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Literature Article

Short Chain Fatty Acids in Intestinal Dysbiosis

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Abstract

We carried out an intense review of the functions of short chain fatty acids in intestinal dysbiosis and we were surprised to detect the utmost importance that exists in their daily impact on the processes of the digestive tract, as well as the extra-digestive ones.

We find the close relationship that exists between these acids, immunity, inflammation and metabolism. What predicts a successful future in its use, not only as a metabolic and immune complement, but as a therapeutic that can minimize the daily processes of chronic inflammation, which millions of human beings in the world experience.

All of this forces us to have these very current acids as priorities in our daily work and dedicate all the time possible to their development as possible antibiotics or as therapeutic sources.

We cannot ignore, when using short chain fatty acids, that patients have sufficient fiber intake, which can be used by multi-specific acids, as well as in parallel the use of diets, such as Paleo; without forgetting stress management, exercise and numerous actions harmful to the Intestinal Microbiome. Remembering the importance of controlling the intake of polyols and increasing polyphenols.

Keywords: *Short Chain Fatty Acids (SCFA); Intestinal Dysbiosis (ID); Gut Microbiota (GM); Inflammatory Bowel Disease (IBD)*

Introduction

The anions with the greatest abundance in the lumen of the large intestine are short chain fatty acids (SCFA), which have good physiological action, as is the case of sodium chloride [1]. More, it is not the only function that these fatty acids have; in some they are complemented by oxalates and sulfates [2]. Furthermore, SCFA, because they are the most abundant, are the regulators of this action.

Being byproducts produced by bacterial fermentation of both fiber and carbohydrates and regulating the transportation of sodium in the colon [3]. Butyrate, acetate and propionate make up 95% of SCFA; The first is the most important, representing more than 60% of the colonocyte's need [4].

Short-chain fatty acids modify phagocytosis and chemotaxis; They induce reactive oxygen species, modify cell function and proliferation. They have anti-inflammatory, anti-microbial and anti-tumor effects, as well as alter intestinal purity; influencing the maintenance of the immune system and intestinal homeostasis [5].

Finally, SCFA originating from the intestinal microbiome modulate brain physiology through immune, vagal, endocrine and humoral pathways. This action is generated through the gut-brain axis, bi-directionally, immensely interconnected [6].

The following functions are not negligible: Protection against pathogens.

Contribution to drug metabolism and incidence in brain processes [7].

Butyrate, Dysbiosis and other aspects. Perhaps one of the most laudable functions of butyrate is the detection of carcinogenic proliferation of the colon. It performs this function by being a capital part of dietary fiber; inducing the development, apoptosis and particularity of the tumor process [8]. It is also a transcendent energy substrate, a nutritional contributor and proliferator of a healthy intestinal mucosa, a reducer of intestinal pH and a strengthener of the intestinal barrier [9]. It is absorbed by the mitochondria, through aerobic oxidation of planar acids to produce acetyl-CoA, which enters the Krebs cycle.

Based on the background that ischemic heart disease and stroke were the most frequent causes of deaths in China in 2017. Lu Y and his group [10] studied the context and found that there are several bacterial factors such as metabolites of tryptophan and endotoxin, as well as trimethylamine oxide, which affect the development of cerebral vascular disease. Likewise, intestinal dysbiosis (ID) also increases the process, by enhancing the inflammatory response.

