The emergence of Akkermansia Muciniphila as a Next-Generation Probiotic for Metabolic Health and Weight Loss

September 26th, 2023

Introduction

Given the evolving landscape of research and shifting trends in nutritional supplementation, it can be challenging to sift through the latest information and make an informed choice when selecting the most suitable probiotic for your health needs. This article summarizes major recent research findings detailing the metabolic benefits of *A. muciniphila*, a next-generation microorganism, studied for the potential therapeutic treatment of common metabolic diseases and weight management.

What is a Next-Generation Probiotic?

Extensive research has established the important connection between gut microbiota and brain function, commonly referred to as the gut-brain axis.[1,2] This scientific and medical consensus underscores the many advantages of maintaining a healthy gut microbiome for mental and overall well-being. Due to the significance of gut health, a new category of probiotics has emerged, known as next-generation probiotics (NGPs), distinguished by their pharmaceutical therapeutic potential for disease prevention and treatment.[3,4] Along with the promising development of specialized genetically modified NGPs, it's worth highlighting that ongoing research in this field has unveiled a world of naturally occurring NGPs, potentially already residing in your gut, demonstrating considerable safety, efficacy, and availability in various products on the market.

What is *Akkermansia Muciniphila*?

Latin for “mucus lover,” *A. muciniphila* possesses a distinctive ability to feed off the mucus lining within the gastrointestinal tract.[5] This microbe is typically found along the large intestine, constituting approximately 0.5-5% of a healthy human's microbiome.[6,7] Remarkably, *A. muciniphila's* primary function revolves around the degradation of mucin proteins, serving as a gatekeeper of intestinal permeability, and thus, influencing the integrity of the gut-brain axis.[8]

In contrast to the majority of gut bacteria, which rely on fiber as their dietary source, *A. muciniphila* assumes a pivotal role within the microbiota ecosystem, not only by consuming mucins to maintain the intestinal mucus lining, but also by producing nutrients, such as short chain fatty acids.[9] These byproducts serve a purpose of nourishing other bacteria and fostering the development of a robust and health-promoting commensal microbiota environment.

Ubiquitous Presence and Distinctive Function

Even before *A. muciniphila's* discovery in 2004, the important connection between gut permeability and inflammatory and neurological diseases, or the gut-brain axis, was well known. Consequently, researchers at the Wageningen University of the Netherlands initially posited that bacteria engaged in metabolizing the gut lining would play a substantial role in interacting with human intestinal cells and shaping various health outcomes. These researchers soon isolated and discovered *A. muciniphila* as the exclusive mucin-degrading bacteria in the human intestines.[10] Further investigation found *A. muciniphila* strains in infants and throughout diverse human populations, along with genetically similar strains in a range of wild animal populations.[11–15] These finding suggest the evolutionary importance and pivotal role of mucus-consuming bacteria in the well-being and growth of animals. Moreover, since its discovery, *Akkermansia* has garnered over 2,000 mentions in PubMed articles in just two decades. Extensive research has revealed robust links between its presence and various health advantages, establishing it as a NGP with numerous potential targets for therapeutic applications.[8]

Although this is not an exhaustive summary of *A. muciniphila* research, the following information provides an overview of important scientific research around *A. muciniphila* and why it has emerged as one of the most promising, naturally occurring, NGPs to treat metabolic disorders and help with weight loss.

A. muciniphila Abundance is associated with Healthy Lifestyle Factors in Humans

Healthy levels of *A. muciniphila* in the gut align with a balanced diet, regular exercise, and favorable eating habits in humans. Individuals who maintain consistent exercise regimens and incorporate polyphenol-rich foods into their diets, such as dark berries, chocolate, coffee, and tea, tend to exhibit healthy levels of this bacterium.[16,17] Interestingly, as a mucus-consuming bacterium that does

not need starch or sugar to survive, *A. muciniphila* has been observed to flourish in the presence of calorie restriction and resiliency during periods of starvation or fasting,[18] demonstrating potential insight to its ubiquity and widespread presence among humans and animals globally.

Another significant factor linked to the presence of *A. muciniphila* is longer food transit time, meaning digestion takes longer in the intestines.[19,20] This results in heightened nutrient absorption and an extended feeling of satiation after eating. Remarkably, extended food transit time, leading to decreased appetite is also a noteworthy effect observed in one of the world's most widely used pharmaceuticals for diabetes management and weight loss—semaglutide, available under brand names Ozempic, Wegovy, and Rybelsus.[21] This phenomenon may be attributed to the natural activation of glucagon-like peptide-1 (GLP-1) by *A. muciniphila*. Semaglutide, in essence, emulates the effects of GLP-1—a hormone typically released in the small intestine, responsible for slowing gastric emptying and increasing satiety.

