

The Mycobiome Frontier – Pre & Post 2020 Status: Integrating Fungal Bioactive Compounds, Probiotics, and Antimicrobial Peptides in Modern Therapeutics and Biotechnology

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Abstract

*The fungal kingdom represents an indispensable resource in modern therapeutics and biotechnology, offering a diverse array of bioactive compounds, probiotics, and antimicrobial peptides (AMPs). Functional fungal polysaccharides (FFPs), such as beta-glucans, chitin, and mannans, are centrally involved in modulating the human gut microbiota, providing novel therapeutic avenues for chronic conditions including diabetes, neurodegenerative disorders, and cancer. These compounds act as prebiotics, nourishing beneficial bacteria and enhancing metabolic parameters such as insulin sensitivity and glucose regulation. Concurrently, fungal probiotics, notably *Saccharomyces boulardii* and *S. cerevisiae*, are gaining recognition for their ability to reestablish eubiosis, enhance gut barrier functions, and modulate immune responses through the secretion of signaling molecules like short-chain fatty acids (SCFAs). Unlike bacterial counterparts, fungal probiotics are often inherently resistant to antibiotics, making them uniquely valuable for patients undergoing antimicrobial treatment. Furthermore, fungi produce potent antimicrobial peptides and specialized secondary metabolites that have historically defined the golden era of antibiotics and continue to serve as essential candidates for combating multidrug-resistant pathogens. In the sphere of biotechnology, the integration of fungal processes supports a circular bioeconomy through the high-yield production of industrial enzymes, organic acids, pigments, and sustainable mycelium-based materials. This synthesis of fungal applications, ranging from immunosuppressive drugs, like cyclosporine to biofuel production, demonstrates the vast potential for personalizing medicine and promoting environmental sustainability. However, the transition to standard medical practice requires large-scale clinical trials to validate safety and efficacy. This review underscores the role of fungi as sustainable biological factories critical for next-generation therapeutic and industrial innovations.*

Keywords: Anticancer, fungal–gut biome, fungal–probiotics, mushrooms, yeast peptides

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INTRODUCTION

The biological sciences are currently witnessing a paradigm shift, moving away from a bacteriocentric view of microbiology toward a more holistic understanding that incorporates the Kingdom Fungi [1]. For much of the 20th century, following the “golden era” of antibiotics initiated by the discovery of penicillin from *Penicillium rubens* and cephalosporin C from *Acremonium chrysogenum*, fungi were primarily viewed through two distinct lenses: as sources of potent pharmaceutical agents or as agents of decay and disease. The fungal kingdom comprises a plethora of eukaryotic species that proliferate in diverse

environments, playing essential roles as decomposers [2], symbionts, and components of the human microbiota [3]. For centuries, fungi have been utilized in food production and traditional medicine, but recent scientific advancements have positioned them as cornerstones of modern biotechnology and therapeutics. The integration of fungal bioactive compounds, probiotics, and antimicrobial peptides offers a transformative approach to managing global health challenges, including metabolic diseases, neurodegeneration, and the rising threat of antimicrobial resistance [2, 4, 5].

However, recent technological advancements in metagenomics, metabolomics, and proteomics have illuminated the “rare biosphere” of the human gut, the mycobiome [6]. Although fungi constitute approximately 0.1% of the total microbial community in the human gastrointestinal tract, their larger cellular volume and distinct metabolic capabilities allow them to exert a disproportionately significant influence on host immunity, metabolic homeostasis, and neurological function [7, 8]. The human gut is now understood not merely as a bacterial reservoir but as a complex ecosystem where inter-kingdom interactions between fungi (mycobiota) and bacteria determine the difference between health and dysbiosis. Fungal Bioactive Compounds and Gut Microbiota Modulation Among the most significant fungal derivatives are functional fungal polysaccharides (FFPs), which are primarily found in the fruiting bodies and mycelia of edible and medicinal mushrooms such as Shiitake (*Lentinula edodes*), Reishi (*Ganoderma lucidum*), and Lion’s Mane (*Hericium erinaceus*) [5, 9]. These complex carbohydrates, including beta-glucans and chitin, are not absorbed in the small intestine; instead, they travel to the colon where they interact directly with the gut microbiota. FFPs act as prebiotics, selectively stimulating the growth of beneficial bacteria, like *Bifidobacterium* and *Lactobacillus*, while suppressing detrimental or opportunistic pathogens [9].

In therapeutic contexts, these bioactive compounds have demonstrated profound effects on metabolic health. For individuals with type 1 and type 2 diabetes, FFPs help stabilize blood sugar by reducing carbohydrate absorption and improving insulin sensitivity. Furthermore, the interaction between FFPs and the gut–brain axis suggests a potential role in preventing or slowing the progression of neurodegenerative diseases like Alzheimer’s and Parkinson’s. By mitigating oxidative stress and neuroinflammation through the modulation of microbial metabolites, fungal compounds help maintain neuronal integrity [3, 10, 11]. The researchers have proven affectivity of such probiotics in improving the rumen digestibility and gut health of cattles also [12]. In oncology, FFPs serve as immunomodulators that activate immune cells, such as macrophages and natural killer cells, potentially reducing tumor growth and enhancing the body’s response to cancer immunotherapy [5, 6, 13].

