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Postbiotics: Emerging functional metabolites for gut health and disease management

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Abstract
Postbiotics, defined as bioactive compounds produced during microbial fermentation, have recently emerged as promising functional metabolites with potential health benefits. Unlike probiotics, which rely on live microorganisms, postbiotics encompass a diverse array of microbial-derived substances such as short-chain fatty acids (SCFAs), peptides, enzymes, cell wall fragments, and extracellular polysaccharides, which confer health benefits even in the absence of live bacteria. Accumulating evidence highlights their role in modulating gut microbiota composition, enhancing mucosal immunity, attenuating inflammation, and maintaining gut barrier integrity. Moreover, postbiotics are associated with potential therapeutic applications in metabolic disorders, inflammatory bowel disease (IBD), colorectal cancer, and infectious diseases. Their stability, safety profile, and ease of formulation position them as viable alternatives or adjuncts to probiotics and prebiotics. This review synthesizes current evidence on the biological mechanisms, clinical applications, and future perspectives of postbiotics, emphasizing their translational potential in gut health and disease management.

Keywords: Therapeutic nutrition, foods, postbiotics, gut microbiota, infectious diseases

Introduction
The human gastrointestinal tract hosts trillions of microorganisms, collectively termed the gut microbiota, which play critical roles in nutrient metabolism, immune regulation, and barrier function. Dysbiosis of the gut microbiota has been linked to numerous diseases, including IBD, obesity, diabetes, and colorectal cancer (Gibson *et al*., 2017; Roberfroid, 2007) [6, 12]. While probiotics and prebiotics have been extensively studied to restore microbial balance, the concept of postbiotics has gained momentum as an innovative approach to harness microbial metabolites without the need for live microorganisms (Sanders *et al*., 2013) [13]. Postbiotics are defined as bioactive compounds produced during microbial fermentation that confer health benefits to the host (Aguilar-Toalá *et al*., 2018) [1]. These metabolites include SCFAs such as acetate, propionate, and butyrate, microbial peptides, enzymes, cell wall components, and other microbial-derived molecules. Their functional properties extend to modulation of immune responses, anti-inflammatory effects, pathogen inhibition, and improvement of gut barrier function. The safety and stability of postbiotics, combined with their capacity to provide consistent therapeutic effects, make them promising candidates for functional foods, nutraceuticals, and therapeutic interventions.

Mechanisms of Action of Postbiotics
Postbiotics exert beneficial effects through multiple mechanisms. SCFAs, the most studied postbiotic metabolites, regulate gut health by serving as energy sources for colonocytes, strengthening epithelial barrier function, and modulating immune responses (Calder, 2006; Kris-Etherton *et al*., 2002) [3, 8]. Butyrate, in particular, has been shown to inhibit histone deacetylases, promoting anti-inflammatory gene expression and suppressing pro-inflammatory cytokines (Shahidi & Ambigaipalan, 2015) [15]. Postbiotic peptides and extracellular polysaccharides can prevent pathogen adhesion to the gut mucosa, enhance mucin production, and stimulate the secretion of immunoglobulin A (IgA), thereby reinforcing mucosal immunity (Slavin, 2005; Scalbert *et al*., 2005) [14, 16]. Additionally, cell wall components such as peptidoglycans and lipoteichoic acids interact with pattern recognition receptors (PRRs) on host immune cells, promoting immune modulation and tolerance. Enzymatic postbiotics can aid in digestion and reduce oxidative stress by scavenging free radicals. Collectively, these multifactorial actions contribute to gut homeostasis and systemic health benefits.

