Understanding the Basics of Postbiotics

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ABSTRACT

Bioactive substances known as postbiotics are produced by probiotics during metabolic activities. These substances, which positively affect the host's health, include short-chain fatty acids, teichoic acids, extracellular polysaccharides, enzymes, and peptides. In contrast to probiotics, postbiotics are components or byproducts of metabolism rather than living microbes. Postbiotics can either boost or inhibit the immune system, reinforcing the body's defenses against infections and lowering inflammation. By strengthening the intestinal barrier, they lower the membrane permeability and inhibit the movement of toxins and pathogens across it. Some postbiotics have direct antibacterial qualities that prevent the proliferation of pathogenic bacteria and encourage a healthy gut microbiome.

INTRODUCTION

Postbiotics are substances produced by probiotic microbes through their metabolic activities, which can have direct or indirect beneficial effects on the host (Zolkiewicz *et al.*, 2020). Fundamentally, postbiotics are either dead bacteria or their byproducts. As the name suggests, postbiotics represent an advanced alternative to probiotics. Probiotics are live bacteria that, when consumed in moderation, help modify gut microbiota and offer a range of health benefits (Scarpellini *et al.*, 2021). The most commonly used probiotics in therapeutic practice include *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, and *Saccharomyces* yeast. Fermented foods are good sources of these friendly microbes. Maintaining the right balance of gut microbes requires probiotics. However, occasional risks associated with probiotics include the potential for increased virulence and the development of antibiotic resistance (Thorakkattu *et al.*, 2022). Thus, it is crucial to develop alternatives that can potentially modulate the gut microbiota safely and effectively. Probiotic components and bacterial products, sometimes known as postbiotics, present an exciting possibility in this regard.

Types

Postbiotics refer to the complex array of metabolic products released by probiotics in cell-free supernatants, which include enzymes, secreted proteins, short-chain fatty acids, vitamins, peptides, biosurfactants, organic acids, amino acids, etc (Thorakkattu *et al*., 2022). In contrast, paraprobiotics consist of either crude cell extracts, which have a complex chemical composition, or inactivated microbial cells of probiotics. These can be intact or ruptured and contain cell components *viz.* teichoic acids, surface proteins and peptidoglycans. Postbiotics primarily encompass cell-free supernatants, exopolysaccharides, enzymes, fragments of cell walls, short-chain fatty acids (SCFAs), bacterial lysates, and metabolites of the gut microbiota (Zolkiewicz *et al*., 2020).

Supernatants

Cell-free supernatants are composed of the active metabolites produced by bacteria and yeast in their surrounding liquid environment. They can be directly created using cell cultures; the microorganisms are incubated, extracted, and then centrifuged. Different supernatants from various bacterial strains serve distinct purposes. For example, the supernatants of *Lactobacillus acidophilus* possess antioxidant properties, while those of *Lactobacillus casei* exhibit anti-inflammatory effects. Additionally, research has shown that supernatants from *L. casei* and *L. rhamnosus* GG cultures reduce oxidative stress in vivo and prevent the invasion of colon cancer cells (Scarpellini *et al*., 2021). Recent studies have also highlighted the antibacterial activity of supernatants from the genera Bifidobacterium and Lactobacillus. These supernatants have been effective in preventing enteroinvasive *E. coli* strains from invading enterocytes in vitro. This antibacterial effect may result from the reinforcement of cell barriers, increased production of protective genes, and inhibition of pathogen adhesion (Khodaii *et al*., 2017). Moreover, the supernatants of *L. plantarum* have a trophic effect on the structure of intestinal barriers; when administered to lambs at an early age, they enhance the intestinal absorption surface and reduce the number of intestinal infections. Finally, it has been demonstrated that the supernatants from two well-known yeast species, *Saccharomyces cerevisiae* and *Saccharomyces boulardii*, can reverse the impaired intestinal peristalsis caused by stress (West *et al*., 2016).

