

Human microbiota as an important modulator of gut health

The brain... the heart... the gut. In recent years, it has become increasingly apparent that overall health and well-being has another foundation stone: the gut. Researchers worldwide continue to find evidence that good gut health is highly influential on many aspects of human health, stretching far beyond the digestive system itself.

The gut exerts influence on health and well-being in many ways, but is, in turn, affected by numerous factors.

Understanding these factors and their impact on the gut microbiota - the collection of bacteria that reside in the human gut - is critical to understanding overall gut health. Unsurprisingly, the gut (and more specifically its microbiota) is the dominant influencer of digestive health - one of the topics of most concern to consumers today. In this whitepaper, we explain and explore the microbiota, the issues caused by dysbiosis and how it can be manipulated to improve gut health.



A global concern

Problems with the gut are nothing new, but today, approximately 40% of consumers globally suffer from functional digestive issues¹. There is a prevalence of digestive diseases, disorders and difficulties that threaten the overall health of millions worldwide - and everyone from scientists and medical professionals, to brands and consumers, is talking about it.

Digestive health has also been gaining popularity for some years as consumers understand how much they themselves can influence and improve their health and well-being. As a result, many are pursuing a more holistic approach that focuses more on prevention, not only cure. When it comes to nutrition, a keyword, for example, is "clean label". As a result, consumers are eager to incorporate ingredients such as probiotics² and prebiotics³ into their daily diets to boost their gut health, and the pressure is on for scientists, brands and manufacturers to continuously develop innovative health solutions.

Inextricable link, unquestionable issue

It is unsurprising that the gut itself (and more specifically its microbiota) is the single largest influencer of digestive health and should therefore be the main target when looking to improve it. The protective role of the gut microbiota in suppressing invading pathogens, a concept known as colonisation resistance, has been extensively researched⁴.

Approximately 40% of people have functional gastro-intestinal disorders that impact their quality of life, including¹:



14% with Irritable Bowel Syndrome (IBS)



10% with functional constipation



3.5% with bloating or distension

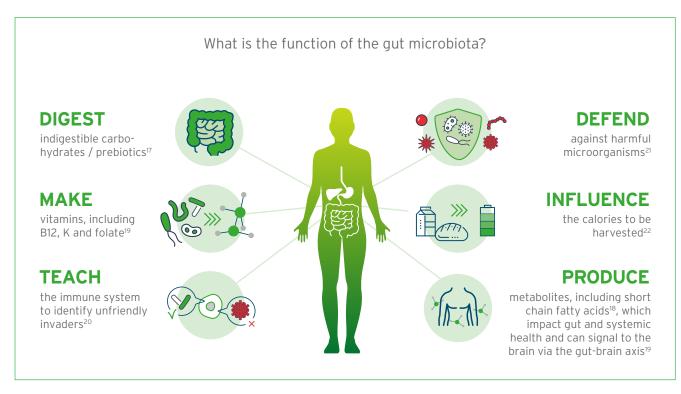
At the same time, good digestive health is a consumer priority worldwide, with more than one third of individuals suffering from digestion problems or discomfort¹. These issues, ranging from stomach discomfort to diagnosed disorders such as IBS, are uncomfortable, embarrassing and unpleasant, and millions of people cope with them on a daily basis. IBS, for example, as one of the more common issues, is a lifelong problem for many consumers and is estimated to affect more than 580 million globally⁵. In IBS patients, abnormal contractions in the gut and a distended bowel can trigger diarrhoea, constipation, or both.

Similarly, constipation is also one of the most common gut health impairments globally – with the biggest problem reported in the western hemisphere, where there is a prevalence of 2-27% 6. Meanwhile, the estimated self-defined constipation rate in Asia is 15-23% in women and approximately 11% in men 7. Due to its high occurrence and difficulties in diagnosis and subsequent treatments, constipation generates high costs in health care systems every year 8.

While a significant number of people look to medicine to remedy their digestive health issues, an increasing number is taking a preventative approach that encompasses healthy eating, fitness and well-being as a more sustainable, long-term solution. Central to it all is achieving and maintaining a healthy gut and its microbiota.



All eyes on the gut microbiota



Source: Adapted from Gut Microbiota for health

The gut microbiota collectively weighs up to 2kg (more than a human brain) and contains around the same number of microorganisms as the total number of cells in the human body⁹. Each individual gut hosts about 100 trillion bacteria in total¹⁰ and over 1,000 bacterial species⁹, many of which are vital in breaking down food and toxins and supporting the immune system.

