R2017-P09
NDB

Final Report **PA Soybean Board** **PI:** Lambert, Joshua D.

Title: Mitigation of ulcerative colitis by dietary soy fiber supplementation

Overall Objective and Experimental Approach: Our objective was to determine the ability of dietary soybean fiber to mitigate dextran sulfate sodium (DSS)-induced ulcerative colitis (UC) in mice.

Male C57BL6 mice received control diet or diets where 20 or 40% of the fiber content was replaced with soybean fiber (SBF). After 2 weeks, mice were treated with 2% DSS in the drinking fluid to induce UC. After 7 days of DSS treatment, mice were euthanized and tissue and plasma samples were collected. Control mice received water for the duration of the experiment (Fig. 1).

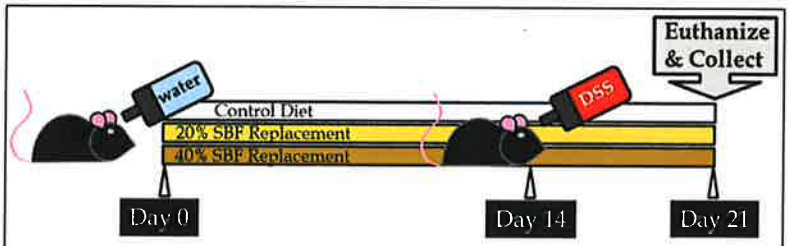

Fig 1. Overall experimental design. Male C57BL/6J mice were randomized to control diet or diets where 20 or 40% of the fiber content was replaced with soybean fiber. After 2 weeks, mice received 2% dextran sulfate sodium (DSS) in the drinking water to induce ulcerative colitis. After 7 days, mice were euthanized. Control mice received water for the entire experiment.

New Data:

The SBF-containing diets were well-tolerated. DSS treatment led to a 10% decrease in body weight compared to water-treated controls (Fig. 2). Treatment with SBF tended to prevent this decrease in body weight. DSS treatment also increased relative spleen weight and decreased colon length, which both indicate increased inflammation (Fig. 2). SBF treatment mitigated both the increase in spleen weight and the decrease in colon length. Taken together, these results indicate that SBF is able to blunt DSS-induced UC.

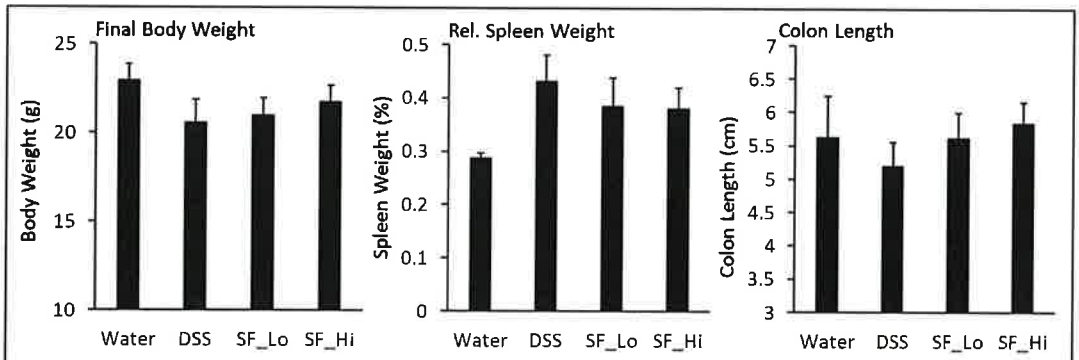

Fig 2. Impact of soy fiber supplementation on gross markers of ulcerative colitis and inflammation in C57BL/6J mice. Mice were pretreated with soybean fiber-supplemented diets for 2 weeks prior to treatment with DSS for 7 days. Soybean fiber replaced 20% or 40% of total fiber in the SF_Lo and SF_Hi groups, respectively. Final body weight was recorded. Following euthanasia, spleen weight was determined and normalized to body weight. Colon length was measured. Each bar represents n = 5 – 10 mice and the error bars represent the standard deviation.

