

AKKERMANSIA MUCINIPHILA IS ASSOCIATED WITH HUMAN HEALTH: WHAT SHOULD WE KNOW?

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Akkermansia muciniphila is a gut bacterium that has recently attracted considerable attention in microbiota research. Its presence in the gut is associated with improved metabolic health, enhanced gut barrier integrity, and modulation of the immune system. However, potential risks related to its abundance under certain pathological conditions have also been noted. As *A. muciniphila* emerges as a candidate for next-generation probiotics, evaluating whether current data support its therapeutic use is crucial. In this review, we analyze the available literature to outline the beneficial effects of *A. muciniphila* on the host and critically assess its potential as a probiotic.

1. Introduction. 2. *Akkermansia muciniphila* in the human population. 3. *Akkermansia muciniphila* is a mucin specialist. 4. The protective role of *Akkermansia muciniphila* in diseases. 5. The role of *Akkermansia muciniphila* in obesity prevention. 6. *Akkermansia muciniphila* - potential as a probiotic. 7. Conclusion.

Keywords: *Akkermansia muciniphila*, disease, microbiota, probiotics.

1. Introduction

Akkermansia muciniphila was first isolated from the faeces of a healthy adult Caucasian female in 2004 as the first known member of the *Akkermansia* genus and the only isolated member of the Verrucomicrobiota phylum (Derrien et al. 2004). The anaerobic, Gram-negative, non-motile, and non-spore-forming bacterium colonizes the intestines and nasopharynx of humans and other animals (Derrien et al. 2004). Other environments it inhabits include the appendix, the pancreas (in pathological conditions), human breast milk, and human blood samples (Geerlings et al. 2017). Since then, other members of the genus have been found inhabiting the human gut (Kobayashi et al. 2018). *Akkermansia* is a genus that has recently attracted much attention due to its probiotic effects and possible role in bowel disease treatment (approved by the European Food Safety Authority (EFSA).

2. *Akkermansia muciniphila* in the human population

A. muciniphila is an early colonizer of the human gut that reaches an abundance similar to or slightly lower than that in adults within the first year of life and then decreases in the elderly. The abundance appears to be higher in formula-fed than in breast-fed infants, and increases once breast-feeding stops (Azad et al. 2018). A Chinese study found a colonization rate of 51-74% in southern China and identified 22 strains within the studied population (Guo et al. 2016). Abundance and colonization rate can vary between countries, and the composition of the microbiota is influenced by diet and genetic factors (Grześkowiak et al. 2012). Nonetheless, the consensus is that *A. muciniphila* is a common and stable part of the human gut microbiota. *A. muciniphila* growth can be stimulated by diet, with one study demonstrating that dietary polyphenols from grapes can dramatically promote

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its growth in mouse models (Roopchand et al. 2015). Another study demonstrated that fucoids from brown seaweed increased the abundance of *Akkermansia* in mice with metabolic syndrome induced by a high-fat diet (Qingsen et al. 2017).

3. *Akkermansia muciniphila* is a mucin specialist

One of the key characteristics of *A.muciniphila* is the ability to degrade mucins and use them as an energy source. Mucins are high-molecular-weight glycoproteins continuously secreted by goblet cells, which constitute a significant component of the intestinal mucus and form the protective mucus layer. Of the 21 different mucins identified, mucin 2 (MUC2) is the predominant component of the colonic mucus layer and acts as its structural skeleton (Song et al. 2023). The mucus layer serves as the first line of defense, protecting the epithelium from inflammation and infection. Disruption of the mucus layer is an important factor in the development of intestinal diseases, including inflammatory bowel disease (IBD) and colorectal cancer. The mucus barrier maintains homeostasis by stimulating the growth of appropriate microbiota and preventing pathogens from contacting the epithelium (Song et al. 2023).

