

Akkermansia muciniphila: Next-Gen Bacteria for Metabolic Health

Research Highlights

- ✓ *Akkermansia muciniphila* is a keystone species inhabiting host intestinal mucus layer and contributes to the maintenance of a healthy gut barrier.
- ✓ A lower abundance of *Akkermansia muciniphila* is associated with poor metabolic health, whereas a higher abundance is linked to better metabolic health.
- ✓ Its membrane protein Amuc_1100 can help maintain host gut barrier integrity, support immune homeostasis, and improve metabolic functions via TLR2 signaling. Amuc_1100 remains active after pasteurization.
- ✓ A human clinical trial demonstrated that pasteurized *Akkermansia muciniphila* is more effective than the live bacterium in improving metabolic health-related parameters.

A unique, mucin-loving keystone species

The gut mucus layer forms a natural defense barrier, and its integrity is vital for maintaining the intestinal health of the host.¹ *Akkermansia muciniphila*, unlike many of the known probiotic species, is a unique commensal microbe inhabiting the mucus layer, where it can interact closely with host intestinal epithelial cells and immune cells. *Akkermansia muciniphila* is known to utilize mucins (key components of mucus) as nutrient and energy sources and produce beneficial short-chain fatty acids (SCFAs).² It is believed that through reinforcing gut barrier function, *Akkermansia muciniphila* supports various bodily functions, such as energy, lipid, and glucose metabolism as well as immune responses.³

Clinical relevance of *Akkermansia muciniphila*

The presence and abundance of *Akkermansia muciniphila* in the gut may be indicative of the host's metabolic health.⁴

- In multiple human cohort studies, the abundance of *Akkermansia muciniphila* is reduced in the microbiomes of individuals with obesity, type 2 diabetes (T2DM), impaired glucose control, high blood pressure, inflammatory bowel diseases, and liver diseases (Figure 1).⁵⁻¹⁰
- Conversely, greater abundance of *Akkermansia muciniphila* is linked with a leaner body weight, lower body fat mass, and greater improvement in insulin sensitivity (Figure 1).^{5,11}