The Rise of Fungal Probiotics While the probiotic market has traditionally been dominated by bacteria, fungal probiotics are emerging as robust alternatives due to their unique biological characteristics [14, 15]. Fungal cells are generally larger than bacteria and possess rigid cell walls made of chitin, which provides superior resistance to harsh environmental conditions such as the low pH of stomach acid and bile salts in the digestive tract [7, 9, 16, 17]. The most widely studied fungal probiotic, *Saccharomyces boulardii*, has been used for decades to treat gastrointestinal disturbances [18], including antibiotic-associated diarrhoea, urinary tract infection [19, 20] and irritable bowel syndrome (IBS).

A critical advantage of fungal probiotics is their inherent resistance to antibiotics, allowing them to be administered concurrently with antimicrobial therapy to prevent dysbiosis. These fungi enhance gut barrier functions by regulating tight junction proteins, thereby preventing the “leaky gut” syndrome associated with systemic inflammation [19, 21]. Moreover, fungi, like *S. cerevisiae* and *Eurotium cristatum*, have shown potential in treating obesity by restoring microbial balance and producing SCFAs that regulate energy metabolism and suppress inflammation. Antimicrobial Peptides and Secondary Metabolites Fungi are prolific producers of natural products (NPs) that serve as antimicrobial, immunosuppressive, and anti-inflammatory agents [17, 20, 22]. The golden era of antibiotics was initiated by the discovery of penicillin from *Penicillium rubens*, and fungi continue to be a primary source for drug discovery. Fungal antimicrobial peptides (AMPs), such as plectasin and peptaibols,

provide potent defence mechanisms against pathogens by inhibiting cell wall synthesis or disrupting plasma membranes [17]. As multi-drug resistant (MDR) pathogens become a global threat, these fungal peptides and secondary metabolites, including lovastatin for cholesterol management and cyclosporine for immunosuppression, remain vital components of the modern pharmacopeia [20].

Biotechnological Integration and the Circular Economy Beyond direct human health, fungi are essential to industrial biotechnology and the development of a circular bioeconomy. Fungal strains are “cell factories” capable of converting organic waste into high-value by-products [21, 22]. They produce a vast range of extracellular enzymes, including amylases for the food industry, proteases for detergents, and cellulases for biofuel production. Additionally, fungi synthesize natural pigments (such as carotenoids and melanin) and organic acids (such as citric and gluconic acids) that serve as eco-friendly alternatives to synthetic chemicals [22, 23]. Recent innovations in mycelium-based materials also offer sustainable solutions for packaging and thermal insulation, utilizing the natural growth patterns of filamentous fungi to create biodegradable products. This review provides a comprehensive synthesis of the therapeutic potential of fungi, ranging from macroscopic edible mushrooms to microscopic yeasts and filamentous fungi. We examine the mechanisms by which Functional Fungal Polysaccharides (FFPs) modulate the gut microbiota to manage chronic conditions such as diabetes, obesity, and neurodegenerative disorders. Furthermore, we explore the emerging field of fungal probiotics, extending beyond the well-established *Saccharomyces boulardii* to include next-generation candidates, like *Pichia kudriavzevii* and *Kluyveromyces marxianus*, and the critical role of Antifungal Peptides (AFPs) in the face of rising antimicrobial resistance [19]. By integrating data from ecology, immunology, and biotechnology, this report establishes a unified framework for understanding the mycobiome’s pivotal role in the future of personalized medicine and sustainable industry. In conclusion, the integration of fungal bioactive compounds, probiotics, and peptides represents a multifaceted approach to modern science. By leveraging the unique metabolic and structural properties of fungi, researchers can develop personalized therapeutic strategies and sustainable industrial processes that address the complex needs of the 21st century.

REVIEW OF LITERATURE: THE HUMAN GUT MYCOBIOME: ECOLOGY AND DYSBIOSIS

The present review follows the PRISMA guidelines and has been written according to the following structured pattern:

The human gastrointestinal tract harbours a dynamic and spatially heterogeneous fungal community. While the bacterial microbiome is dominated by the phyla *Firmicutes* and *Bacteroidetes*, which collectively comprise nearly 90% of the community, the mycobiome is characterized by lower diversity but significant stability in core taxa [1, 6, 19]. Metagenomic analyses across diverse geographical cohorts – spanning Europe, North America, and Asia – have identified the phyla *Ascomycota* and *Basidiomycota* as the predominant fungal lineages in the human gut. Within these phyla, the genera *Saccharomyces*, *Candida*, and *Malassezia* are the most ubiquitous in healthy adults. Research suggests the existence of a “core mycobiome” consisting of species, such as *Saccharomyces cerevisiae*, *S. limpetus*, and *Candida albicans*, wherein *Aspergillus versicolor*, *Cryptococcus* spp., *Cladosporium herbarum*, *Debaryomyces hansenii*, *Galactomyces* spp., *Geotrichum* spp., *Malassezia* spp., *Penicillium commune*, and *Trichosporon* spp., have been found growing synergistically in over 60% of healthy samples (Jadaoul et al., 2025) [19, 24]. At least 267 distinct fungal taxa have been detected in the human gut, a number far lower than the diversity observed among gut bacteria. The gut microbiome overall is highly diverse, comprising a relatively stable core of roughly 200 shared species alongside a more variable pool of about 800 or more species that shift with geography, diet, and health (Figure 1). Whether a comparable, well-defined “core gut mycobiome” exists for fungi remains unresolved. The studies have also reported a wide range of additional fungal genera throughout the gastrointestinal tract, with communities dominated by members of the *Zygomycota*, and *Chytridiomycota*. This consistency suggests that these organisms are not merely transient passengers derived from diet or the environment but are adapted commensals with specific ecological niches within the host.