These findings suggest that structural changes in GM are closely linked to host metabolism and structure regulation. So, the physiology of GM is significant, to delve into the potential mechanism in the treatment of IBD. Chen and Vitetta [11] comment in gastroenterology that butyrate, due to the actions of the microbiota, increases in the positive management of antagonists in inflammatory bowel disease; that is, anti-TNF with positive effects enhance the action of butyrate. All of this is vital knowledge for future therapy. Above all, due to the failures that occur in the management of anti-TNF treatment. Which forces us to continue searching for therapeutic approaches that correct ID. And therefore, butyrate levels increase. Likewise, Aden K., *et al*. [12] conclude that metabolic profiles of stool samples could be used to identify patients who will achieve clinical remission in IBD. Apparently, the increase in IBD has occurred due to changes that are not genetic, but environmental. Therefore, ID is the cause of the increase in the process, which is why management with bacteriotherapy has been proposed, which includes the use of probiotics, prebiotics and fecal microbiota transplantation [13]. Various therapies have been used for ID, including Infliximab, even though the responses are variable, so knowledge of these and other procedures must be deepened [14]. Sometimes bacterial diversity and richness are observed, which is stimulating in this therapy. Given by the presence of *Lachnospiraceae* and *Blautia*. Observing the development of SCFA and a decrease in pathogens.

Repeated or improper use of antibiotics has led to bacterial resistance, creating significant threats to many people with common bacterial infections. This has stimulated management with probiotics, which although some of the actions are known, such as, for example, production of antimicrobial substances, potentiation of the intestinal barrier and others, are not well understood. Furthermore, probiotics, like other substances, turn out to be foreign bodies and are often blocked by the immune system itself, which is why the addition of substances that prevent their rejection (Smectite Clay) has been considered [15-17]. This last aspect is significantly addressed by Dolai and Borody, who state why treatments with probiotics are not decisive, and point out ways to increase their effectiveness, so that there is long-term success [18].

Short chain fatty acids (SCFA)

Metabolites of the intestinal microbiota, are produced by the fermentation of indigestible carbohydrates, being extremely interesting, since they modulate intestinal inflammation, and could be an alternative to antibiotics [19]. There is often a lot of talk about them, since they maintain intestinal homeostasis and they usually do so through GM itself, by educating the immune system, through the fermentation of dietary fiber, highlighting the activity of butyrate. The latter has an anti-inflammatory impact, inhibiting neutrophils, dendritic cells, macrophages and effector T cells [20].

SCFA are saturated in nature and comprise 1 to 6 carbon atoms; Within them are butyrate, propionate, valerate, formate, caproate and acetate. All of them, preferably butyrate, impact various functions, especially energy metabolism, so they must be considered as part of the therapy in patients with ID [21].

GM has been involved in Parkinson's disease, along with permeability and the inflammatory process. All of this must be considered, since it has been determined that calprotectin increases, while SCFA decrease in this condition, depending on sex. The problem was confirmed by observing a reduction in SCFA in feces [22]. SCFA, together with the intestinal immune system, promote inflammatory intestinal diseases. The gut microbiome and gut immune system contribute to inflammatory bowel diseases. Both can determine IBD. Therefore, it is suggested to evaluate their clinical effect [23].

SCFA are absorbed by the intestines and excreted through feces, knowledge that is used for their determination and probable therapeutics. Still, the results are contradictory; although what is determined is that SCFA increase in capillary permeability [24]. Butyrate and acetate in hypertensive rats, as well as treatments with specific bacteria, generate control of arterial hypertension [25].

SCFA butyrate can protect against the development of obesity in children, as well as metabolic syndrome. This does not occur with the administration of selective prebiotics [26].

In vegan patients, it has not been determined whether the effect of the diet has to do with it, or with the personal composition of the GM and its metabolism [27]. It has already been established that GM modulates the physiology of the commensal, having reiterated that this action is linked GM to epigenetic mechanisms [28]. GM impacts host metabolism, with SCFA having significant action. For this, serum fatty acids, both local and specific, fecal SCFA and GM were determined, detecting that the ratio of *Firmicutes/Bacteroidetes* was linked in healthy patients to serum levels of fatty acids; while it did not appear in lupus disease and it was observed that the *Firmicutes/Bacteroidetes* proportion decreased [29].

