

## **Prebiotic inulin and resistant starch mixture-specific effect on distal colonic fermentation and metabolic health**

Emanuel E. Canfora<sup>1</sup>, Gerben D.A. Hermes<sup>2</sup>, Mattea Müller<sup>1</sup>, Jacco Bastings<sup>1</sup>, Veerle Dam<sup>3</sup>, Elaine E. Vaughan<sup>3</sup>, Marco A. van Den Berg<sup>4</sup>, Jens J. Holst<sup>5</sup>, Koen Venema<sup>1,6</sup>, Erwin G. Zoetendal<sup>2</sup>, Ellen E. Blaak<sup>1</sup>

<sup>1</sup>Human Biology, School for Nutrition and Translational Research in Metabolism (NUTRIM), Maastricht University Medical Center+, Maastricht, the Netherlands

<sup>2</sup>Laboratory of Microbiology, Wageningen University&Research, Wageningen, the Netherlands

<sup>3</sup>Sensus BV (Royal Cosun), Roosendaal, the Netherlands

<sup>4</sup>DSM Biotechnology Center, Delft, the Netherlands

<sup>5</sup>NovoNordisk Center for Basic Metabolic Research and Department of Biomedical Sciences Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

<sup>6</sup>Centre for Healthy Eating & Food Innovation, Maastricht University – Campus Venlo, Venlo, the Netherlands

## Abstract

**Background:** Metabolic issues such as obesity, diabetes and dyslipidemia have increased substantially over the past decades. Infusions of the short-chain fatty acid (SCFA) acetate in the distal colon improved metabolic parameters in men. Here, we hypothesized that combining rapidly and slowly fermentable prebiotic/fiber mixes will enhance distal colonic acetate production and improve metabolic health.

**Methods:** In vitro gut model studies showed that certain mixes yielded high distal colonic acetate production. Subsequently, lean and prediabetic overweight/obese men were included in two randomized crossover studies. In one study, participants consumed long-chain inulin+resistant starch (IN+RS), IN or maltodextrin (PLA) prior to a clinical investigation day. The second trial studied B-glucan+RS (BG+RS) versus BG and PLA. Breath hydrogen, indirect calorimetry, plasma metabolites/hormones were assessed during fasting and postprandial conditions. Gut microbiota composition and SCFA were also determined.

**Results:** In lean men, IN+RS increased breath hydrogen and fasting plasma butyrate, which was accompanied by increased energy expenditure, carbohydrate oxidation and PYY and decreased postprandial glucose concentrations (all  $P < 0.05$ ) compared to PLA. In prediabetic men, IN+RS increased plasma acetate compared to IN or PLA ( $P < 0.05$ ), but did not affect metabolic parameters. BG+RS increased plasma butyrate compared to PLA ( $P < 0.05$ ) in prediabetic men, but did not affect other fermentation/metabolic markers in both phenotypes. IN+RS induced more pronounced shifts in fecal microbiota versus BG+RS; shifts were individual-specific.

**Conclusion:** Administration of IN+RS the day prior to investigation improved metabolic parameters in lean but not in prediabetic individuals, demonstrating that effects were phenotype- and mix-specific. No effects were found for BG+RS, indicating addition of the prebiotic IN to the RS was essential to the effect. Longer-term consumption is anticipated to change the microbiota, therefore, such a study is being prepared to determine whether long-term changes in fermentation patterns can be directly related to changes in human energy and substrate metabolism in overweight/obese individuals.