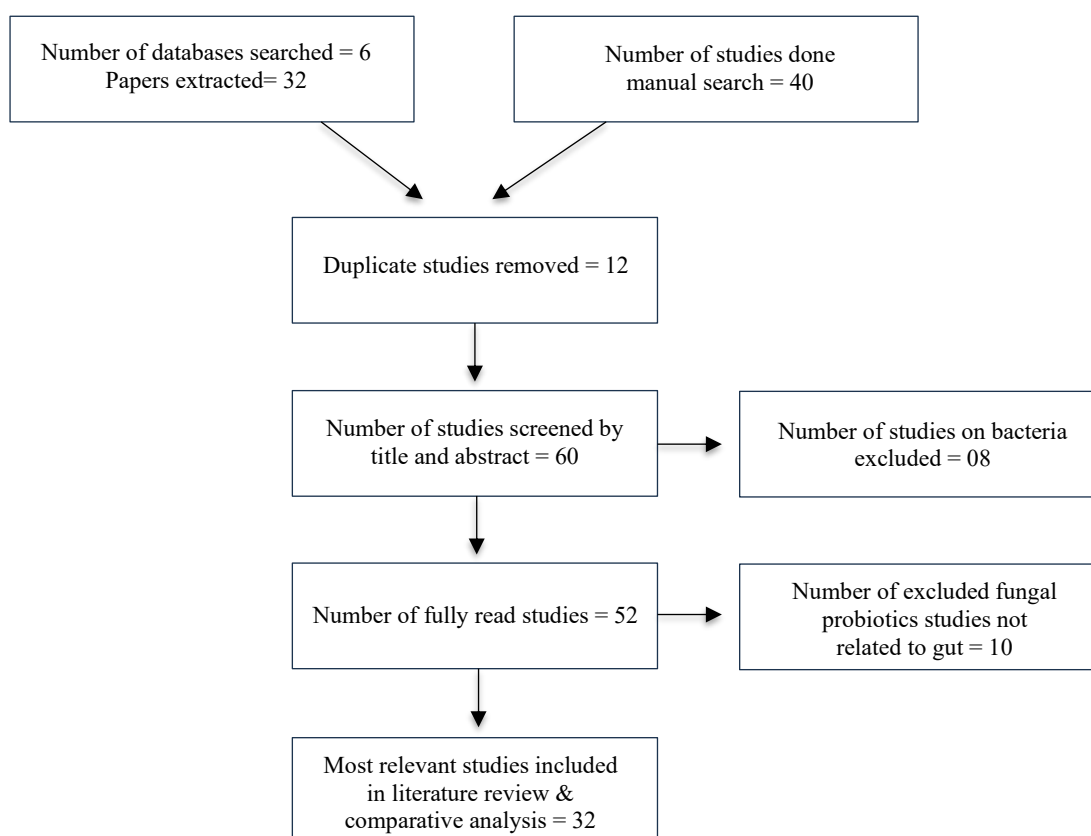


Figure 1. Composition, diversity, and enterotypes.

Analogous to bacterial enterotypes, fungal communities can be categorized into four distinct “myco-enterotypes”: *Saccharomyces* type, *Candida* type, *Aspergillus* type, and a mixed type [12, 19]. These enterotypes appear to be strongly influenced by long-term dietary patterns and geographic location rather than transient factors like Body Mass Index (BMI) or sex. For instance, high-carbohydrate diets have been positively correlated with an increased abundance of *Candida* species, whereas diets high in animal protein and saturated fats tend to suppress *Candida* but may select for other, potentially pro-inflammatory taxa. The geographic variance is substantial; studies comparing residents of Hong Kong and Yunnan found pronounced differences in fungal enrichment, highlighting the environmental determinants of mycobiome assembly.

Fungal–Bacterial Interactions and Colonization Resistance

The stability of the gut ecosystem is maintained through a delicate balance of competitive and synergistic interactions between fungi and bacteria. This cross-kingdom talk is essential for colonization resistance, the mechanism by which the indigenous microbiota prevents the overgrowth of pathobionts. In a healthy state, commensal bacteria suppress fungal blooms through the competition for nutrients and the secretion of inhibitory metabolites. For example, *Lactobacillus rhamnosus* has been shown to deplete essential nitrogen and carbon sources, thereby forcing *Candida albicans* to alter its metabolic gene expression and reducing its capacity for hyphal transition and virulence.

Conversely, fungi can influence bacterial composition. *Saccharomyces cerevisiae* abundance is positively correlated with beneficial Short-Chain Fatty Acid (SCFA)-producing bacteria such as *Faecalitalea* and *Megamonas* [4, 19]. In contrast, *Candida* abundance often exhibits a negative correlation with beneficial taxa, like *Bifidobacterium adolescentis* and *Eubacterium hallii*, suggesting an antagonistic relationship. When bacterial populations are decimated by broad-spectrum antibiotics, this inhibitory pressure is released, often leading to fungal overgrowth, a phenomenon clinically manifesting as antibiotic-associated diarrhoea or candidiasis.

Mechanisms of Pathogenesis in Ulcerative Colitis (UC)

Ulcerative Colitis (UC) serves as a critical model for understanding the pathological consequences of fungal dysbiosis [1]. The disease is characterized by a thinning of the protective Mucin 2 layer and increased intestinal permeability, conditions that allow opportunistic fungi to interact directly with the epithelial lining [6, 8, 9]. In active UC, the mycobiota diversity collapses, and the community often becomes dominated by *Candida* species.

