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Abstract

The Contribution of Short-Chain Fatty Acids to Health Benefits May Depend on the Site of Absorption: A Mechanistic Study Design †

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Abstract: The fermentation of dietary fibres in the human colon generates short-chain fatty acids (SCFAs) that potentially mediate the health benefits associated with high fibre intake. In the colonic lumen, SCFAs support gut health and stimulate the release of the appetite-regulating hormones glucagon-like peptide 1 (GLP-1) and peptide-YY (PYY). In addition, SCFAs act as fuel for colonocytes and serve as precursors for substrate metabolism in the liver. The SCFAs that ultimately reach the systemic circulation may influence physiological processes in organs at a distance. Yet, when consuming plant-based fermented foods containing SCFAs, the SCFAs are absorbed in the small intestine and will not reach the colon, which might affect their physiological effects. We hypothesise that, compared to colonic delivery, a larger fraction of SCFAs will reach the systemic circulation and that the stimulation of gut hormone release will be less pronounced. To test this hypothesis, we designed two randomised crossover human intervention studies in healthy participants in which SCFAs will be targeted either to the small intestine (test day 1) or colon (test day 2) using standard capsules or capsules with a colon delivery coating, respectively. Study 1 will assess the systemic bioavailability of postprandial concentrations of labelled SCFAs after oral administration of stable isotope 13C-labelled SCFAs and intravenous administration of ^{2}H-labelled SCFAs. In study 2, postprandial concentrations of GLP-1 and PYY, glucose, and insulin will be quantified after the administration of capsules with unlabelled SCFAs. These studies will clarify the importance of the site of administration on the kinetics of SCFAs and the gut hormone release that will contribute to elucidating the role of SCFAs as health-supporting metabolites.

Keywords: short-chain fatty acids (SCFAs); systemic bioavailabilityglucagon-like peptide 1 (GLP-1); peptide YY (PYY); stable isotope; targeted delivery

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