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A Current Overview of Next-Generation Probiotics and Their Prospects in Health and Disease Management

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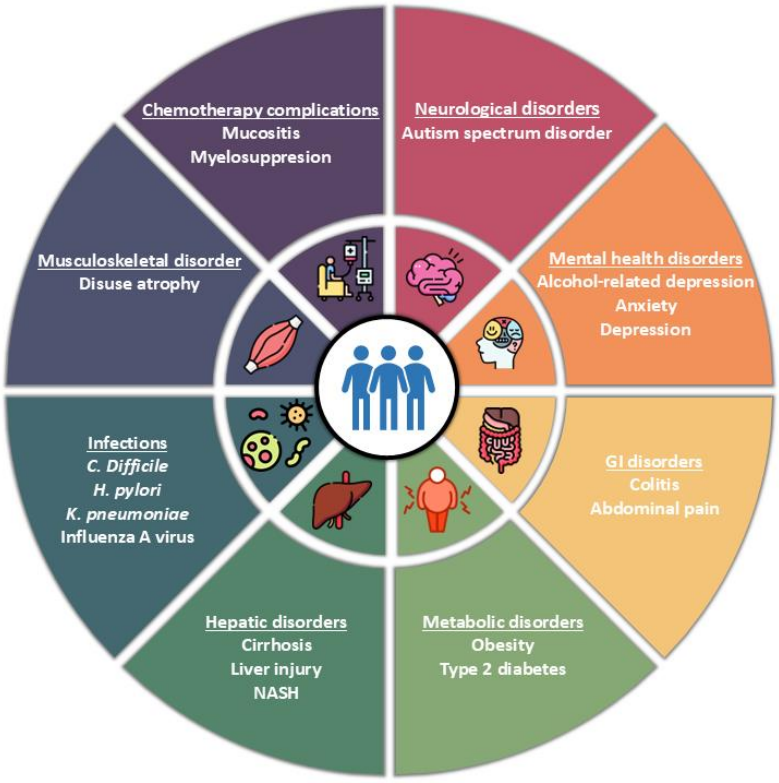
Abstract: Traditional probiotics have been extensively studied, and their effectiveness in gut modulation is well established. However, emerging research has shifted focus to previously understudied probiotic strains, now known as next-generation probiotics (NGPs), with the aim of harnessing their unique potential to elicit targeted therapeutic effects in disease management. This study aims to provide a comprehensive review on the recent evidence on NGPs by exploring their potential roles and applications in human health and agricultural settings. The literature search was conducted systematically across four databases with the keywords “next generation probiotics” and “gut health” or treatment” or “therapy”. The findings of this review identified promising NGPs, including *Akkermansia muciniphila*,

Bacillus sp., *Bacteroides* sp., *Enterococcus* sp., *Faecalibacterium* sp., *Parabacteroides* sp., and *Streptomyces* sp. These NGPs can elicit targeted effects in specific disease states while simultaneously restore gut dysbiosis by promoting beneficial bacteria, elevated short-chain fatty acid levels, and stimulate immunomodulatory effects to reduce inflammation. These modes of action are closely linked to one another, acting as a positive feedback loop to reduce inflammation in the host. Besides, other niche NGPs that are lesser-studied also show therapeutic effects in disease management, highlighting the importance of further research into these species to uncover potential mechanistic pathways for treating various illnesses. In summary, NGPs can offer targeted therapeutic effects in addition to probiotic effects in the gut, providing a multi-faceted approach in treating various health conditions. The development of therapeutics with these NGPs could offer alternatives to current treatment strategies to improve disease outcomes and prognosis. Nevertheless, future research is essential to better elucidate the exact mechanisms, safety profiles, and therapeutic applications of these NGPs.



Graphical abstract: The potential therapeutic applications of NGPs.

Keywords: next-generation probiotics; gut modulation; microbiota; gut health; agriculture; life biotherapeutics; SDG 3 Good health and well-being

1. Introduction

Probiotics have been a fundamental component of the human diet for centuries, with a crucial role in promoting gut health and overall well-being. Long before the formal introduction of the concept, humans were already incorporating probiotics into their diet via the consumption of fermented foods such as bread, wine, kefir, and cheese products[1]. In the early 1900s Elie Metchnikoff introduced the probiotic concept, stating that "the dependence of the intestinal microbes on the food makes it possible to adopt measures to modify the flora in our bodies and to replace the harmful microbes by useful microbes". This was based on his findings that regular consumption of fermented dairy products such as yogurt in Bulgarian rural people enhanced their longevity. He proposed that the effects of gastrointestinal metabolism which contributed to illness and aging were mitigated by the consumption of *Bulgarian bacillus* from the yogurt by the Bulgarians[2]. Subsequently in 1953, the term "probiotic" was first introduced by Werner Kollath, defining it as an "active substance that is essential for a healthy development of life"[2]. Over the years, scientific research and technology advancements have expanded our understanding of probiotics and their applications in health management. Currently, probiotics are defined as "live microorganisms identified on the basis of comparative microbiota analyses that, when administered in adequate amounts, confer a health benefit on the host"[3]. Probiotics are widely commercialized and marketed to consumers as dietary supplements, functional foods, and beverages[4]. They are often promoted for their health benefits, such as improving gut health, boosting immunity, and enhancing overall well-being which can be attributed to the gut modulation properties of the probiotics[5,6]. Moreover, probiotics are also often used in agriculture to improve the growth performance of cultivated plants and livestock[7,8]. The most common probiotic strains that are frequently used in research and commercially available products are the lactic-acid bacteria (LAB), *Lactobacillus* sp. and *Bifidobacterium* sp[9]. These strains are often chosen for their proven effectiveness in supporting digestive health and their ability to survive the harsh environment in the gastrointestinal (GI) tract[10].

Nevertheless, advancements in genome and metagenomic sequencing technologies have significantly enhanced our understanding of the human gut microbiota and its critical role in health maintenance. These innovations allow for a more comprehensive and precise analysis of the microbial communities residing in the gut, revealing complex interactions between the host microbiota and the pathophysiology of various diseases. For example, gut dysbiosis has been associated with dermatological, gastrointestinal, hepatic, metabolic, mental health, and neurological disorders[11–16]. Therefore, emerging research has been focused on exploring other microorganisms, often referred to as next-generation probiotics

(NGPs), that can demonstrate targeted beneficial effects. This approach offers personalized treatment strategies for managing specific diseases, tailoring the treatment to individual conditions to optimize therapeutic outcomes. In contrast to the traditional probiotics such as *Lactobacilli* and *Bifidobacteria* which have well-established effects on host health, NGPs are bacteria species that were not previously studied and used as probiotics. Some examples of NGPs are *Akkermansia muciniphila*, *Bacillus* sp., *Bacteroides* sp., *Enterococcus* sp., *Faecalibacterium* sp., *Parabacteroides* sp., and *Streptomyces* sp. Furthermore, a closely related concept to NGPs is live biotherapeutics (LBP), which refers to probiotic strains investigated for potential development as pharmaceutical products. The U.S. Food and Drugs Administration (FDA) has stated that probiotics that were on the market prior to the adoption of the dietary supplement regulations (Dietary Supplement and Education Act of 1994) in October 1994 can be used as a dietary supplement ingredient, which may subsequently be developed into a dietary supplement[17]. Based on the statement, NGPs will be developed as LBPs. The FDA defines LBP as "a biological product that: (i) contains live organisms, such as bacteria; (ii) is applicable to the prevention, treatment, or cure of a disease or condition of human beings; and (iii) is not a vaccine"[18]. This distinction highlights the potential for NGPs to be developed as therapeutic products to manage specific health conditions (Figure 1).

