

## Abstract

# Identifying a Complex Carbohydrate Mixture in Context of a High-Protein Diet That Is Able to Steer Microbial Fermentation to Improve Metabolic Health: The DISTAL Study <sup>†</sup>

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**Abstract:** Background: The microbial metabolites short-chain fatty acids (SCFAs) are proposed to largely contribute to improvements in metabolic health associated with dietary fiber (saccharolytic) fermentation. Nevertheless, towards the distal colon, fermentable carbohydrates become depleted, and gut bacteria switches towards protein (proteolytic) fermentation. This yields a diversity of metabolites like branched-chain fatty acids (BCFAs), often considered detrimental to metabolic health. We previously demonstrated that acute SCFA administration to the distal, but not the proximal colon, led to beneficial alterations in human substrate and energy metabolism. Hence, we hypothesize that a switch from proteolytic to saccharolytic fermentation in the distal colon has the most pronounced metabolic health effects and aimed to identify a complex carbohydrate mixture capable of inducing such a microbial substrate switch. Methods: The TIM-2 model, an in vitro computer-controlled dynamic model, was used to mimic colonic fermentation, simulating amongst others body temperature, luminal pH, microbial metabolite absorption, and peristalsis. TIM-2 was inoculated with standardized pooled microbiota from individuals with overweight/obesity and disturbed glucose homeostasis. After an overnight adaptation period, pre-digested proteins were added to the model to create a high protein background. Subsequently, either separately or in combination, potato fiber, native inulin from chicory, pectin from sugar beet, or no fibers (protein control) were administered. Samples of the lumen and dialysate were taken at various time points and assessed for proximal (0–8 h) and distal (8–24 h) SCFA and BCFA levels. Results: Of all the tested combinations, combining potato fiber and pectin resulted in the highest distal SCFA production (26.3 vs 6.4 mmol) and SCFA:BCFA ratio (13.3 vs 2.2) compared to the protein control. Discussion: The combination of potato fiber and pectin was best able to increase distal SCFA production in pooled microbiota of individuals who were overweight/obese. To assess whether these results translate to improvements in metabolic health, we are currently conducting a 12-week double-blind placebo-controlled randomized study. 44 individuals who are overweight/obese and have a disturbed glucose homeostasis are randomized to supplementation with a potato fiber/pectin mixture or placebo (maltodextrin) while consuming an eucaloric high protein diet (25 E% protein). The primary outcome will be the change in peripheral insulin sensitivity.

**Keywords:** dietary fibers; SCFA; metabolic health; obesity



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**Informed Consent Statement:** Not applicable (for data presented here).

**Data Availability Statement:** The datasets presented in the abstract are not readily available as current investigations are still ongoing but will be made available upon reasonable request. Requests to access the dataset should be direct to t.vandeuren@maastrichtuniversity.nl.

**Conflicts of Interest:** The authors declare no conflict of interest.

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