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Review Article

# Gut Microbiome's Next Generation Probiotic: Akkermansia Overview and Supplementation Health Benefits

Subhendu Nayak <sup>1#</sup> , Meghan McLean <sup>1#</sup> , Swetaleena Mishra <sup>2#</sup> , Ranjan			
Kumar Sahoo <sup>2</sup> *, and Durga Madhab Swain <sup>3</sup> *	Received: April 23, 2024		
<sup>1</sup> Vidya Herbs, 7 Otis Stone Hunter Road, Bunnell, Florida, USA	Published: May 10, 2024		
<sup>2</sup> Department of Biotechnology, Centurion University of Technology and Management,	© All rights are reserved by <b>Durga Madhab</b>		
Bhubaneswar, Odisha, India	Swain., et al.		
<sup>3</sup> MU Bond Life Sciences Center, University of Missouri, Columbia, USA			
*Corresponding Author: Durga Madhab Swain, MU Bond Life Sciences Center, University			
of Missouri, Columbia, USA and Ranjan Kumar Sahoo Department of Biotechnology,			
Centurion University of Technology and Management, Bhubaneswar, Odisha, India.			
<sup>#</sup> These authors contributed equally			

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## Abstract

A bacterium known as *Akkermansia muciniphila* (*AkkermansiaA. muciniphila*) was detected in human feces in 2004. It is defined as a gram-negative, anaerobic, and mucin-degrading microbe belonging to the Verrucomicrobia species. Although the majority of A. muciniphila is found in the human intestinal tract playing a role in the gut microbiome, there are also smaller levels detected in breast milk and oral cavities as well as in the pancreas and appendix. Evidence suggests that having *A. muciniphila* present in the gut microbiome has positive effects on human health. As a result, *A. muciniphila* has been shown to have health benefits when taken as a dietary supplementation where it is considered a promising next-generation probiotic. However, the large-scale production of *A. muciniphila* remains a challenge due to its need for a stable environment. While culturing A. muciniphila in a mucin-based medium is one option, other strategies that use plate-based mediums have also been explored. Currently, both live and pasteurized forms of *A. muciniphila* are available on the market and shown to have promising outcomes in animal models. Additionally, researchers are investigating various prebiotics to increase the abundance of *A. muciniphila* in the human gut. This article presents a detailed summary of the phenotypic characteristics of *A. muciniphila* and its associations with various human health condition illnesses. Finally, the paper explores *A. muciniphila*'s potential as an effective next-generation probiotic.

Keywords: Akkermansia muciniphila; Gut Microbiome; Intestinal Mucin; Probiotic

### Introduction

The microorganisms in the human body have been extensively studied, with particular attention given to the gut microbiota. Research has shown that the gut microbiome plays a crucial role in maintaining health and preventing various diseases. Several illnesses, such as inflammatory bowel syndrome [1]., eating disorders [2], cancer [3], type 2 diabetes [4], and psychological disorders [5] have been associated with changes in the gut microbiota. The gut microbiota consists of several species, with Firmicutes and Bacteroidetes being the dominant bacteria, accounting for 90% of the gut's bacteria [6]. Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia are among other species that have been reported in the gut microbiota. In the gastrointestinal tract, A. muciniphila is the sole species reported in the Verrucomicrobia phylum family. It was discovered and isolated from the stool of a healthy individual [7]. A. muciniphila depends on mucin as a carbon, nitrogen, and energy source which differentiates it from most other bacteria in the gut microbiome [8]. Recent studies have shown that it comprises 1% to 3% of the gut microbiome in feces

and is present in over 90% of healthy adults tested [9]. However, its levels tend to decrease in older people [9]. Most of the research studies that reveal the existence of *A. muciniphila* in the human digestive system are conducted through metagenomic analysis. However, only a few studies have reported the isolation of this bacterium.