Postbiotics in Gut Health
Postbiotics have demonstrated significant potential in enhancing gut health. SCFAs, especially butyrate, improve intestinal barrier integrity by upregulating tight junction proteins such as occludin and claudin, reducing intestinal permeability and preventing “leaky gut” syndrome (Calder, 2006) [3]. Postbiotics also modulate the composition of gut microbiota by promoting the growth of beneficial bacteria like Lactobacillus and Bifidobacterium while inhibiting pathogenic organisms (Gibson *et al*., 2017) [6]. In addition, postbiotics attenuate local gut inflammation by suppressing pro-inflammatory cytokines (IL-6, TNF-α) and increasing anti-inflammatory cytokines (IL-10), thereby reducing

susceptibility to gastrointestinal disorders such as IBD and colitis (Shahidi & Ambigaipalan, 2015) [15]. Clinical studies have reported that supplementation with postbiotic preparations can improve stool consistency, reduce gastrointestinal discomfort, and support digestive health, particularly in populations with functional bowel disorders.

Therapeutic Potential in Disease Management
Beyond gut health, postbiotics show promise in managing systemic and chronic diseases. In metabolic disorders such as obesity and type 2 diabetes, SCFAs regulate glucose and lipid metabolism, enhance satiety through modulation of gut-brain hormonal signaling (GLP-1 and PYY), and improve insulin sensitivity (Kris-Etherton *et al*., 2002) [8]. In IBD, postbiotics reduce mucosal inflammation, improve barrier integrity, and decrease oxidative stress, complementing conventional therapies (Sanders *et al*., 2013) [13]. Emerging evidence also suggests potential anticancer effects, particularly in colorectal cancer, where butyrate induces apoptosis in malignant cells and inhibits tumour proliferation (Calder, 2006) [3]. Furthermore, postbiotics exhibit antimicrobial properties against gastrointestinal pathogens, including Salmonella, Escherichia coli, and Clostridium difficile, through competitive exclusion and production of antimicrobial metabolites (Scalbert *et al*., 2005) [14].

Advantages of Postbiotics over Probiotics and Prebiotics
Postbiotics offer distinct advantages compared to probiotics and prebiotics. Unlike probiotics, they do not require viable microorganisms, eliminating concerns about microbial survival during storage, transit through the gastrointestinal tract, or risk of translocation in immunocompromised individuals (Roberfroid, 2007) [12]. Compared to prebiotics, which require fermentation by resident gut microbiota to produce beneficial metabolites, postbiotics provide direct bioactive effects with predictable outcomes. Additionally, postbiotics are more stable, easier to formulate into functional foods or supplements, and have a favorable safety profile, making them suitable for vulnerable populations, including infants, elderly, and immunocompromised patients (Aguilar-Toalá *et al*., 2018) [1].

Current Evidence from Clinical Trials and Studies
Several clinical studies support the efficacy of postbiotics in improving human health. For instance, fermented milk and yogurt containing postbiotic metabolites have been shown to enhance immune responses, reduce gastrointestinal infections, and improve bowel function (Sanders *et al*., 2013) [13]. Randomized controlled trials have reported decreased incidence of diarrhea in children receiving postbiotic supplementation and improved metabolic markers in adults with obesity (Gibson *et al*., 2017) [6]. Furthermore, in patients with IBD, oral postbiotic formulations have been associated with reduced inflammatory markers and improved mucosal healing (Shahidi & Ambigaipalan, 2015) [15]. Despite these promising results, the field remains in its early stages, and more large-scale, multicenter trials are needed to standardize dosing, identify active metabolites, and clarify long-term effects.

Future Perspectives and Challenges
The future of postbiotics in functional foods and therapeutics is promising but faces challenges. Standardization of postbiotic preparations is essential, including defining bioactive components, concentrations, and stability during processing. Personalized nutrition approaches, integrating postbiotics with an individual's gut microbiome profile, may optimize efficacy. Advanced technologies such as metabolomics, metagenomics, and artificial intelligence can aid in identifying novel postbiotic molecules and predicting their biological effects (Roberfroid, 2007) [12]. Regulatory frameworks for postbiotic products are still evolving, requiring clear definitions and safety evaluations to support commercialization.