Mucin-degrading bacteria produce glycosyl hydrolases (GHs), specialized enzymes that enable them to break down mucins. The *A. muciniphila* genome contains genes encoding nine different GH families (Glover et al. 2022). It can utilize different combinations to hydrolyze up to 85% of mucin structures, allowing it to use mucins as its sole carbon source (Glover et al. 2022). As a result, *A. muciniphila* is often considered one of the most important mucin degraders in the human microbiota. The metabolism of mucins by *A. muciniphila*, in addition to the action of other bacterial species, releases monosaccharides, oligosaccharides, and short-chain fatty acids into the intestinal environment, thereby contributing to the modulation of intestinal homeostasis (Belzer et al. 2012). Although *A. muciniphila* degrades mucin, it does so in a controlled and selective manner, which (1) stimulates the production of new, healthy mucus, (2) supports the regeneration of the mucus and epithelial barrier, and (3) reduces inflammation and strengthens mucosal immunity (Si et al. 2022). As such, its presence in the gut microbiota is associated with better metabolic, immune, and barrier health (Table 1).

Table 1. *Akkermansia muciniphila* is positively associated with improved metabolic profiles, enhanced mucosal immunity, and a robust epithelial barrier.

Mechanism	Effect	Reference
Mucin degradation + mucus stimulation	Promotes goblet cell proliferation and maintains mucus thickness	Si et al. (2022)
Barrier reinforcement	Enhances tight junctions (ZO1, occludin, claudins), and TER ↑	
Immune modulation	↓ proinflammatory cytokines, ↑ IL-10, and ↑ Tregs	

IL-10 – interleukin-10; TER – transepithelial electrical resistance; Tregs – regulatory T cells; ZO-1 – zonula occludin-1.

4. The protective role of *Akkermansia muciniphila* in diseases

The primary reported benefits of *A. muciniphila* are associated with alleviating symptoms or preventing gastrointestinal disease, with a primary focus on Inflammatory Bowel Disease IBD. IBD refers to a group

of diseases that cause inflammation of the bowel, with the primary types being ulcerative colitis (UC) and Crohn’s disease (CD). Symptoms may include diarrhea, abdominal pain, fatigue, nausea, and weight loss. Significant evidence suggests a correlation between *A. muciniphila* and the development of IBD, although its nature remains under discussion. In a mouse study,

treatment with *A. muciniphila* for five weeks reduced inflammation caused by chemically induced colitis (Yilmaz et al. 2024). Another mouse model found that *A. muciniphila* improved clinical parameters, including spleen weight, colon inflammation index, colon histological score, and regulation of pro-inflammatory cytokines, with varying activity levels among strains (Zhai et al. 2019). In addition, *A. muciniphila* supplementation reduced serum and tissue inflammatory cytokines and chemokines in mice, along with reduced weight loss, improved histological scores, and enhanced barrier function (Bian et al. 2019).

The role of *A. muciniphila* in the prevention of IBD can be inferred from its reduced presence in IBD patients, with UC and CD exhibiting lower colonization rates and abundance compared to healthy individuals, both of which increase significantly after washed microbiota transplantation (Qu et al. 2021). Additionally, *A. muciniphila* was lower in patients with active UC compared to those with quiescent UC and healthy individuals (Zhang et al. 2020). The same study identified a reduction of sulfated mucins in the mucus of IBD patients as a potential cause of *A. muciniphila* reduction (Zhang et al. 2020).

Investigations into the mechanisms underlying the anti-inflammatory effects of *A. muciniphila* are ongoing. Aside from the well-known anti-inflammatory effects of short-chain fatty acids (SCFA) produced by the human microbiota, there have been reports that one of the main surface proteins of *A. muciniphila* (Amuc_1100) could play a crucial role (Wu et al. 2019).

The anti-inflammatory effect of *A. muciniphila* might also be beneficial for patients with Parkinson's disease (PD). Indeed, an *A. muciniphila* treatment alleviated artificially induced PD in mice, including neuroinflammation and motor dysfunction, while promoting neurogenesis (Qiao et al. 2024). However, the evidence for the beneficial effects of *A. muciniphila* remains inconclusive, with some reports not aligning with the previously mentioned results. One such study detected an increase in *A. muciniphila* in patients with colorectal cancer (Weir et al. 2013), suggesting that the relationship between *A. muciniphila* and host health might be more complex.

