

Evaluation of the Effect of Two Mixes of Prebiotic Fibers in the Simulator of the Human Intestinal Microbial Ecosystem (SHIME®)

Natarajan Ranganathan¹, Massimo M², Ghyselinck J², Pinheiro I²,

P Ranganathan¹, K Hanlon¹, A Irvin¹, Usha Vyas¹

¹Kibow Biotech Inc., Newtown Square ,PA 19073 ²ProDigest BVBA, Ghent, Belgium



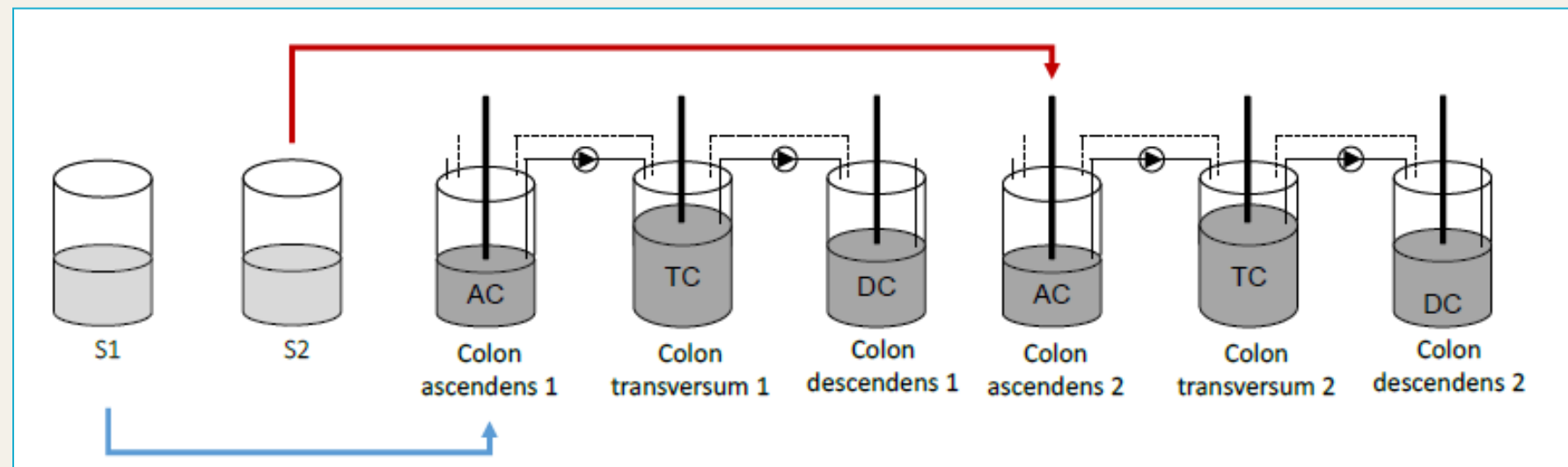
INTRODUCTION

The role of dietary fibers and prebiotics on the gut microbiome and various health benefits is reaching newer heights. Various clinical studies have documented the beneficial health properties of various single prebiotic dietary fibers. Here we have studied the effects of our proprietary prebiotic fiber formulation with and without addition of a *Bacillus* probiotic on the activity and composition of the human gut microbiome.

