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REVIEW ARTICLE

Postbiotics: Emerging Therapeutic Agents in Modern Medicine

[1]Naglaa R.A. Mohamed*, [2]Nagwa A. Tharwat, [3]Amr M. Abdou
[1]Department of Botany and Microbiology, Faculty of Science, Cairo University, 12592, Egypt
[2]Department of Botany and Microbiology, Faculty of Science, Cairo University, Giza 12613, Egypt
[3]Department of Microbiology and Immunology, National Research Centre 12622 Dokki, Giza, Egypt

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Corresponding Author:
Naglaa Ramadan Atta
Microbiology Department, Faculty of Science, Cairo University
Tel.: (+20) 1150940983
Naglaaramadan@gstd.sci.cu.edu.eg

ABSTRACT

Postbiotics, defined as bioactive compounds produced during microbial fermentation, have emerged as a promising alternative to traditional probiotics, offering unique therapeutic potential and applications across various sectors. This review comprehensively explores postbiotics' classification, mechanisms of action, and therapeutic applications, focusing on their use in the food industry, human health, functional foods, and biomedical applications. In the food industry, postbiotics enhance food safety, shelf life, and functional properties while promoting gut health through non-living microbial metabolites. Postbiotics can help improve human health by affecting the immune system, enhancing metabolism, and aiding digestion, making them good options for treating long-term illnesses like inflammatory bowel disease and metabolic syndrome. Additionally, incorporating postbiotics into functional foods offers the possibility of delivering health benefits beyond basic nutrition. In the biomedical field, their potential applications range from wound healing to tissue regeneration, where postbiotics' anti-inflammatory and antioxidant properties can play a key role. This review highlights the growing evidence supporting the broad spectrum of postbiotics' therapeutic capabilities, positioning them as a versatile and sustainable option in modern medicine and industry. Despite the promising outlook, we need further research with clinical trials to fully understand their efficacy and establish appropriate guidelines for their application.

INTRODUCTION

The human gut microbiome, a diverse and dynamic community of trillions of microorganisms, plays an essential role in immune modulation, metabolic regulation, and overall health maintenance [1] Disruption of this microbial balance is associated with various diseases, underscoring the importance of preserving gut homeostasis [2].

Historically, probiotics have been the focus of microbiome-targeted therapies. According to the Food and Agriculture Organisation of the United Nations and the World Health Organisation (FAO/WHO), probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host."[3], probiotics are typically composed of lactic acid bacteria such as *Lactobacillus* and *Bifidobacterium* species. These microorganisms, generally recognized as safe (GRAS), are commonly delivered through fermented products like yogurt or non-fermented vehicles such as cereals, juices, and nutritional supplements. Their health-promoting effects are mediated by suppressing pathogenic microbes, enhancing intestinal barrier function, and modulating immune responses through pathways such as tight junction signaling [4].

Complementing probiotics, prebiotics are described by the International Scientific Association for Probiotics and Prebiotics (ISAPP) as"a substrate that is selectively utilized by host microorganisms to confer a health benefit" [5]. Prebiotics, present in dietary fibers, human milk oligosaccharides (HMOs), phenolics, and polyunsaturated fatty acids, stimulate the growth and activity of beneficial microbes. When combined, probiotics and prebiotics form synbiotics, synergistic formulations designed to optimize microbial colonization and host benefits[6].

Recently, attention has shifted to postbiotics, defined as non-viable microbial cells, their components, or metabolites that exert biological effects on the host. These include secreted molecules and byproducts such as enzymes, peptides, teichoic acids, polysaccharides, and organic acids, either released during fermentation or upon microbial lysis[7]. The ISAPP further defines postbiotics as "preparations of inanimate microorganisms and/or their components that confer a health benefit to the host" [8].

Postbiotics are typically derived from bacteria and fungi, including *Lactobacillus, Bifidobacterium, Streptococcus, Eubacterium, Faecalibacterium*, and *Saccharomyces*, found in fermented foods like yogurt, kombucha, and pickled vegetables[9]. Commercial postbiotics are now available as supplements or food additives for gastrointestinal and immune support [10].

