



Propionate: Friend or Foe

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Introduction

Key Points of discussion:

1. Total SCFAs contents are important or their relative proportions
2. Propionate is health promoting or damaging
3. Probiotics or prebiotics should be targeted to increase or decrease propionate production

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Butyrate and Propionate Protect against Diet-Induced Obesity and Regulate Gut Hormones via Free Fatty Acid Receptor 3-Independent Mechanisms

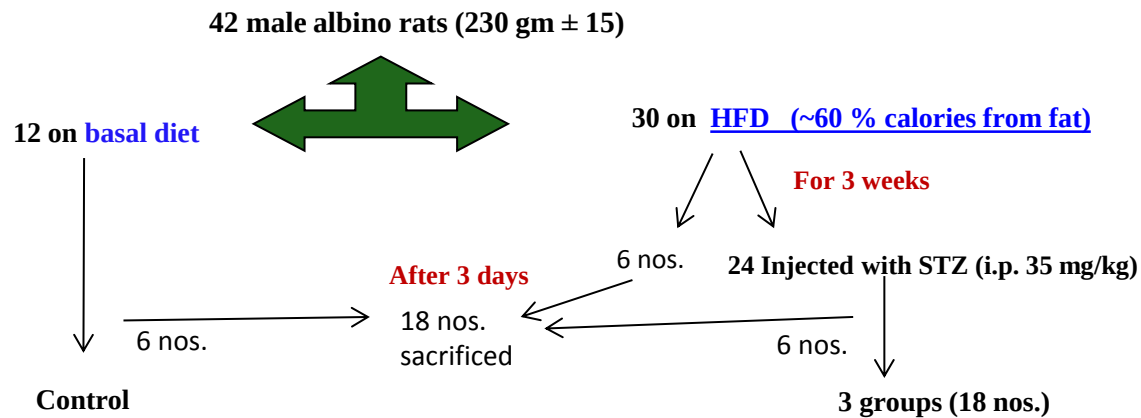
Hua V. Lin^{1*}, Andrea Frassetto¹, Edward J. Kowalik Jr¹, Andrea R. Nawrocki¹, Mofei M. Lu¹, Jennifer R. Kosinski¹, James A. Hubert¹, Daphne Szeto¹, Xiaorui Yao¹, Gail Forrest¹, Donald J. Marsh²

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Abstract

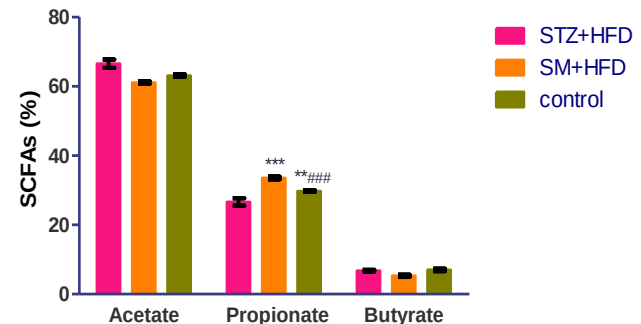
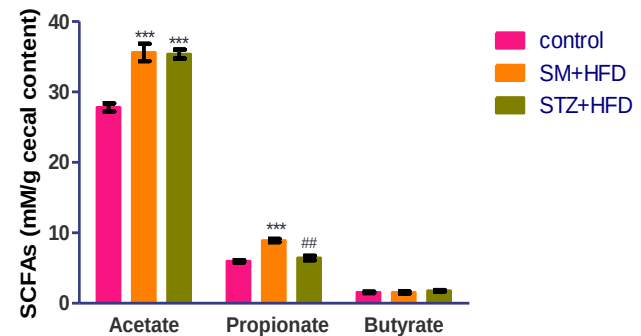
Short-chain fatty acids (SCFAs), primarily acetate, propionate, and butyrate, are metabolites formed by gut microbiota from complex dietary carbohydrates. Butyrate and acetate were reported to protect against diet-induced obesity without causing hypophagia, while propionate was shown to reduce food intake. However, the underlying mechanisms for these effects are unclear. It was suggested that SCFAs may regulate gut hormones via their endogenous receptors Free fatty acid receptors 2 (FFAR2) and 3 (FFAR3), but direct evidence is lacking. We examined the effects of SCFA administration in mice, and show that butyrate, propionate, and acetate all protected against diet-induced obesity and insulin resistance. Butyrate and propionate, but not acetate, induce gut hormones and reduce food intake. As FFAR3 is the common receptor activated by butyrate and propionate, we examined these effects in FFAR3-deficient mice. The effects of butyrate and propionate on body weight and food intake are independent of FFAR3. In addition, FFAR3 plays a minor role in butyrate stimulation of Glucagon-like peptide-1, and is not required for butyrate- and propionate-dependent induction of Glucose-dependent insulinotropic peptide. Finally, FFAR3-deficient mice show normal body weight and glucose homeostasis. Stimulation of gut hormones and food intake inhibition by butyrate and propionate may represent a novel mechanism by which gut microbiota regulates host metabolism. These effects are largely intact in FFAR3-deficient mice, indicating additional mediators are required for these beneficial effects.