The pathogenicity of *Candida* in this context is driven by morphological plasticity. The transition from the commensal yeast form to the invasive filamentous (hyphal) form is a key virulence factor. Filamentous *Candida albicans* secretes aspartyl proteases that actively degrade the mucin barrier, facilitating epithelial invasion and triggering a potent immune response. This invasion stimulates epithelial cells to secrete pro-inflammatory cytokines, particularly Interleukin-8 (IL-8), which recruits neutrophils and perpetuates mucosal inflammation. Furthermore, *Candida tropicalis* has been implicated in the direct disruption of tight junction proteins, further exacerbating “leaky gut” and allowing the translocation of microbial products into systemic circulation.

Interestingly, the interaction is bidirectional and involves metabolic cross-feeding. *Candida*-dominated communities in UC patients have been linked to enhanced haemoglobin biosynthesis. Since iron is a limiting nutrient for many pathogenic bacteria, this fungal activity may essentially “feed” bacterial pathobionts, creating a self-reinforcing cycle of dysbiosis and inflammation. However, the fungal kingdom is not monolithic in its effects. Certain “Mucosa-Associated Fungi” (MUC), including *Saccharomyces cerevisiae* and *Saccharomycopsis fibuligera*, play a protective role. These fungi stimulate CD4+ T cells to produce Interleukin-22 (IL-22), a cytokine critical for epithelial repair and the production of antimicrobial peptides (AMPs). This finding highlights a potential therapeutic avenue: manipulating the mycobiome to favour IL-22-inducing strains could promote mucosal healing in IBD patients [9, 24].

FUNCTIONAL FUNGAL POLYSACCHARIDES (FFPS): PREBIOTICS FOR METABOLIC AND NEURAL HEALTH

Functional Fungal Polysaccharides (FFPs) are complex carbohydrates derived from the cell walls and intracellular contents of edible and medicinal mushrooms. These compounds, which include β -glucans, α -glucans, heteroglycans, chitin, and mannans, resist hydrolysis by human digestive enzymes [25]. Upon reaching the colon, they serve as fermentable substrates for the gut microbiota, acting as potent prebiotics.

Biochemical Mechanisms of Microbiota Regulation

The therapeutic efficacy of FFPs is primarily mediated through the modulation of the *Firmicutes* to *Bacteroidetes* ratio and the subsequent production of SCFAs. *Firmicutes* are particularly adept at degrading these complex polysaccharides into butyrate, acetate, and propionate [19, 26].

- *Butyrate*: This SCFA is the preferred energy source for colonocytes. It enhances the expression of tight junction proteins (e.g., occludin, claudin-1), thereby reinforcing the intestinal barrier. Furthermore, butyrate acts as a histone deacetylase (HDAC) inhibitor, suppressing the expression of pro-inflammatory cytokines in macrophages and dendritic cells.
- *Acetate and Propionate*: These metabolites enter the portal circulation and reach the liver and peripheral tissues. Propionate inhibits hepatic lipogenesis, while acetate serves as a substrate for cholesterol synthesis and regulation.

Specifically, polysaccharides from *Ganoderma lucidum* (Reishi) have been shown to reverse the dysbiosis associated with high-fat diets (HFD) in murine models. Treatment with GLPs (*G. lucidum* polysaccharides) significantly increases the abundance of *Bacteroidetes* while suppressing *Firmicutes*, thereby reducing the *Firmicutes/Bacteroidetes* (F/B) ratio associated with obesity [3, 6]. This modulation is accompanied by an enrichment of anti-inflammatory genera such as *Dehalobacterium* and *Enterococcus*, creating a gut environment resistant to metabolic endotoxemia [10, 16].

Metabolic Syndrome: Diabetes, Obesity, and Dyslipidemia

The global epidemic of metabolic syndrome – comprising obesity, type 2 diabetes (T2D), and dyslipidemia, has necessitated the search for novel dietary interventions. FFPs offer a multi-pronged therapeutic approach [17].

- *Diabetes Mellitus*: In T2D models, polysaccharides from *Inonotus obliquus* (Chaga) and *Morchella esculenta* (Morel) have demonstrated remarkable hypoglycemic effects. These compounds improve insulin sensitivity not only by reducing systemic inflammation but also by modulating gut-derived signaling molecules. By promoting the growth of SCFA-producing bacteria, FFPs enhance the secretion of Glucagon-Like Peptide-1 (GLP-1) from enteroendocrine L-cells. GLP-1 enhances glucose-dependent insulin secretion and promotes satiety. Additionally, *Grifola frondosa* (Maitake) polysaccharides have been shown to modulate bile acid metabolism, transforming primary bile acids into secondary bile acids that activate the TGR5 receptor, further improving glucose homeostasis [3, 19].
- *Lipid Metabolism*: Hyperlipidemia is a major risk factor for cardiovascular disease. *Poria cocos* polysaccharides have been shown to improve lipid profiles and prevent the progression of Non-Alcoholic Steatohepatitis (NASH). The mechanism likely involves the physical sequestration of bile acids in the gut (preventing their reabsorption) and the SCFA-mediated inhibition of HMG-CoA reductase in the liver, the rate-limiting enzyme in cholesterol synthesis. Clinical trials with *Lentinula edodes* (Shiitake) polysaccharides have demonstrated improved dietary fiber intake and gut microbiota profiles in subjects with hypercholesterolemia, although significant lipid reduction in human trials remains variable and warrants further investigation [3].

The Gut–Brain Axis: Implications for Neurodegeneration

The concept of the “gut–brain axis” describes the bidirectional communication between the enteric nervous system and the central nervous system (CNS), mediated by neural, endocrine, and immune pathways. Dysbiosis and the resulting systemic inflammation (inflammaging) are increasingly recognized as drivers of neurodegenerative conditions like Alzheimer’s Disease (AD) and Parkinson’s Disease (PD) [4].

- *Hericium erinaceus* (*Lion’s Mane*): This mushroom stands out for its neuroprotective properties. Its polysaccharides and secondary metabolites (erinacines and hericenones) have been shown to stimulate the synthesis of Nerve Growth Factor (NGF). In murine models of AD, administration of *H. erinaceus* extracts improved cognitive function and reduced amyloid-beta plaque burden. The gut-mediated mechanism involves the restoration of barrier integrity [27, 28], which prevents the translocation of bacterial Lipopolysaccharides (LPS). LPS is a potent inflammatory trigger that, upon reaching the brain, activates microglia and drives neuroinflammation. By sealing the gut barrier, *H. erinaceus* essentially dampens this peripheral inflammatory drive.
- *Other Neuroprotective Fungi*: Polysaccharides from *Amanita caesarea* and *Polygonatum sibiricum* have also shown efficacy in alleviating neuroinflammation and oxidative stress in Alzheimer’s models. These findings suggest that modulating the gut microbiota with FFPs could be a viable prophylactic strategy for delaying the onset of cognitive decline [5].

Oncology: Immunomodulation as Adjuvant Therapy

In oncology, fungal polysaccharides are valued not necessarily for direct cytotoxicity against cancer cells, but for their ability to function as Biological Response Modifiers (BRMs). They potentiate the host’s immune system to recognize and eliminate malignant cells [6].

- *Mechanism of Immunostimulation*: FFPs interact with Pattern Recognition Receptors (PRRs) such as Dectin-1, Complement Receptor 3 (CR3), and Toll-like Receptors (TLR-2/4) on immune cells within the Gut-Associated Lymphoid Tissue (GALT). This interaction triggers the release of pro-inflammatory cytokines (TNF-alpha, IL-beta, IFN-gamma) and activates Natural Killer (NK) cells, macrophages, and cytotoxic T-lymphocytes [29].

Clinical Evidence [19]

- *Ganoderma lucidum*: Polysaccharides from Reishi have been documented to reduce colorectal cancer growth and inhibit tumorigenesis in colitis-associated cancer models. This is achieved partly by modulating the Wnt/ β -catenin signaling pathway and partly by enhancing the population of beneficial bacteria that produce anti-tumorigenic metabolites.
- *Grifola frondosa*: The “D-fraction” of Maitake polysaccharides has demonstrated specific anti-hepatocellular carcinoma effects. In diabetic mice, it improves microbial balance, suggesting a link between metabolic health and cancer prevention.
- *Inonotus obliquus*: Chaga extracts have been shown to inhibit tumor growth in models of colitis-associated cancer, highlighting the connection between chronic inflammation and carcinogenesis.

DISCUSSION

Fungal Probiotics and Expanding the Repertoire

While the probiotic market has been historically dominated by bacterial genera, such as *Lactobacillus* and *Bifidobacterium*, fungal probiotics offer distinct advantages that make them robust candidates for next-generation therapeutics. Fungi are eukaryotic, meaning they are intrinsically resistant to antibacterial antibiotics. This allows them to be administered concurrently with antibiotic courses to prevent dysbiosis and secondary infections, like *Clostridium difficile*, a utility where bacterial probiotics often fail due to susceptibility.

Saccharomyces Boulardii: The Clinical Standard

Saccharomyces boulardii is the archetype of fungal probiotics and the most extensively studied (Table 1). Its efficacy in preventing and treating Antibiotic-Associated Diarrhea (AAD) and *Clostridium difficile* infections (CDI) is supported by robust clinical evidence [14, 18].

Mechanisms of Action

- **Toxin Degradation**: *S. boulardii* secretes a specific protease (54-kDa serine protease) that directly degrades *C. difficile* toxins A and B, neutralizing their cytopathic effects on the gut epithelium.
- **Immune Stimulation**: It stimulates the secretion of secretory IgA (sIgA) in the gut, enhancing the mucosal immune barrier against pathogens.
- **Trophic Effects**: It releases polyamines (spermine, spermidine) that aid in the maturation and turnover of enterocytes, accelerating mucosal recovery after injury.

Table 1. Therapeutic probiotics of fungal bioactives and their mechanisms of action.

Fungal species	Bioactive class	Target condition	Mechanism of action
Ganoderma lucidum	Polysaccharides (β -glucans)	Diabetes, Cancer	Increases <i>Bacteroides/ Firmicutes</i> ratio; Immunostimulation.
Hericium erinaceus	Diterpenoids (Erinacines)	Neurodegeneration (AD/PD)	Promotes NGF synthesis; Reduces neuroinflammation via gut-brain axis.
<i>S. boulardii</i>	Probiotic Yeast	<i>C. difficile</i> Infection, Diarrhea	Toxin degradation; IgA stimulation; Trophic effects.
Pleurotus ostreatus	Polysaccharides (Pleuran), Chitin	Hyperlipidemia, Infection	Prebiotic for <i>Lactobacillus</i> ; Antioxidant; Cholesterol lowering.
Inonotus obliquus	Polysaccharides	Type 2 Diabetes	Enhances insulin sensitivity; Inhibits lipogenesis.
Lentinula edodes	Polysaccharides (Lentinan)	Cognitive Decline	Modulates gut microbiota; Neuroprotection.

Emerging Fungal Probiotics

Research is now looking beyond *Saccharomyces* to identifying probiotic potential in other yeasts and filamentous fungi found in traditional fermented foods [7].

- *Kluyveromyces marxianus*: Commonly found in kefir and dairy products, this yeast has demonstrated superior adhesion properties to intestinal epithelial cells compared to *S. boulardii*. It exhibits significant anti-inflammatory activity and has been shown to modulate the immune response in vitro, making it a promising candidate for inflammatory bowel diseases.

- *Pichia kudriavzevii*: Isolated from fermented cocoa and cereal products, this strain is notable for its resistance to low pH and bile salts, essential traits for surviving gastric transit. It produces phytase, an enzyme that breaks down phytate in plant foods, thereby enhancing mineral absorption (iron, zinc, calcium). Furthermore, in vivo studies have suggested it possesses cholesterol-lowering properties.
- *Debaryomyces hansenii*: A marine-associated yeast found in high-salt environments (and cheese), *D. hansenii* has shown potential in enhancing innate immunity. Animal studies indicate it can increase phagocytic activity and the respiratory burst response in leukocytes, suggesting a role in boosting non-specific immunity against infections.
- *Filamentous Fungi (Aspergillus oryzae)*: Traditionally used in Koji fermentation for sake and soy sauce, *A. oryzae* acts as a probiotic by secreting a vast array of digestive enzymes (amylases, proteases, lipases). These enzymes assist the host in nutrient digestion. Moreover, *Aspergillus oryzae* supports the growth of beneficial lactic acid bacteria, fostering a synergistic gut environment. Studies in livestock and aquaculture have shown that supplementation with *Aspergillus oryzae* improves growth performance and immune markers.

Bioactive Fungal Metabolites: Beyond Polysaccharides

Fungi are prolific producers of low-molecular-weight secondary metabolites with profound health implications.

- *Gamma-Aminobutyric Acid (GABA)*: Filamentous fungi possess the glutamate decarboxylase enzyme, allowing them to synthesize GABA, a major inhibitory neurotransmitter. Fermentation of oats and soybeans by *Aspergillus oryzae* and *Rhizopus* species significantly enriches the GABA content of the food substrate. Dietary GABA from fungal sources has been linked to blood pressure reduction (antihypertensive), stress relief, and the regulation of insulin secretion, offering potential applications in managing anxiety and metabolic syndrome.
- *Ergosterol and Vitamin D2*: Ergosterol is the primary sterol in fungal cell membranes. It possesses direct anti-inflammatory and anti-hyperlipidemic effects, reducing the absorption of dietary cholesterol. Crucially, ergosterol is the precursor to Vitamin D2 (ergocalciferol). When mushrooms are exposed to UV light (sunlight or artificial UV), they convert ergosterol into Vitamin D2. This makes fungi the only significant non-animal dietary source of Vitamin D, which is vital for bone health and immune regulation.
- *L-Carnitine*: Essential for the transport of fatty acids into the mitochondria for beta-oxidation, L-carnitine plays a key role in energy metabolism. Filamentous fungi, like *Rhizopus oligosporus* and *Aspergillus oryzae*, have been found to produce significant amounts of L-carnitine during solid-state fermentation. This has implications for weight management, athletic performance, and the treatment of metabolic disorders involving impaired fatty acid oxidation.
- *Statins*: Perhaps the most commercially successful fungal metabolite is lovastatin, originally isolated from *Aspergillus terreus* (and found in Red Yeast Rice fermented by *Monascus purpureus*). Lovastatin inhibits HMG-CoA reductase, the rate-limiting enzyme in cholesterol biosynthesis, and remains a cornerstone of cardiovascular disease prevention.

Industrial and Environmental Applications

The utility of fungi extends into industrial biotechnology, creating a circular economy that indirectly supports human health through environmental sustainability.

- *Myc-Materials and Textile Innovation*: The vegetative mycelium of fungi is being engineered to create sustainable alternatives to leather, plastics, and construction materials. Mycelium-based composites are grown on agricultural waste substrates, binding them into durable, biodegradable forms used for thermal and acoustic insulation and packaging. “Myco-leather” offers a cruelty-free, low-carbon alternative to animal leather, reducing the environmental footprint of the textile industry.
- *Bioremediation and Enzymatic Valorization*: Fungi are nature’s premier decomposers, producing powerful lignocellulolytic enzymes (laccases, peroxidases, cellulases) that can degrade complex organic pollutants. *Pleurotus ostreatus* (Oyster mushroom) is extensively used in mycoremediation

to break down petroleum hydrocarbons, pharmaceutical residues (like sulfonamides), and agricultural pesticides in contaminated soil and water. This enzymatic prowess is also harnessed to valorize agricultural waste (e.g., wheat straw, corn stover) into biofuels and high-protein animal feed, contributing to sustainable resource management [30].

FUTURE PERSPECTIVES

The fungal kingdom represents a frontier of immense biological complexity and therapeutic potential. The “myco-blindness” of the past is rapidly dissipating as we recognize fungi as integral components of the human holobiont.

- *Precision Mycobiome Manipulation*: Developing targeted antifungal therapies or probiotic cocktails that specifically modulate the fungal community to treat IBD and metabolic disorders.
- *Standardization*: Establishing rigorous protocols for the extraction and characterization of fungal bio-actives to ensure consistency and safety in clinical applications.
- *Synthetic Biology*: Utilizing fungal hosts for the heterologous expression of complex pharmaceuticals and creating “designer” AFPs with enhanced stability and potency [31, 32].