ID can influence the decrease in SCFA, which will affect homeostasis; The determination of feces is the most economical and reliable methodology (gas chromatography and mass spectrometry). In colorectal cancer (CRC), there is a decrease in acetic acid and an increase in propionic and isovaleric acid. Therefore, it is suggested as a non-invasive method in patients with CRC [30].

Functions of SCFAs (metabolites important in the intestinal microbiome) [31,32]:

- Impact immunity, inflammation and metabolism.
- Impact the health and illness of the host.
- Energy source for cells of the ileum and colon.
- Modulate brain physiology.
- Strengthen the intestinal epithelial barrier.
- Anti-inflammatory, anti-microbial and anti-tumor.

- Affect reactive oxygen species.
- Reducer of intestinal pH.
- Contribution to drug metabolism.
- Alter intestinal purity.
- Modify cell function and proliferation.
- Regulation of genetic expression (Defense functions).
- Regulation of the physiology of innate immune cells (macrophages, dendritic cells and neutrophils).
- Regulation of T and B cell differentiation.
- Regulation of specific adaptive T and B cell immunity.
- Modify phagocytosis and chemotaxis.
- Raw materials in the synthesis of lipids and sugars.
- Promote apoptosis.
- Increase insulin sensitivity.
- Potential effect, to improve human health.

Conclusion

The above highlights the importance of SCFA, since based on powerful functions, we can aspire to improve the context of human health. Who doesn't want their patients to improve their immunity, want to live with less chronic inflammation and strengthen their metabolism.

For all these reasons, we must put SCFA in the first line of management, since with their knowledge and application we will achieve transcendent impacts on the population that suffers from various digestive disorders and not only digestive, but extra-digestive disorders, which could improve with SCFA.

Bibliography

1. Dudeja PK and Ramaswamy K. "Intestinal anion absorption". In physiology of the gastrointestinal tract (Fourth Edition) (2006).
2. Kiela PR and Ghishan FK. "Physiology of intestinal absorption and secretion". *Best Practice and Research Clinical Gastroenterology* 30.2 (2016): 145-159.
3. Liu H., *et al*. "Butyrate: A double-edged sword for health?" *Advances in Nutrition* 9.1 (2018): 21-29.
4. Parada DV., *et al*. "Short chain fatty acids (SCFAs). Mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases". *Frontiers in Immunology* 10(2019): 277.
5. Tan J., *et al*. "The role of short-chain fatty acids in health and disease". *Advances in Immunology* 121 (2014): 91-119.
6. Tan C., *et al*. "Dysbiosis of gut microbiota and short-chain fatty acids in acute ischemic stroke and the subsequent risk for poor functional outcomes". *Journal of Parenteral and Enteral Nutrition* 45.3 (2021): 518-529.
7. Silva YP., *et al*. "The role of short-chain fatty acids from gut microbiota in gut-brain communication". *Frontiers in Endocrinology (Lausanne)* 11 (2020): 25.

8. Bravo JJ., *et al*. "Butyrate and colorectal carcinogenesis". *Cirugía Española* 68.1 (2000): 57-64.

9. Hajjar R., *et al*. "The role of butyrate in surgical and oncological Outcomes in colorectal cancer". *American Journal of Physiology, Gastrointestinal and Liver Physiology* 320.4 (2021): G601-G608.

10. Lu Y., *et al*. "Microbiota-derived short-Chain fatty acids: Implications for cardiovascular and metabolic diseases". *Frontiers in Cardiovascular Medicine* 9 (2022): 900381.

11. Chen J and Vitetta L. "Butyrate in inflammatory bowel diseases therapy". *Gastroenterology* 158.5 (2020): 1511-1513.

12. Aden K., *et al*. "Metabolic functions of gut microbes associate with efficacy of tumor necrosis factor antagonists in patients with inflammatory bowel diseases". *Gastroenterology* 157.5 (2019): 1279-1292.e11.

13. Yoshimatsu Y., *et al*. "Bacteriotherapy for inflammatory bowel disease". *Inflammation and Regeneration* 41.1 (2021): 3.