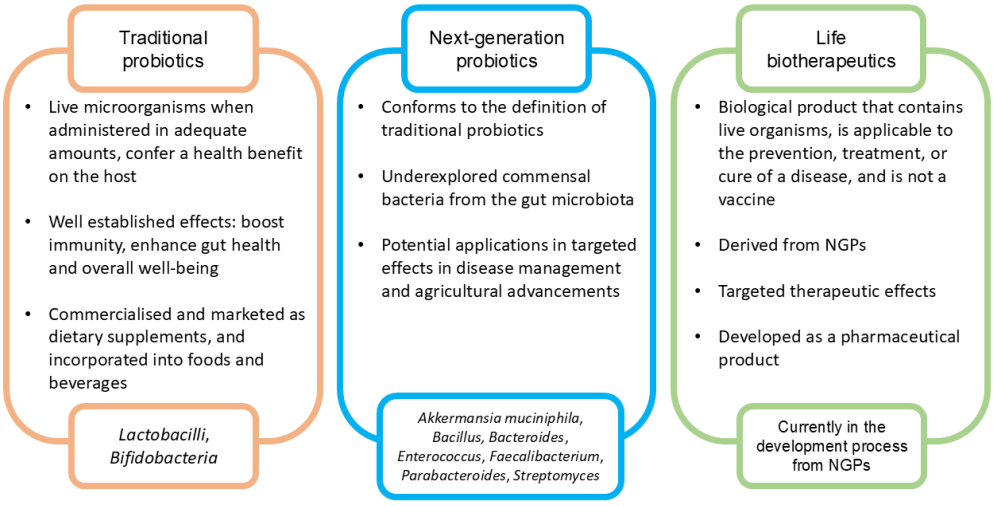


Figure 1. Comparison between traditional probiotics, next-generation probiotics, and life biotherapeutics.

Given the increasing interest in the beneficial effects of NGPs, this review aims to provide a comprehensive analysis of the current evidence on their efficacy. In addition, this review explores the potential applications of NGPs in promoting human health and advancing agriculture systems, underscoring their potential roles in therapeutic and sustainable practices. This review also highlights the promising bacterial candidates for NGPs, offering

valuable insights that can serve as a foundation for future search and development of NGPs and LBPs in these emerging fields.

2. Methods

The literature search for this review was conducted systematically across four databases, namely Embase, Ovid Medline, PubMed, and Scopus using the keywords: "next generation probiotics" AND "gut health" OR "treatment" OR "therapy". Additional studies were retrieved from Google Scholar to supplement the literature search. Original articles in English which reported on the therapeutic effects of NGPs in both human and animal model studies from January 2019 to November 2024 were included. Studies which utilized well-established, commercially available probiotics such as *Lactobacillus* sp. and *Bifidobacteria* sp. were excluded. Articles without experimental intervention were excluded (e.g., reviews). The results from the search were imported for further title screening, full-text review, and data extraction.

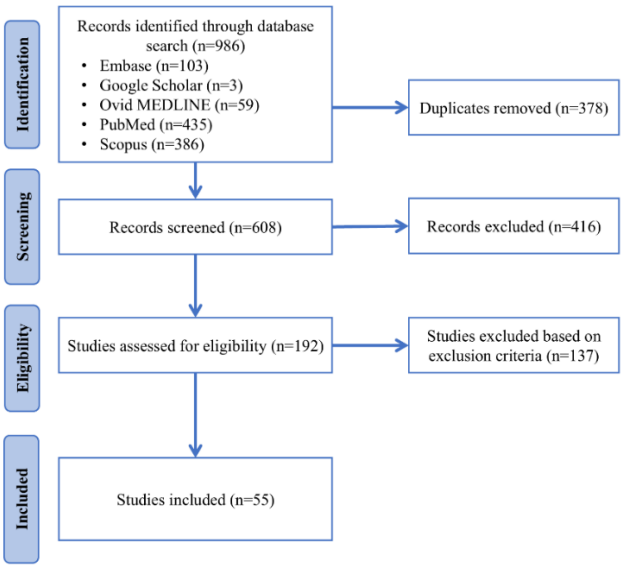


Figure 2. Flow chart illustrating the literature search conducted for this review.

3. Next-Generation Probiotics and Their Potential Applications

Based on the literature search, 986 studies were identified and 378 duplicates were removed. A total of 608 records were screened and 192 studies were assessed for eligibility. Upon full-text review, 137 studies were excluded based on the exclusion criteria and 55 studies were included in this review. The included articles reported on the beneficial effects of various bacterial species in both human and animal models (Table 1), of which these effects will be discussed further in the following sections.

Table 1. A summary of recent evidence on the efficacy of next-generation probiotics against various targeted conditions in humans and animals.

Probiotics	Targeted condition	Host	Key findings	Study
Akkermansia muciniphila	Acute colitis	Mice	• Improved symptoms of acute colitis • Reduced proinflammatory cytokines • Increased goblet cell numbers, and enhanced mucin expression in the gut barrier • Upregulation of NLRP3	[19]
	Alcohol-related depressive behaviors	Mice	• Improved depressive behaviors • Reduced serum LPS, alleviated neuroinflammation, normalized depression-related gene expression, and increased 5-HT levels in the hippocampus • Improved intestinal barrier integrity, maintained goblet cell numbers, and increased occludin expression • Increased abundance of *Lactobacillus* and *Bifidobacterium animalis*	[20]
	Chronic stress-induced anxiety and depression-like behaviour	Mice	• Improved anxiety and depressive behaviors • Increased serum 5-HT levels • Alleviated HPA-axis hyperactivity by reducing corticosterone and glucocorticoid receptors • Reduced intestinal inflammation • Restored imbalance in *Bacillota* and *Bacteroidota* while increasing *Actinobacteriota*, and reducing *Campylobacteria*	[21]
	Depression	Mice	• Improved depressive-like behavior • Upregulation of β-alanyl-3-methyl-l-histidine and edaravone • Normalization of depression-related biomarkers	[22]
		Mice	• Improved depressive-like behavior • Increased 5-HT in the gut and prefrontal cortex • Regulation of gut serotonin via inhibition of SERT expression in gut	[23]
	Diabetes complicated with Alzheimer's disease	Zebrafish	• Improved blood glucose, BMI, and diabetes indexes • Enhanced memory, anxiety, aggression, and social preference behaviors	[24]
	Effects on normal diet	Mice	• Reduction in adipose tissue and liver weight • Reduction in TG, TC, LDL, Glu while increasing HDL • Reduced inflammatory markers • Improved gut barrier function • Reduced *Bacillota*, increased *Bacteroidota* and *Verrucomicrobia* in the gut microbiota	[25]