*A. muciniphila's* ability to break down and utilize mucin as a sole source of nitrogen and carbon is of great significance in the human gut. This enables other bacteria to thrive and develop by consuming the byproducts of mucin degradation. *A. muciniphila's* metabolites additionally have been found to influence the host's inflammatory status. *In vitro* or *in vivo*, it has been discovered that it can regulate the immune system, enhance gut barrier function, and improve metabolism in cases of obesity and diabetes [10]. The results indicated a correlation between the existence of *A. muciniphila* and the wellbeing of individuals, as its prevalence notably diminishes in various health conditions. In the future, *A. muciniphila* can be utilized to indicate specific diseases that vary in their seriousness. Recent

research has promoted the use of *A. muciniphila* as a probiotic due to its advantageous impact on the human body. Many studies have been published that reported the safety of A. muciniphila as a probiotic for obese humans and its beneficial role. Depommier., et al. suggest that it is a safe probiotic for obese people which improves the patient's metabolism system [11]. A clinical trials study by Depommier., et al. (NCT05114018) found that pasteurized A. mu*ciniphila* improved insulin sensitivity and total plasma cholesterol leading to a slight decrease in body weight. Supporting this finding, another clinical trial by Hibberd., et al. (NCT01978691) found A. muciniphila reduced the waist-hip ratio, increased energy intake, and body fat mass changed upon taking the probiotic [11]. This review presents an overview of A. muciniphila, its characteristics, potential applications, and challenges associated with live culture versus pasteurized as a probiotic in human experimentation.

### **Characteristics of Akkermansia**

In 2004, Muriel Derrien discovered Akkermansia muciniphila in the human intestine and found the bacterium to use mucin as its sole energy (7). A. muciniphila is a non-spore-forming, oval-shaped bacterium belonging to the Verrucomicrobia species. It is present in healthy individuals' gut microbiota, making up approximately 1-3% of the total gut microbiome [12]. It is a Gram-negative, nonmotile bacterium and the first and only member of the Verrucomicrobia species found in the human gut [13]. At first, aerobic tolerance has been observed in A. muciniphila, previously categorizing it as a strict anaerobe. Recent discoveries indicate that it can now be classified as an aerotolerant anaerobe since it has demonstrated the ability to withstand small quantities of oxygen [14].

A. muciniphila can break down intestinal mucin glycoproteins using various enzymes, including glycosyl hydrolases, proteases,

sulphatases, and sialidases, utilizing them as carbon and nitrogen sources [15]. This process leads to the creation of short-chain fatty acids (SCFAs), including acetate. Acetate is a type of fatty acid with a short carbon chain, propionate, and 1,2-propanediol, along with succinate and sulfate [16]. A. muciniphila helps in the degradation process of mucin, which results in the promotion of mucin turnover and thickening. This, in turn, strengthens the intestinal barrier and reduces the gut's permeability to microbial products. Due to the metabolites A. muciniphila secretes, it can lead to the activation of important antimicrobial mechanisms. For example, A. muciniphila activates Paneth cells to enhance the production of antimicrobial peptides through a mechanism that builds barriers. The colon absorbs SCFAs, which are produced from gut mucin glycoproteins. These SCFAs provide colonocytes with energy and stimulate regulatory T cells, reducing inflammation [17]. Other bacteria in the gut microbial community, including Anaerostipes caccae, Anaerobutyricum hallii, and Faecalibacterium prausnitzii, utilize SCFAs to synthesize butyrate and propionate (16) Not only does A. muciniphila use metabolites to unlock health benefits, but it also uses its outer membrane proteins to stimulate positive effects. For example, A. muciniphila outer membrane protein Amuc\_1100 can influence immune responses by activating Toll-like receptor 2 (TLR2). Immune, epithelial, and endothelial cells express TLRs that identify microbial structures. This recognition can initiate both pro- and anti-inflammatory responses and affect the regulation of the host's metabolism [18]. The European Food Safety Authority (EFSA) conducted an upbeat assessment of the safety of pasteurized A. muciniphila in 2021 [19]. This assessment marks the beginning of a new era of probiotics: next-generation probiotics [20]. A. muciniphila has many benefits (Figure 1) and can be used as a biomarker of a healthy metabolic profile. Its depletion signals intestinal dysbiosis across various diseases (Table 1).