14. Zhuang X., *et al*. "Fecal microbiota alterations associated with clinical and endoscopic response to infliximab therapy in Crohn's disease". *Inflammatory Bowel Diseases* 26.11 (2020): 1636-1647.

15. Wan MLY., *et al*. "Probiotics interaction with foodborne Pathogens: a potential alternative to antibiotics and future challenges". *Critical Reviews in Food Science and Nutrition* 59.20 (2019): 3320-3333.

16. Han., *et al*. "Smectite promotes probiotic biofilm formation in the gut for cancer immunotherapy". *Cell Reports* 34.6 (2021): 108706.

17. Akhtar M., *et al*. "Gut microbiota-derived short chain fatty acids are potential mediators in gut inflammation". *Animal Nutrition* 8 (2022): 350-360.

18. Dolai S and Borody T. "Editorial: Prerequisites for a successful probiotic therapy in dysbiosis". *Journal of Gastrointestinal Infection* 12 (2022): 83-85.

19. Vergara DM and González SME. "Short chain fatty acids (butyric acid) and intestinal Diseases". *Nutrición Hospitalaria* 34.4 (2017): 58-61.

20. Gonçalves P., *et al*. "A cross-talk between microbiota-derived short-chain fatty acids and the host mucosal immune system regulates intestinal homeostasis and inflammatory bowel disease". *HAL Open Science Pasteur* (2019): 02122775.

21. den Besten G., *et al*. "The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism". *Journal of Lipid Research* 54.9 (2013): 2325-2340.

22. Aho VTE., *et al*. "Relationships of gut microbiota, Short-chain fatty acids, inflammation, and the gut barrier in Parkinson's disease". *Molecular Neurodegeneration* 16.1 (2021): 6.

23. Deleu S., *et al*. "Short chain fatty acids and its producing organisms: An overlooked therapy for IBD?". *EBioMedicine* 66 (2021): 103293.

24. De la Cuesta ZJ., *et al*. "Higher fecal short-chain fatty acid levels are associated with gut microbiome dysbiosis, obesity, hypertension and cardiometabolic disease risk factors". *Nutrients* 11.1 (2019): 51.

25. Robles-Vera I., *et al*. "Probiotics prevent dysbiosis and the rise in blood pressure in genetic hypertension: role of short-chain fatty acids". *Molecular Nutrition* 64.6 (2020): 1900616.

26. Holmes ZC., *et al*. "Short-chain fatty acid production by gut microbiota from children with obesity differs according to prebiotic choice and bacterial community composition". *mBio* 11.4 (2020): e00914-20.

27. Prochazkova M., *et al*. "Vegan diet is associated with favorable effects on the metabolic performance of intestinal microbioma". *Frontiers in Nutrition* 8 (2022): 783302.

28. Yuille S., *et al*. "Live biotherapeutics-derived short-chain fatty acids as potent class I HDAC inhibitors". Poster Number: 1011. Keystone Symposia. Abstracts Microbiome: The antimicrobial efficacy and phytochemical analysis of the stem bark of *Azadirachta indica* (Neem) (2019).

29. Rodríguez-Carrio J., *et al*. "Intestinal dysbiosis is associated with altered short-chain fatty acids and serum-free fatty acids in systemic lupus erythematosus". *Frontiers in Immunology* 8 (2017): 23.

30. Niccolai E., *et al*. "Evaluation and comparison of short chain fatty acids composition in gut diseases". *World Journal of Gastroenterology* 25.36 (2019): 5543-5558.

31. Yao Y., *et al*. "Role of short-chain fatty acids in immunity, inflammation and metabolism". *Critical Review in Food Science and Nutrition* 62.1 (2022): 1-12.

32. Selber-Hnatiw S., *et al*. "Metabolic networks of the human gut microbiota". *Microbiology* 166.2 (2020): 96-119.

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