

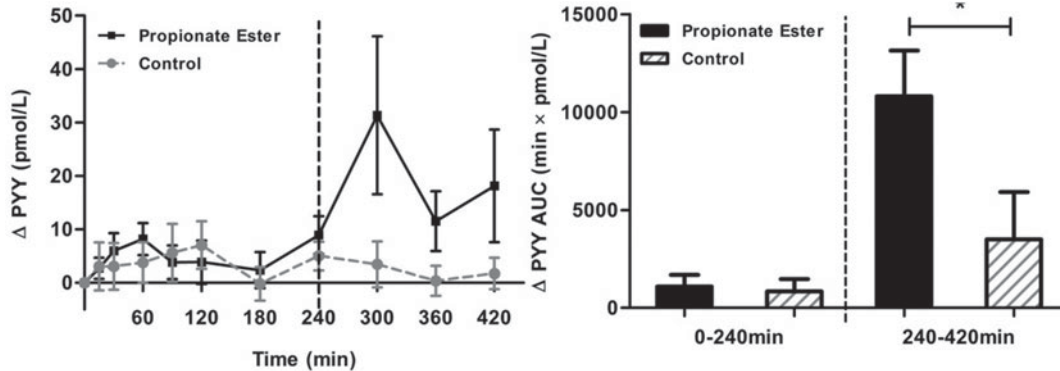
Targeted delivery of propionate to the colon stimulates the release of anorectic gut hormones and suppresses appetite in humans

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Recent evidence suggests that short chain fatty acids (SCFA) trigger the release of the anorectic gut hormones peptide YY (PYY) and glucagon like peptide-1 (GLP-1) by stimulating the free fatty acid receptors (FFAR) 2 and 3 on enteroendocrine L cells⁽¹⁾. Of the SCFA produced by colonic fermentation of available carbohydrates, propionate has been shown to have the highest affinity for FFAR2⁽²⁾. We hypothesised that increasing colonic propionate would stimulate gut hormone secretion and reduce energy intake. To elevate colonic propionate levels we have developed a novel propionate ester molecule whereby propionate is chemically bound by an ester bond to inulin. The majority of the bound propionate should only be released when the inulin polymer is fermented by the colonic microbiota, thus providing targeted colonic delivery.

To assess the site and extent of propionate release, 9 volunteers consumed a standardised breakfast containing 100 mg of ¹³C labelled propionate ester and 10 g of unlabelled ester. Breath H₂ and ¹³CO₂ enrichment were collected over 24 h to investigate gut transit times. Breath H₂ started to increase at 180 min and peaked at 240 min. More than 80% of the ¹³C recovered in breath appeared co-incident with and after breath H₂ onset, suggesting delivery of the majority of the bound propionate to the colon.



Plasma PYY levels after ingestion of propionate ester vs. control. Dotted lines signify the time point after which >80% propionate ester enters the colon. Data are presented as means ± SEM, **P* < 0.05.

This propionate ester (10 g/d) and an inulin control (10 g/d) were then administered to 20 volunteers in a randomised crossover study to determine its effect on food intake and gut hormone concentrations. Ingestion of 10 g propionate ester significantly increased plasma PYY and GLP-1 (*P* < 0.05) and reduced *ad libitum* food intake (1175 ± 103 kcal control vs. 1013 ± 94 kcal propionate ester; *p* < 0.01).

In conclusion, these data suggest that an acute increase in colonic propionate can elevate plasma PYY and GLP-1 levels and reduce food intake in humans. Elevating propionate levels in the colon may therefore offer a potential strategy to protect against weight gain and the metabolic consequences of obesity.

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