Postbiotics exert beneficial effects through various microbial products, including proteins, lipids, carbohydrates, vitamins, organic acids, and structural cell wall components [11]. However, their composition can be influenced by food processing techniques such as heat, pressure, irradiation, and sonication, which may affect both microbial integrity and metabolite production[12]. Analytical methods like matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry and high-performance liquid chromatography (HPLC) are employed for postbiotic characterization [13].

The use of postbiotics has gained attention due to safety concerns associated with live probiotics, especially in vulnerable populations such as immunocompromised individuals, infants, and elderly patients [14,15]. Unlike probiotics, postbiotics eliminate risks related to microbial translocation and infection and offer advantages such as stability, standardization, and extended shelf life[16]. Additionally, they pose a lower risk of transmitting antibiotic-resistance genes, a growing concern with live microbial therapies [17].

Given these benefits, postbiotics emerge as a promising alternative to traditional probiotics. This review will explore their classification, mechanisms of action, and therapeutic applications, highlighting their potential to address current limitations in probiotic-based interventions.

Probiotics, Prebiotics, Synbiotics, and Postbiotics

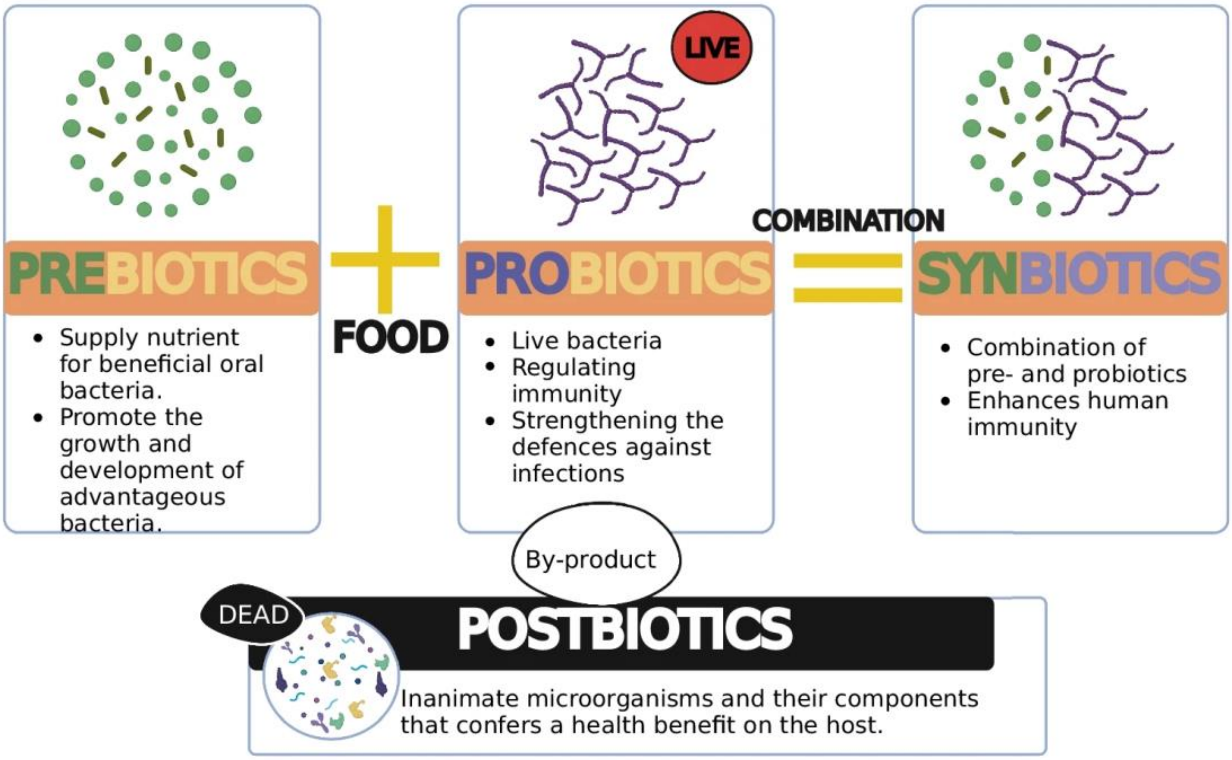

Fig. 1: This figure shows the combination of prebiotics and postbiotics forming synbiotics and potbiotics, which is defined as probiotics by-products [18].