METHODS

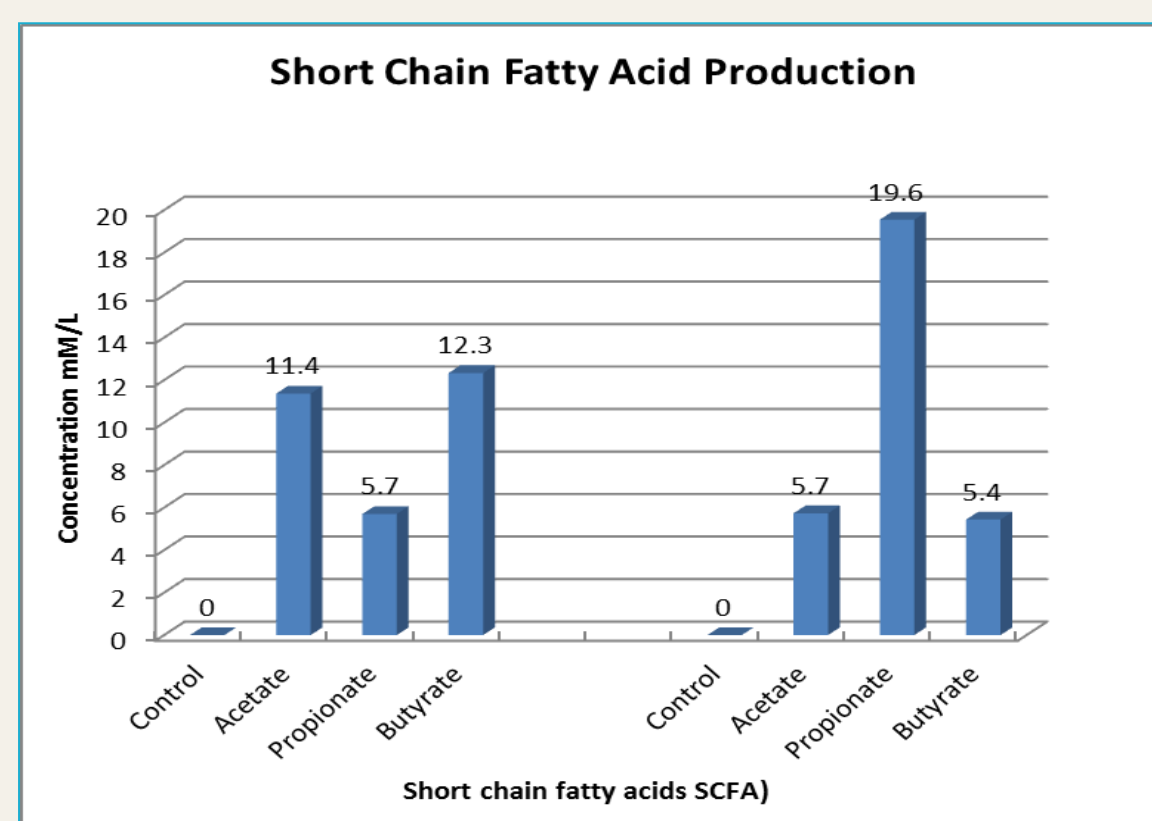
A TWINSHIME® setup was used, which allowed for simultaneous comparison and testing of two samples. Each segment of the TWINSHIME® consisted of a succession of 4 reactors simulating the different parts of the gastrointestinal tract.

The experiment was carried out as a three stage setup: In the stabilization period which was two weeks the colon reactors were inoculated with a fresh fecal sample, in a basic nutritional matrix to support maximum gut diversity. The next two weeks were the control/reference period where the nutrient matrix was further dosed and the baseline microbial community and activity were determined. This was followed by a three week treatment period where the SHIME reactor was operated under nominal conditions, but with the prebiotic fiber with and without the *Bacillus* probiotic added to the normal composition. Various metabolites and microbial composition were analyzed.