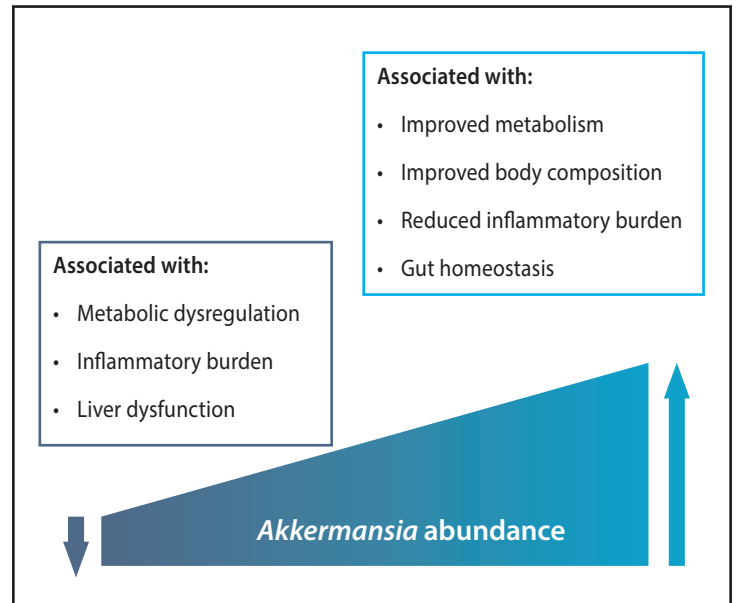


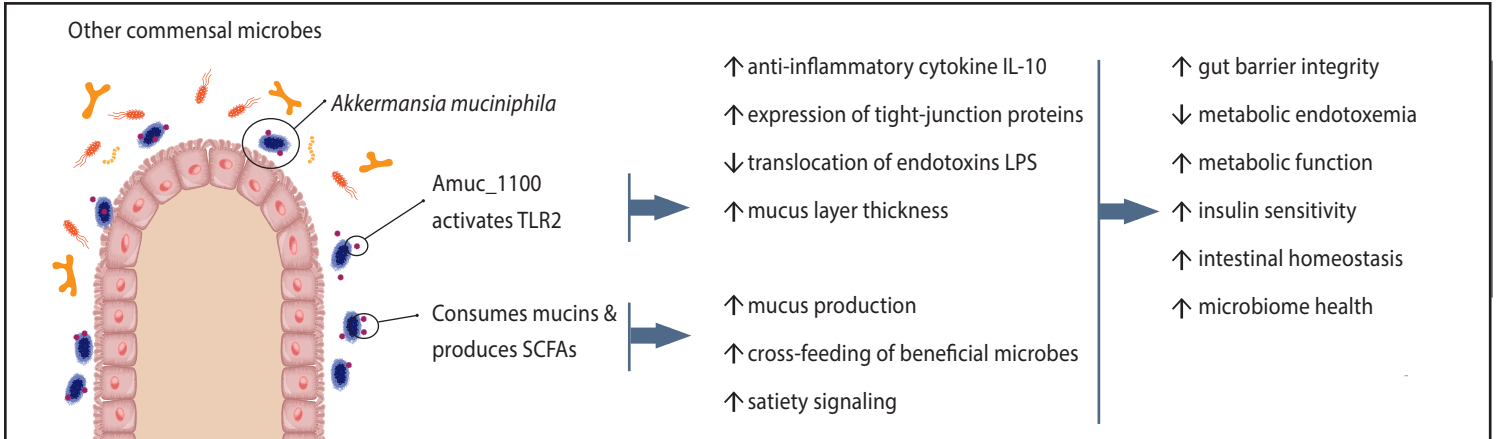
Figure 1. The inverse relationship between *Akkermansia muciniphila* abundance in the gut and host metabolic health.

Proposed mechanisms of actions of *Akkermansia muciniphila*

Recent intervention studies in animals demonstrated *Akkermansia muciniphila* administration reversed high-fat diet-induced metabolic disorders, fat-mass gain, metabolic endotoxemia, adipose tissue inflammation, and insulin resistance.¹² As seen in Figure 2, *Akkermansia muciniphila* has been demonstrated to exert several mechanisms of action such as:

- Enhance mucin production by increasing the number and density of goblet cells (mucin-producing cells), which helps restore the thickness of the mucus layer.¹³
- Increase the expression of tight-junction proteins within the intestinal epithelium to augment the integrity of tight junctions.¹⁴
- Its membrane protein Amuc_1100 binding to Toll-like receptor 2 (TLR2), leading to activation of anti-inflammatory pathways, prevention of lipopolysaccharides (LPS) translocation, and improvement in mucin secretion and gut barrier.¹⁵

More important, researchers discovered that mice receiving pasteurized *Akkermansia muciniphila* had a greater reduction in body weight, fat-mass gain, plasma lipids, and insulin-resistance markers than mice receiving the live bacterium.¹⁵ Research found that the protein Amuc_1100 remained heat-stable after pasteurization, and its administration alone recapitulated most of the observed metabolic benefits *in vivo*. This suggests that pasteurization enhances the effects of *Akkermansia muciniphila* by increasing accessibility of Amuc_1100 to the host.¹⁵



IL: interleukin; LPS: lipopolysaccharides; SCFAs: short-chain fatty acids; TLR2: toll-like receptor 2

Human clinical trial of *Akkermansia muciniphila*

The metabolic benefits seen in animal studies led to the first human clinical trial investigating the health-promoting potential of *Akkermansia muciniphila* (both alive and pasteurized) in people who were overweight or obese and insulin-resistant.

Thirty-two volunteers received either placebo, live *Akkermansia muciniphila* (10 billion CFU/day), or pasteurized *Akkermansia muciniphila* (10 billion CFU/day) for three months and were asked not to change their diet and exercise habits. The study found:¹⁶

- The supplementation of pasteurized form but not of live form markedly improved insulin sensitivity and reduced insulinemia and plasma total cholesterol levels compared with volunteers supplemented with placebo.
- Compared with placebo, pasteurized *Akkermansia muciniphila* decreased body weight, hip circumference, and waist circumference by an average of 5.0 lb., 1.0 in., and 0.6 in., respectively.
- Compared with placebo, pasteurized *Akkermansia muciniphila* decreased plasma LPS levels (metabolic endotoxemia) by an average of 117%.
- Both live and pasteurized *Akkermansia muciniphila* for three months were safe and well-tolerated.

Summary

Given the correlation between abundance of *Akkermansia muciniphila* and health status, efforts have been made to restore and promote abundance of *Akkermansia muciniphila*, such as increasing intake of polyphenol-rich foods (e.g., EGCG, berberine),^{17,18} supplementing selected probiotic strains,^{19,20} and exercise.²¹ Today, daily supplementation of *Akkermansia muciniphila* has become a reality. While a balanced diet and regular exercise are the cornerstones for maintaining healthy weight and minimizing metabolic syndrome risks, this next-generation bacteria, pasteurized *Akkermansia muciniphila*, offers a novel solution to support metabolic health in those who are overweight or obese.

References:

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