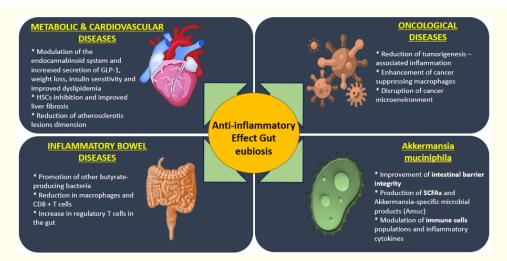


Figure 1: Possible health benefits of Akkermansia muciniphila in people. Akkermansia muciniphila has been shown to play a beneficial function in modifying intestinal and extraintestinal disorders through the direct and indirect control of immune system response, inflammatory, and endocrine pathways, as well as its significant influence on gut ecology. Hepatic stellate cells, or HSCs; glucagon-like peptide-1, or GLP-1; and short-chain fatty acids, or SCFAs.

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Administered of Droduct	Machanism of Astion	Satting	Doculto	Doforonas
Administered of Product	Mechanism of Action Expansion of cytotoxic T-lymphocytes in	Setting Mice with DSS-in-	Results	Reference
Pasteurized <i>A. muciniphila</i> or the outer membrane protein Amuc_1110	the colon and mesenteric lymph nodes Reduction in macrophage and CD8+ cy- totoxic T lymphocyte levels in the colon of mice with DSS-induced colitis Reduction in markers of DNA damage; cell apoptosis; abnormal proliferation of	duced colitis and CAC	Improvement of CAC symp- toms; delayed tumor develop- ment; decreased number and area of tumor lesions. Amelioration of colitis symp- toms; improvement of histo- logic damage	Wang L., <i>et</i> <i>al</i> . 2020
Amus 2100 (a Q a satul	colonic epithelial cells	Miss with DCC in	Ampliquetion of colitic curve	Oian V. at
Amuc_2109 (a β- acetyl- aminohexosidase secreted by <i>A. muciniphila</i> )	Reshaped gut microbiota. Reduced expression of pro-inflammatory	Mice with DSS-in- duced colitis	Amelioration of colitis symp- toms.	Qian K., et al. 2022
Amuc_1434 (a recom-	cytokines Enhanced TRAIL-mediated apoptosis	LS174T cancer cells	Inhibition of proliferation and	Meng X., et
binant enzyme derived from <i>A. muciniphila</i> able to degrade Muc2)	pathway. Enhanced expression of p53, resulting in		enhanced apoptosis of LS174T cells in vitro.	al. 2020
411 8	blockade of G0/G1 cell cycle phase			
Akk-Evs	Increased infiltration of GZMB+, IFN-γ+ CD8+ lymphocytes, and M1 macrophages in tumour tissue.	PCa-bearing mice	Reduced tumor burden	Luo Z., <i>et</i> <i>al</i> . 2021
Three strains of pasteur- ized <i>A. muciniphila</i> with anti-lipogenic activity <i>in</i> <i>vitro</i>	Increased expression of IRS-1; reduced expression of leptin gene in adipose tissue	HFD-fed mice	Three strains of pasteurized A. muciniphila with anti-lipogenic activity in vitro	Yang M., <i>et</i> <i>al</i> . 2020
	Increased gut production of GLP-1 and PYY			
	Inhibition of low-grade intestinal inflam- mation, restoration of damaged gut integrity			
	Reduced expression of perilipin-2 (a protein involved in the regulation of lipolysis) in adipose tissues			
	Reduced expression of lipogenic-adip- ogenic markers (as PPARγ) in adipose tissue and liver			
Pasteurized A. muciniphila	Reduced expression of gut GLUT2, GLUT5, and SGLT1 with consequent decrease in carbohydrate absorption	HFD-fed mice	Reduced body and fat mass weight.	Depom- mier C., <i>et</i> <i>al</i> . 2020
	Reduced expression of perilipin-2 (a protein involved in the regulation of lipolysis) in adipose tissues			
Live and pasteurized <i>A. muciniphila</i> and its EVs	Reshaped gut microbiota.	Quiescent and LPS-	Amelioration of liver biochem-	Rafter S., et
	Reduced expression of TLR2 and TLR4	activated HSC and HFD-fed mice treated with CCl4	istry Reduced expression of fibrosis and inflammatory	al. 2020
			Reduced expression of fibrosis markers via activated HSC	
			Attenuation of liver histopatho- logical damage	

**Table 1:** Studies reporting on the beneficial effects of the administration of pasteurized *A. muciniphila* or its components.