We examined the impact of dietary SBF on 4 plasma markers inflammation: interleukin (IL)-1β, tumor necrosis factor (TNF)α, IL-6, and monocyte chemoattractant protein (MCP)1. DSS treatment led to a significant increase in the levels of all 4 markers measured compared to water-treated controls (Fig. 3). For both IL-1β and TNFα, SBF treatment mitigated DSS-induced changes (Fig. 3). By contrast, SBF treatment had no effect on IL-6 levels and appeared to exacerbate increases in MCP-1 levels. These results indicate that SBF can modulate some inflammatory markers associated with UC *in vivo* but that additional studies are needed to better characterize the spectrum of anti-inflammatory changes and understand the mechanism of action.

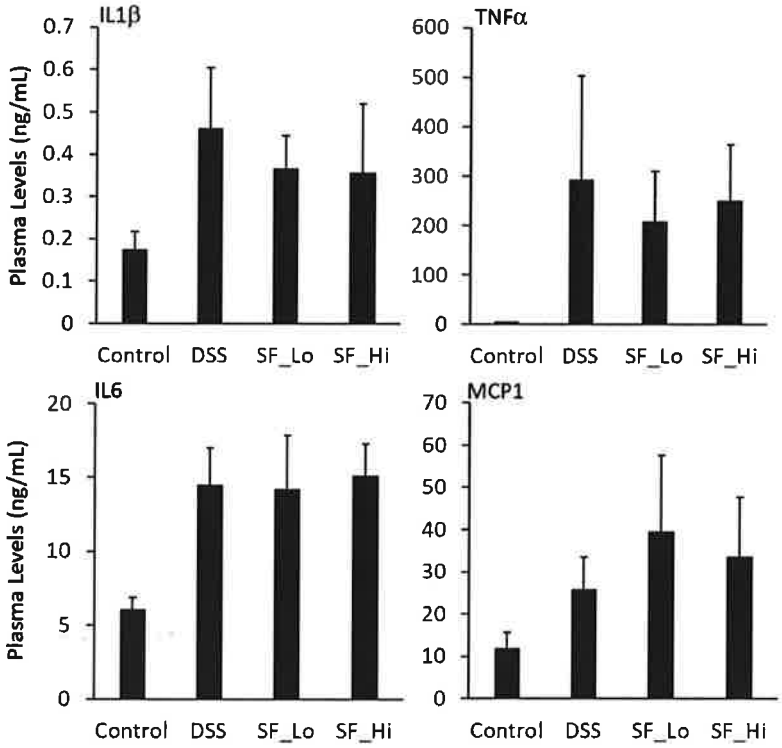

Fig 3. Impact of soy fiber supplementation on plasma markers of inflammation in C57BL/6J mice. Mice were pretreated with soybean fiber-supplemented diets for 2 weeks prior to treatment with DSS for 7 days. Soybean fiber replaced 20% or 40% of total fiber in the SF_Lo and SF_Hi groups, respectively. Plasma levels of cytokines were measured by ELISA. Each bar represents n = 5 – 10 mice and the error bars represent the standard deviation.

Ongoing and Future Studies:

We are currently examining the impact of SBF treatment on inflammatory gene expression in the colon tissues. These data will help us better understand the local effects of SBF in the gastrointestinal tract and more clearly demonstrate the potential beneficial effects of SBF in the context of UC.

Future studies will focus on three directions:

1. Replication of the experiments conducted to date to confirm the observed results and increase the robustness of the findings.

2. Expand the results to a model of inflammation-driven colon cancer by examining the impact of dietary SBF on the development of colon cancer in azoxymethane (AOM)/DSS treated mice.

3. Characterize the potential anti-inflammatory synergy of SBF in combination with other soybean components including: soy protein, soy isoflavones, and soybean oil derived phytochemicals such as tocopherols.

Conclusions:

The present results indicate the consumption of SBF may improve markers of gastrointestinal inflammation and may be useful in the prevention and management of UC. Further studies are needed to confirm the results of this study and to better understand the underlying mechanisms of action.