Table 1: Recent Studies on Postbiotics and Their Role in Gut Health and Disease Management

Study	Year	Key Findings	Postbiotic Components	Health Implications
Asefa *et al*.	2025 [2]	Postbiotics enhance gut barrier integrity and modulate immune responses.	Short-chain fatty acids (SCFAs), bacteriocins, exopolysaccharides (EPS), teichoic acids.	Effective in managing irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), and metabolic disorders.
Meena *et al*.	2025 [10]	Postbiotics bridge the gap between current research and real-world applications.	SCFAs, EPS, bacteriocins, vitamins.	Potential therapeutic agents for chronic diseases, offering a safer alternative to live probiotics.
Ji *et al*.	2023 [7]	Postbiotics regulate gut microbiota composition and functionality.	SCFAs, EPS, bacteriocins.	Beneficial for gastrointestinal health, metabolic regulation, and immune modulation.
Prajapati *et al*.	2023 [11]	Postbiotics influence gut microbiota composition and functionality.	EPS, bacteriocins, SCFAs.	Contribute to gut health, immune system regulation, and pathogen inhibition.
Calvanese *et al*.	2025 [4]	Postbiotics offer advantages over live probiotics.	SCFAs, EPS, bacteriocins.	Enhanced stability and bioavailability, suitable for immunocompromised individuals.
Kumar *et al*.	2024 [9]	Postbiotics have bioactive properties and therapeutic potential.	SCFAs, EPS, bacteriocins.	Aid in improving gut health, regulating the immune system, inhibiting pathogen growth, and reducing inflammation.
Chen *et al*.	2025 [5]	Postbiotics exhibit bioactivity and safety advantages.	SCFAs, EPS, bacteriocins.	Suitable for individuals with compromised immune systems or allergies to certain bacterial strains.

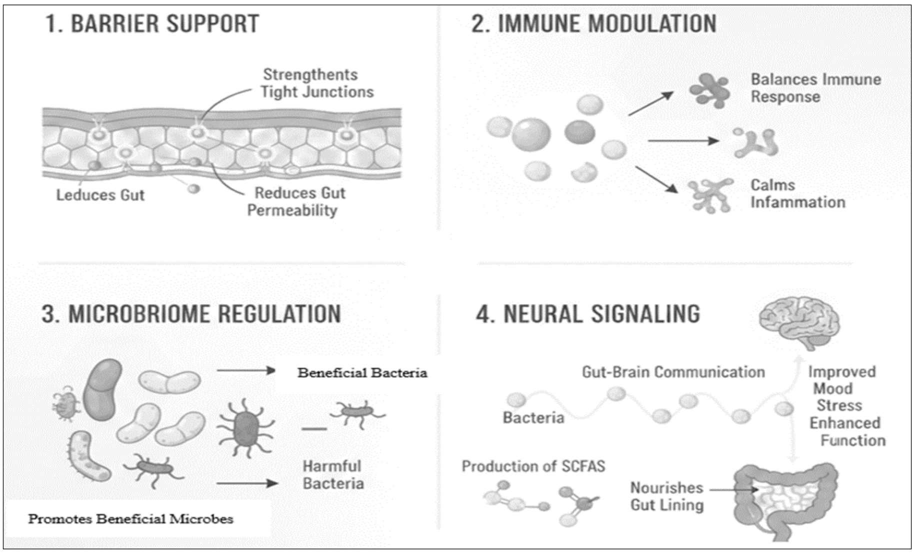

Fig 1: Mechanisms of Postbiotics in gut health

Conclusion

Postbiotics represent a novel and promising category of functional metabolites with significant potential to enhance gut health and manage a variety of diseases. Their multifaceted mechanisms, including immune modulation, antimicrobial activity, and metabolic regulation, make them attractive alternatives or complements to probiotics and prebiotics. With further research, clinical validation, and technological advancement, postbiotics could become integral components of functional foods, nutraceuticals, and therapeutic strategies, offering safe, stable, and effective solutions for maintaining gastrointestinal and systemic health.

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