Study Design:



Feeding of high fat diet resulted in

Increase	Body Weight Fasting blood glucose Plasma Insulin GHb FFAs Triglyceride Total Cholesterol LDL-Cholesterol LDL-Cholesterol Propionate proportions (%)
Decrease	OGTT Total number of bacteria Bifidobacteria most significantly



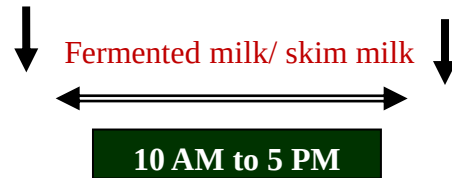
Effect of HFD feeding on SCFAs in caecal contents after 24 days. * Mean values were significantly different from those of the control. *P<0.05, **P<0.01, ***P<0.001. # Mean values were significantly different from those of the HFD+SM group. #P<0.05, ##P<0.01, ###P<0.001.

Singh et al. 2014

Grouping of diabetic rats

Sr. No.	Group	Feed
1.	HFD+SM	HFD+Skim milk (Diabetic milk control)
2.	HFD +LGG	HFD+Milk fermented with reference probiotic LGG
3.	HFD + 17	HFD+Milk fermented with <i>L. rhamnosus</i> NCDC 17

Feeding schedule



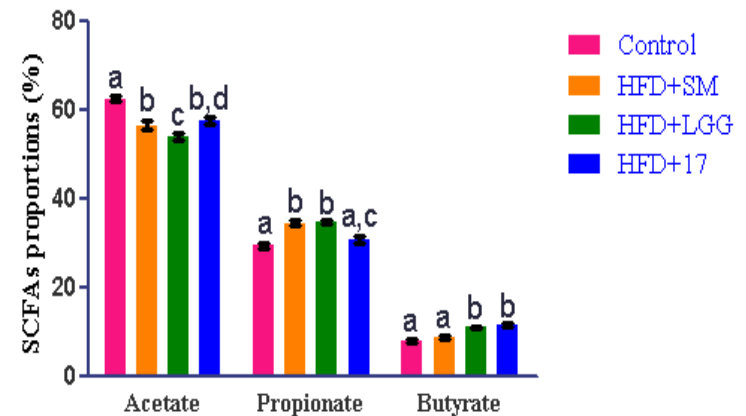
HFD + water

[Composition of diets](#)

Feeding for 6 weeks

Feeding of *L. rhamnosus* NCDC 17

Decrease 	Fasting blood glucose GHb FFAs Triglyceride Total Cholesterol LDL-Cholesterol LDL-Cholesterol TBARS in RBC and liver Propionate proportions (%) Expression of TNF- α and Il-6 in epididymal fat
Increase 	OGTT Plasma Insulin Activities of catalase, SOD and GPx in RBC and liver Total number of bacteria Bifidobacteria most significantly Acetate proportions (%) Expression of proglucagon and PC1 in cecum