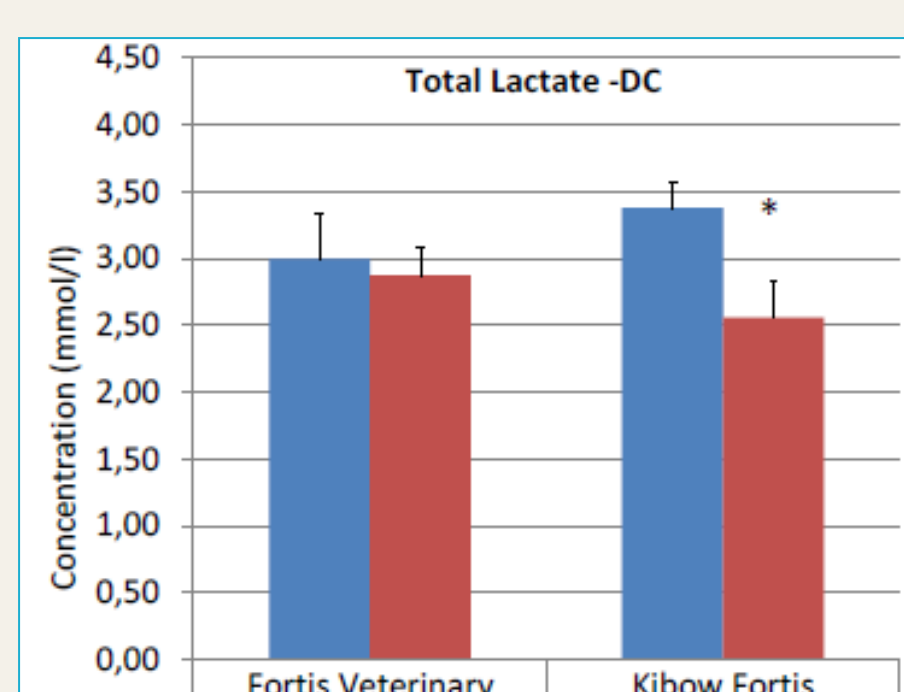
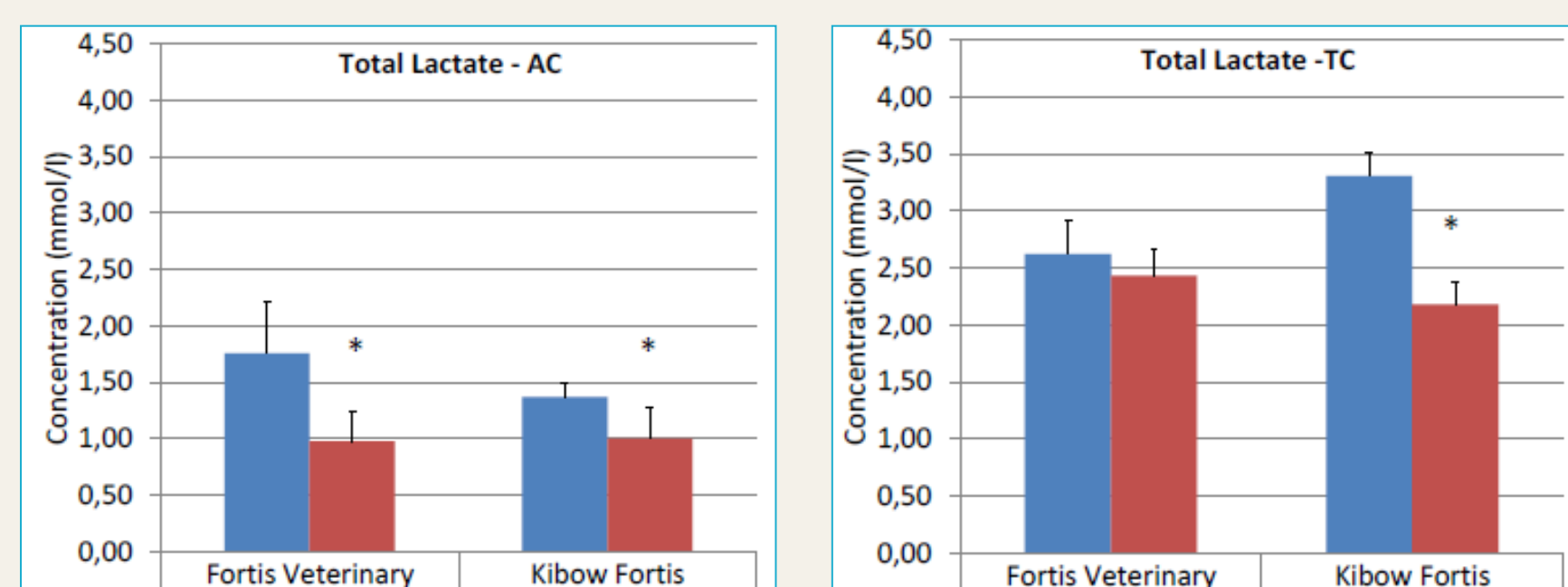


S1-stomach, S2-small intestine. The colonic reactor compartments were continuously stirred reactors with constant volume and pH control.