Probiotics	Targeted condition	Host	Key findings	Study
	Enterotoxigenic *Escherichia coli* infection (ETEC)	Piglets	• Reduced diarrhea rates • Improved small intestinal morphology, and increased CD4+ T lymphocyte proportion in blood • Enhanced gene expression related to intestinal barrier and antioxidant indices • Reduced expression of ETEC virulence factor genes in the ileum and colon	[26]
	Liver injury	Mice	• Alleviated liver and colon damage caused by HFD/CCl-4 • Reduced inflammatory cytokines • Decreased expression of fibrosis and inflammation biomarkers in tissues	[27]
		Mice	• Enhanced gut epithelium, mucosal layer thickness, and intestinal integrity • Reduced liver inflammation and hepatocyte damage	[28]
	Mucositis induced by chemotherapy	Mice	• Improved mucosal health and epithelial barrier integrity by reducing intestinal permeability and bacterial translocation • Reduction of pro-inflammatory cytokines • Increased anti-inflammatory cytokines	[29]
	NASH	Mice	• Reduced hepatic inflammation • Protected intestinal barrier and downregulated hepatic TLR2 expression • Promoted growth of intestinal barrier-protecting bacteria	[30]
	Obesity	Mice	• Reduction in HFD-induced obesity • Improved intestinal inflammation and intestinal barrier integrity • Increased goblet cell density	[31]
	Ovalbumin-induced food allergy	Mice	• Mitigated weight loss and reduced serum levels of IgE • Decreased injury in the proximal jejunum • Reduced inflammatory markers • Restored gut dysbiosis by reducing *Staphylococcus* and yeast levels	[32]
Akkermansia muciniphila and *Faecalibacterium prausnitzii*	Immobilization-induce muscular atrophy	Mice	• Improved grip strength but did not increase muscle mass • Enhanced immune function • Increased ZO-1 expression, promoting IL-10 and inhibiting IL-6 • Decreased expression of ubiquitin-proteasome genes and myostatin • Increasing expression of genes regulating mitochondrial biogenesis	[33]
Bacillus coagulans MTCC 5856	Gut health	Humans	• Increased relative abundance of *Prevotella*, *Faecalibacterium*, *Blautia*, *Megasphaera*, and *Ruminococcus* • Maintained balance of *Bacteroidota* and *Bacillota*	[34]
Bacillus licheniformis	Chronic diarrhea	Cats	• Improved symptoms after 7 days of intervention administration	[35]

Probiotics	Targeted condition	Host	Key findings	Study
			• Significant increase in *Blautia* sp., *Ruminococcus torques*, and *Ruminococcus gnavus* with a decrease in *Clostridium perfringens*	
Bacillus sp. AM1	Chemically induced colitis	Mice	• Lower levels of colon damage • Reduction in inflammatory markers	[36]
Bacillus strains	Growth performance and nutrient digestibility	Broilers	• Improved growth performance • Improved nutrient digestibility • Increased *Streptococcus*, and reduced *Akkermansia* abundance	[37]
Bacteroides fragilis	Chemotherapy-induced myelosuppression and GI adverse effects	Humans	• Reduced myelosuppression by lesser reduction of white blood cell and neutrophil counts • Lowered rates of GI symptoms	[38]
	Colitis	Mice	• Blocked activation of NF-κB pathway and inflammatory cytokines by TNF- α • Improved weight loss, colon length, and gut barrier function	[39]
	Clostridium difficile infection	Mice	• Alleviated gut barrier destruction, epithelial stress, and pathogenic colitis • Improved survival rates • Increased bacterial diversity and abundance *A. muciniphila*	[40]
	LPS-induced systemic inflammation	Mice	• Reduced systemic release of cytokines • Induced IL-10 secretion	[41]
Bacteroides fragilis and *Bacteroides ovatus*	LPS-induced systemic inflammation	Mice	• Preserved gut microbiota diversity • Cytokine production modulation	[42]
Bacteroides salyersiae CSP6	Colitis	Mice	• Improved symptoms: body weight loss, colon contraction, intestinal bleeding, mucosal damage • Reduced pathogenic *Escherichia-Shigella* while increased *Dubosiella* sp. and *Bifidobacterium longum* • Increased anti-inflammatory compounds: equol, 8-deoxylactucin, and tiglic acid	[43]
Bacteroides uniformis	DSS-induced ulcerative colitis	Mice	• Alleviated colitis severity and increased occludin	[44]
Bacteroides xylanisolvens AY11-1	Colitis	Mice	• Alleviated body weight loss, colon length contraction, intestinal bleeding, and mucosal damage • Restored gut dysbiosis and increased *Blautia* sp. and *Prevotellaceae* UCG-001	[45]
Bacteroides sp.	Gut health	Broilers	• Enhanced IgA levels • Produces isovaleric acid to regulate macrophage and intestinal epithelial cell cytokine production	[46]
	Liver cirrhosis	Mice	• Improved liver/body weight ratio	[47]

Probiotics	Targeted condition	Host	Key findings	Study
Christensenella minuta	Colitis	Mice	• Normalized hepatic fibrosis biomarkers: COL1A1 • Upregulation of propionic acid in the cecum and liver • Alleviation of colitis symptoms • Promoted regeneration of intestinal epithelial cells via upregulation of IGF-1 • Increased beneficial bacteria: *Dubosiella*, *Lactobacillus murinus*, *Desulfovibrio fairfieldensis* • Decreased pathogenic bacteria: *Clostridia* UCG014, *Ileibacterium*, *Parasutterella* • Elevated propionic acid levels	[48]
Clostridium beijerinckii R8	Diarrhea	Goat kids	• Reduced diarrhea rates and fecal scores through reduced intestinal permeability • Improved intestinal immune response and antioxidant capacity • Inhibited *Escherichia-Shigella* while stimulated *Lactobacillus* growth	[49]
Corynebacterium pseudodiphtheriticum 090104	Hypermucoviscous Carbapenem-Resistant *Klebsiella pneumoniae* ST25 lung infection	Mice	• Reduced lung bacterial counts and lung tissue damage • Modulated leukocyte recruitment to the lungs • Influenced production of TNF-α, IFN-γ, and IL-10 in the respiratory tract and serum	[50]
Dysosmobacter welbionis J115T	Obesity and metabolic disorders	Mice	• Counteracted diet-induced obesity and fat mass gain • Protected against brown adipose tissue inflammation • Improved glucose tolerance, lower insulin resistance, and reduced white adipose tissue hypertrophy	[51]
Enterococcus faecalis EC-12	Stress-induced GI discomfort	Humans	• Significantly improved abdominal pain and stomach rumbling • No effect on mental symptoms or salivary cortisol levels • Significant increase in tryptamine levels in faecal metabolite composition	[52]
	Depression	Mice	• Decreased anxiety-like and anti-depressive behavior • Increased expression of neurotransmitter receptor genes • Significant increase in *Butyricicoccus* and *Enterococcus*	[53]
Enterococcus faecium	Surgical antibiotic prophylaxis	Human	• Reduction in *Streptococcus gallolyticus* and *Roseburia*	[54]
	Parasite control	Horses	• Parasite eggs and oocysts were not found in horses after treatment • Increased phagocytic activity	[55]
Escherichia coli 1917-pSK18a-MT	Cadmium induced liver injury	Mice	• Alleviated cadmium-induced hepatic steatosis, inflammatory cell infiltration, and liver fibrosis • Improved colonic barrier function	[56]

Probiotics	Targeted condition	Host	Key findings	Study
Faecalibacterium duncaniae	Influenza	Mice	• Restored gut dysbiosis by increasing the abundance of *Verrucomicrobiota* • Reduced viral load in the lungs • Reduced lung inflammation and alleviation of alveolar wall thickening and inflammatory cell infiltration • Increased gene expression of lung barrier markers • Restoration of SCFA levels associated with increased *Dubosiella* and *Muribaculaceae* • Reduced systemic bacterial translocation to the spleen	[57]
Faecalibacterium prausnitizii	NASH	Mice	• Improved glucose homeostasis, preventing hepatic lipid accumulation and liver damage • Reduced liver fibrosis and inflammation • Hepatic steatosis alleviation was associated with regulation of gene expression related to hepatic steatosis	[58]
	Sleep deprivation-induced intestinal barrier injury and gut dysbiosis	Mice	• Enhancement of goblet cell count and Mucin2 levels • Reduced inflammation associated with increased tight-junction protein expression and decreased macrophage infiltration • Suppressed pro-inflammatory cytokine expression and apoptosis • Reduced *Klebsiella* and *Staphylococcus* and increased *Akkermansia* • Increased fecal butyrate levels	[59]
Luoshenia tenuis	Weight control	Mice	• Decreased body weight gain and food intake • Alleviation of abnormal glucose and lipid metabolism • Reduced inflammatory responses	[60]
Odoribacter laneus	Glucose control and inflammation in obesity	Mice	• Reduced circulating succinate • Inflammatory profile modulation	[61]
Paeniclostridium sp.	Chemically induced colitis	Mice	• Lower levels of colon damage • Reduction in inflammatory markers	[36]
Parabacteroides distasonis	Chronic abdominal pain	Mice	• Reduced colonic hypersensitivity • Reduced activation in response to capsaicin, inflammatory soup, and bradykinin stimulations	[62]
Parabacteroides goldsteinii	Autism-spectrum disorder	Mice	• Reduced intestinal and systemic inflammation • Improved disease outcomes in autism spectrum disorder • Enhanced neuropeptide-related signaling, suppressed abnormal cell proliferation and inflammation in the intestine	[63]

Probiotics	Targeted condition	Host	Key findings	Study
			• Enhanced ribosomal, mitochondrial, and antioxidant activities while reducing glutamate receptor signaling in the hippocampus	
	Helicobacter pylori infection	Mice	• Reduced *H. pylori*-induced gastric inflammation • Lowered cholesterol levels	[64]
Prevotella copri	Obesity and type 2 diabetes	Mice	• Improved glucose tolerance • Lowered creatinine serum levels	[65]
Rouxiella badensis subsp. *Acadiensis*	Gut health	Mice	• Enhanced intestinal epithelial barrier • Elevated antimicrobial peptide α defensin levels • Demonstrated antibacterial effects against *Staphylococcus aureus* and *Salmonella enterica* serovar Typhimurium	[66]
Rummeliibacillus stabekisii	Growth performance	Nile tilapia	• Increased weight gain, feed conversion ratio, and feed efficiency • Elevated intestinal digestive enzymes • Enhancement of cumulative survival when challenged with *Aeromonas hydrophila* and *Streptococcus iniae* • Improved immune functions • Enhanced the abundance of *Bacillus* and *Lactobacillus* sp. while reduced *Streptococcus* and *Staphylococcus*	[67]
Streptomyces amritsarensis	Disease resistance	Grass carp	• Improved survival rates after pathogen infection • Significant upregulation of antioxidant- and immune-related genes	[68]
Streptomyces chartreusis	Growth performance	Common carp fingerlings	• Significantly improved growth performance • Significant increase in serum total immunoglobulin and lysozyme activity	[69]
Streptomyces sp.	*Vibrio parahaemolyticus* infection	Giant freshwater prawn	• Improved survival rates compared to antibiotic group • Increased growth rates by 17% • Enhance immune function	[70]
		Whiteleg shrimp	• Stimulated antimicrobial producers to protect against *V. parahaemolyticus* infection • Increased diversity in the gut microbiota	[71]
		Artemia franciscana nauplii	• Increased survival rates after treatment • Protective effect against *V. parahaemolyticus* infections	[72]

Probiotics	Targeted condition	Host	Key findings	Study
	Aeromonas hydrophila infection	Zebrafish larvae	• Significantly improved larvae survival • Reduced colonization of *A. hydrophila* by 67.53% • Upregulation of genes involved in immune response • Inhibited virulence factor production, expression of virulence genes, and quorum sensing	[73]

BDNF: brain-derived neurotrophic factor; BMI: Body Mass Index; CCl-4: carbon tetrachloride; DSS: dextran sodium sulfate; GI: gastrointestinal; Glu: glucose; HDL: high-density lipoprotein; HFD: High-fat diet; HPA: hypothalamic-pituitary-adrenal; LDL: low-density lipoprotein; LPS: lipopolysaccharide; NASH: non-alcoholic hepatic steatohepatitis; NLRP3: (NOD-, LRR-, and pyrin domain-containing protein 3); SCFA: short-chain fatty acid; SERT: serotonin transporter; TC: total cholesterol; TG: triglycerides.

The capabilities of these potential next-generation probiotics can be harnessed and applied in the management of disease in humans. Additionally, the potential applications of these probiotics have also been demonstrated to extend into agriculture, enhancing the growth performance and health of livestock.

3.1. Akkermansia muciniphila

Recent research has focused on the potential of *A. muciniphila* as an NGP as the altered abundance of this mucin-degrading bacterium is associated with various physiological dysfunctions, e.g.: GI disorders, hepatic disorders, and metabolic conditions[74–77]. This Gram-negative anaerobic bacterium, belonging to the *Verrucomicrobia* phylum, resides in the mucus layer of the GI tract[78]. *A. muciniphila* degrades mucin in the GI tract to produce short-chain fatty acids (SCFAs) such as acetate and propionate which act as substrates for other commensal bacteria and the surrounding intestinal epithelial cells (IECs)[79]. This helps to regulate the IECs to strengthen gut barrier integrity. Moreover, the immuno-modulatory effects of SCFAs play a role in the reduction of inflammation during diseased states[80]. For instance, in mice with dextran sodium sulfate (DSS) induced acute colitis, *A. muciniphila* has been shown to improve gut integrity by increasing goblet cell numbers, reducing inflammatory cell infiltration, and enhancing mucin expression in the gut barrier. The improved symptoms of acute colitis in the mice could also be attributed to the upregulation of NLRP3 proteins which is crucial for immune regulation and gut homeostasis during inflammation[19].

Interestingly, *A. muciniphila* has been shown to elicit anti-depressive effects in several studies[20–23]. Cheng *et al.* reported that the NGP ameliorated the hypothalamic-pituitary-adrenal (HPA) axis hyperactivity by reducing corticosterone and glucocorticoid receptors while increasing serotonin levels, thereby improving anxiety and depressive behaviors in the mice. Similarly, Guo *et al.* observed increased levels of serotonin post-treatment with *A. muciniphila*[20,23]. Additionally, Ding *et al.* found that supplementation with the NGP normalized depression-related biomarkers such as corticosterone, dopamine, and brain-derived neurotrophic factor (BDNF), indicating symptom improvement[22]. In depression models, *A. muciniphila* also reduced intestinal inflammation, restored gut microbiota imbalance in *Bacillota* and *Bacteroidota*, increased *Actinobacteria*, *Lactobacillus*, and *Bifidobacterium animalis*[21]. Since depression has been associated with intestinal inflammation and gut dysbiosis[81,82], the counteractive effects of *A. muciniphila* against these features in depressive models suggest its potential as a therapeutic intervention. These findings indicate that supplementation with *A. muciniphila* can lead to anti-depressive

effects which target key mechanisms of depression pathophysiology, including hyperactivity of the HPA axis, neurotransmitter imbalances, and gut dysbiosis. Therefore, *A. muciniphila* hold promise as an NGP to be utilized as an adjunct to antidepressants or as an alternative treatment strategy.

A. muciniphila has also demonstrated hepatoprotective effects when supplemented in mice with liver injuries caused by a high-fat diet and carbon tetrachloride, underscoring its potential application in the management of hepatic disorders[27,28]. It was reported that liver and colon damage in the treated mice was alleviated, evident from the marked decrease in expression of fibrosis and inflammatory markers in the tissues[27]. Moreover, supplementation with the NGP enhanced the gut epithelium, mucosal layer thickness, and intestinal integrity within the GI tract of the mice[28]. Furthermore, Han *et al*. reported that *A. muciniphila* inhibited nonalcoholic steatohepatitis (NASH) through the downregulation of hepatic toll-like-receptor 2 (TLR2), thus hindering the activation of TLR2 by lipoteichoic acid enriched hepatic γδT17 cells, subsequently lowering inflammation in the liver[30].

In the context of obesity management, Shin *et al.* reported that the use of *A. muciniphila* in mice on HFD reduced HFD-induced obesity while simultaneously improving intestinal inflammation and intestinal barrier integrity[31]. A separate study done by Ashrafian *et al*. explored the effects of both live and pasteurized *A. muciniphila* on a normal diet. Both types of *A. muciniphila* were found to reduce adipose weight by decreasing the total concentrations of triglycerides[25]. In addition, supplementation of the probiotic reduced liver weight and reduced inflammatory markers in the mice. The gut barrier functions in the mice were also improved, alongside the reduction of harmful bacteria and increased abundance of beneficial bacteria like *Bacteroidota*, and *Verrucomicrobia* including *A. muciniphila*[25]. This shows that *A. muciniphila* has the potential to be used as a probiotic to promote gut health and maintain a healthy weight.

Apart from applications in human diseases, *A. muciniphila* has the potential to be used to improve immune function in livestock. It was reported that supplementing weaned piglets with *A. muciniphila* was effective in reducing diarrhea rates caused by enterotoxigenic *Escherichia coli* (ETEC). Lan *et al.* reported reduced expression of ETEC virulence factor genes in the ileum and colon of the piglets, resulting in lower rates of infection and disease progression. The small intestinal morphology of the piglets was also improved, accompanied by an increase in CD4+ T lymphocyte proportion in blood, suggesting an improvement in immune function following *A. muciniphila* supplementation[26]. The use of this NGP in

livestock could prevent infections through its immunomodulatory effects to enhance the growth and production of livestock.

3.2. Bacillus sp.

Bacillus sp. is a group of Gram-positive bacteria with some members recognized as opportunistic pathogens that can cause disease in humans or animals[83,84]. However, there are strains of *Bacillus* sp. that have garnered significant interest for their probiotic properties[85,86]. For example, *Bacillus coagulans* MTCC 5856 maintained the balance of *Bacteroidota* and *Bacillota* in the human gut while increasing the relative abundance of beneficial bacteria such as *Prevotella*, *Faecalibacterium*, *Blautia*, *Megasphaera*, and *Ruminococcus*[34]. These bacteria are known to be essential in maintaining gut health, improving immune function, and reducing inflammation. As an example, *Prevotella* breaks down dietary fiber in the gut which increases SCFA content in the gut, thereby maximizing energy extraction from fiber[87]. In a separate study, *Bacillus* sp. AM1 was found to ameliorate colon damage in mice with bisphenol A (BPA)-induced colitis by significantly reducing the inflammation markers IL-1β and IL-6 within the gut[36]. The research aimed to explore potential therapeutic options for addressing the growing health risks associated with BPA exposure[88]. The results suggest that *Bacillus* sp. have the potential to mitigate the harmful effects of BPA, including its impact on gut health, inflammation, and metabolic disruptions.

In addition, probiotics containing *Bacillus amyloliquefaciens* and *Bacillus pumilus* were shown to improve broiler growth performance and nutrient digestibility. Supplementation with these *Bacillus* strains led to a reduction in *Akkermansia* species associated with low weight gain in the gut microbiota of broilers. Moreover, these probiotics stimulated an increase production of protease and amylase which improved nutrient digestibility in the broilers, supporting growth performance[37]. Furthermore, Lee *et al*. reported that supplementation of *Bacillus licheniformis* in cats effectively improved symptoms of chronic diarrhea. The increase in beneficial bacteria such as *Blautia* sp., *Ruminococcus torques*, *Ruminococcus gnavus*, and the decrease in harmful *Clostridium perfringens* could potentially be a mechanism of symptom improvement by *Bacillus* strains. These data suggest that the use of *Bacillus* sp. as an NGP could have broad applications, extending from human to animal health.

3.3. Bacteroides sp.

Bacteroides sp. are another group of NGP of interest due to their capabilities in producing SCFAs from the degradation of non-digestible plant- or animal-based glycan from

dietary sources[89]. This production of SCFAs can promote the growth and increased abundance of other beneficial bacteria within the host gut microbiota, which in turn improves host digestive health and immunity. Similar to other probiotics, *Bacteroides fragilis* has shown promise in improving gut health, as demonstrated by He *et al*. which investigated the effects of the NGP on colitis. Treatment with *B. fragilis* led to improvements in weight loss, colon length, and gut barrier function, mirroring the positive effects of established probiotics. Additionally, this NGP further reduced inflammation by blocking the activation of NF-κB pathway and suppressing the release of inflammatory cytokines by TNF- α[39]. Similar findings were reported in studies using *Bacteroides salyersiae* CSP6, *Bacteroides xylanisolvens* AY11-1, and *Bacteroides uniformis* as the interventions for colitis in mice[43–45]. In addition, supplementing *Bacteroides* sp. in colitis restores gut dysbiosis, contributing to symptom improvement[43,45]. As shown by *B. salyersiae* CSP6 supplementation, the abundance of pathogenic *Escherichia-Shigella* decreases, while the levels of probiotic *Dubosiella* sp. and *Bifidobacterium longum* increase within the gut microbiota[43]. Moreover, supplementation of *B. fragilis* in a randomized controlled trial involving participants experiencing GI adverse effects associated with chemotherapy-induced myelosuppression demonstrated beneficial effects. *B. fragilis* effectively reduced myelosuppression, by maintaining white blood cell and neutrophil counts, consequently protecting the participants from GI adverse effects associated with chemotherapy[38].

Furthermore, *B. fragilis* shows potential as a therapeutic option for managing bacterial infections. In a study involving mice infected with *Clostridium difficile* (currently known as *Clostridioides difficile*), supplementation with this NGP helped alleviate gut barrier destruction, epithelial stress, and pathogenic colitis. These improvements could be linked to the increased bacterial diversity and abundance of *A. muciniphila* within the gut, contributing to improved survival rates in the infected mice[40]. Studies have also explored the role of *B. fragilis* in mitigating lipopolysaccharide (LPS)-induced systemic inflammation[40,42]. Lipopolysaccharides are a component of the outer membrane of Gram-negative bacteria which act as an endotoxin when released into the bloodstream of the host during bacterial infections. This triggers the inflammatory response in the host, stimulating the immune cascade, resulting in systemic inflammation. Supplementation of *B. fragilis* in LPS-induced systemic inflammation has shown immunomodulatory effects whereby systemic release of pro-inflammatory cytokines was reduced, effectively reducing inflammation[41,42].

In agricultural applications, *Bacteroides* sp. have been shown to promote intestinal mucosal immunity in broilers by enhancing immunoglobulin A (IgA) levels which improves the gut health in the livestock. The underlying mechanism could be attributed to the

production of isovaleric acid by the *Bacteroides* sp. which is a SCFA that regulates the immune functions of IECs. The upregulation of cytokine production in IECs to stimulate the production of IgA in the gut of broilers supports the overall gut and immune health in the livestock[46]. These findings show that *Bacteroides* sp. could potentially be used as an NGP in the health maintenance of livestock to increase poultry production in the agriculture industry.

3.4. Enterococcus sp.

Traditionally known for their role in the fermentation of various foods such as dairy products, *Enterococcus* sp. has attracted interest for their potential as NGPs. *In-vitro* studies have highlighted their promise as safe probiotic strains which have exhibited cholesterol-lowering effects and bacteriocin production[90,91]. The bacteriocins produced by *Enterococcus* sp. have demonstrated antagonistic activity against a range of pathogens such as *Bacillus cereus, Escherichia coli, Listeria ivanovii, Listeria monocytogenes, Pseudomonas aeruginosa*, and *Staphylococcus aureus*[92–94]. Ongoing research continues to explore the full scope of probiotic uses of *Enterococcus* sp. through *in-vivo* studies.