#### Present in the gut: Next-generation probiotic

The gut microbiome largely influences the host's immune, physiological, and pathological processes. The occurrence and development of diseases, including metabolic diseases, immunerelated diseases, neurologic and psychiatric diseases, pregnancy complications, and adverse pregnancy outcomes, are significantly impacted by gut microbiota dysbiosis. Probiotics have a long history of safe consumption and can regulate intestinal microflora balance. They offer a range of health benefits, including preventing necrotizing enterocolitis, reducing crying in infants with colic, improving the quality of life for IBS patients, preventing diarrhea in children's hospitals, and reversing intestinal inflammation caused by antibiotics. The popularity of probiotics has led to a multibillion-dollar industry worldwide, which is expected to exceed \$65.9 billion by 2024 (http://www.zionmarketresearch.com/report/ probiotics-market). Probiotics are mainly unregulated, and their clinical efficacy is unreliable. However, they can aid in disease prevention (Zion Market Research, 2021). They have been found to reduce the incidence of necrotizing enterocolitis in newborns with very low birth weights.

Next Generation Probiotics (NGPs) are a new class of active biological agents that differ from traditional probiotics. They contain live or pasteurized organisms that are applicable for dietary supplementation to aid in the recovery of their levels in humans to gain health benefits. NGPs are being widely studied and reported as they can play an essential role in the future intervention or treatment of human diseases. Some potential NGP candidates are *Akkermansia muciniphila, Faecalibacterium prausnitzii, Bacteroides fragilis, Eubacterium hallii,* and Roseburia spp. By understanding the levels of *A. muciniphila* in healthy individuals, the needed dose of supplementation can be provided to those with depleted amounts.

### Human breast milk

Human breast milk is rich in nutrients that offer immunological and other health benefits to newborn babies. Research on human milk indicates that it serves as a source of commensal microorganisms that aid the development of the infant's gut. A study revealed the presence of *A. muciniphila* in human breast milk for the first time and it remains present in colostrum breast milk all the way to breast milk six months after birth. The mean concentrations were 1.25 log number of gene copies/mL in colostrum breast milk and 1.20 log number of gene copies/mL in breast milk six months after birth. This study also found that *A. muciniphila* was more abundant in mothers who were overweight than in average mothers. In another study conducted in 2014, *A. muciniphila*-like species were detected in human breast tissue samples of 43 women aged between 18 and 90 years using 16S rRNA sequencing [22]. It was found in milk samples from 11 women after a caesarean section [23]. The Akkermansia genus was detected in breast milk from healthy Korean mothers [24], as well as the bacterial extracellular vesicles, which play a role in transporting crucial mediators in intracellular signaling via the transfer of macromolecular cargoes. Interestingly, mothers with a genetic predisposition to coeliac disease were shown to have increased levels of *A. muciniphila* in their breast milk [25]. One hypothesis on why it can be present in human breast milk due to its ability to use human milk oligosaccharides [26].