CONCLUSION

The fungal kingdom constitutes a multifaceted reservoir of bioactive agents and bioprocesses with immediate relevance to therapeutics, medical and industrial biotechnology. The fungal-derived functional metabolites exert reproducible modulatory effects on the gut microbiota, acting as prebiotic substrates that selectively enrich beneficial taxa and alter microbial metabolism for improving host metabolism and immunity. The eukaryotic probiotics of *Saccharomyces* sp. origin offer complementary mechanisms for restoring eubiosis and reverting the ill effects of antibiotic exposure, with expanding clinical evidence against various other dysbiosis-related indications. Fungi also act as a potential source of antimicrobial peptides, specialized secondary metabolites, and continuing to supply scaffolds for next-generation antimicrobials against multidrug-resistant pathogens. The structural diversity and biosynthetic plasticity of fungal metabolites may provide tractable leads for medicinal biotechnology and synthetic biology approaches aimed at overcoming current resistance mechanisms.

In industrial and environmental biotechnology, fungal systems contribute to a circular bioeconomy through high-yield enzyme production, organic acid fermentation, pigment biosynthesis, and the generation of sustainable mycelium-based materials. These applications demonstrate how fungal bioprocesses can couple value creation with reduced environmental footprint, supporting both decarbonization and resource-recovery objectives in manufacturing and materials science. However, it requires, mechanistic clarity and standardization in metabolite composition, probiotic strains, dosing regimens, and manufacturing processes along with rigorous clinical validation, including adequately powered randomized controlled trials with standardized endpoints, safety monitoring, and stratification by host microbiome and metabolic phenotype, must be researched in future to accelerate effective translation. The regulatory frameworks must evolve in parallel to accommodate complex biologics and live biotherapeutic products, with clear criteria for quality control, potency assays, and post-market surveillance. Realizing this potential will depend on coordinated efforts in basic science, translational research, and regulatory science to ensure safety, efficacy, and equitable access. When coupled with robust clinical trials and scalable bioprocessing, fungal-based solutions are poised to contribute substantially to personalized medicine and a more sustainable industrial landscape. In conclusion, the integration of fungal biology into mainstream biomedical research is not just an academic exercise but a necessity. From the macroscopic mushrooms that nourish and heal, to the microscopic yeasts that guard our gut, fungi act as essential architects of human health. Harnessing their power through biotechnology and precision medicine offers novel solutions to some of the most pressing health challenges of our time.

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REFERENCES

1. Zhang Y, Wang L, Peng L. The role of intestinal fungi in the pathogenesis and treatment of ulcerative colitis. *Microorganisms*. 2025;13(4):794. doi: 10.3390/microorganisms13040794.
2. Divyashree S, Shruthi B, Vanitha P, Sreenivasa M. Probiotics and their postbiotics for the control of opportunistic fungal pathogens: A review. *Biotechnol Rep*. 2023;38:e00800. doi: 10.1016/j.btre.2023.e00800.
3. Li M, Yu L, Zhao J, Zhang H, Chen W, Zhai Q, et al. Role of dietary edible mushrooms in the modulation of gut microbiota. *J Funct Foods*. 2021;83:104538. doi: 10.1016/j.jff.2021.104538.
4. Roustana N, Aslan M, Yesilcimen Akbas M, Ozcan F, Sar T, Taherzadeh MJ. Effects of fungal based bioactive compounds on human health: Review paper. *Crit Rev Food Sci Nutr*. 2024;64(20):7004–7027. doi: 10.1080/10408398.2023.2178379.
5. Chander M. Fungal-derived nutraceuticals & bioactive compounds with physiotherapeutic and health-promoting properties: A comprehensive review. *Int J Fungi*. 2025;2(2):1–9. doi: 10.37591/IJF.v02i02.228797.
6. Barcan AS, Barcan RA, Vamanu E. Therapeutic potential of fungal polysaccharides in gut microbiota regulation: Implications for diabetes, neurodegeneration, and oncology. *J Fungi*. 2024;10(6):394. doi: 10.3390/jof10060394.
7. Hussain A, Rabbani N, Areeb M, Ali SA. Fungi as probiotics: Properties and applications. In: *Fungal biotechnology*. 1st ed. CRC Press; 2025. p. Chapter 22.
8. Törös G, El-Ramady H, Prokisch J, Velasco F, Llanaj X, Nguyen DH, Peles F. Modulation of the gut microbiota with prebiotics and antimicrobial agents from *Pleurotus ostreatus* mushroom. *Foods*. 2023 May 16;12(10):2010.
9. Eberl A, Saqib S, Korpela K, Virtanen S, Sipponen T, Salonen A, et al. Bacterial and fungal profiles as markers of infliximab drug response in inflammatory bowel disease. *J Crohns Colitis*. 2021;15(6):1019–1031. doi: 10.1093/ecco-jcc/jjaa252.
10. Chander M, Paul M. Therapeutic & diagnostic applications of biosurfactants of microbial origin. *Int J Multidiscip Res*. 2025;7(1):1–25. doi: 10.36948/ijfmr.2025.v07i04.50288.
11. Kosgey JC, Jia L, Fang Y, Yang J, Gao L, Wang J, et al. Probiotics as antifungal agents: Experimental confirmation and future prospects. *J Microbiol Methods*. 2019;162:28–37. doi: 10.1016/j.mimet.2019.05.001.
12. Wang L, Li M, Liu C, Li X, Wang P, Chang J, et al. Effects of fungal probiotics on rumen fermentation and microbiota in Angus cattle. *Animals*. 2025;15(18). doi: 10.3390/ani15182746
13. Haifer C, Paramsothy S, Kaakoush NO, Saikal A, Ghaly S, Yang T, et al. Lyophilised oral faecal microbiota transplantation for ulcerative colitis (LOTUS): a randomised, double-blind, placebo-controlled trial. *Lancet Gastroenterol Hepatol*. 2022;7(2):141–151. doi: 10.1016/S2468-1253(21)00400-3.
14. Kumar R, Salwan R, Chander M. The synthesis of medicinally important pharma molecules from carbohydrate building blocks. *Int J Nov Res Dev*. 2023;8(5):e138–148.
15. Wu Y, Hu S, Wu C, Gu F, Yang Y. Probiotics: Potential novel therapeutics against fungal infections. *Front Cell Infect Microbiol*. 2022;11:793419. doi: 10.3389/fcimb.2021.793419.
16. Bulut SD, Döndaş HA, Celebioglu HU, et al. Recent insights about probiotics related pharmabiotics in pharmacology: Prevention and management of diseases. *Probiotics Antimicrob Proteins*. 2025;17:2262–2292. doi: 10.1007/s12602-025-10613-3.
17. Miguel UF de, Sara A, Enriqueta GG, Cotter PD. Antifungal peptides as therapeutic agents. *Front Cell Infect Microbiol*. 2020;10:518678. doi: 10.3389/fcimb.2020.00105.
18. Abid R, Waseem H, Ali J, Ghazanfar S, Ali GM, Elsbali AM, et al. Probiotic yeast *Saccharomyces*: Back to nature to improve human health. *J Fungi*. 2022;8(5). doi: 10.3390/jof8050444.
19. Corbu VM, Gheorghe-Barbu I, Dumbravă AŞ, Vrâncianu CO, Şesan TE, et al. Current insights in fungal importance: A comprehensive review. *Microorganisms*. 2023;11(6). doi: 10.3390/microorganisms11061384.
20. Neha B, Samiksha S, Rashmi P, Sumit KD, Sahil, Vimal P. Role of fungal metabolites in pharmaceuticals, human health, and agriculture. In: Abd-Elsalam KA, Mohamed HI, editors. *Nanobiotechnology for plant protection: Fungal metabolites*. Elsevier; 2024. p. 519–535. doi: 10.1016/B978-0-323-95241-5.00005-8.