Enterococcus faecalis EC-12 has been investigated for its potential role as an NGP in the management of mental health disorders and related complications. For instance, Kambe *et al.* reported that supplementation of the NGP in depressed mice resulted in reduced anxiety-like behavior[53]. The behavioral changes were linked to an increased expression of the neurotransmitter receptor gene *Adrb3*. It was proposed that the increase in *Adrb3* alters tryptophan metabolism, affecting serotonin levels in the brain[95]. In a separate study by Li *et al*., stress-induced GI discomfort in humans was ameliorated by supplementing EC-12, with notable improvements abdominal pain and stomach rumbling. Based on the fecal metabolite analysis, subjects in the EC-12 group showed elevated levels of tryptamine. This tryptophan metabolite can interact with colonic cells to improve GI motility and mucus secretion[96]. However, the supplement did not elicit any effect on the mental symptoms or salivary cortisol levels, indicating that there was no significant effect on stress levels[52].

From an agricultural perspective, supplementation of *Enterococcus faecium* was effective in parasite control for horses. After supplementation of the NGP, an increase in phagocytic activity was observed in the treated horses. Moreover, nematode eggs of *Strongylus* sp. and *Eimeria* sp. oocysts were not found in horses after treatment[55], indicating the potential of this NGP in supporting health in livestock. By enhancing immune function and reducing parasite burden, *E. faecium* supplementation helps prevent diseases in these animals, contributing to overall well-being and productivity in agricultural settings.

3.5. Faecalibacterium sp.

Fluctuations in *Faecalibacterium* sp. in the gut has been associated with various diseases that involve inflammation, with their abundance positively correlated with symptom alleviation[97–100]. The anti-inflammatory effects of *Faecalibacterium* sp. have been linked to their ability to restore SCFA levels in the gut, which results in the inhibition of NFκB and the subsequent production of interleukin (IL)-8. They further inhibit the production of pro-inflammatory cytokines, effectively dampening the inflammatory response[97]. Therefore, studies have been investigating the role of *Faecalibacterium* sp. as an NGP to harness their therapeutic potential for disease treatment.

Faecalibacterium duncaniae has shown promising effects in the treatment of influenza A. Chollet *et al.* reported reduced viral load in the lungs of influenza A virus-infected mice[57]. Symptom improvements were observed including alleviation of inflammation in the lungs, decreased inflammatory cell infiltration, and reduced alveolar wall thickening. There was also an increase in gene expression of lung barrier markers, indicating the protective effects of *F. duncaniae* on the lung tissue barrier. Similar to previous studies on *Faecalibacterium* sp., the administration of this NGP resulted in an increase in SCFA levels in the gut which was attributed to the increase in *Dubosiella* and *Muribaculaceae* populations. As influenza can cause secondary bacterial infections[101], the study further challenged the influenza-infected mice with *Streptococcus pneumoniae*. Supplementation of *F. duncaniae* prevented systemic translocation of *S. pneumoniae* to the spleen, thereby protecting the mice from systemic bacterial infection[57].

Another member of the genus, *Faecalibacterium prausnitzii*, has demonstrated promising therapeutic effects as an NGP. In mice with NASH, supplementation of *F. prausnitzii* provided hepatoprotective effects, as shown by improved glucose homeostasis, prevention of hepatic lipid accumulation, and reduced liver damage[58]. The NGP also reduced fibrosis and inflammation, preventing further liver damage. Furthermore, *F. prausnitzii* upregulated the expression of transport proteins involved in lipid metabolism to alleviate hepatic steatosis in NASH mice. Moreover, in a mouse model for sleep-deprivation induced intestinal barrier injury and gut dysbiosis, administration of *F. prausnitzii* suppressed pro-inflammatory cytokines, and increased the expression of anti-apoptotic protein Bcl-2 to reduce excessive apoptosis of cells[59]. The supplement displayed gut protective effects as it enhanced goblet cell counts, tight-junction protein expression and decreased macrophage infiltration. These are essential in maintaining gut homeostasis and safeguarding the gut barrier.

3.6. Parabacteroides sp.

First characterized as *Bacteroides distasonis* and *Bacteroides goldsteinii*, these strains were reclassified in 2006 as *Parabacteroides distasonis* and *Parabacteroides goldsteinii* in 2006 to reflect their distinct chemotaxonomic and phylogenetic differences from members of the genus *Bacteroides*[102]. These commensal bacteria exhibit probiotic effects, including immunomodulation and the production of SCFA such as acetate, propionate, and butyrate[103,104]. The combined impacts of these probiotic properties suggest that *Parabacteroides* may play a role in controlling inflammation, particularly during diseased states to regulate immune responses to improve therapeutic outcomes. Lin *et al.* explored the effects of *Parabacteroides goldsteinii* in autism-spectrum disorder (ASD)[63]. Supplementation with *P. goldsteinii* reduced intestinal and systemic inflammation which was associated with improved disease outcomes in ASD. In addition, the NGP also reversed chronic inflammation-related deficits in neurotransmission. Although the underlying causes of ASD are complex, maternal immune activation (MIA) has been highlighted as one of the underlying mechanisms of ASD[105]. In this regard, *P. goldsteinii* could target the inflammatory mechanism in ASD for symptom alleviation.

Apart from its potential use in neurological disorders, *Parabacteroides* sp. supplementation also offers benefits in GI disorders. Administration of *P. goldsteinii* reduced *Helicobacter pylori*-induced gastric inflammation in a mouse model by lowering serum cholesterol levels and altering the gut microbiota composition[64]. *H. pylori* is known to modify host cholesterol by glycosylation and attach the glycosylated cholesterol onto its surface to evade host immune detection. Moreover, this modification increases their resistance towards antibiotics, thus reducing the efficacy of antimicrobial treatments against *H. pylori* infections. Therefore, the cholesterol-lowering properties of *P. goldsteinii* could be leveraged in the treatment of *H. pylori* infections to prevent the pathogen from evading the host immunity and antibiotic interventions. Another member of the genus, *Parabacteroides distasonis*, demonstrated antihyperalgesic effects in chronic abdominal pain in mice. The mechanisms for pain relief were linked to the direct interaction of *P. distasonis* with the nociceptors, decreasing their activation levels for stimuli like capsaicin and bradykinin[62].

3.7. Streptomyces sp.

Streptomyces sp. is a group of spore-forming, filamentous, Gram-positive bacteria renowned for their remarkable probiotic potential[106,107]. This is due to their ability to produce useful secondary metabolites with antimicrobial, antifungal, antioxidant, and anticancer properties[108–111]. Most notably, the development of antibiotics such as chloramphenicol, erythromycin, streptomycin, tetracycline, and vancomycin originate from *Streptomyces* sp.[112]. This puts further emphasis on the role of *Streptomyces* sp. as a source

of bioactive compounds. Additionally, the dormant spores of *Streptomyces* sp. are highly resilient, enabling them to withstand harsh environmental conditions[113,114]. This advantage allows *Streptomyces* sp. to preserve its bioactive compounds during transport up till the point of use, ensuring their stability and efficacy.

