Bifidobacterium animalis subsp. lactis HN019 live probiotics and postbiotics: production strategies and bioactivity evaluation for potential therapeutic properties

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B. animalis subsp. *lactis* HN019 is a commercially available well-characterized probiotic with documented effects on human health, such as the ability to enhance the immune function and to balance the intestinal microbiome. Therefore, optimizing the manufacturing process to increase biomass yields and viability is currently of interest. Moreover, the growing demand of vegan grade food supplements further addresses scientific research towards the design of alternative growth media for lactic acid bacteria (probiotics).

Besides the established use of live probiotic cells, alternative supplements like non-viable cells and/or probiotic derived bioactive molecules, indicated as postbiotics, might be considered as potential next generation biotherapeutics. In fact, the latter may present lower variability during storage, as well as easier production processes and scale-up.

In this work, to better characterize the physiology of *B. lactis* HN019, medium design together with different fermentation strategies (batch, fed-batch and *in situ* product removal) on lab-scale bioreactors were combined to increase the titer of viable cells up to $2.9\pm0.1\times10^{10}$. On the other hand, exopolysaccharides (EPS) were isolated from the fermentation broth, characterized, and tested, in comparison to live cells and whole heat inactivated broth for the first time up to date, in *in vitro* biological assays, using differentiated CaCo-2 cells challenged by LPS of *S. Minnesota*.

Interestingly, all samples demonstrated immune-modulating properties by downregulating the expression of TLR-4 and NF-kB in LPS challenged cells. In addition, the proposed treatments, and EPS in particular, showed the ability to restore the integrity of the tight junctions by up-regulating the expression of zonulin.