fluid, serum and bronchoalveolar lavage (BAL) of mice after oral administration of *L. rhamnosus* CRL1505 (10^8 CFU/g daily) [5]. Intake of *L. rhamnosus* CRL1505 essentially primes the immune system, allowing it to respond earlier to an infectious agent and clear the infection [8, 10]. It has been shown in a murine model that when mice were challenged with IFV or RSV, blocking IL-10 receptors significantly reduced the capacity of *L. rhamnosus* CRL1505 to prevent lung tissue damage by limiting coagulation, revealing that stimulation of this cytokine by *L. rhamnosus* CRL1505 is partly responsible for the probiotic's health benefits [10].

Efficacy

Pre-clinical animal studies

There are substantial pre-clinical data supporting the digestive and respiratory health benefits of *L. rhamnosus* CRL1505. Published, peer-reviewed animal studies include viral and bacterial challenge experiments, as well as normo- and malnutrition models. The health outcomes of these studies can be summarized as follows:

- *L. rhamnosus* CRL1505 stimulates the immune system, intra- and extra-intestinally [4].
- Oral administration of *L. rhamnosus* CRL1505 enhances resistance to the enteric pathogen *Salmonella typhimorium*, in well- and malnourished mice [4,5].

- Oral administration of *L. rhamnosus* CRL1505 heightens resistance to the airway pathogen *Streptococcus pneumoniae* serotype 14, in well- and malnourished mice [4,5], and increases anti-pneumococcal immunoglobulin A (IgA) in airway tissue [4].
- Oral administration of *L. rhamnosus* CRL1505 counters bacteraemia in well- and malnourished mice [4,5].
- Priming of mice with orally administered *L. rhamnosus* CRL1505 led to an earlier immune response to a nasal challenge with respiratory syncytial virus A2 (RSV) and influenza virus A/PR/8/34 (H1N1) (IFV), and reduced lung damage [1,7,10].
- Heat-inactivated *L. rhamnosus* CRL1505 can partially deliver the benefits of the live probiotic when administered intranasally in a model of viral respiratory infection (poly(I:C)) and RSV challenge [8].
- Orally administered *L. rhamnosus* CRL1505 offsets alterations in B cell development resulting from malnutrition [6].

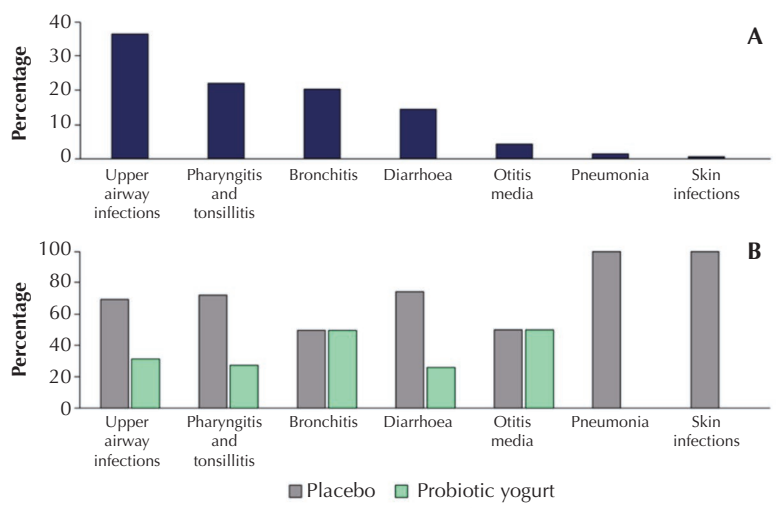

Figure 1 - Distribution of infections in the study cohort according to the type of infection (**A**), and a comparison of the proportions of children consuming the placebo or probiotic yogurt (**B**). Adapted from Villena *et al* [9]

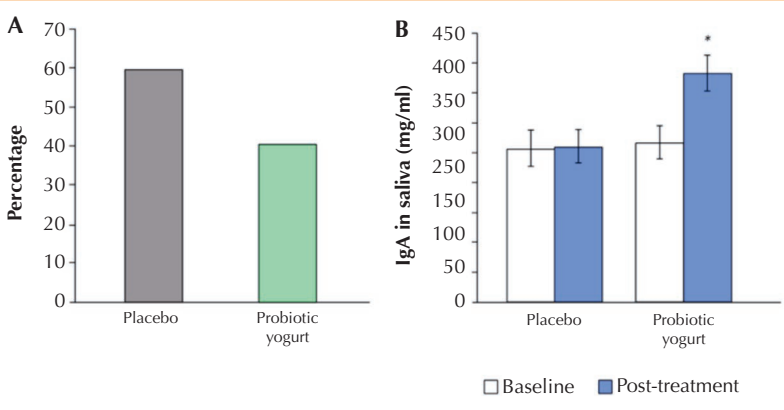

Figure 2 - Antibiotic use throughout the study period (**A**) and IgA concentrations in children's saliva (**B**). Adapted from Villena *et al* [9]

Clinical relevance

A randomized, double-blind, placebo-controlled trial conducted by Villena and colleagues (2012) [9] on 298 preschool children (aged 2–5 years old) who consumed either yogurt containing *L. rhamnosus* CRL1505 (>10^8 CFU/g) or a placebo yogurt for 5 days/week for 6 months showed:

- Significantly fewer infections in children consuming the probiotic-containing yogurt. Only 34% of children in the *L. rhamnosus* CRL1505 group showed symptoms of infection compared with 66% in the control group.
- Significantly fewer children in the probiotic group presented with upper respiratory tract infection (69% of cases were observed in the placebo group), pharyngitis and tonsillitis (72% of cases were reported in the placebo group), and acute diarrhoea (74% of cases occurred in the placebo group) (Fig. 1).
- Children in the *L. rhamnosus* CRL1505 group used significantly fewer antibiotics during the study period than the placebo group; 60% of antibiotic use was in the placebo group (Fig. 2A).
- Saliva IgA concentrations were significantly higher in the probiotic group than in the placebo group after the 6-month intervention (Fig. 2B), suggesting a similar mechanism to that observed in the pre-clinical trials.

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Sacco in a nutshell

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