Probiotics

The World Health Organization defines probiotics as "living microorganisms that, when administered in sufficient quantities, confer a health benefit on the host"[6]. Most probiotics are Gram-positive bacteria, particularly from the *Lactobacillus* and *Bifidobacterium* genera[19], though other non-pathogenic strains, including specific *Escherichia coli*[20], *Enterococcus* [21], *Pediococcus*, and *yeasts* like *Saccharomyces boulardii*, have also demonstrated probiotic properties[22–24]. Additional beneficial effects have been observed from commensal bacteria such as *Streptococcus oralis* and *S. salivarius* [25].

Probiotics contribute to intestinal homeostasis through diverse mechanisms, including regulating innate and adaptive immune responses, inhibiting pathogens, enhancing nutrient bioavailability, and supporting intestinal barrier integrity[26]. They also help alleviate food intolerances and enhance systemic functions such as digestion and immune surveillance [27].

These benefits arise through various mechanisms, including metabolite cross-feeding, direct cell-to-cell interactions, and signaling pathways [28].

In clinical settings, Probiotics have demonstrated potential in managing diseases including allergies, infectious diarrhea, inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), infant colic, and certain malignancies. They additionally promote mucosal immunity and may mitigate the adverse effects of broad-spectrum antibiotics by reinstating gut microbial equilibrium[29,30]. Their role as adjuncts in antibiotic therapy continues to be explored [31].

Prebiotics

Prebiotics are defined as non-digestible food components that selectively promote the growth or activity of beneficial gut microorganisms, thereby improving host health [32]. Prebiotics are typically indigestible by human enzymes, including compounds like fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), resistant starches, and glucose-derived oligosaccharides [32]. By supporting beneficial microbes, prebiotics indirectly produce bioactive metabolites, including postbiotics, thus forming an essential link in gut microbial modulation[33].

Synbiotics

Synbiotics are formulations, including probiotics and prebiotics, as described in Figure 1, to synergistically improve microbial survival and function in the gastrointestinal tract. This dual strategy enhances gut microbial balance, supports digestive and immune functions, and mitigates gastrointestinal disorders [34]. Notably, the interaction between probiotics and prebiotics in synbiotics promotes the generation of postbiotic compounds such as short-chain fatty acids, thereby amplifying the overall health benefits, together, these components represent an integrated approach to modulating the microbiota for therapeutic gain[35].

Postbiotics

Postbiotics are bioactive compounds produced during fermentation by probiotic organisms or derived from their inactivated forms. These include short-chain fatty acids (SCFAs), cell wall fragments, exopolysaccharides (EPS), enzymes, and metabolites, which can be obtained through natural fermentation or thermal inactivation. Although various terms, such as pseudoprobiotics, paraprobiotics, and cell-free supernatants, have been used, "postbiotics" is the most commonly accepted term in current literature [36,37].

These compounds exert various health-promoting effects, including immune modulation, anti-inflammatory, antibacterial, antiviral, antioxidant, and anti-cancer activities [38]. Notably, postbiotics avoid the risks associated with live microbial administration, such as microbial translocation or antibiotic resistance transfer. Their defined chemical structures, stable shelf life, and safety profile make them suitable for applications in both food and pharmaceutical industries[39]. The specific benefits of postbiotics depend on the originating probiotic strain and the nature of the bioactive compounds produced.

Classification of Postbiotics

Gut microorganisms depend on the host for essential nutrients to grow and thrive. In turn, they produce a variety of low-molecular-weight metabolites that support microbial development, cell signaling, stress resistance, and beneficial microbial proliferation. These metabolites, often bioactive compounds, can also be released into the host environment, modulating cellular and metabolic pathways with potential physiological benefits. Using bioengineering, recombinant probiotics can be developed to produce such bioactive compounds. However, their specific effects depend on the microbial species or consortia used [8].

Postbiotics are classified either by their constituent elements or physiological properties. The primary constituents include short-chain fatty acids, enzymes, vitamins, peptides, teichoic acids, bacterial lysates as shown in Figure 2, inactivated or dead bacteria, proteins (e.g., lactocepin, p75), organic acids (e.g., propionic acid), lipids (e.g., butyrate, lactate), and carbohydrates (e.g., teichoic acids) [40]. Their physiological functions span immunomodulatory, anti-inflammatory, antioxidant, anti-hypertensive, anti-proliferative, hypo-cholesterolemic, and anti-obesogenic activities [41].

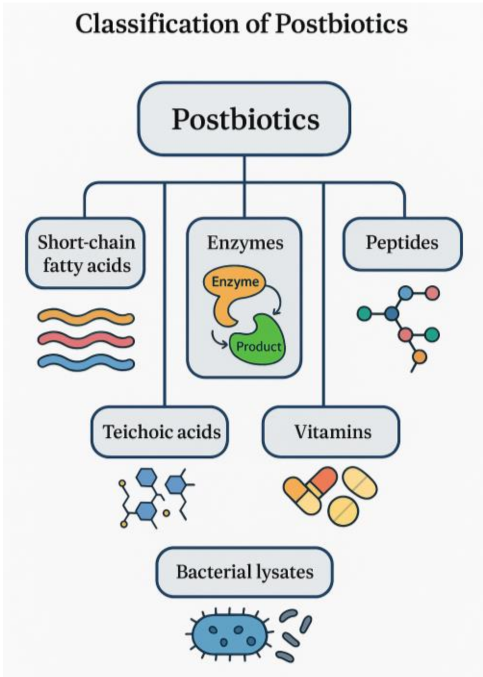

Fig. 2: A Schematic representation shows different types of postbiotics.

Short-Chain Fatty Acids (SCFAs):

SCFAs, primarily acetate, propionate, and butyrate, are the major end-products of bacterial fermentation of dietary fibers. [42] Their production is influenced by microbial composition, pH, substrate availability, and hydrogen pressure [43]. SCFAs are abundant in the colon and play key roles in maintaining gut barrier integrity, modulating metabolism, and supporting immune function [44]. Butyrate, particularly, serves as an energy source for colonocytes and exhibits potent anti-inflammatory properties. Its clinical relevance includes the management of colonic diseases and glucose homeostasis [45].

Enzymes:

Microbial enzymes are bioactive proteins critical to metabolic and physiological functions, such as catalase and superoxide dismutase (SOD), mainly when expressed in genetically modified *Lactobacillus* strains, can ameliorate inflammatory conditions like Crohn's disease and chemically-induced colon cancer [46,47].

Peptides:

Postbiotic peptides, including antimicrobial peptides (AMPs), disrupt bacterial membranes and act as immunomodulators[48]. Bacteriocins, a well-studied group of AMPs, have potent antibacterial properties. They are categorized into four classes based on structure and stability [49]. Nisin and lysosphine are notable examples showing effectiveness against resistant pathogens,although clinical application remains limited due to production and stability issues [50,51].

Teichoic Acids (TAs):

TAs, including lipoteichoic acids, are glycopolymers found in Gram-positive bacterial walls and influence cell rigidity, permeability, and immune response [52]. They modulate host immunity through interactions with Toll-like receptors (TLRs) and influence cytokine production and T-cell responses, contributing to immunomodulation, anticancer, and antioxidant effects[53].

Vitamins:

Gut bacteria, particularly *Bifidobacteria* and *Lactobacilli*, synthesize essential vitamins like B12, K2, folate, and riboflavin [30,54,55]. These vitamins are critical for systemic health and are absorbed by colonocytes via specific transport mechanisms. Vitamin K2, for instance, supports bone and cardiovascular health [56].

Bacterial Lysates (BLs):

BLs are derived from lysed Gram-positive or Gram-negative bacteria and act through the gut-lung axis to stimulate systemic immunity. Clinical evidence suggests their efficacy in reducing asthma and Chronic Obstructive Pulmonary Disease (COPD) exacerbations, as well as mitigating allergic rhinitis and dry eye syndrome caused by blue light exposure [57].