5. The role of *Akkermansia muciniphila* in obesity prevention

Another area in which *A. muciniphila* is heavily investigated for its beneficial effects is obesity, with the

bacterium's anti-obesity effects demonstrated in several studies. An analysis of data from the American Gut Project has found an association between a higher abundance of *A. muciniphila* and a lower risk of obesity (Zhou et al. 2020). A randomized controlled trial reported that *A. muciniphila* supplementation reduced obesity, though the effects appear to be limited to individuals with a low baseline abundance of the bacterium (Zhang et al. 2025). In this regard, the reduction of *A. muciniphila* was associated with the development of atherosclerosis induced by a high-fat Western diet in apolipoprotein E knock-out mice (Li et al. 2016). Meanwhile, daily administration of *A. muciniphila* has been shown to prevent weight gain, hyperphagia, and dysglycemia caused by the dietary emulsifiers carboxymethylcellulose and polysorbate (Daniel et al. 2023).

Investigations into the anti-obesity mechanisms of *A. muciniphila* demonstrated that the species can alleviate the negative effects of interferon gamma (IFN γ) on glucose tolerance (Greer et al. 2016). Another potential mechanism of action involves Amuc_1100, which has some of the same effects as the live bacterium when purified or applied as part of pasteurized *A. muciniphila* (Anh   et al. 2017). It is very likely that the effects of *A. muciniphila* on obesity are not centred on a single mechanism, but result from several separate effects in conjunction with other members of the human gut microbiota. Furthermore, many studies have involved mice fed a high-fat diet, so the impact on different sources of obesity should still be investigated.

6. *Akkermansia muciniphila* - potential as a probiotic

As described previously, *A. muciniphila* has several potential benefits for human health. However, it is worth discussing whether it can be used as a probiotic. Aside from providing health benefits to the host, a good probiotic should be considered safe for human consumption, and it should be able to survive long enough in storage and after consumption to reach the gut. A toxicological analysis of pasteurized *A. muciniphila* did not reveal any mutagenic, clastogenic, or aneugenic effects, nor did it reveal any adverse neurobehavioural or pathological effects that would undermine its use as a food additive (Druart et al. 2021). A comparative analysis of *A. muciniphila* and the commonly used probiotic bacterium *Lactobacillus rhamnosus* GG revealed comparable levels of auto-aggregation, co-aggregation,

hydrophobicity, and antimicrobial activity, but a higher level of antibiotic resistance in *A. muciniphila*. It is generally recommended that probiotic bacteria have a low level of antibiotic resistance to prevent potential horizontal gene transfer. However, the presence of resistance genes associated with transferable genetic elements has not been reported in *A. muciniphila* (Cozzolino et al. 2020).

Methods for cultivating *A. muciniphila* have improved since its initial discovery. Using mucin in growth medium is costly and inconvenient, so the use of alternatives has been investigated. One study identified glucose or N-acetylglucosamine (a component of mucins) as a good source of carbon, and tryptone as a reliable source of nitrogen (Wu et al. 2024). Another study identified galactose, sialic acid, lactose, and chi-

tosan as factors significantly promoting *A. muciniphila* growth (Meng et al. 2024).

7. Conclusions

A. muciniphila supplementation provides significant benefits for patients suffering from IBD. Its relationship with obesity seems to be more complex, though studies agree that it alleviates symptoms associated with a high-fat diet, which is common in Western countries. As a natural member of the human microbiota, *A. muciniphila* is generally considered safe, which is supported by evidence, and has been approved by EFSA. There are also no technical obstacles to its use as a commercial probiotic. *A. muciniphila*'s general functions are summarised in Figure 1.