Effect of probiotic feeding on SCFAs in caecal contents after 6 weeks. Values are mean $\pm$ SEM. Values with different superscript letters are significantly different ($P < 0.05$)

- These observations suggest that HFD feeding increase the propionate ratio and first lead to obesity and then diabetes.
- Our results are contradictory to well established understanding for propionate being beneficial in obese condition as it was thought to lower lipogenesis and serum cholesterol levels ([Hosseini et al. 2011](#)).
- However, our results are coherent with finding of [Schwartz et al. \(2010\)](#) which showed increase in faecal propionate levels in overweight people and [Yang et al. \(2013\)](#) exhibited fermentation of different cereal grains by obese microbiota resulted in elevated propionate production compared with that of normal weight.
- [Payne et al. \(2011\)](#) also reported significantly higher levels of propionate and total SCFAs in fecal sample of obese children in comparison to normal weight children.

Thank you...

Composition of diets

Sr No.	Component	Basal diet	High Fat Diet (%)
		Normal Chow (%)	
1	Starch	53	25
2	Casein	20	20
3	Sucrose	10	10
4	Fat	7*	35**
5	Cellulose	5	5
6	Vitamin mixture	1	1
7	Mineral mixture	3.5	3.5
8	Choline Chloride	0.2	0.2
9	Methionine	0.3	0.3

*(soyabean oil) ** (7% soyabean oil and 28% Lard)

Vitamin and Mineral mixture as per AOAC, 1990.



Propionate as a health-promoting microbial metabolite in the human gut

Elham Hosseini, Charlotte Grootaert, Willy Verstraete, and Tom Van de Wiele

Propionate is a major microbial fermentation metabolite in the human gut with putative health effects that extend beyond the gut epithelium. Propionate is thought to lower lipogenesis, serum cholesterol levels, and carcinogenesis in other tissues. Steering microbial propionate production through diet could therefore be a potent strategy to increase health effects from microbial carbohydrate fermentation. The present review first discusses the two main propionate-production pathways and provides an extended gene-based list of microorganisms with the potential to produce propionate. Second, it evaluates the promising potential of arabinoxylan, polydextrose, and L-rhamnose to act as substrates to increase microbial propionate. Third, given the complexity of the gut microbiota, propionate production is approached from a microbial-ecological perspective that includes interaction processes such as cross-feeding mechanisms. Finally, it introduces the development of functional gene-based analytical tools to detect and characterize propionate-producing microorganisms in a complex community. The information in this review may be helpful for designing functional food strategies that aim to promote propionate-associated health benefits.

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Microbiota and SCFA in Lean and Overweight Healthy Subjects

Andreas Schwartz¹, David Taras², Klaus Schäfer², Silvia Beijer³, Nicolaas A. Bos³, Christiane Donus⁴ and Philip D. Hardt⁴

Obesity has recently been linked to the composition of human microbiota and the production of short chain fatty acids (SCFAs). However, these findings rely on experimental studies carried out using rather small and defined groups of volunteers or model animals. Our aim was to evaluate differences within the human intestinal microbiota and fecal SCFA concentration of lean and obese subjects. A total of 98 subjects volunteered to take part in this study. The BMI in kg/m² of 30 volunteers was within the lean range, 35 were overweight and 33 were obese. The fecal microbiota was characterized by real-time PCR analyses. With the primers used herein we were able to cover 82.3% (interquartile range of 68.3–91.4%) of the total microbiota detectable with a universal primer. In addition, the concentration of SCFA was evaluated. The total amount of SCFA was higher in the obese subject group ($P = 0.024$) than in the lean subject group. The proportion of individual SCFA changed in favor of propionate in overweight ($P = 0.019$) and obese subjects ($P = 0.028$). The most abundant bacterial groups in faeces of lean and obese subjects belonged to the phyla *Firmicutes* and *Bacteroidetes*. The ratio of *Firmicutes* to *Bacteroidetes* changed in favor of the *Bacteroidetes* in overweight ($P = 0.001$) and obese subjects ($P = 0.005$). Our results are in line with previous reports suggesting that SCFA metabolism might play a considerable role in obesity. However, our results contradict previous reports with regard to the contribution of various bacterial groups to the development of obesity and this issue remains controversial.