Mechanisms of Action of Postbiotics

Postbiotics exert a range of biological activities through multiple mechanisms of action mentioned in Figure 3.

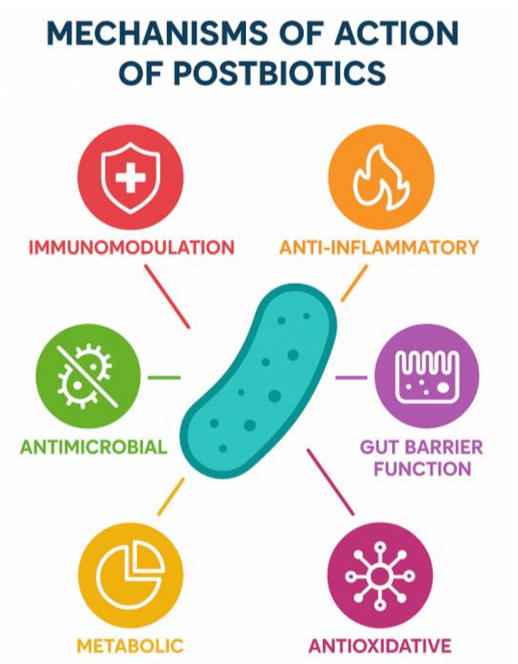

Fig. 3: Different mechanisms of action of postbiotics

Immunomodulation

Postbiotics, particularly SCFAs like butyrate and propionate, are pivotal in modulating the immune system. Butyrate promotes the differentiation of regulatory T cells (Tregs) in the gut, while propionate facilitates the development of peripheral Tregs [58]. These SCFAs exert their effects by binding to G-protein-coupled receptors (GPCRs) such as GPR43 and GPR109A, leading to the inhibition of histone deacetylase (HDAC) activity and subsequent suppression of pro-inflammatory cytokines like Tumor necrosis factor (TNF-α)[59].

Additionally, components derived from probiotic cultures, such as supernatants and cell wall fragments from *Bifidobacterium breve* and *Bacillus coagulans*, have been shown to enhance dendritic cell maturation, increase Interleukin 10(IL-10) production, and decrease TNF-α release. Lipoteichoic acid and peptidoglycan, constituents of microbial cells, activate immunological receptors, thereby modulating cytokine production [60]. Furthermore, postbiotics influence mucosal immunity by enhancing the production of secretory IgA, contributing to a balanced immune response [61].

Anti-inflammatory Effects

Postbiotics exhibit significant anti-inflammatory properties by inhibiting various pro-inflammatory signaling pathways. For instance, heat-treated *Bifidobacterium longum* CECT-7347 has demonstrated efficacy in reducing gastrointestinal disturbances and acute inflammatory responses, while also activating immunological pathways associated with specific immune responses.[40] Moreover, SCFAs like butyrate suppress the activation of nuclear factor κB (NF-κB) and reduce the production of pro-inflammatory cytokines, thereby mitigating inflammation [40]. However, it is essential to note that prolonged anti-inflammatory effects may increase the risk of infectious diseases, highlighting the need for balanced immune system modulation [62].

Antimicrobial activity

Postbiotics possess antimicrobial properties by producing metabolites such as peptides, bacteriocins, organic acids, and volatile substances. These compounds inhibit the proliferation of harmful bacteria and mitigate food spoilage. The antibacterial efficacy of postbiotics is influenced by factors such as the target bacterium type, the specific probiotic source, and the concentration of postbiotics used [63].

In vitro studies have demonstrated that supernatants from *Bifidobacterium* and *Lactobacillus* cultures exhibit antibacterial activity, preventing the adhesion of pathogenic bacteria to intestinal cells. Additionally, postbiotics can modulate gene expression in the host, enhancing the expression of resistance genes and strengthening the intestinal barrier [64].

Gut Barrier Function

Postbiotics contribute to gut health by reinforcing the epithelial barrier and reducing inflammation. SCFAs, particularly butyrate, enhance intestinal barrier function by upregulating the expression of tight junction proteins such as claudin-1, occludin, and ZO-1. Butyrate also stimulates goblet cells to secrete mucin, especially MUC2, which prevents pathogenic bacteria from damaging enterocytes [65].

Furthermore, butyrate activates hypoxia-inducible factor (HIF) in the hypoxic regions of the colon, promoting intestinal epithelial barrier function, antimicrobial defense, and mucus production. These mechanisms collectively enhance the gut's mechanical barrier, reducing intestinal permeability and improving overall gut health [66].

Metabolic and Antioxidative Effects

Postbiotics offer physiological and nutritional advantages through their metabolic and antioxidative activities. They encompass non-viable microorganisms, subcellular components, and metabolic byproducts like SCFAs, vitamins, and enzymes. Postbiotics have been observed to demonstrate anti-obesity and antidiabetic effects by elevating energy expenditure, reducing adipocyte formation, and regulating lipid and carbohydrate metabolism[67].

In terms of antioxidative activity, postbiotics contain enzymes such as (SOD), catalase (CAT), and glutathione peroxidase (GPx), which mitigate the detrimental impacts of reactive oxygen species (ROS). These enzymes protect cells from oxidative stress, contributing to cellular health and reducing the risk of chronic diseases [68].

Different Applications of Postbiotics

Postbiotics exhibit a broad spectrum of biological activities that contribute to human health, though many of their mechanisms and effects remain under active investigation.

Applications in the Food Industry

Fermentation is a primary avenue for postbiotic production, with *Lactobacillus* and *Bifidobacterium* species frequently utilized as producer strains [40]. In the dairy industry, exopolysaccharides from starter cultures are especially valuable, enhancing rheological properties and reducing moisture content in fermented products [69]. Postbiotics from *Lactobacillus plantarum* also act as natural bio-preservatives, notably extending the shelf life of soy-based foods [70].

A commercially approved example is MicroGARD, a postbiotic derived from *Propionibacterium freudenreichii* subsp. *Shermanii* is used widely in dairy and food preservation. Fermentation-induced enrichment of vitamin B content and reduction of toxic compounds further highlight the potential of postbiotics in food applications [40].

Application in Functional Foods

Postbiotics are integral to functional food (FF) development, enhancing nutritional value and health benefits. Postbiotic-enriched foods, such as cell-free fractions of fermented milk, have shown protective effects against Salmonella infection in murine models [71]. Formulations incorporating *B. breve* and *Streptococcus thermophilus* postbiotics in infant milk substitutes have been linked to reduced rates of food intolerances and respiratory allergies, with minimal adverse effects [72].

Pharmaceutical Applications

Although many postbiotic products are still in preclinical or experimental stages, their promise in pharmaceutical applications is growing. For example, biosurfactants from *Lactobacillus gasseri* exhibit anti-biofilm activity against Methicillin-Resistant *Staphylococcus aureus* (MRSA), offering a potential therapeutic avenue[8]. Owing to their pharmacological stability and efficacy, postbiotics are being considered for integration into pharmaceutical formulations [39].

Biomedical Applications

Postbiotics have shown promising immunomodulatory and antimicrobial effects in various biomedical contexts. For instance, heat-killed *Lactobacillus paracasei* enhanced vaccine-induced antibody production and NK-cell activity in older people [73]. In pediatric populations, postbiotics offer new strategies for managing infectious diseases, food allergies, and even graft-versus-host disease through gut microbiome modulation [36,58]. A combination of postbiotic butyrate and active vitamin D may prove beneficial in treating infectious or autoimmune colitis [74]. Their role in immune regulation is further emphasized by findings that postbiotic metabolites influence CD4+

T-cell differentiation, with implications for allergic rhinitis[٧٥] . Additionally, their ability to reduce intestinal uropathogenic reservoirs and inhibit pathogen growth supports their potential to manage urinary tract infections [76]. Several postbiotic molecules also promise to address obesity, coronary artery disease, and oxidative stress by reducing inflammation and pathogen adherence in the gut [77].