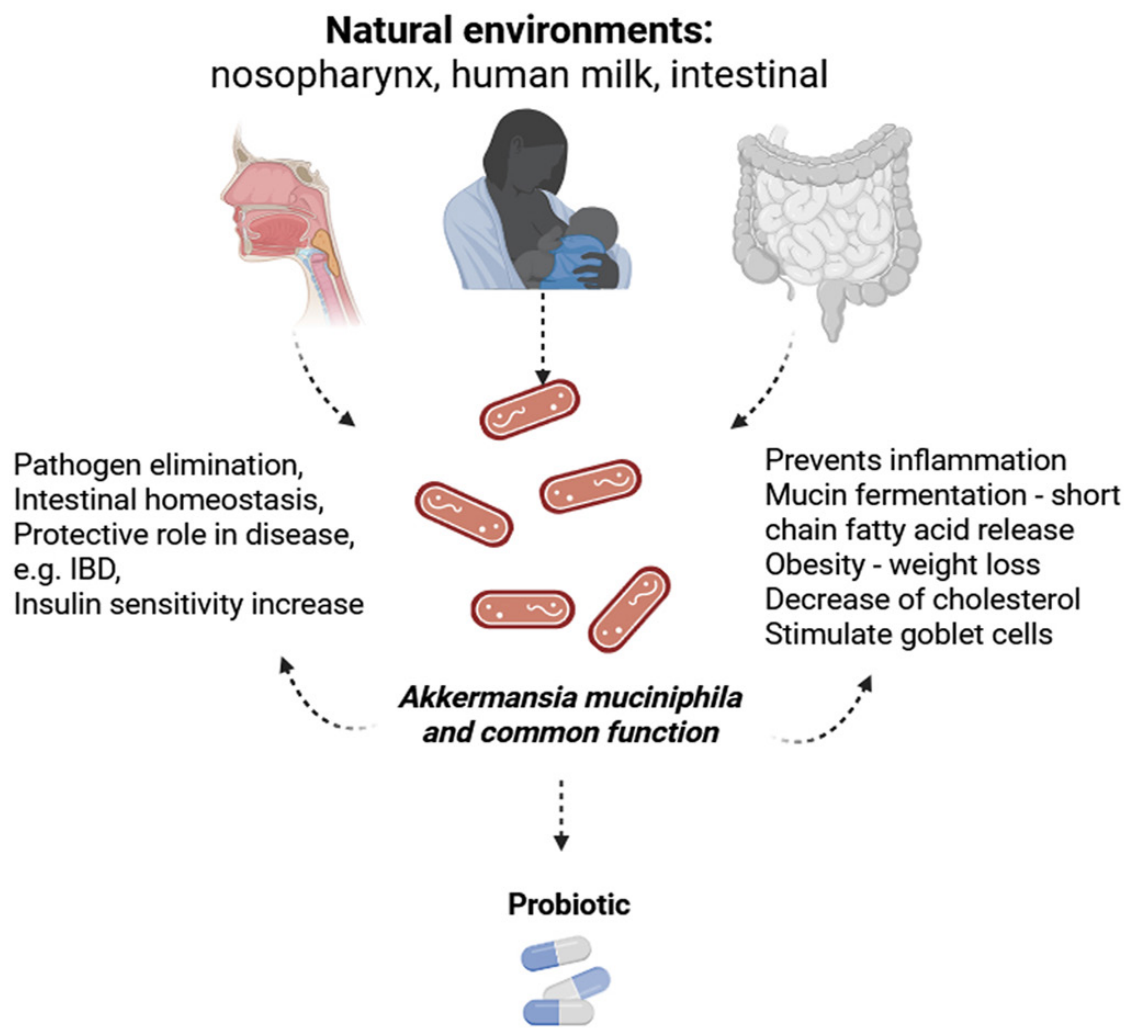


Figure1. Summary of the role of *A.muciniphila* in health and disease. Illustration created using Biorender (www.biorender.com). Agreement number: CA28PV7H2E



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Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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