Treating and Reversing Metabolic Disorders

In contrast to the presence of *A. muciniphila* at healthy levels, mounting evidence underscores its lack of presence as a risk factor for metabolic conditions such as obesity, type 2 diabetes, nonalcoholic fatty liver disease, and cardiovascular disorders.[22–27] These associations with metabolic health not only suggest that *A. muciniphila* in humans may act as a preventive measure against metabolic and cardiovascular conditions linked to high body-mass index, but also offer indications of its therapeutic potential in treating and enhancing outcomes for individuals affected by these conditions. One study, which examined the abundance of *A. muciniphila* in a group of 11 overweight and 38 obese individuals, revealed positive correlations with improved overall metabolic profiles and heightened clinical success following caloric restriction.[28] This, in turn, has the potential to enhance the quality of life for overweight individuals and increase the likelihood of successful weight loss treatments.

Studies conducted on rodents have strongly supported the connection between *A. muciniphila* and the reduction of metabolic diseases. In these studies, daily administration of live A. muciniphila reversed metabolic conditions induced by a high-fat diet in mice.[29,30] Improved conditions included decreased fat mass, metabolic endotoxemia, inflammation in adipose tissue, and insulin resistance. Pasteurized *A. muciniphila* also contributed to reducing the development of fat mass, insulin resistance, and dyslipidemia in mice.[31–37] Furthermore, research on rodents has demonstrated that *A. muciniphila* supplementation leads to a decrease in cholesterol and serum triglyceride levels in metabolic disease

models.[31,38,39] It has been effective in preventing nonalcoholic fatty liver disease by regulating the expression of genes related to fat synthesis and inflammatory markers in the liver of mice.[39] Additionally, in mouse models of atherosclerosis, it has been shown to reduce the severity of atherosclerotic lesions.[40] *A. muciniphila* has also shown promise in mitigating diabetes in both type 2 and type 1 diabetes mouse models by lowering gut permeability and reducing inflammation.[41,42] Other studies have indicated that *A. muciniphila* supplementation reduces the severity of inflammatory bowel disease, alcoholic liver disease, colitis-associated tumorigenesis, and progeria in mice.[30,35,43–46] Currently, human clinical studies are underway to validate the promising results on metabolic disorder treatments observed in rodent studies.

Promising Future Research on *A. muciniphila*: Effects on Neurological Health and Immunity

While compelling data has established numerous potential direct benefits of *A. muciniphila* in reducing the severity of metabolic conditions and improving weight loss, research also sheds light on its potential systemic effects on immune response and neurological pathways.

A. muciniphila plays a role in fortifying gut barrier function by maintaining mucous linings, which can prevent the leakage of harmful substances and pathogens into the bloodstream, triggering immune responses.[29,47] Furthermore, enhancements in metabolic health due to *A. muciniphila* may indirectly influence the immune system. Obesity and metabolic disorders are often linked to chronic low-grade inflammation, which can impair immune function. Additionally, *A. muciniphila* is associated with anti-inflammatory properties and was found to stimulate the production of regulatory T (Treg) cells in the gut of Multiple Sclerosis mouse models.[48] Treg cells are instrumental in maintaining immune tolerance and preventing excessive immune responses, guarding against autoimmune reactions such as allergies and chronic inflammation. Due to its immunomodulatory potential, *A. muciniphila* is being explored for its potential in enhancing cancer immunotherapy treatments. Although further investigation is required, it has shown promise in improving the clinical response to checkpoint inhibitor immunotherapies.[49–51]

In terms of neurological health, *A. muciniphila* can generate beneficial short-chain fatty acids (SCFAs) like acetate and propionate during mucin fermentation.[9] SCFAs can exert anti-inflammatory and neuroprotective effects. Some studies also propose that *A. muciniphila's* influence in maintaining the gut-brain barrier may extend to improving the integrity of the blood-brain barrier, a pivotal defense mechanism safeguarding the brain from harmful substances.[1,2,52]

Nevertheless, ongoing research in the context of neurological disorders has stirred controversy. While certain reports have observed positive correlations between *A. muciniphila* abundance and the severity of conditions such as Parkinson's disease and Multiple Sclerosis,[53–58] other studies have demonstrated beneficial effects of *A. muciniphila* abundance on Alzheimer's Disease and seizure models.[59,60] No studies have provided evidence for the direct role of *A. muciniphila* in the etiology of neurological disorders and confounding factors, like microbiota environment, chronic constipation, dietary changes, and drug treatments, have been cited variables skewing data in humans.[8]

Collectively, these findings underscore the complexities of drawing conclusions solely from associations with a single bacterium, without considering the intricacies of the entire microbiome ecosystem. It's crucial to understand that the composition of the gut microbiota can have multifaceted and diverse effects on health.

Why Choose Akkermy's Probiotic Formula

At Akkermy we believe in the science-backed evidence of the health benefits of *A. muciniphila* abundance, but we understand that the gut is a complex ecosystem, relying on additional bacteria and nutrients to optimally thrive. We have designed a formula to also include *Bacillus coagulans*, a well-tolerated bacteria with strong evidence in effectively minimizing gastrointestinal discomfort,[61] and added essential vitamins (B and D) and the mineral chromium.

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