Guar Gum-Induced Changes in Gut Microbiota Metabolic Activity and Intestinal Immune Response Augments Susceptibility to Experimental Colitis

Devendra Paudel, Sangshan Tian, Grace Joseph, Eleni Prodes, Divek V. T. Nair, Vishal Singh

The Pennsylvania State University

Objectives: Guar gum is a common food additive found in many processed foods. Both preclinical and clinical studies documented the beneficial effect of guar gum on gastrointestinal health. We, therefore, hypothesized that guar gum might attenuate the severity of ulcerative colitis (UC), an inflammatory bowel disease (IBD) that chiefly affects the large intestine.

Methods: To test the effect of guar gum on colitis, wild-type (WT) mice were fed diets containing either cellulose (insoluble fiber as control) or guar gum (soluble fiber, 7.5% w/w) for four weeks. Acute and chronic colitis was induced via epithelial injury [dextran sulfate sodium (DSS, 1.4% w/v) in drinking water for 7 days] or immune hyperactivation [IL-10 receptor neutralization by weekly injections of αIL-10R mAb (1 mg/mouse, intraperitoneally) for 4 weeks], respectively. Colitis development was examined by serological, biochemical, histological, and immunological parameters.

Results: Unexpectedly, experimental mice maintained on a guar gum-containing diet (GuD) exhibited increased susceptibility to both acute and chronic colitis. Relative to the control group, GuD-fed mice experienced greater occurrence of rectal bleeding, diarrhea, splenomegaly, and displayed higher levels of pro-inflammatory markers [serum amyloid A (SAA) and lipocalin 2 (Lcn2)]. Analysis of the composition of gut microbiota and their metabolites revealed elevated branched chain amino acids and reduced butyrate in the GuD-fed groups compared to control, among other differences in gut microbiota community structure. Depletion of gut microbiota with broad spectrum antibiotics reversed colitis susceptibility, suggesting that GuD-induced alterations in gut microbiota might contribute to the severity of experimental colitis. Besides differences in gut microbiota activity, a substantial decrease in colonic IL-18 production (>3 folds) was observed in mice fed GuD. Remarkably, supplementation of recombinant IL-18 (rIL-18) alleviated colitis in GuD-fed mice, suggesting that reduced colonic IL-18 upon GuD feeding increases susceptibility to colitis.

Conclusions: Collectively, our study demonstrates that food additive guar gum adversely impacts the gut microbiota activity and colonic immune response and increases susceptibility to colonic inflammation.

Funding Sources: Crohn's & Colitis Foundation.