Probiotics and prebiotics as a therapeutic strategy for inflammatory bowel disease

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Abstract

Inflammatory bowel disease (IBD) is the collective term for a group of idiopathic intestinal conditions typified by ulcerative colitis (UC) and Crohn’s disease (CD). An underlying factor in the development of IBD appears to be a dysregulated immune response to the host microflora. Due to the involvement of the intestinal bacteria in the pathogenesis of IBD, manipulation of the microflora by probiotics, prebiotics or combinations thereof (synbiotics) has been identified as a potential treatment option.

The primary aim of this thesis was to identify probiotics and/or prebiotics with the potential to reduce the severity of experimental colitis. The specific aims were to i) screen a range of candidate probiotic strains for capacity to reduce symptoms of DSS-colitis, ii) characterize the effects of DSS within the small intestine, iii) assess, in vitro, the effect of probiotics on intestinal epithelial cell integrity, iv) assess the potential for the prebiotic, fructooligosaccharide, to reduce the severity of DSS-colitis alone, and in symbiotic combination with a probiotic strain.

It was found that treatment with L. reuteri BR11 and B. lactis Bb12 partially reduced the severity of experimentally-induced colitis. This was the first description of L. reuteri BR11 as a potential new probiotic. Interestingly, L. rhamnosus GG exacerbated some indicators of injury. This study supported the idea that probiotics could be beneficial in the treatment of IBD, however, it highlighted the importance of screening strains for therapeutic benefits. L. reuteri BR11 was shown to maintain total mucin production in DSS-treated rats, indicating one potential mechanism by which it partially protects the colon from DSS-induced damage. In addition, it was demonstrated that DSS altered the morphology of the
small intestine of colitic rats. This supports recent studies which indicate small intestinal manifestations of DSS-induced colitis. Again, *L. reuteri* BR11 was the most successful bacterial strain at normalizing these changes.

Using an *in vitro* cell culture system, it was found that treatment of Caco-2 cell monolayers with DSS increased caspase 3/7 activity, indicative of increased apoptosis. Further to this, it was demonstrated that incubation of Caco-2 cells with *L. reuteri* BR11 significantly reduced the extent of apoptosis, again highlighting a beneficial mechanism by which *L. reuteri* BR11 may have prevented intestinal damage.

It was found that 6% w/w FOS, alone, and in combination with *L. reuteri* BR11, could not prevent DSS-colitis. The lack of a beneficial effect in *L. reuteri* BR11-treated rats may have been due to an increased DSS dose in this study. Alternatively, FOS may have led to an over-production of organic acids, promoting colonic injury.

In summary, this thesis explores the rapidly advancing area of probiotics and prebiotics for the treatment of IBD. It describes the capacity for *L. reuteri* BR11 and to a lesser extent, *B. lactis* Bb12, to partially reduce the severity of DSS-colitis. The use of prebiotics and synbiotics was largely unsuccessful in this study, however, further investigations into these areas are warranted. This thesis provides support for future investigations into the use of probiotics and prebiotics for the treatment of IBD.