Recent research has highlighted the potential applications of *Streptomyces* sp. in the aquaculture industry to improve growth performance and disease resistance in the cultured marine animals. For example, *Streptomyces* sp. supplementation in aquatic animals prevented *Vibrio parahaemolyticus* infections[70–72]. Goh *et al.* reported that supplementing giant freshwater prawns (*Macrobrachium rosenbergii*) with *Streptomyces* sp. MUM 195J enhanced immune function in the prawns, and improved growth and survival rates even after *Vibrio parahaemolyticus* infection[70]. In a study involving whiteleg shrimp (*Litopenaeus vannamei*), an increase in bacterial diversity and *Bacteriovorax* populations were observed in the shrimp microbiota post-treatment with *Streptomyces* sp. RL8. *Bacteriovorax* are a group of bacteria that prey on Gram-negative bacteria such as *V. parahaemolyticus* to cause cell lysis, thus limiting the proliferation of the pathogenic bacteria[115]. The foodborne pathogen is known to cause gastroenteritis in humans and vibriosis in aquatic animals[116,117], thus the inhibitory effects of *Streptomyces* sp. can prevent infections by *V. parahaemolyticus*. Additionally, there are increasing reports on the emergence of antibiotic-resistant *V. parahaemolyticus* in our surrounding environment[118]. *Streptomyces* sp. could be used as an NGP to manage the proliferation of *V. parahaemolyticus* in aquatic environments to reduce the spread of antibiotic resistance to preserve the efficacy of antimicrobial treatments. Furthermore, *Streptomyces amritsarensis* (N1-32) improved survival rates of grass carp after *Aeromonas veronii* challenge. This was linked an enhanced immune response of the fish due to N1-32 regulating the humoral immunity and gene expression of cytokines[68]. Similar findings were reported by Arghideh *et al.* as the supplementation of *Streptomyces chartreusis* significantly improved the growth performance of common carp fingerlings. The effects of *S. chartreusis* were associated with the significant increase in serum total immunoglobulin and lysozyme activity, indicating an enhancement of immune function in the treated carp fingerlings[69]. Based on the positive outcomes of various studies, *Streptomyces* sp. holds promise as NGPs that could be deployed in the aquaculture industry. Their potential to promote the health and growth of the cultured species could significantly boost production to meet the growing global demand for sustainable aquaculture.

3.8. Other Niche Next-Generation Probiotics

In addition to the NGPs that are more extensively studied, there is increasing attention on the probiotic potentials of lesser-studied microorganisms. These bacteria could

harbor unique properties that might provide new solutions in therapeutics. One example is *Corynebacterium pseudodiphtheriticum* 090104, a respiratory commensal bacterium which exhibited protective effects against hypermucoviscous carbapenem-resistant *Klebsiella pneumoniae* lung infection in a mouse model[50]. Incorporation of the NGP in the nasal treatment for the mice decreased bacterial counts of *K. pneumoniae* in the lungs and reduced lung tissue damage. These effects were linked to the regulation of the respiratory innate immune response as it modulated leukocyte recruitment to the lungs, reduced TNF-α, and increased IFN-γ and IL-10 levels by the NGP[50].

Other than combating bacterial infections, niche NGPs have also shown beneficial effects in improving features of metabolic disorders. For instance, although the supplementation of *Dysosmobacter welbionis* J115T did not have significant impact on the gut microbiota, there was reduced fat mass gain, resulting in decreased development of diet-induced obesity in the mouse model. The NGP also protected the mice from brown adipose tissue inflammation, improved glucose tolerance by lowering insulin resistance, and reduced white adipose hypertrophy[51]. Another study on the effects of NGPs on obesity utilized *Odoribacter laneus* as the intervention. The findings indicate that *O. laneus* reduced circulating succinate levels and modulated obesity-related inflammation in the treated mice [61]. Obesity is associated with elevated circulating succinate which can contribute to inflammation and insulin resistance[119]. The depletion of succinate following *O. laneus* treatment suggests its potential as an NGP for managing obesity and its associated metabolic disruptions. Furthermore, the potential of *Prevotella copri* in the management of obesity and type 2 diabetes was also explored Novotny-Nuñez *et al*. The study found that *P. copri* supplementation reduced liver weights and serum creatinine levels while enhancing glucose tolerance, indicating improvements in the typical features of obesity and type 2 diabetes. The study also reported no adverse effects during the treatment with *P. copri*[66]. Therefore, *P. copri* has the potential to be an NGP that effectively manages co-morbidities such as obesity and type 2 diabetes. Given the varying effects of these niche NGPs, there is a need to unearth the probiotic potentials of these understudied microorganisms to fully understand their therapeutic applications.

4. Discussion

In recent years, technological advancements in next-generation sequencing, gnotobiotics, metagenomics, and metabolomics have profoundly transformed our understanding of probiotics[120,121]. As high-throughput sequencing technologies become more accessible, there have been more comprehensive studies on the human gut microbiota which uncover beneficial commensal bacteria that can influence host health. These

breakthroughs in microbiome research have highlighted the complex interactions between the gut microbiome and the host, illuminating the potential roles of NGPs in maintaining overall health and disease management. This review identified NGPs which have shown beneficial effects in the management of various diseases in humans including gastrointestinal, hepatic, metabolic, neurological disorders, and bacterial and viral infections (Table 1 and Figure 3). Some examples of candidates for NGPs are *A. muciniphila*, *Bacillus* sp., *Bacteroides* sp., *Enterococcus* sp., *Faecalibacterium* sp., and *Parabacteroides* sp. In addition, several NGPs have been proven effective in improving the growth performance and disease resistance of livestock, offering valuable benefits to the agricultural industry (Table 1 and Figure 4). These NGPs include *A. muciniphila*, *Bacillus* sp., *Bacteroides* sp., *Clostridium beijerinckii* R8, *E. faecium*, *Rummeliibacillus stabekisii*, and *Streptomyces* sp.

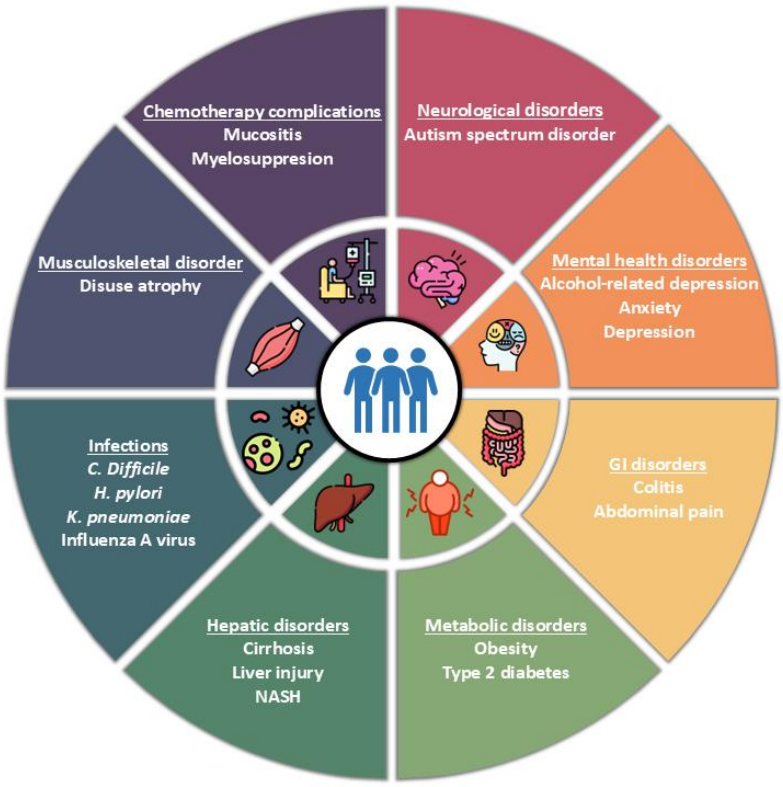


Figure 3. A summary of the potential therapeutic applications of NGPs in humans.