Various studies have indicated the existence of a core gut microbiota, comprising prevalent gut microbiota, species, genes and essential functions, which are observed in most individuals and persist over time¹¹. Similarly, it is widely known that the microbiota breaks down indigestible food components to make them available for the human host and facilitates nutrient absorption¹³. Thus, the microbiota also has a systemic metabolic impact¹⁴. But in addition to this, the gut microbiota (directly or indirectly through the production of specific metabolites) also contributes to gut physiology, gut mobility and intestinal barrier homeostasis^{15, 16}.

Microbiome or microbiota?

These two terms are often used interchangeably but they define different aspects. The term "microbiome" refers to the microorganisms and their activities in an entire habitat (in this case the human body). The term "microbiota" covers a community of microorganisms residing in a particular environment (in this case, the human gut)¹².



The gut microbiota collectively weighs up to 2kg (more than a human brain) and contains around the same number of microorganisms as the total number of cells in the human body

Every person's microbiota composition is different, with each gut containing various species, each represented by numerous different strains and different quantities. However, broad commonalities can be seen, depending on many factors, including diet. And, with a range of disease thought to be linked in some way to the gut and the composition and activity of the microbiota²⁰, it has become increasingly clear that any conversation about digestive health should also consider the gut microbiota and the factors that influence it (such as nutrition).

A balanced approach

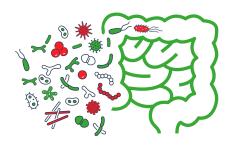


A healthy gut microbiota is complex and dynamic, with the ability to restore to equilibrium after disturbances such as pathogenic infection or antibiotic therapy¹¹. Microbiota composition fluctuates, but balance is crucial for it to perform all of its functions properly. A healthy balance, for example, ensures that beneficial bacteria such as bifidobacteria are present, while the growth of potentially

harmful bacteria is inhibited. The gut microbiota changes as we age, and alterations in the composition and activity are associated with some diseases. The scientific community is actively working to understand better which microbes are associated with health and disease, and whether an increase in risk-related bacteria or a loss of helpful species could be causal^{21,22}.



The gut microbiota is complex and dynamic, with the **ability to restore to equilibrium after disturbances** such as pathogenic infection or antibiotic therapy¹¹



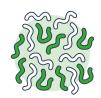
Source: Adapted from Gut Microbiota for health

The bifidobacteria brief

As one of the important genera of bacteria that make up the gastrointestinal tract microbiota in humans, a presence of *Bifidobacterium* has been implicated to be important for a healthy gut microbiota²³. The beneficial bifidobacteria produce metabolites such as short-chain fatty acids by breaking down fibres, thereby alleviating gastrointestinal symptoms like abdominal pain or bloating²⁴, inhibiting the growth of bad bacteria and reducing the gut pH¹⁶. The various bifidobacteria species also have influence on protecting the gut barrier¹⁶.

As a dynamic collection of bacteria and other microorganisms, there is always the possibility that the gut microbiota will be disrupted by unhealthy diet, medication or infection. This disruption can be characterised by a decline in bacterial species that benefit the body's health, an increase in harmful, disease-causing bacteria, or a restriction of the overall bacterial species richness. This type of imbalance is known as dysbiosis, and can be accelerated by exercising to exhaustion, disease and ageing²⁵.





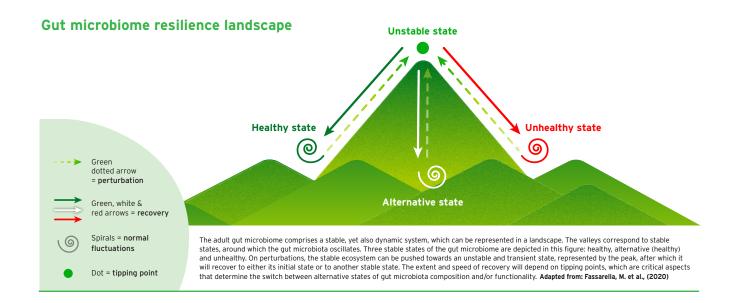
Bifidobacteria

Short-chain fatty acids

Resilience of gut microbiota

The gut microbiota's ability to self-regenerate after any perturbation (disturbance) is known as the resilience phenomenon²⁶. Impaired ability to come back to the pre-perturbation healthy composition and activity may lead to long-lasting dysbiosis. As such, maintaining a resilient micro-biota may be important for health^{11,27}. There is growing evidence that a disrupted microbiota can contribute to the pathogenesis of gastrointestinal disorders including inflammatory bowel disease (IBD), irritable bowel

