Lyophilized Symbiotic Mitigates Mucositis Induced by 5-Fluorouracil

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Mucositis is an adverse effect of cancer chemotherapies using 5-fluorouracil (5-FU). It is characterized by mucosal inflammation, pain, diarrhea, and weight loss. Some studies reported promising healing effects of probiotic strains associated with prebiotics as adjuvant treatment of mucositis. The development of alternative or adjuvant treatments is needed and the use of probiotics;synbiotic as promising candidates for adjuvant treatment of mucositis recently attracted attention. This study aimed todevelop a symbiotic and lyophilized product, based on milk, supplemented with WPI and FOS, fermented by strains L. casei BL23, L. plantarum B7, and L. rhamnosus B1, which would be able to reduce the intestinal inflammation, to control the pro-inflammatory immune response, and to decrease intestinal permeability, in a murine model of mucositis induced by 5-FU. A lyophilized synbiotic product containing skimmed milk, supplemented with whey protein isolate (WPI) and with fructooligosaccharides (FOS), and fermented by Lacticacaseibacillus casei BL23, Lactiplantibacillus plantarum B7, and Lacticaseibacillus rhamnosus B1. Regards the intestinal permeabiity, this parameter was determined in vivo by quantifying blood radioactivity after oral administration of 99mTc- DTPA. Finally, histological damages caused by 5-FU-induced mucositis were monitored. L. casei BL23, L. plantarum B7, and L. rhamnosus D1, submitted to lyophilization counts after rehydration of the product, reached populations greater than 2×10^9 CFU/g. The Symbiotic treatment significantly reduced ($p < 0.05$) the loss, compared to 5-FU (inflamed control group) and L. casei BL23, besides a slight weight loss in the Naive group without inflammation; in addition, the Symbiotic formulation showed discrete destruction and reduction of villi, moderate inflammatory infiltrate with mucosal and submucosal involvement, with moderate loss of crypts, can be observed. Finally, animals treated with matrix and Symbiotic exhibited significantly decreased ($p < 0.001$) intestinal permeability compared to the 5-FU inflamed control group. Overall, the symbiotic formulation presented anti-inflammatory potential in 5-FU-induced mucositis, reducing animal weight loss intestinal permeability, modulating genes implicated in the intestinal epithelial barrier, controlling pro-inflammatory cytokine levels, and reducing mucosal damage caused by chemotherapy. Indeed, the consumption of the symbiotic formulation caused a reduced score of inflammation in the duodenum, ileum, and colon, as well as decreased levels of pro-inflammatory cytokines IL- 1?, IL-6, IL-17, and TNF-? in the mice ileum. Therefore, the symbiotic product developed in this work thus represents a promising adjuvant treatment of mucositis.Overall, this work opens new perspectives for the development of functional symbiotic products for target populations, in the context of mucositis, based on smart selection of matrices and bacterial consortia.

References

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