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Short Communication

Short Chain Fatty Acids: Production, Benefits, and Caution

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Carboxylic acids with aliphatic chains are referred to as fatty acids. Fatty acids can be classified as short (<6 C), medium (6-12 C), and long (>12 C) depending on the length of the aliphatic tail. Short Chain Fatty Acids (SCFAs) includes formate (1 C), acetate (2 C), propionate (3 C), butyrate (4 C) and valerate (5 C) [1].

Fermentation of resistant carbohydrates (e.g. fructo-oligosaccharides, inulin, resistant starch, sugar alcohols, and polysaccharides from plant cell wall) in the mammalian gut by anaerobic bacteria produces SCFAs [2]. Moreover, amino acids can also be fermented to produce SCFAs by human colonic bacteria [3]. Interestingly, SCFAs can also be produced endogenously by the host via several pathways such as fat oxidation during starvation, alcohol metabolism in the liver, and propionyl Co-A activity [4-6]. The majority of SCFAs production in the gut is dependent on bacteria, however, some specific foods such as vinegar, sourdough bread, and some dairy products also contain SCFAs [7]. Acetate, propionate, and butyrate are major forms of SCFAs in the large intestine (around 80% of all SCFAs) and are usually present in 60:20:20 molar ratios respectively in the stool [8].

SCFAs produced in the gut can defuse into epithelium in unionized form or can be transported into the cell by mono-carboxylate transporters such as MCT-1 and DMCT-1 [9]. In the caecum and colon, 95% of SCFAs are rapidly absorbed and the remaining 5%are retained in feces. Within the colon, approximately 60% of absorbed SCFAs move to lamina propria and systemic circulation, while the remaining 40% is utilized by colonocytes [10]. SCFAs produced in the gut also interact with receptors present on colonocytes as well as immune cells which play a crucial role in the exertion of many of their observed effects. Free Fatty Acid receptor 2 (FFAR2) also known as G- protein-coupled Receptor 43 (GPR43) interacts with SCFAs with a preference for shorter SCFAs with EC50 values as C2=C3>C4 (humans) and C2>C3>C4 (mice) [11]. The second receptor which is activated by SCFAs is FFAR3/GPR41, which prefers longer SCFAs (C3, C4, and C5).

SCFAs predominantly improve host health in several ways such as mucus production, maintenance of epithelial integrity, anti-tumor effects, anti-inflammatory effects on host epithelium, and effects on immune cells [12,13]. Butyrate has been shown to inhibit nuclear translocation of NF-κb and HDAC. Macrophages polarize towards the M2 phenotype and downregulate the production of IL-6 and IL-12 in response to butyrate. It also downregulated dendritic cells activation in lamina propria and thus promotes tolerance. Neutrophils exposed to SCFAs downregulate inflammatory receptors on their membrane and decrease the expression of neutrophilic TNF-α and nitric oxide.

It is important to note that under certain circumstances, for example during infection, SCFAs may exert unfavorable effects by down-regulating pro-inflammatory activities. In a study local addition of SCFAs to the site of subcutaneous infection impaired neutrophil phagocytosis and increased bacterial load [14]. However, in another study, propionate was found to enhance the IL-6-dependent recruitment of neutrophils in the gut during *Citrobacter rodentium* infection [15]. It should be noted that during gut infection many factors are at play such as diverse microbiota and their metabolites. Modulation of immune activities to the extent of pro- or anti-inflammatory by SCFAs depends on the immunological milieu at the site of infection. The effect of specific SCFAs on the host may not be always translated to other

SCFAs as individual SCFAs may have specific effects which may depend on their availability, absorption, receptor binding, etc. Moreover, the potency of each SCFA varies across disease models. Thus caution should be taken when demonstrating or interpreting the effects of these metabolites. The majority of studies associate the positive effect of SCFAs with the protection of disease, however, it should be noted that the opposite may also occur. For instance, consumption of SCFAs in drinking water results in their accumulation in renal tissue and severe T-cell mediated inflammation [16]. Most of the studies lack supportive data on humans as they are unable to provide an adequate dose of fermentable fiber or fail to effectively examine putative mechanisms in animal models and their translation to the human context. There is a need to effectively design studies in collaboration with immunologists, nutritionists, and dietitians so that they can be translated to clinical findings.

Bibliography

1. Layden BT., et al. "Short chain fatty acids and their receptors: new metabolic targets". Translational Research 161.3 (2013): 131-140.
2. Richards LB., et al. "The effects of short-chain fatty acids on the cardiovascular system". PharmaNutrition 4.2 (2016): 68-111.
3. Macfarlane J. "Proteolysis and amino acid fermentation". Human colonic bacteria (1995): 75-100.
4. Knowles SE., et al. "Production and utilization of acetate in mammals". Biochemical Journal 142.2 (1974): 401-411.
5. Sarkola T., et al. "Ethanol, acetaldehyde, acetate, and lactate levels after alcohol intake in white men and women: effect of 4-methylpyrazole". Alcoholism: Clinical and Experimental Research 26.2 (2002): 239-245.
6. Walter JH., et al. "Measurement of propionate turnover in vivo using sodium [2H5] propionate and sodium [13C] propionate". Clinica Chimica Acta 182.2 (1989): 141-150.
7. Darzi J., et al. "Do SCFA have a role in appetite regulation?". Proceedings of the Nutrition Society 70.1 (2011): 119-128.
8. Cummings J., et al. "Short chain fatty acids in human large intestine, portal, hepatic and venous blood". Gut 28.10 (1987): 1221-1227.
9. Dawson AM., et al. "Absorption of short chain fatty acids in man". Proceedings of the Society for Experimental Biology and Medicine 117.1 (1964): 97-100.
10. Fleming SE., et al. "Absorption of short-chain fatty acids from the rat cecum in vivo". The Journal of Nutrition 121.11 (1991): 1787-1797.
11. Kimura I., et al. "Free fatty acid receptors in health and disease". Physiological Reviews 100.1 (2019).
12. Gill PA., et al. "Short chain fatty acids as potential therapeutic agents in human gastrointestinal and inflammatory disorders". Alimentary Pharmacology and Therapeutics 48.1 (2018): 15-34.
13. Silva YP., et al. "The role of short-chain fatty acids from gut microbiota in gut-brain communication". Frontiers in Endocrinology 11 (2020): 25.
14. Corrêa RO., et al. "Bacterial short-chain fatty acid metabolites modulate the inflammatory response against infectious bacteria". Cellular Microbiology 19.7 (2017): e12720.
15. Kim MH., et al. "Short-chain fatty acids activate GPR41 and GPR43 on intestinal epithelial cells to promote inflammatory responses in mice". Gastroenterology 145.2 (2013): 396-406.
16. Park J., et al. "Chronically elevated levels of short-chain fatty acids induce T cell–mediated ureteritis and hydronephrosis". The Journal of Immunology 196.5 (201): 2388-2400.

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