RESULTS

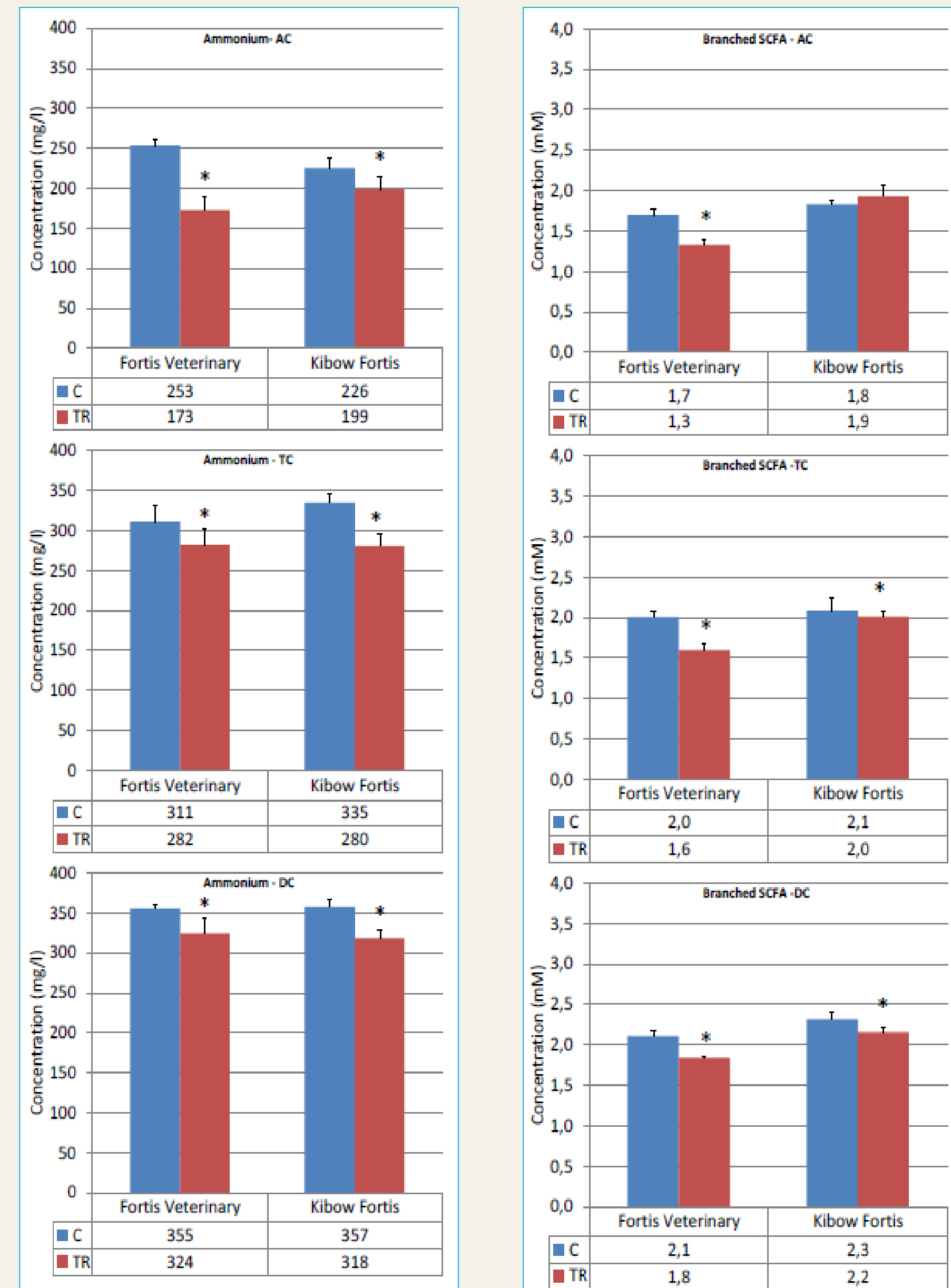


Both fiber products stimulated the production of the main short chain fatty acids (SCFA) and were associated with an increase in acetate and butyrate. The fiber containing *Bacillus* probiotic shifted the SCFA profile from an acetate-dominant profile to a propionate-dominant profile



Lactate levels in three sections of the colon. (Blue bar is the control and Red bar is the treatment group) Lactate levels were lower than the control in both the treatment groups.

RESULTS contd....



Both products lowered ammonium and branched chain fatty acid (b-SCFA) concentration. Decreased levels of ammonium and b-SCFA production is considered as beneficial, as the production of ammonium and b-SCFAs results from protein degradation and reflects proteolytic activity of the gut microbiome.

