

Antiviral potential of topically applied lactobacilli in the respiratory tract: from mechanisms to application

Irina Spacova

Abstract

Viral respiratory tract infections are a major cause of hospitalization and mortality worldwide. While probiotics for the gastrointestinal tract show promise in the prevention of viral respiratory tract infections, topical application of probiotic bacteria directly to the respiratory tract is emerging as a more targeted alternative with distinct potential benefits.

We recently summarized the mechanisms through which topically applied beneficial bacteria could impact the course of viral infection (Spacova *et al.*, 2021, Trends in Molecular Medicine). On one hand, probiotics administered to the upper airways can directly stimulate respiratory mucosal immunity, thus bypassing the gut-lung axis. On the other hand, our experimental data suggests that beneficial lactobacilli can also directly inhibit the infectivity of human coronaviruses (*e.g.*, HCoV-299) or the respiratory syncytial virus (RSV) *in vitro*.

Consequently, we took an important step in translating these experimental findings to the clinic through rational selection of beneficial lactobacilli based on their probiotic and adaptation factors and their effective formulation for application in the human airways. We formulated a throat spray with three beneficial lactobacilli capable of antiviral action and validated that the freeze-dried lactobacilli maintained their immunostimulatory properties *in vitro*. The throat spray was then tested in a randomized double-blind placebo-controlled trial in COVID-19 primary care patients, resulting in high compliance for spray use and self-sampling. We observed an increase in lactobacilli abundances during spray use and a trend towards lower SARS-CoV-2 viral loads in the upper respiratory tract of the lactobacilli spray group compared to the placebo group after 3 weeks of study. These results pave the way for rational selection of beneficial lactic acid bacteria against respiratory viruses for topical applications to prevent or treat respiratory viral diseases in primary care patients.