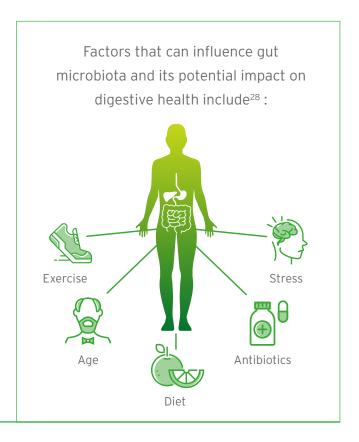
syndrome (IBS) and coeliac disease^{26,30}. The 'tipping points' that mark the critical switch of the microbiota to an unhealthy state are only beginning to be understood, and the responses are highly individual-specific. However, it is becoming apparent that the mechanisms shaping and determining gut microbiota resilience will allow the development of modulatory strategies to increase resilience of healthy states, or rather decrease and ultimately overcome unhealthy states³⁰.



Balancing the gut microbiota

So, if dysbiosis is a key factor in the development and prevalence of digestive health issues, how can the microbiota be 'rebalanced'? There is a huge potential to sustain, improve or restore the microbiota in at-risk or diseased individuals.

Diet has repeatedly been shown to be one of the most important factors affecting the gut microbiota. The microbiota's composition and the activity of the microbiota are important throughout the lifespan. Indeed, more than 50% of the variation of gut microbiota have been related to dietary adjustments – and major changes in diet during adulthood can modify the microbiota in a matter of days²⁷. Specific foods and dietary patterns all influence the abundance of different types of bacteria, which in turn can affect both overall gut health and digestive health specifically^{28,29}. In particular, prebiotics have shown themselves to be popular solutions that positively influence the gut and, in turn, digestive health³¹.



The exciting future of digestive health



Balancing the microbiota via external dietary influences is a game-changer for consumer health. As they become more aware of the effects of lifestyle and diet on holistic health and well-being, scientists and new product development teams are exploring the potential of supplements and functional foods and drinks that positively influence our gut health.

At FrieslandCampina Ingredients, our world-leading experience in infant, performance and medical nutrition has allowed us to develop ingenious digestive health solutions that work with the body's natural processes to address gut health conditions and digestive problems. With decades of expertise in the science of prebiotic effects, their development and their application as ingredients, we are eager to unlock the secrets of the microbiota and provide consumers with the means to improve their gut health easily.

Interested?

Interested in learning more about the gut microbiota, or the digestive health solutions offered by FrieslandCampina Ingredients? Get in touch with our team today via email at info@biotis.com to start the conversation.

References

- Sperber, A. et al. Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. Gastroenterology, 160, 99–114 (2021).
- Hill C, Guarner F, Reid G, et al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol. 11(8):506 514 (2014).
- Gibson, G. R., Hutkins, R. W. & Prescott, S. L. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) Consensus Statement on the Definition and Scope of Prebiotics. Nat Rev Gastroenterol Hepatol 14, 491–502 (2017).
- Litvak & Bäumler. The founder hypothesis: A basis for microbiota resistance, diversity in taxa carriage, and colonization resistance against pathogens, 15(2):e1007563 2019.
- 5. Official Statistics United Nations.
- Camilleri, M., et al. Chronic Constipation. Nature Reviews Disease Primers, 3:17095, 2017.
- Gwee, K., et al. Primary Care Management of Chronic Constipation in Asia: The ANMA Chronic Constipation Tool. J Neurogastroenterol Motil, 19(2). ;149-160, 2013.
- 8. Rantis, P.C., Jr., et al., Chronic constipation—is the work-up worth the cost? Dis Colon Rectum, 40(3):280-6, 1997.
- Sender, R., Fuchs, S. & Milo, R. Revised Estimates for the Number of Human and Bacteria Cells in the Body. PLoS Biol. 14, 1-21 (2016).
- 10. Can gut bacteria improve your health? Harvard Health Publishing, 2016.
- Fassarella, M. et al. Gut microbiome stability and resilience: elucidating the response to perturbations in order to modulate gut health. Gut. 2021 Mar;70(3):595-605.
- Berg, G., Rybakova, D., Fischer, D. et al. Microbiome definition re-visited: old concepts and new challenges. Microbiome 8, 103 (2020). https://doi.org/10.1186/s40168-020-00875-0
- Krajmalnik-Brown, R et al. Effects of gut microbes on nutrient absorption and energy regulation. Nutrition in Clinical Practice: official publication of the American Society for Parenteral and Enteral Nutrition vol. 27.2 (2012): 201-14.
- Koh, A. et.al. From Dietary Fiber to Host Physiology: Short-Chain Fatty Acids as Key Bacterial Metabolites. Cell. 2016;165(6):1332-1345.

