DOCTORAL THESIS

Iron absorption and regulatory mechanisms: effects of fructooligosaccharide and other prebiotics

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Abstract

Iron deficiency is the most prevalent nutrient deficiency in the world, leading to long-term developmental and health consequences in populations at risk. Also known as prebiotics, non-digestible oligosaccharides such as fructooligosaccharide (FOS), inulin, galactooligosaccharide (GOS) and lactulose resist digestion by gastric acid and pancreatic enzymes *in vivo*, but are preferentially fermented by beneficial intestinal bacteria once they reach the colon. Prebiotics have been shown to increase the absorption of minerals such as iron from diets, but results from studies reported in the literature at times are contradictory, and mechanisms involved are still unclear. A better understanding of the role of FOS and other prebiotics in iron absorption may lead to new dietary modification strategies to increase intake of iron absorption enhancers in plant-based diets. The objectives of this study were therefore to determine the effects of prolonged FOS, as well as Synergy 1 (a combination of long- and short-chain FOS), inulin, GOS and lactulose supplementation on iron status of anemic rats; and to assess the enhancing effects of FOS on iron absorption and elucidate the regulatory mechanism involved using the Caco-2 cell culture model.

In our animal studies, male Sprague-Dawley rats were first fed a low-iron diet for 14 days prior to prebiotics supplementation to achieve an iron-deficient status. Rats receiving the low-iron diet (12 ppm Fe) showed significantly lower non-heme iron concentrations in liver, spleen and kidney, as well as lower hemoglobin level than rats receiving a normal diet (45 ppm Fe), confirming iron-deficiency anemia.

At the onset of the feeding trials, anemic rats were further divided into groups with or without supplementation of prebiotics. Prebiotics were provided to the rats by dissolving in water at 5% (w/v). Rats were kept on their respective test diets for 28 or 35 days, and all had free access to food and water during the feeding trials. The results showed significantly higher hemoglobin and non-heme iron levels in anemic rats with FOS or GOS supplementation, suggesting that both FOS and GOS could have positive effects on the iron status of anemic subjects with a low-iron intake. Rat colon contents also showed significant changes in short-chain fatty acid (SCFA) concentrations, presumably due to fermentation of prebiotics by intestinal microflora.

Changes in the expression of Duodenal cytochrome b (Dcytb) and Divalent metal transporter 1 (DMT-1) in Caco-2 cells were measured by Western Blot and Real Time PCR. Our results confirmed that Caco-2 cells 14 days post confluence provided a stable research model for gene expression studies related to iron absorption. At low iron level, especially with FOS or SCFA supplementation, Dcytb and DMT-1 expression levels were increased in Caco-2 cells. While at high iron level, expression of Dcytb or DMT-1 was mostly down-regulated. Effects of SCFA were much more pronounced than FOS at different iron concentrations, suggesting that any effects of dietary FOS on improving iron status would require fermentation by the intestinal microflora. Further studies on other prebiotics (e.g., GOS and lactulose) and different combinations of SCFA are warranted.

Key words: iron, anemia, FOS, Caco-2, Dcytb, DMT-1

Table of contents