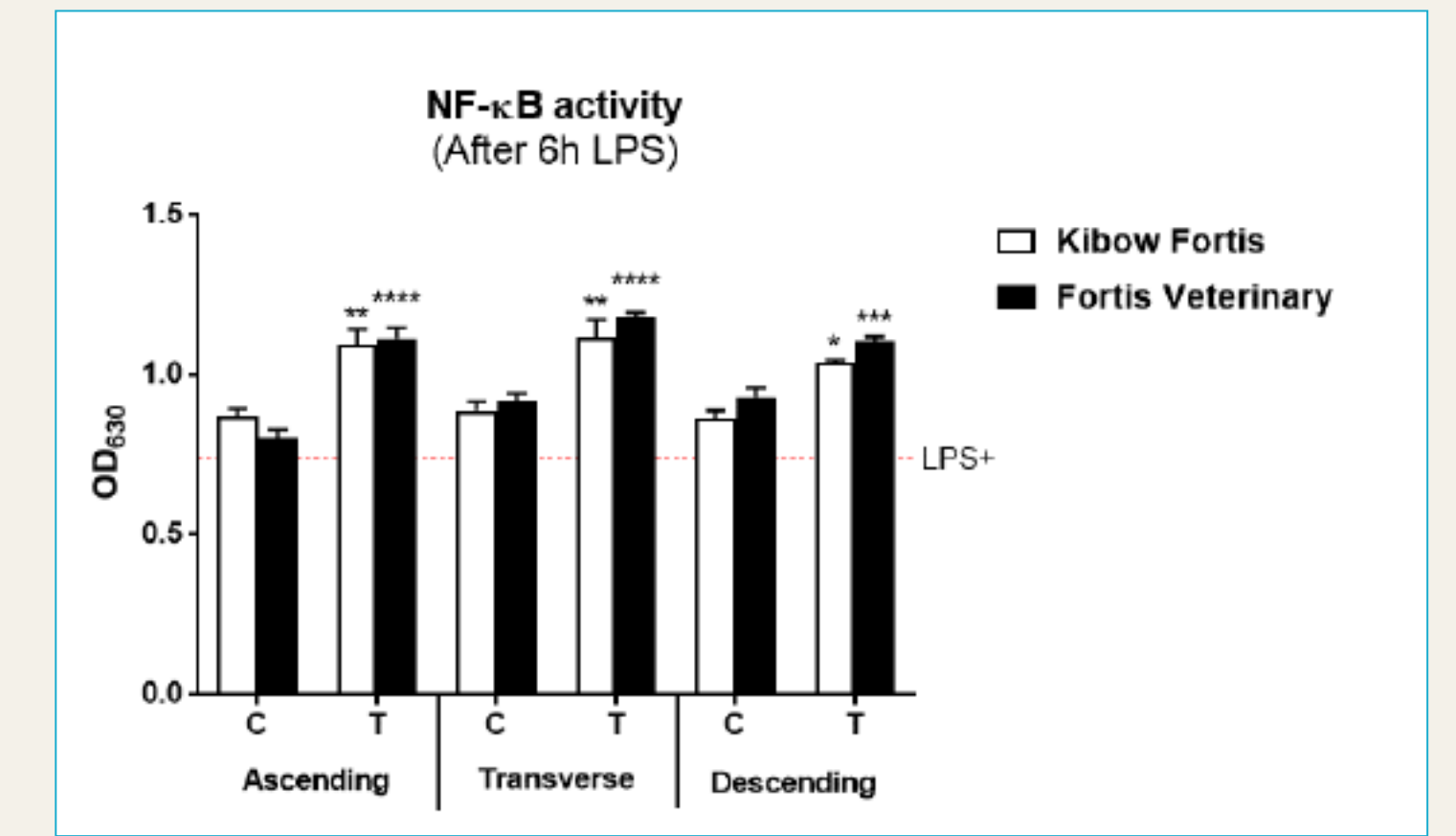


Effect of the multifiber composition on the beneficial microbial populations in the ascending colon (AC), transverse colon (TC) and the descending colon (DC) assessed with qPCR.