- Ge X, Pan J, Liu Y, Wang H, Zhou W, Wang X. Intestinal Crosstalk between Microbiota and Serotonin and its Impact on Gut Motility. Curr Pharm Biotechnol. 2018;19(3):190-195.
- Picard C, Fioramonti J, Francois A, Robinson T, Neant F, Matuchansky C. Review article: bifidobacteria as probiotic agents -- physiological effects and clinical benefits. Aliment Pharmacol Ther. 2005;22(6):495-512.
- Flint, HJ. et al., The role of the gut microbiota in nutrition and health. Nat Rev Gastroenterol Hepatol. 2012 Sep 4;9(10):577-89.
- Blaak, E. E. et al. Short chain fatty acids in human gut and metabolic health. Benef. Microbes 11, 411-455 (2020).
- Amon, P. & Sanderson, I. What is the microbiome? Arch. Dis. Child. Educ. Pract. Ed. 102, 258-261 (2017).
- 20. https://.worldmicrobiomeday.com.
- Ghosh ST, Das M, Jeffery IB and O'Toole PW. Adjusting for age improves indentification of gut microbiome alterations in multiple diseases. eLife 2020:9:e50240.
- An R, Wilms E, Masclee AAM, Smidt H, Zoetendal EG, Jonkers D. Age-dependent changes in GI physiology and microbiota: time to reconsider? Gut. 2018 Dec;67(12):2213-2222.
- 23. O'Callaghan, A. & van Sinderen, D. Bifidobacteria and their role as members of the human gut microbiota. Front Microbiol. 2016 Jun 15:7:925.
- Hungin APS, Mitchell CR, Whorwell P, et al. Systematic review: probiotics in the management of lower gastrointestinal symptoms - an updated evidence-based international consensus. Aliment Pharmacol Ther. 2018;47(8):1054
 –1070.
- Ticinesi A, Tana C, Nouvenne A. The intestinal microbiome and its relevance for functionality in older persons. Curr Opin Clin Nutr Metab Care. 2019;22(1):4-12.
- Sommer F, Anderson JM, Bharti R, Raes J, Rosenstiel P. The resilience of the intestinal microbiota influences health and disease. Nat Rev Microbiol. 2017;15(10):630-638.
- Dogra SK, Doré J, Damak S. Gut Microbiota Resilience: Definition, Link to Health and Strategies for Intervention. Front Microbiol. 2020;11:572921.
- 28. Rinninella, E. et al. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms 7, (2019).
- David, L.A. et al. Diet rapidly and reproducibly alters the human gut microbiome. 2014 Nature 505(7484):559-63.
- Dogra, S.K. et al. Gut Microbiota Resilience: Definition, Link to Health and Strategies for Intervention. Front Microbiol. 2020 Sep 15;11:572921.
- Wilson, B., Rossi, M., Dimidi, E. & Whelan, K. Prebiotics in irritable bowel syndrome and other functional bowel disorders in adults: A systematic review and metaanalysis of randomized controlled trials. Am. J. Clin. Nutr. 109, 1098-1111 (2019).





The Netherlands

Stationsplein 4 3818 LE Amersfoort The Netherlands Tel: +31 (0)33 713 33 33

Health benefit solutions

FrieslandCampina in Ingredients

Asia-Pacific

3 Temasek Avenue #11-01 Centennial Tower Singapore 039190 Tel: +65 6580 8100

Please visit www.biotis.com or email info@biotis.com

Potential consumer benefits are not to be considered as health claims. They should be considered as potential leads that might be developed into health claims complying with the local legal requirements. The information contained herein is, to the best of our knowledge, correct. The data outlined and the statements are intended only as a source of information. No warranties, expressed or implied, are made. On the basis of this information it is suggested that you evaluate the product on a laboratory scale prior to use in a finished product.

The information contained herein should not be construed as permission for violation of patent right.

China

2506, West Tower of Twin Towers B12 Jianguomenwai Ave, Chaoyang Dist. Beijing 100022 China Tel: +86 10 6566 6099

North America

61 S. Paramus Road, Suite 535 Paramus, NJ 07652, USA Tel: +1 551 497 7300

Latin America

Rua Fradique Coutinho 30 - 6° - Cj. 61 Condomínio Edifício WinWork Pinheiros 05416-000 São Paulo, Brasil Tel: +55 11 2395 1700