Exopolysaccharides

Microorganisms produce biopolymers with diverse chemical properties, including a complex variety of exopolysaccharides (EPSs) that can be formed when they are expelled from within the bacterial cell wall. While EPSs are not a new postbiotic, as they are already used in the food industry as water-binding, emulsifying, and stabilizing agents (Singh and Saini, 2017), they may also possess novel immunomodulatory properties through interactions with dendritic cells and macrophages, leading to increased proliferation of T and NK lymphocytes. The EPS derived from *Lactobacillus casei* has been effective in increasing the efficacy of the foot-and-mouth vaccine. Uronic acid, an EPS from *Lactobacillus helveticus* and also found in green tea, has antioxidant potential linked to its iron-binding properties. One notable characteristic of EPSs is their ability to inhibit cholesterol absorption. Additionally, kefiran, an EPS produced by *Lactobacillus kefiranofaciens*, has been shown in animal models to delay the onset of atherosclerosis (Scarpellini *et al*., 2021).

Enzymes

Reactive oxygen species (ROS) can damage lipids, proteins, carbohydrates, and nucleic acids, prompting microorganisms to evolve defense mechanisms. Essential to their survival are antioxidant enzymes like glutathione peroxidase (GPx), peroxide dismutase, catalase, and NADH-oxidase, which originally function within cells as protective strategies. Studies have found that two strains of *Lactobacillus fermentum* exhibit significant antioxidant activity make the font as italics for "in vitro" and contain high levels of GPx (Kullisaar *et al*., 2002). Additionally, *Lactobacillus plantarum* has been shown to have higher GPx concentrations. Remarkably, genetically modified strains of lactobacilli that produce SOD-catalase were able to alleviate Crohn's disease symptoms in a mouse model, compared to their wild-type counterparts (LeBlanc *et al*., 2011).

Short-chain fatty acids (SCFAs)

SCFAs are well-known by-products of the gut microbiota's fermentation of plant polysaccharides. They include fatty acid salts and acids such as acetic, propionic, and butyric acid. For enterocytes, butyrate acts as the primary trophic agent and energy source. Butyrate also possesses immunosuppressive properties, potentially contributing to the development of dietary tolerance by increasing the expression of certain immunosuppressive cytokines like TGF-β, IL-10, and type 1 interferons (Lee *et al*., 2017). In patients with ulcerative colitis, rectal administration of butyrate significantly reduces colon inflammation compared to a placebo. Interestingly, intestinal colonization with *Roseburia intestinalis*, a major butyrate producer, can prevent atherogenesis in a mouse model. This study also noted a significant decrease in endotoxemia, likely due to the closing of the intestinal barrier, along with reduced levels of inflammatory markers in the serum and aorta, such as lipopolysaccharide and TNF-α (Zolkiewicz *et al*., 2020).

Bacterial Lysates

Bacterial lysates (BLs) are produced by chemically and mechanically breaking down Gram-positive and Gram-negative bacteria. Their safe clinical use is well-established in internal medicine, infectious disease medicine, and pediatrics. The gut-lung axis theory, which describes the interaction between the respiratory immune system and the gastrointestinal system, specifically the gut-associated lymphoid tissue (GALT), supports their use in preventing bacterial and viral infections. Mechanistic studies have shown that orally administered lyophilized BLs reach Peyer's patches in the small intestine, where they stimulate dendritic cells and activate T and B lymphocytes. These lymphocytes then travel through the mucous membrane of the respiratory tract, leading to increased IgA production and activation of the innate immune system (Scarpellini *et al*., 2021).

Metabolites

This section explores the wide array of compounds produced by bacteria, including aromatic amino acids, vitamins, and metabolites derived from phenolic compounds. These compounds have potent antioxidant and signaling properties and are highly bioavailable, making their role in the microbe-host interaction crucial. Folate produced by intestinal bacteria can have both beneficial and detrimental effects. On the positive side, folate supplementation lowers the risk of stroke compared to controls. On the negative side, folate supplementation or overproduction may accelerate carcinogenesis in individuals at risk for colorectal cancer or those already diagnosed with the disease, suggesting a U-shaped relationship between health and disease for this postbiotic (Zolkiewicz *et al*., 2020).

Clinically, gut microbes can synthesize vitamin B_{12} and other B complex vitamins from scratch. For example, incorporating *Lactobacillus acidophilus* into a yoghurt matrix has been associated with increased vitamin B_{12} production and, more importantly, a reduced incidence of anaemia (Mohammad *et al*., 2006).

Potential Mechanisms of Postbiotic Action

Postbiotics have diverse effects on the human body, including immune regulation, protection against infections, lipid and cholesterol metabolism, and antioxidant and anticancer properties (Thorakkattu *et al*., 2022).