#### Ageing

Many clinical trials have found that the amount of A. muciniphila in the human gut typically decreases as one age (8). Recent studies show that A. muciniphila is more abundant in healthy older adults with longer lifespans [27]. Van., et al. conducted preclinical studies and found that A. muciniphila has the potential to slow down ageing (16). It was found here that A. muciniphila supplementation thickened the gut mucus layer in senescent mice, improving their immune system. Prematurely aged mice experienced an extension of their healthy lifespan after being transplanted with A. muciniphila. This outcome was likely due to the increase in secondary bile acid levels. Shin., et al. found that when it is orally administered, it improves gut health and homeostasis, restores cognitive function and muscle atrophy, and extends the healthy lifespan of aged mice [28]. Cerro., et al. study on aged mice found that A. muciniphila supplementation improved immune cell function and reduced oxidative stress and pro-inflammatory cytokines [29]. Ma., et al. conducted a study that showed that aged mice exhibited improved glucose sensitivity, hepatosplenomegaly, inflammation, antioxidant capacity, and intestinal barrier function after being supplemented with A. muciniphila [30]. These findings suggest that it could positively regulate host metabolism and immune function during ageing [31]. Plant-based supplements like curcumin, ginseng, and apple polyphenols can extend lifespans and have anti-ageing effects [32] Beta-carotene may help with aging by affecting telomerase activity [33]. Additionally, many plant supplements can increase the abundance of A. muciniphila to a certain extent. Studies suggest that it has anti-ageing potential, but it is unclear if plant supplements increase its abundance. These findings introduce new ideas in ageing-related research [34].

#### Pregnancy

Genetic and environmental factors, including diet, cultural behavior, and socioeconomic status, influence obesity. Obesity also alters intestinal microbiota composition, with lean individuals having more Bacteroidetes and obese individuals having more Firmicutes, potentially improving energy extraction and adipose tissue storage. Pregnant women who are obese have significant health risks, but

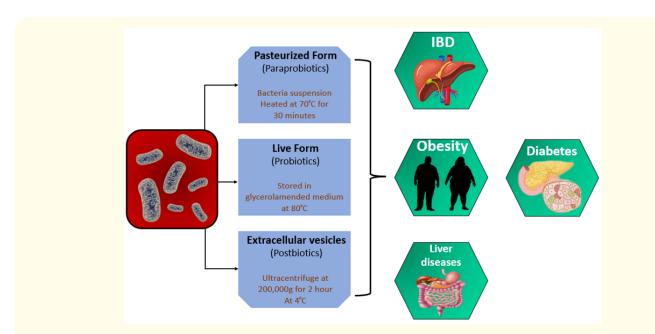
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little research has been done on the connections between obesity and the composition of their gut flora [35]. A woman's body undergoes several physiological changes throughout pregnancy to provide the best conditions for the fetus's growth and development. The human intestinal microbiota, consisting of around 100 trillion organisms, is crucial for the health of expectant mothers and their children's development. Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria, which constitute 70-90% of all bacteria in the digestive tract, produce 3.3 million genes and millions of metabolites involved in biochemical changes. During pregnancy, there are significant changes in the gut microbiome, marked by a decrease in individual richness (alpha-diversity) and an increase in intersubject beta-diversity. Although they may be impacted by certain factors such as diet, antibiotic treatments, gestational diabetes, or pre-pregnancy body mass index, it is essential to note that these changes are crucial for a healthy pregnancy. The observed changes could be influenced by other factors, like the condition of the host's immune and endocrine systems. In the first trimester, the gut microbiome composition in pregnant women is like that of non-pregnant women in good health, with a predominance of Firmicutes, particularly clostridial, over Bacteroidetes. Additionally, the gut microbiota during pregnancy has been identified as a crucial factor determining offspring health, potentially influencing the development of atopy and autoimmune phenotypes in the offspring [36].

#### Akkermansia Alive vs Pasteurized in Supplementation

A.muciniphila in both live and pasteurized forms has shown positive effects on cardiometabolic risk factors in various mice models and humans with metabolic syndrome. There are multiple suggested mechanisms by which these positive effects occur. A mechanism involving a protein called Amuc\_1100 can bind to toll-like receptor 2 (TLR2). This binding helps improve gut barrier function and reduce inflammation. Additional mechanisms are currently being investigated to explain the beneficial effects of pasteurized A. muciniphila on glucose homeostasis. For example, a recent study showed that supraphysiological doses of a protein called P9, which live A. muciniphila secretes, increase Glucagonlike peptide-1 (GLP-1) secretion [37]. This plays a critical role in glucose homeostasis as GLP-1 is a peptide that communicates with the pancreas to secrete insulin and suppress glucagon secretion. However, this effect is absent when A. muciniphila is pasteurized. Ashrafian., et al. demonstrated that both live and pasteurized forms of A. muciniphila could modulate lipid and immune homeostasis and improve health by regulating gut microbiota. However, the dominant effects were observed in the pasteurized form. An increasing amount of research indicates that certain naturally occurring gut bacteria are underrepresented in the intestinal tracts of individuals with type 2 diabetes (T2D) and that the stability of the gut barrier and the generation of butyrate are critical activities of these bacteria for maintaining insulin and glucose ho-

