Gut-level benefits of butyrate

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hort-chain fatty acid butyrate plays a critical role in the health of the gut. Several mechanisms have been described which support this role and they are detailed below.

Butyrate is a natural product of fermentation by certain bacteria in the gut and is produced from fibrous material in the diet (Miller et al., 2003). It is the product of the anaerobic fermentation of short-chain fatty acids (SCFAs) in the colon. It is an essential nutrient for colonic cells, particularly epithelial cells (Cook and Sellan, 1998).

SCFAs, butyrate

Animals do not directly produce SCFAs, which are the major end products of the fermentation of undigested carbohydrate (dietary fiber) in the colon by commensal gut bacteria. These bacteria use the residue present in the colon to produce SCFAs, which are then absorbed into the gut wall and used as metabolic fuels by enterocytes (Cook and Sellan, 1998).

Homeostasis, immune function

Although butyrate is the least abundant of the three major SCFAs, it is the most important for colonocyte health. Butyrate is also a product of the fermentation of dietary fiber in the gut and is produced by bacteria in the gut (Miller et al., 2003).

Butyrate forms from a simple four-carbon fatty acid

Butyrate forms from a simple four-carbon fatty acid (Figure) produced in the colon by phylogenetically diverse group of Gram-positive anaerobic bacteria belonging to the Firmicutes phylum (Louis and Flint, 2009). The main route for synthesis of butyrate is the catabolism of carbohydrates through the Embden-Meyerhof-Parnas pathway and the subsequent condensation of two molecules of acetyl-CoA (Miller and Wolin, 1996).

Antimicrobial activity

In addition to the cellular barrier function, butyrate acts through other mechanisms to help reduce infection. For example, antimicrobial peptides (AMPs) are a critical part of innate immunity (Brogden et al., 2003). The two major families of AMPs are the defensins (Ganz, 2003) and cathelicidins (Zanerti, 2004). The cathelicidin identified in humans is LL-37, which has strong antimicrobial activity (Gudmundsson et al., 1996). Research has shown that butyrate up-regulates LL-37 production in cultured human colon epithelial cells (Hase et al., 2002).

Butyrate is active against shigella infections and butyrate increases levels of LL-37, the question arises as to whether butyrate could be a product of the commensal flora that helps protect from shigellosis. Butyrate treatment for cecal fistula infected rabbits resulted in reduced clinical symptoms, up-regulation of the rabbit homologue to LL-37, reduced inflammation and a lower bacterial load in the feces (Raqi et al., 2006).

Antimicrobial peptides play a key role in the innate immune system. For example, cathelicidins and defensins are produced by epithelial cells in the gut to form a mucosal barrier that is more efficient in nutrient absorption and more resistant to attack by invading pathogens. Researchers have shown that supplementing feeds with unique fermentation metabolites can provide prebiotic-like activity in a laboratory model of poultry digestion known as the “Intestinal Activity Model” (IAM). One of the more surprising IAM results from the model was that the production of butyrate in the intestinal lumen changes in bacterial populations not only reduced pathogen growth (Nsereko et al., 2014) but resulted in a significant increase in the production of butyrate (Nsereko et al., 2015).

Butyrate also plays an extensive role in gut homeostasis (Hodin, 2010), including support for the gut barrier function. It facilitates the creation and maintenance of cellular tight junctions or zonula occludens (Peng et al., 2007, Peng et al., 2009), which are the closely associated areas of two cellular membranes that together form a mucosal barrier that is more efficient in nutrient absorption and more resistant to attack by invading pathogens. There also have been reports of more direct effects of butyrate on the immune system of mammals, including work that it interacts with cytokines (the messaging system of immunity). For example, butyrate may increase levels of the anti-inflammatory cytokine interleukin-10 (Brogden et al., 2003). Butyrate also may regulate or modulate immunity in broiler chickens (Zhang et al., 2011).

References