Immunomodulatory Effects

Within the gut environment, butyrate stimulates the differentiation of regulatory T cells (Tregs), while propionate supports the development of peripheral Tregs. Various components of postbiotics, including supernatants and cell wall fragments extracted from *Bacillus coagulans* cultures, also induce the production of anti-inflammatory cytokines and promote immune responses mediated by T helper type 2 (Th2) cells (Jensen *et al*., 2010).

Functional Foods

Postbiotics-rich formulations have been developed using milk as a medium with *Streptococcus thermophilus* and *Bifidobacterium breve* as the probiotics. The effectiveness of these foods is assessed through randomized clinical trials. For example, in infants with a family history of atopy, postbiotics from *B. breve* and *S. thermophilus* reduced the incidence of symptoms related to food or inhalation allergies during the early months of life. Moreover, these benefits persisted even after discontinuing the supplementation. The administration of these postbiotics was also associated with a milder course of acute diarrhea in infants (Scarpellini *et al*., 2021).

Methods Used to Obtain and Identify Postbiotics

Several methods have been developed using various cell disruption techniques, such as heat and enzymatic treatments, solvent extraction, sonication, and additional extraction and purification steps, including centrifugation, dialysis, freeze-drying, and column purification (Zolkiewicz *et al*., 2020).

Commercially available postbiotics

So, far, there are few postbiotics-rich products, which are available in markets abroad (Liang *et al*., 2023). Some of them are listed below in Table 1.

Table 1. Commercially available postbiotics with probiotic used

Product name	**Corresponding microorganism**
Epicor	*Sac. cerevisiae*
Del-Immune V®	*L. rhamnosus*
LBiome	*L. fermentum* and *L. delbrueckii*
HK L-137	*L. plantarum* L-137
Lyofast LPR A	*L. rhamnosus and L. plantarum*
Hylak® forte	*Ent. faecalis, L. Acidophilus & L. helveticus*
Totipro	*Lactic acid bacteria* (LAB)
Lacidophilin tablets	Bacteriocin-producing LAB
FreshQ®	*L. rhamnosus* and *L. paracasei*
Dairy Safe™	Nisin-producing and nisin-resistant *Lac. lactis* strains

CONCLUSION

Postbiotics is an emerging area of research and application with great potential for improving the health of mankind through various mechanisms. Due to their ability to enhance health outcomes and reduce the need for antibiotics, postbiotics are becoming increasingly valuable in modern industry and healthcare. Further, they are more stable than probiotics and thus can be effectively used in the food industry for developing health foods.

REFERENCES

Jensen, G. S., Benson, K. F., Carter, S. G., & Endres, J. R. (2010). GanedenBC 30™ cell wall and metabolites: anti-inflammatory and immune modulating effects in vitro. *BMC immunology*, *11*, 1-14.

Khodaii, Z., Ghaderian, S. M. H., & Natanzi, M. M. (2017). Probiotic bacteria and their supernatants protect enterocyte cell lines from enteroinvasive Escherichia coli (EIEC) invasion. *International journal of molecular and cellular medicine*, *6*(3), 183.

Kullisaar, T., Zilmer, M., Mikelsaar, M., Vihalemm, T., Annuk, H., Kairane, C., & Kilk, A. (2002). Two antioxidative lactobacilli strains as promising probiotics. *International journal of food microbiology*, *72*(3), 215-224.

LeBlanc, J. G., del Carmen, S., Miyoshi, A., Azevedo, V., Sesma, F., Langella, P., ... & de LeBlanc, A. D. M. (2011). Use of superoxide dismutase and catalase producing lactic acid bacteria in TNBS induced Crohn's disease in mice. *Journal of Biotechnology*, *151*(3), 287-293.

Lee, C., Kim, B. G., Kim, J. H., Chun, J., Im, J. P., & Kim, J. S. (2017). Sodium butyrate inhibits the NF-kappa B signaling pathway and histone deacetylation, and attenuates experimental colitis in an IL-10 independent manner. *International immunopharmacology*, *51*, 47-56.

Liang, Bing, and Dongming Xing. "The current and future perspectives of postbiotics." *Probiotics and Antimicrobial Proteins* 15.6 (2023): 1626-1643.

Mohammad, M. A., Molloy, A., Scott, J., & