

Colon cancer is a complex disease that involves numerous genetic alterations that change the normal colonic mucosa into invasive adenocarcinoma. In the current study, the protective effects of inulin (prebiotic), *Lactobacillus casei* (*L. casei*, probiotic) and their combination (synbiotic) on 1,2- dimethylhydrazine (DMH)-induced colon cancer in male Swiss mice were evaluated. Animals were divided into: Control group, DMH-treated group, DMH plus inulin, DMH plus *L. casei* and DMH plus inulin plus *L. casei*-treated groups. Fecal microbiome analysis, biochemical measurements, histopathological examination of the colon tissues, immunostaining and Western blotting analysis of bcatenin, GSK3b and JNK-1 were performed. The prebiotic-, probiotic- and synbiotic-treated groups showed decreased levels of carcinoembryonic antigen and a lower number of aberrant crypt foci compared to the DMH-treated group with the synbiotic group exhibiting a superior effect. Furthermore, all treatments showed a body weight-reducing effect. Administration of inulin, *L. casei* or their combination increased the expression level of phospho-JNK-1 while they decreased the expression level of b-catenin and phospho-GSK3b. Remarkably, *L. casei* treatment resulted in enrichment of certain beneficial bacterial genera i.e. *Akkermansia* and *Turicibacter*. Therefore, administration of *L. casei* and inulin as a synbiotic combination protects against colon cancer in mice.