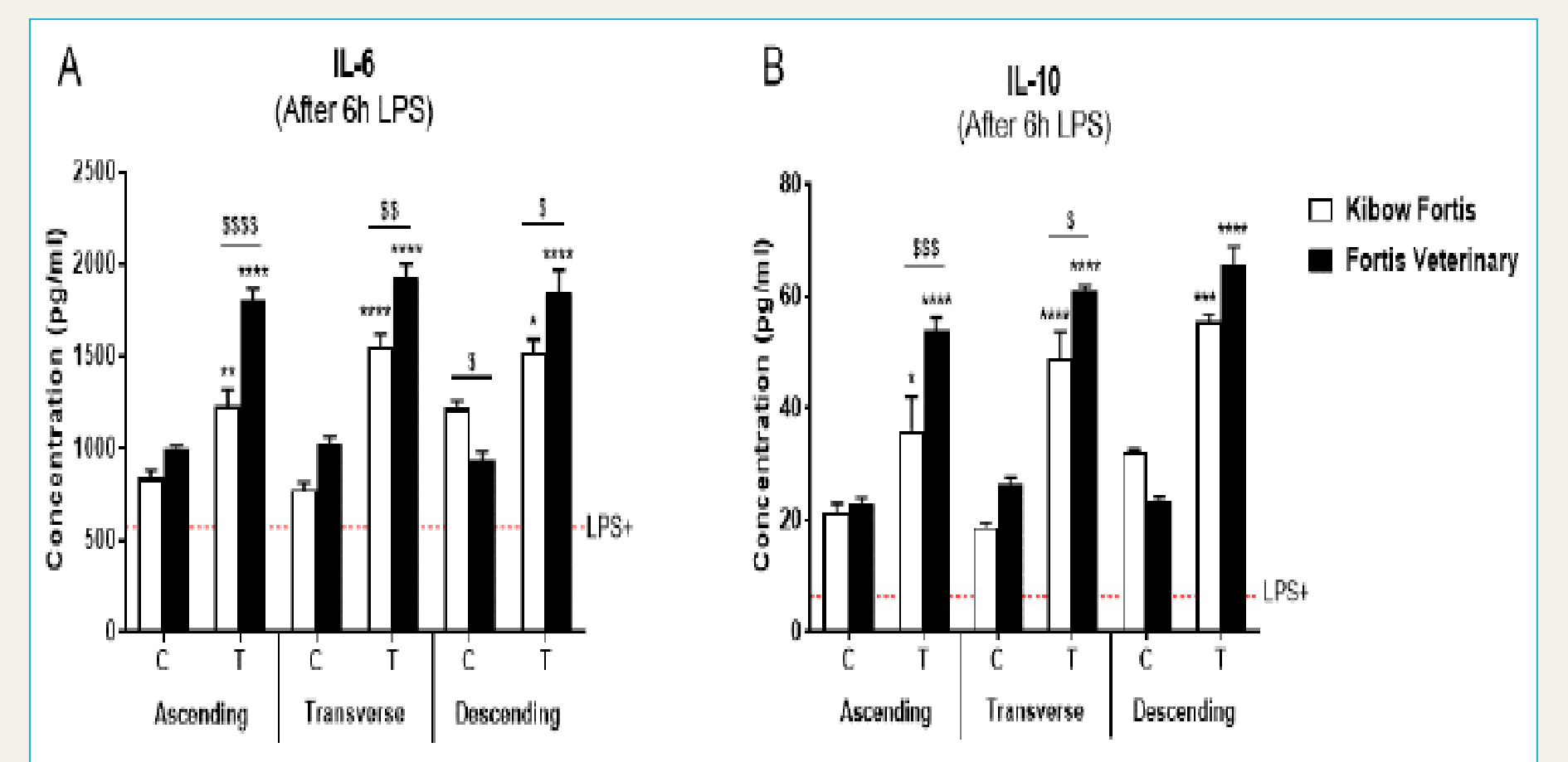
Each bar represents the average copy numbers over the control and treatments periods.

qPCR results showed both products could stimulate growth of *Lactobacillus* and *Bifidobacterium* the beneficial gut microbes.