Applications in Human Health

Skin Health

The skin microbiome is key in maintaining barrier integrity and preventing pathogenic colonization. Alterations in its composition are associated with conditions such as acne, eczema, and psoriasis [78,79]. Recent studies suggest modulating skin microbiota can improve disease outcomes[79]. A probiotic mix of *Bifidobacterium lactis*, *Lacticaseibacillus rhamnosus*, and *Bifidobacterium longum* enhanced psoriasis treatment outcomes when combined with topical steroids [80]. Postbiotic preparations from *Lactococcus chungangensis* promoted wound healing in diabetic mice by stimulating cytokine and growth factor expression, facilitated by compounds like palmitic and palmitoleic acids [81]. Similarly, stearic and linoleic acids present in these preparations contribute to tissue regeneration [82]. In atopic dermatitis, topical application of *Vitreoscilla filiformis* postbiotics restored the skin barrier and rebalanced the skin microbiota [83,84].

Oral health

Oral dysbiosis is linked to dental caries, gingivitis, and periodontitis [85–87]. Diet-induced pH changes in the oral cavity promote the growth of acidogenic bacteria like Streptococcus mutans, which demineralize teeth and further perpetuate dysbiosis[85]. Biotic interventions, including probiotics and postbiotics, are being explored to rebalance the oral microbiome. For instance, *Lactococcus lactis* disrupted pathogenic biofilms and reduced harmful bacterial abundance. Its bacteriocin, Nisin, has demonstrated antimicrobial activity against key oral pathogens, indicating its potential for postbiotic oral health applications[87].

Vaginal Health

The vaginal microbiome, dominated by lactic acid bacteria, maintains a protective acidic environment that inhibits pathogens such as *Gardnerella vaginalis* and *Candida albicans* [86] *Lacticaseibacillus rhamnosus* AD3, originating from the vaginal tract, produces beneficial metabolites that help restore healthy flora and combat infections [88] Postbiotic gels containing lactic and acetic acids have shown therapeutic efficacy comparable to antibiotics [86,89,90] Disruptions in vaginal microbiota composition are linked to higher preterm labor risks, especially with reduced *Lactobacillus* populations and increased presence of *Atopobium vaginae* and *Gardnerella vaginalis* [86,91] Notably, *Lactobacillus crispatus* protects preterm birth, partly due to its D-lactate production and immunomodulatory properties[٩٢] . However, further research is needed to optimize delivery methods and assess safety, especially for pregnant populations.

Metabolic Modulation and Anti-Atherosclerotic Properties

Postbiotics modulate lipid metabolism, contributing to cardiovascular health. Propionate exerts cholesterol-lowering effects similar to statins or nutraceuticals like curcumin and K-monacolin. Kefiran conjugates have demonstrated anti-atherogenic activities by preventing cholesterol buildup in macrophages and reducing systemic lipid levels while exerting anti-inflammatory effects. In obese mouse models, *Lactobacillus*-derived BLs reduce triglycerides and LDL cholesterol while increasing HDL levels [93]. These effects are mediated through peroxisome proliferator-activated receptors (PPARs), also therapeutic targets of fibrate drugs [93].

Detoxification and Wound Healing

Postbiotics contribute to detoxification by activating autophagy pathways. Bacterial peptidoglycan stimulates autophagy via the NOD1 receptor [94], and *L. fermentum* postbiotics induce autophagy in HepG2 hepatic cells, offering protection against hepatotoxic insults. Urolithin A, a microbial metabolite, modulates mitophagy and may prevent or delay age-related muscle decline. Interestingly, *L. reuteri* sonication-derived BLs increase oxytocin-producing cells in the hypothalamus and raise systemic oxytocin levels, enhancing wound healing capacity[95]. Animal and human studies have confirmed these interventions' efficacy and safety [95].

Limitations and Challenges

Despite their promise, postbiotics may exert weaker effects on gut metabolism and gene regulation compared to live probiotics. For example, *B. breve* M-16V live cultures demonstrated superior immunomodulation to their inactivated counterparts, especially in suppressing spleen cell pro-inflammatory cytokines[96].

