The impact of prebiotics, probiotics, and gut-derived metabolites on intestinal health and skeletal muscle metabolic and oxidative capacity

Document status and date:
Published: 16/01/2025

DOI:
10.26481/dis.20250116bo

Document Version:
Publisher's PDF, also known as Version of record

Impact paragraph

Diet, lifestyle, and genetic makeup are factors that influence the health and disease state of people. In recent years, there has been growing public and scientific interest in the role of the gut microbiota in human health. The gut microbiota, a complex and dynamic network of microorganisms, plays a crucial role in numerous bodily functions, including nutrient processing, immune system regulation, and maintaining overall physical and mental health. Prebiotics and probiotics can significantly modulate this microbial balance, promoting health and preventing disease by enhancing beneficial bacteria growth and activity. However, modern lifestyles and certain environmental factors such as poor diet, use of antibiotics, a sedentary lifestyle, and high levels of stress often lead to reduced microbial diversity. This can lead to dysbiosis, which is an imbalance in the intestinal microbiota composition and -activity that can contribute to disease development.

Recognizing the vital role of the gut microbiome, scientific interest on how to leverage this knowledge to enhance health outcomes is increasing. Understanding how to modulate the gut microbiota through dietary interventions can potentially lead to new interventions to prevent disease and maintain health. This thesis aims to establish the potential of prebiotics, probiotics, and gut derived metabolites to improve gut health and gut derived signals, thereby influencing overall well-being.

Evaluating the effects of prebiotics and probiotics on metabolic health

The comprehensive review in chapter 2 of this thesis explores various *in vitro*, *ex* vivo, and *in vivo* models used to investigate the effects of prebiotics and probiotics on gut and metabolic health. This review identifies the benefits and limitations of each model, emphasizing the importance of selecting appropriate models based on specific research objectives and considering aspects of the gut microbiota, such as microbial interactions and fermentation patterns.

In this review, it is proposed to combine different *in vitro* models to study various aspects of prebiotics and probiotics. These models range from fermentation models, which assess the effects of predigested prebiotics and probiotics on microbiota composition, to cellular and engineered digestion and absorption models. Combining these models is essential for advancing dietary intervention research. Providing a clear framework for future research, including integrating microfluidics in organoid models, can narrow the gap between *in vitro* and *in vivo* systems, thus enhancing the translation of *in vitro* mechanistic results. However, results should be validated in *in vivo* systems as current *in vitro* models still have limitations in mimicking systemic responses and neuronal as well as humoral mechanisms. The advancement of available *in vitro* models is particularly relevant for microbiologists, gastroenterologists, physiologists, and researchers in nutritional and metabolic health, as it enhances the ability to translate scientific discoveries into clinical applications. The review's impact lies in its ability to guide future research towards more standardized and effective methodologies, thereby accelerating progress in understanding and utilizing prebiotics and probiotics for health benefits.

Intestinal health and gluten sensitivity

An example of a diet-related health condition that significantly affects quality of life is gluten sensitivity, which includes conditions such as celiac disease (CeD) and non-celiac wheat sensitivity (NCWS). Celiac disease affects about 1% of the population worldwide (79), while estimates for NCWS range from 0.6 to 13% (80). This means that millions of people face the daily challenge of avoiding gluten, a protein found in wheat, barley, and rye. Even a small amount of gluten can trigger severe physical reactions, making everyday activities like grocery shopping, dining out, and social gatherings sources of anxiety and stress. This constant vigilance can significantly impact the quality of life for those affected. Individuals suffering from celiac disease often report that dietary restrictions and the constant risk of gluten exposure negatively impact their quality of life (81). Currently, the only way to manage these conditions is to adhere to a strict gluten-free diet, but hidden gluten in many food products poses a persistent threat. Hidden gluten refers to gluten that is not obvious or expected in various food items, such as sauces, soups, and even some medications, making it difficult to completely avoid. Studies report adherence rates to a gluten free diet ranging from 36% to 90%, with a median adherence rate of 70% (82). This uncertainty can lead to a fear of accidental gluten intake, causing considerable mental and physical distress.

Finding ways to reduce the risk of accidental gluten exposure is crucial for improving patients' quality of life. The research in chapter 3 of this thesis explores a novel approach to manage this. It demonstrates that consumption of a specific probiotic, *Bifidobacterium longum* NCC 2705 (BL NCC 2705), is safe for individuals with celiac disease and non-celiac wheat sensitivity. This probiotic produces a serine protease inhibitor (serpin), which helps to prevent the breakdown of gluten into its harmful components, thereby reducing the likelihood of an adverse reaction upon inadvertent gluten intake.

Importantly, this finding addresses both the physical and mental burdens associated with accidental gluten intake. For individuals with celiac conditions, the fear of hidden gluten can cause significant stress and anxiety, limiting their social participation. By offering a potential safeguard against these accidental exposures, this probiotic can help alleviate the mental burden, enabling these individuals to engage more freely in social activities such as dining out. This can significantly improve their quality of life by reducing the constant vigilance and stress related to gluten exposure. Clinicians can offer nutritional advice instead of drugs, dietitians can provide more effective dietary plans, and the food industry can develop new products incorporating these probiotics.

Relevance and impact of personalized prebiotic supplementation

Interest in personalized nutrition has increased because it allows for dietary interventions tailored to individual characteristics, including each person's unique gut microbiota composition. This approach addresses specific needs more accurately, and allows for more effective and targeted health interventions. Personalized prebiotic supplementation is particularly relevant as it has been associated with optimization of physical performance and overall health by considering individual variability in gut microbiota.