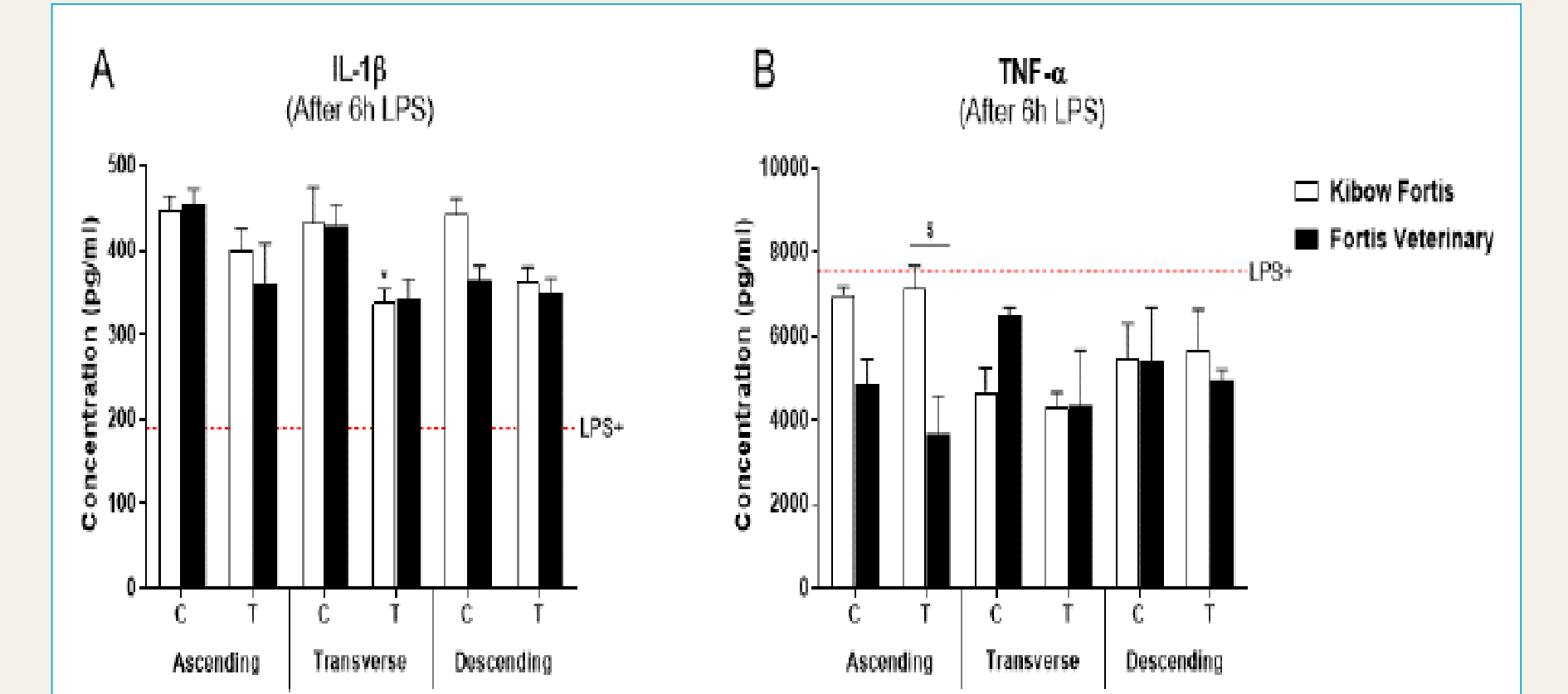
RESULTS contd....