meostasis. This study sought to investigate the notion that enteral exposure to microorganisms with these putative roles could safely enhance clinical glycemic control measures and contribute to the overall dietary management of diabetes. These anaerobic bacteria, when combined into a probiotic, would improve dietary management through the following means: (1) producing two new probiotic formulations in a current good manufacturing practice (cGMP) facility that contains three (WBF-010) or five (WBF-011) distinct strains; (2) determining stable live-cell concentrations; (3) verifying safety at target concentrations administered in both animal and human studies; and (4) carrying out a 12-week parallel, doubleblind, placebo-control. This is the first RCT in which T2D-afflicted humans are given four out of the five strains [38]. For A. muciniphila to become pasteurized, many researchers achieve this by heating A. muciniphila so it can no longer survive. Plovier., et al. pasteurizes A. muciniphila by using a suspension of bacteria and heating it to 70°C for 30 minutes (10). This method of using pasteurized A. muciniphila harnesses the metabolites that it creates to have positive health benefits. It is also thought that the pasteurized forms of bacteria can reduce the risk of infection. Recently, significant attention has been paid to using para probiotics (Figure 2), nonviable bacterial supplements in pasteurized forms, as an alternative to live bacteria. In one example, they examined pasteurized A. muciniphila found in the High Fat Diet (HFD) model. In this HFD model, 45% of energy as lipids was provided and used to study altered enteric neuron activity in the proximal part of the intestine, which characterizes diabetes. 60% lipid diet caused ectopic fat deposits in insulin-sensitive tissues and the gastrointestinal tract, hindering the study of intestinal hyper-contractility. Abot., et al. found that pasteurized A. muciniphila reduced weight gain and improved glucose and insulin levels in high-fat diet mice [39]. This improvement in glucose homeostasis without compensatory hyperinsulinemia is of great interest to delay/prevent pancreas exhaustion during insulin-resistance progression. Druart., et al. conducted a study that showed that using pasteurized A. muciniphila as a food ingredient is safe for rats [40]. Grajeda-Iglesias., et al. conducted another study that showed how pasteurized A. muciniphila was more effective than the live version in increasing the levels of polyamines, short-chain fatty acids, 2-hydroxybutyrate, and several bile acids in the intestine. These metabolites have been linked to human health [41]. Furthermore, recent studies have focused on postbiotics, which use deactivated cell components to promote well-being [42]. In the case of A. muciniphila, research has begun to explore the potential use of its extracellular vesicles (eVs) as postbiotics. A study showed that A.muciniphila and its eVs might be used as probiotics, prebiotics, and postbiotics to prevent metabolic diseases by affecting the endocannabinoid system and PPAR gene expression [43]. An in vitro study demonstrated that treatment with A. muciniphila or its eVs could impact the expression of genes related to the serotonin system. Therefore, A. muciniphila may be utilized as a therapy for serotonin modulation [44].



**Figure 2:** *A. muciniphila*'s function as a probiotic of the future for a range of metabolic disorders. It has been established that *B. muciniphila* is essential for the control of the immunological and metabolic systems since its identification in 2004. It is currently recognized as a "next-generation probiotic" for the treatment of metabolic disorders such diabetes, liver disease, obesity, and cancer. Furthermore, the extracel-lular vesicles pasteurized postbiotics are currently being employed for the same disorders and have shown to be effective in treating them.