21. Sharma E, Chander M, Kaur K. Diagnosis management & treatment of urinary tract infections: A recent perspective. *Int J Curr Res Acad Rev.* 2024;12(8):11–34. doi: 10.20546/ijcrar.2024.1208.002.
22. Ferrão J, Bell C, Chaquisse E, Garrine C, Fernandes TH. The synbiotic role of mushrooms: Is germanium a bioactive prebiotic player? A review article. *Am J Food Nutr.* 2020;7:26–35.
23. Zhang F, Zuo T, Yeoh YK, Cheng FW, Liu Q, Tang W, et al. Longitudinal dynamics of gut bacteriome, mycobiome and virome after fecal microbiota transplantation in graft-versus-host disease. *Nat Commun.* 2021;12(1):65. doi: 10.1038/s41467-020-20240-x.
24. Chander M. *Rauwolfia serpentina*: A comprehensive phytochemical study of its bioactive metabolites. *Emerg Trends Metab.* 2024;1(2):14–40.
25. Leonardi I, Gao IH, Lin WY, Allen M, Li XV, et al. Mucosal fungi promote gut barrier function and social behavior via type 17 immunity. *Cell.* 2022;185:831–846. doi: 10.1016/j.cell.2022.01.017.
26. Wang X, Cui Y, Sang C, Wang B, Yuan Y, Liu L, et al. Fungi with potential probiotic properties isolated from Fuzhuan brick tea. *Food Sci Hum Wellness.* 2022;11(3):686–696. doi: 10.1016/j.fshw.2021.12.02.
27. Ghosh K, Harikrishnan R, Mukhopadhyay A, Ringø E, et al. Fungi and actinobacteria: Alternative probiotics for sustainable aquaculture. *Fishes.* 2023;8(12). doi: 10.3390/fishes8120575.
28. American Society for Microbiology. Fungi used in food production could lead to new products. Available from: <https://asm.org/press-releases/2023/october/fungi-used-in-food-production-could-lead-to-new-pr>.
29. Chander M, Kaur J. Aquatic ecosystems: A review on prospecting of anticancer molecules from fungi & other microbes. *Int J Fungi.* 2024;1(2).
30. Chen S, Yi M, Yi X, Zhou Y, Song H, Zeng M. Unveiling the fungal frontier: mycological insights into inflammatory bowel disease. *Front Immunol.* 2025;16:1551289. doi: 10.3389/fimmu.2025.1551289.
31. Huang H, Wang Q, Yang Y, Zhong W, He F, Li J. The mycobiome as integral part of the gut microbiome: Crucial role of symbiotic fungi in health and disease. *Gut Microbes.* 2024;16(1): 2440111. doi: 10.1080/19490976.2024.2440111.
32. Jaddaoui IE, Sehli S, Idrissi NA, Bakri Y, Belyamani L, Ghazal H. The gut mycobiome for precision medicine. *J Fungi.* 2025;11(4). doi: 10.3390/jof11040279.