Obesity (2009) **18**, 190–195. doi:10.1038/oby.2009.167



Impact of dietary fiber fermentation from cereal grains on metabolite production by the fecal microbiota from normal weight and obese individuals.

Yang J¹, Keshavarzian A, Rose DJ.

⊕ Author information

Abstract

Gut bacteria may influence obesity through the metabolites produced by dietary fiber fermentation (mainly, short-chain fatty acids [SCFA]). Five cereal grain samples (wheat, rye, maize [corn], rice, and oats) were subjected to in vitro digestion and fermentation using fecal samples from 10 obese and nine normal weight people. No significant differences in total SCFA production between the normal weight and obese groups were observed [279 (12) vs. 280 (12), mean (standard error), respectively; $P=.935$]. However, the obese microbiota resulted in elevated propionate production compared with that of normal weight [24.8(2.2) vs. 17.8(1.9), respectively; $P=.008$]. Rye appeared to be particularly beneficial among grain samples due to the lowest propionate production and highest butyrate production during fermentation. These data suggest that the dietary fibers from cereal grains affect bacterial metabolism differently in obese and normal weight classes and that certain grains may be particularly beneficial for promoting gut health in obese states.



ORIGINAL ARTICLE

The metabolic activity of gut microbiota in obese children is increased compared with normal-weight children and exhibits more exhaustive substrate utilization

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Objective: The gut microbiota contribute otherwise impossible metabolic functions to the human host. Shifts in the relative proportions of gut microbial communities in adults have been correlated with intestinal disease and have been associated with obesity. The aim of this study was to elucidate differences in gut microbial compositions and metabolite concentrations of obese versus normal-weight children.

Materials and methods: Fecal samples were obtained from obese ($n = 15$; mean body mass index (BMI) s.d. score = 1.95) and normal-weight ($n = 15$; BMI s.d. score = -0.14) Swiss children aged 8–14 years. Composition and diversity of gut microbiota were analyzed by qPCR and temperature gradient gel electrophoresis (TGGE).

Results: No significant quantitative differences in gut microbiota communities of obese and normal-weight children were identified. Microbial community profiling by TGGE revealed a high degree of both intra- and intergroup variation. Intergroup comparison of TGGE profiles failed to identify any distinct populations exclusive to either obese or normal-weight children. High-pressure liquid chromatography analysis identified significantly higher ($P < 0.05$) concentrations of short-chain fatty acids (SCFA) butyrate and propionate in obese versus normal-weight children. Significantly lower concentrations of intermediate metabolites were detected in obese children, suggesting exhaustive substrate utilization by obese gut microbiota.

Conclusions: Our results indicate that a dysbiosis may be involved in the etiology of childhood obesity. In turn, aberrant and overactive metabolic activity within the intestine could dictate survival or loss of individual microbial communities, leading to the altered population ratios previously identified in adult obesity.

Nutrition and Diabetes (2011) 1, e12; doi:10.1038/nutd.2011.8; published online 18 July 2011



Summary

I would like to share part of my research work which is somewhat controversial in our understanding towards short chain fatty acids (SCFAs) produced during fermentation by gut microbiota.

Title of talk- 'Propionate: Friend or Foe'

Key Points of discussion:

1. Total SCFAs contents are important or their relative proportions
2. Propionate is health promoting or damaging
3. Probiotics or prebiotics should be targeted to increase or decrease propionate production

- **Based on these observations, reduction of propionate production and/or propiogenic bacteria in the gut can be aimed at to develop therapeutic strategies to combat obesity and diabetes.**