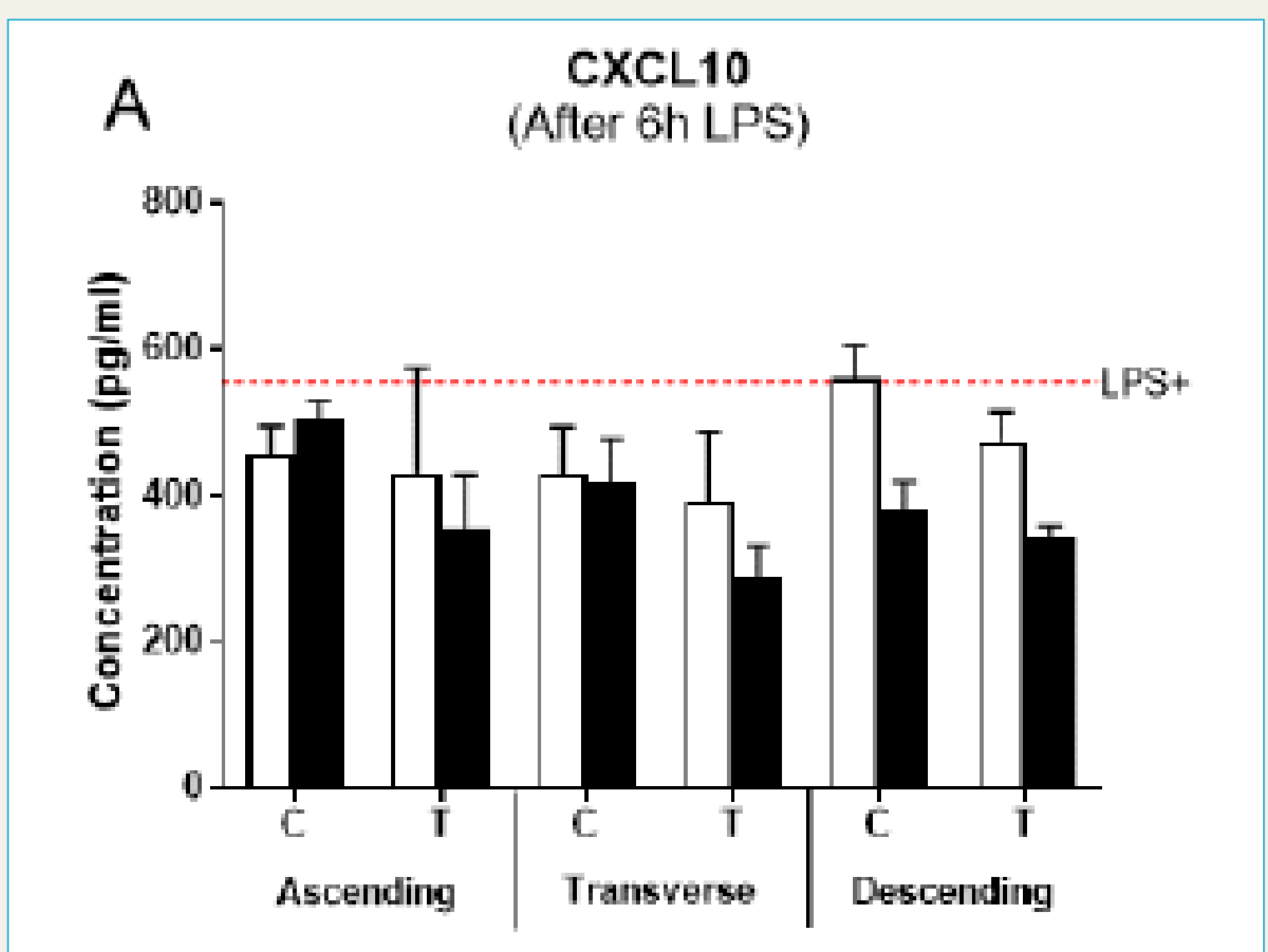
Both formulations were able to increase NF-kB activity compared to the control samples. Improper regulation of NF-kB has been linked to cancer, inflammatory and autoimmune disease, and improper immune development.



Both Formulations were able to increase/potentiate LPS induced IL-6 and IL-10 levels, two cytokines involved in gut immune homeostasis.



Both Formulations were able to decrease levels of IL-1B and TNF-a which are pro-inflammatory cytokines.



Both Formulations were also able to decreasing concentrations of CXCL-10, a chemokine responsible for the recruitment of several immune cells such as monocytes/macrophages, T cells, natural killer (NK) cells and dendritic cells (DCs).

SUMMARY/CONCLUSIONS

When the SHIME® reactors were supplemented with the prebiotic fiber product with and without the *Bacillus* probiotic: number of beneficial microbes increased, SCFA production increased, b-SCFA and ammonium production decreased, and immune cytokines were regulated. However the fiber product with the added *Bacillus* probiotic showed the most pronounced and consistent results among the different areas of the simulated colon.