The efficacy of postbiotics also depends on the inactivation method used. Techniques such as air drying, freeze drying, and spray drying significantly influence the viability and bioactivity of derived postbiotics. Traditional thermal methods (e.g., pasteurization, Tyndallization) may alter products' nutritional, sensory, and flavor profiles, necessitating a balance between microbial safety and functional preservation. Novel inactivation approaches such as electric fields, ultrasonication, high pressure, ionizing radiation, pulsed light, and plasma may offer safer, more stable outcomes while retaining functional properties [97].

Moreover, the accurate quantification and characterization of postbiotic components remain critical. Techniques like flow cytometry are emerging as alternatives to traditional plate counting, improving quality control and product standardization. However, clinical use is hampered by inconsistent recommendations. A recent study found that postbiotic use was often guided by anecdotal experiences of patients or pharmacists rather than standardized clinical evidence. In some cases, such as supplementation with inactivated *L. acidophilus* and micronutrients, adverse effects, including dehydration, abdominal distension, and vomiting, have been reported[9].

Conclusion and Future Perspectives

Postbiotics, non-viable microbial cells, structural components, and metabolic byproducts, have gained increasing recognition for their wide-ranging health benefits. These include immunomodulatory, anticancer, anti-obesogenic, antioxidant, and metabolic effects. Unlike probiotics, postbiotics deliver these advantages without the risks associated with live microorganisms, offering greater safety, enhanced shelf life, and ease of storage and transport. Their application spans clinical settings and the food industry, where they serve as both therapeutic agents and functional food ingredients.

While the beneficial effects of postbiotics are well-documented, the precise mechanisms through which they exert these effects remain under active investigation. Further research is required to unravel the complex signaling pathways and molecular interactions involved in immune regulation, inflammation control, and metabolic modulation. A deeper mechanistic understanding will support the design of more effective postbiotic interventions tailored to specific health conditions.

In parallel, developing reliable biomarkers for postbiotics is a critical area of future research. Identifying and quantifying these markers will enable a more accurate assessment of therapeutic efficacy, optimal dosage, and intervention timing. Moreover, it will allow the detection of postbiotic deficiencies associated with particular disease states, paving the way for early diagnosis and intervention strategies.

Advanced delivery systems are also needed to enhance the functional impact of postbiotics. Many postbiotic compounds face degradation in the gastrointestinal tract before reaching their intended site of action. Innovations such as microencapsulation, bioengineered carriers, and simulation models of the human gut are expected to play a pivotal role in improving bioavailability and targeted delivery.

Postbiotics also present opportunities for managing infectious diseases, particularly those involving immune dysregulation. Their potential as adjunct therapies for viral infections, including SARS-CoV-2, is increasingly being explored. This includes their role in modulating immune responses, mitigating inflammation, and managing long COVID and other post-viral syndromes, where immune and microbial imbalances persist after the acute phase of infection.

Further progress in the field will depend on robust clinical validation. Large-scale, randomized clinical trials are necessary to confirm the efficacy and safety of postbiotics in diverse populations and health conditions. Additionally, establishing transparent and standardized regulatory frameworks will be essential to support the integration of postbiotics into both pharmaceutical products and functional food markets, ensuring consumer safety and consistent product quality.

Another promising direction is the integration of postbiotic science with broader microbiome research. Metagenomic, metabolomic, and systems biology approaches can offer deeper insights into how postbiotics influence host-microbiota interactions and systemic health. Such interdisciplinary integration will advance the development of precision postbiotics formulations tailored to individual microbiome compositions and personalized health needs.

Each postbiotic compound may serve multiple physiological functions, but the mechanisms behind these multifunctional effects remain to be fully elucidated. Although numerous beneficial outcomes have been observed, the scientific basis for these effects requires further clarification through well-designed experimental studies.

In summary, postbiotics represent a dynamic and promising frontier in microbiome-based health strategies. Their ability to enhance immune responses, support gut and metabolic health, and reduce disease risk without the complications associated with live microbial therapies positions them as valuable tools for future preventative and therapeutic approaches. As our understanding of the human microbiome continues to evolve, postbiotics are poised to become integral components of personalized medicine and next-generation functional nutrition.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this review article. No financial or personal relationships with individuals or organizations have influenced the content or conclusions of this work.

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