## Development of A. muciniphila for clinical use

A. muciniphila has been the subject of extensive research, most of which has focused on its associations with different illnesses. However, studies haven't yet established whether the microbe causes these illnesses. Numerous research that concentrated on direct therapies with A. muciniphila primarily used animal models. It has demonstrated potential safety for human interventions; it is a bacterium that is not involved in food production or medicine use. After two weeks of oral treatment, both live and pasteurized A. muciniphila are safe and tolerated in overweight individuals, according to studies that indicate no adverse outcomes even when plentiful [45]. The researchers studied different stages of clinical symptoms and their scientific development in the coming era (Table 2). The ingestion of probiotics, which are beneficial microorganisms, can affect the microbiome in the gut. Probiotics can provide health benefits to the host. Next-generation sequencing methods have led to the discovery of novel microbes linked to promoting health. These newly identified microbes are being referred to as next-generation probiotics (NGPs), and their safety, formulation. A. muciniphila has shown promise as a potential nextgeneration probiotic due to its numerous health benefits. Growing research indicates that Akkermansia may play a significant role as a therapeutic probiotic against several metabolic disease and may also can lower cholesterol, reduce body weight, and slow down the ageing process. Furthermore, it exhibits encouraging indicators of enhancing immunotherap"s effectiveness against specific

malignancies. By Q3 202, Vidya Herbs hope to have completed the necessary human clinical investigations and be able to provide US consumers with a stabilized live culture of Akkermansis. Leading global innovator in the field of nutraceuticals, Vidya Herbs, is at the forefront of converting A. muciniphil''s therapeutic potential into tangible health benefits. Apart from creating significant human clinical trials, the business has also created an encapsulating technique that is pending a patent. Encircling the solid particles with a thin, continuous layer is the new stabilization technique for Akkermansia [46].

#### **Conclusion and Perspectives**

An emerging area of research is focused on the study of communication between probiotic bacteria during transit and intestinal bacteria. *A. muciniphila* has been shown to have beneficial effects on the immune system and metabolic regulation. Due it its natural presents in the gut microbiome, it is considered a next-generation probiotic that has the potential to lead to health benefits as a dietary supplement. It is believed to stimulate host health and prevent pathogens. Based on the market research it was found that two companies namely, Vidya Herbs and A-Mansia Biotech are producing Akkermansia strain and making it commercially available. Vidya Herbs is conducting clinical trials on their live *Akkermansia muciniphila* (VHAKM) which, to date, will have the largest amount of potency/CFU (100 B CFU/gm) on the market. However, no significant evidence currently links this bacterium to malnutrition, so

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Condition	Clinical Development Utilising A. muciniphila	Reference
Crohn's disease	A. muciniphila's capacity to repair the intestinal barrier and lower inflammation has made it a promising therapeutic target for Crohn's disease.	Zheng., <i>et al.</i> , 2023
Breast Milk	A. muciniphila's function in the composition of breast milk and its possible advantages for a baby's gut health, including the development of the immune system and defence against infections, have been studied.	Kostopoulos., <i>et al.</i> , 2020
Cystic fibrosis	The effects of A. muciniphila supplementation on the makeup of the gut microbiota and general health in people with cystic fibrosis are still being studied.	Wang., <i>et al.</i> , 2023
Cancer	According to preliminary research, A. muciniphila may function in cancer therapy, especially if it helps improve immunotherapy response and alter the tumour microenvironment.	Pellegrino., <i>et al.</i> , 2023
Obesity	Due to its ability to lower inflammation in adipose tissue and improve metabolic parameters, A. muciniphila has drawn interest for its anti-obesity qualities.	Xu., <i>et al.</i> , 2020

Table 2: Clinical development in different stages.

further studies should focus on this topic. Finally, more research must be conducted, particularly in human clinical trials, to assess the mechanisms of action and long-term effects of *A. muciniphila* before it is used for therapeutic applications.

## **Author's Contribution**

SN and DMS proposed the review. MM and SN gave valuable inputs. SM wrote the manuscript. DMS gave valuable suggestion for writing the manuscript. All authors read and approved the manuscript.

## **Conflict of Interest**

The Authors declare no conflict of interest.

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