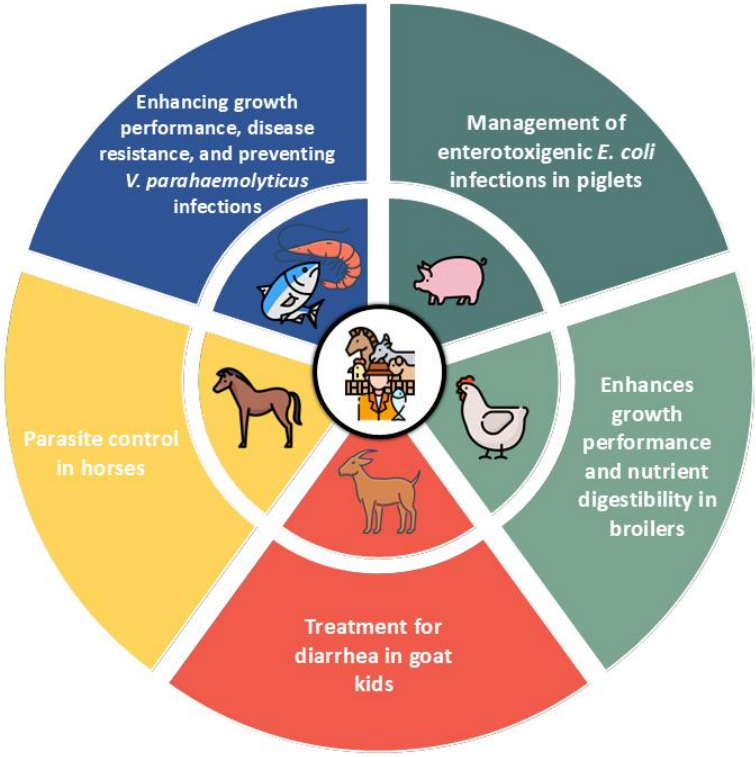


Figure 4. A summary of the potential applications of NGPs in agriculture including livestock cultivation and aquaculture farming.

Traditional probiotics are well known for their role mainly affecting the GI tract by restoring gut dysbiosis to improve gut health and improve general overall wellbeing. In contrast with that, the NGPs included in this study have shown potential for targeted therapeutic use, as their modes of action have been shown to target specific pathways of disease states. For instance, *A. muciniphila* supplementation was able to alleviate anxiety and depressive behaviors by targeting the underlying mechanisms of depression. The NGP increased serum serotonin levels and alleviated HPA-axis hyperactivity in depressed mice, both of which are hallmark features of depression[20,122]. Another example is the reduced myelosuppression by *B. fragilis* in which supplementation of this NGP maintained white blood cell and neutrophil counts in patients receiving chemotherapy. Furthermore, the NGP simultaneously reduced the rates of GI symptoms associated with the chemotherapy[38]. In addition, NGPs have shown targeted effects in metabolic disorders such as obesity, evident by the reduction of serum succinate levels by *O. laneus* to improve treatment outcomes[61]. Moreover, *P. goldsteinii* demonstrated cholesterol-lowering effects which hindered the virulence of *H. pylori* in the gut of infected mice, hence effectively reducing *H. pylori*-induced gastric inflammation[64]. Therefore, these examples highlight how NGPs can offer more targeted approaches in the treatment of various diseases to enhance the efficacy of the management strategies with minimal adverse effects.

In addition to their targeted effects, the NGPs in this review shared similar modes of actions in the gut across varying disease models which can be summarized as follows: (i) restoration of gut dysbiosis by promoting the growth of beneficial bacteria; (ii) elevation of SCFAs to support gut health; and (iii) immunomodulatory effects to reduce inflammation. For example, both *B. salyersiae* and *Christensenellaceae minuta* increased the abundance of *Dubosiella* in mice with colitis[43,48]. *Dubosiella* sp. is a murine commensal bacterium that maintains the balance of Th17/regulatory T cell responses while producing SCFAs like propionate and L-lysine to alleviate mucosal barrier injury[123]. Therefore, the alleviation of colitis symptoms in mice could be associated with the increase in *Dubosiella* sp. by *B. salyersiae* and *C. minuta* which enhanced the beneficial effects of the murine commensal bacterium. The NGPs have also shown their capabilities in increasing SCFA levels, which could be attributed to their own production of SCFAs as well as the growth enhancement of beneficial bacteria which produce SCFAs. The elevation of SCFAs helps to prevent damage to the colonic epithelium by maintaining the integrity of the epithelial barrier. The SCFAs regulate the tight-junction proteins, preventing an increase in gut permeability to reduce the risk of triggering an inflammatory response that could lead to intestinal inflammation[80]. In addition, SCFAs have also been shown to play a role in glucose homeostasis and lipid metabolism[124]. Therefore, the ability of NGPs to increase SCFA levels could be harnessed to develop treatment strategies in metabolic disorders for hyperglycemia and weight control. In terms of immunomodulatory effects, the supplementation of NGPs typically reduced inflammation in the disease models via the inhibition of pro-inflammatory cytokines such as TNF- α and IL-6 while inducing the secretion of IL-10[33,39,41,50]. The reduction in inflammatory burden brought on by supplementation of NGPs could be useful in the treatment of chronic inflammatory diseases.

Ultimately, these mechanisms are closely interconnected, as the restoration of gut dysbiosis promotes the growth of beneficial bacteria, leading to increased SCFA production. The increase in SCFA levels can then trigger immunomodulatory effects that help to reduce inflammation, thus creating a positive feedback loop that supports host health. Nevertheless, the majority of studies reviewed here were conducted in animal models, and uncertainty remains on whether the effects and mechanisms observed will be effectively translated to humans. Therefore, further research and clinical trials with these NGPs are necessary to clarify these outcomes. However, it is important to note the potential risks of developing NGPs from potential pathogenic species such as members of *Bacillus* sp., *Parabacteroides* sp., and *Enterococcus* sp. For example, *Bacillus cereus* can infect the GI tract and cause food poisoning; *P. distasonis* has been associated with extraintestinal abdominal infections and abscesses; and *Enterococcus* sp. is a common cause of urinary tract infections[125–127].

Therefore, ensuring the safety of the specific strains used to develop NGPs is crucial to avoid potential infections as this can exacerbate the prognosis of existing health conditions. This is particularly important to ensure the safe use of the NGPs in demographics that are at a higher risk of infection such as children, elderly, and immunocompromised individuals. Furthermore, the antibiotic resistance profiles of the NGPs need to be fully elucidated to avoid conferring antibiotic resistance within the gut microbiota to avoid compromising the efficacy of antimicrobial treatments. Therefore, careful selection and thorough assessment of the safety profiles of the NGPs are essential to minimize the risks and ensure their safe use in therapeutic applications.

5. Conclusion

Based on the findings, numerous NGPs show significant promise for the treatment of various diseases in both humans and animals, offering valuable therapeutic effects to manage a wide range of illnesses. The current review highlights growing evidence supporting the use of *A. muciniphila*, *Bacillus* sp., *Bacteroides* sp., *Enterococcus* sp., *Faecalibacterium* sp., *Parabacteroides* sp., and *Streptomyces* sp. as NGPs. As research continues to demonstrate the effectiveness of these probiotics, future studies could focus more on identifying and characterizing specific strains within these genera to target health conditions more precisely. Although research on other niche NGPs remain scarce, the existing data suggests that these underexplored species also hold promise in generating beneficial effects for disease management. Therefore, the potential of these NGPs should not be undermined, as the key solutions for treating certain diseases could lie within these lesser-studied species. In conclusion, the findings from this review provide a valuable framework for guiding future research in NGPs. As research in NGPs is essential to gain a deeper understanding of their exact mechanisms of action, safety profile, and therapeutic applications. This can open new avenues for developing targeted therapeutics, thus offering alternatives to current treatments to improve therapeutic outcomes.

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