Influence of dietary glycosaminoglycans and *Bifidobacterium longum* in the gliadin-mediated inflammatory response(s) of intestinal epithelial cells (Caco-2)

J. M. Laparra and Y. Sanz

*Microbial Ecophysiology and Nutrition Group, Institute of Agrochemistry and Food Technology (IATA), Spanish National Research Council (CSIC), Valencia, Spain*

Celiac disease is a chronic enteropathy triggered by the ingestion of cereal gluten proteins (gliadins), whose interaction with intestinal epithelial cells seems to precede the onset of the gliadin-induced inflammatory events characteristic of the disease. Proteoglycans (GAGs) are one of the major components of the extracellular matrix of muscle tissue, and their biological functions are determined by their structure\(^{(1)}\). The objective of this study was to evaluate the influence of GAGs, alone and as coadjuvant of a potential probiotic bifidobacterial strain, in the pro-inflammatory effects of gliadins on intestinal epithelial cells.

GAGs (Chondroitin/dermatan sulphate structures) were isolated from cooked haddock\(^{(2)}\). Gliadins, with/without GAGs, were subjected to a simulated gastrointestinal digestion and incubated in the presence or absence of cell suspensions (10\(^8\) cfu/ml) of *Bifidobacterium longum* IATA-ES1. Caco-2 cell cultures were incubated (6 h) with the dialysates obtained from *in vitro* digestions. The production of tumour necrosis factor (TNF-\(\alpha\)) and interleukin (IL)-1\(\beta\), was determined by ELISA. Gliadin-derived peptides induced a significantly higher (\(P<0.05\)) production of TNF-\(\alpha\) (131.2\(\pm\)30.4 pg/ml) and IL-1\(\beta\) (86.4\(\pm\)7.8 pg/ml) compared to controls (TNF-\(\alpha\), 50.4\(\pm\)8.1 and IL-1\(\beta\), 37.2\(\pm\)1.1 pg/ml). The addition of GAGs either during or after *in vitro* digestion of gliadins failed (\(P>0.05\)) to reduce the TNF-\(\alpha\) production, but abolished (\(P<0.05\)) the IL-1\(\beta\) production. Cell cultures exposed to gliadin digest incubated in the presence of the *B. longum* showed a significant (\(P<0.05\)) reduction of TNF-\(\alpha\) (30.3\(\pm\)7.5 pg/ml) and IL-1\(\beta\) (38.2\(\pm\)13.1 pg/ml). The addition of GAGs to the digestes inoculated with *B. longum* reduced the TNF-\(\alpha\) production to levels similar as those of controls (53.4\(\pm\)3.3 pg/ml), and IL-1\(\beta\) production to levels lower (25.9\(\pm\)8.8 pg/ml) than those induced in the presence of *B. longum* alone. Therefore, it has been demonstrated that dietary GAGs inhibits the IL-1\(\beta\) production induced by gliadin peptides in Caco-2 cells, *B. longum* IATA-ES1 inhibits the TNF-\(\alpha\) and IL-1\(\beta\) production, and the combination of both ingredients exerts additive effects on IL-1\(\beta\) production.

AGL2008–01440/ALI and Consolider Fun-C-Food CSD2007–00063 from the Spanish Ministry of Science and Innovation (MICINN, Spain). The post-doctoral contract to M. Laparra from Juan de la Cierva (MICINN, Spain) is fully acknowledged.