Chapter 4 of this thesis builds on the potential of personalized prebiotic supplementation to enhance endurance exercise performance. The study demonstrates that tailored dietary interventions can improve time to exhaustion during physical activity, which is highly relevant for athletes aiming to optimize their training and performance. Beyond athletics, personalized prebiotic supplementation may also support individuals facing physical challenges due to chronic illnesses or age-related skeletal muscle decline, helping to improve their everyday performance and quality of life. Personalized approaches may also benefit individuals with chronic health conditions, such as diabetes or metabolic disorders and potentially alleviating disease symptoms. Additionally, for the aging population, maintaining muscle function and metabolic health is crucial for sustaining physical capabilities and quality of life, and personalized nutrition offers a promising avenue for supporting their well-being.

The impact of this research is multifaceted. Scientifically, it advances our understanding of the gut-muscle axis and the role of gut microbiota in physical performance, paving the way for future studies in personalized nutrition. Clinically, the findings highlight the potential for integrating personalized dietary recommendations into practice, offering more effective strategies for managing metabolic health and supporting patients with chronic conditions. Societally, promoting better health outcomes through tailored nutrition can reduce healthcare costs and improve the overall well-being of diverse populations, including athletes, the elderly, and individuals with metabolic disorders. For the industry, this research offers a new way to design and launch tailored sports nutrition products, meeting the growing demand for personalized health and performance solutions.

Impact of gut derived metabolites on skeletal muscle

Chapters 5 and 6 of this thesis reveal significant insights into the metabolic effects of gut-derived metabolites, specifically short-chain fatty acids (SCFAs), on skeletal muscle. These studies demonstrate that a specific SCFA ratio can enhance glucose uptake in skeletal muscle cells and induce a shift towards more oxidative skeletal muscle fiber types, which are associated with better endurance and energy efficiency. This dual impact may be particularly relevant for people with diabetes, as enhance glucose uptake in muscle cells can lead to better blood sugar control, potentially reducing the risk of complications such as neuropathy, retinopathy, and cardiovascular diseases. By incorporating dietary strategies that increase a specific ratio of SCFA production, individuals with diabetes could potentially achieve more stable blood glucose levels, improving their overall metabolic health and quality of life, though results will have to be validated in a clinical study.

Similarly, the elderly, who often face the challenge of age-related muscle decline and decreased muscle mass, can benefit from these findings. Enhanced glucose uptake and a shift towards more oxidative muscle fibers could help to increase the skeletal muscle function of the present myotubes, which might mitigate the effects of sarcopenia, leading to improved muscle strength, endurance, and overall physical capabilities. This can significantly enhance their independence and quality of life by reducing mobility issues and the risk of falls and fractures. For athletes, SCFAs may improve energy efficiency in muscle cells, allowing athletes to train more effectively and perform at higher levels. Tailoring diets to boost a specific SCFA profile, based on their personal microbiota composition, could help athletes optimize skeletal muscle function, endurance, and recovery, enhancing their overall athletic performance.

Scientifically, these studies advance our understanding of the gut-muscle axis, showing how gut-derived metabolites influence muscle metabolism and function. This mechanistic insight is vital for developing targeted nutritional interventions aimed at enhancing metabolic health and physical performance. Clinically, the potential to modulate SCFA production through diet offers novel approaches to managing diabetes and age-related muscle decline, potentially reducing healthcare burdens. For the general public, maintaining a healthy gut microbiota through diet could lead to significant health benefits, enhancing metabolic health and physical performance, and improving overall well-being. This research highlights the broader societal benefits of dietary strategies that support gut health, offering practical solutions for improving quality of life across various populations.

Future studies should aim to further elucidate the specific pathways through which SCFAs exert these effects and explore the optimal types and dosages of dietary interventions for different populations to maximize health benefits. Additionally, studies should aim to investigate the impact of other nutritional compounds or the food matrix on the efficacy of prebiotics and probiotics. These findings could be valuable for patients and elderly providing new strategies for managing health conditions, offering potential improvements in muscle function and quality of life. Dietitians could use this information to develop more effective dietary plans while food and beverage companies, as well as those producing prebiotic and/or probiotic supplements, could use these insights to develop targeted nutritional products.

Conclusion

This thesis supports the potential of gut microbiota modulation through prebiotics, probiotics, and gut derived metabolites in enhancing human health. By exploring the intricate relationships between diet, gut microbiota, and various health outcomes, this research provides valuable insights that can form the basis for future scientific studies, clinical practices, new food products and public health strategies. The findings have significant implications for managing chronic diseases, improving athletic performance, and promoting overall well-being through personalized nutrition.

To ensure that these insights will be effectively disseminated and utilized, it is crucial to involve and inform target groups. Researchers and healthcare professionals can be engaged through scientific publications, conferences, and collaborative projects, ensuring that the latest findings are integrated into clinical practice and further research. Patients and athletes can benefit from tailored educational materials and practical guidelines. Dietitians can apply these findings in their dietary recommendations, while companies in the food and beverage industry can use this knowledge to develop innovative products. Continued research in this field will be crucial for developing more effective and targeted dietary interventions, ultimately leading to better health outcomes and improved quality of life for diverse populations.

References

1. Kurppa K, Mulder CJ, Stordal K, Kaukinen K. Celiac disease affects 1% of global population: who will manage all these patients? Gastroenterology. 2024;167(1):148-58.
2. Catassi C, Catassi G, Naspi L. Nonceliac gluten sensitivity. Current Opinion in Clinical Nutrition & Metabolic Care. 2023;26(5):490-4.
3. Rose C, Law GU, Howard RA. The psychosocial experiences of adults diagnosed with coeliac disease: a qualitative evidence synthesis. Quality of Life Research. 2024;33(1):1-16.
4. Hall N, Rubin G, Charnock A. Systematic review: adherence to a gluten-free diet in adult patients with coeliac disease. Alimentary pharmacology & therapeutics. 2009;30(4):315-30.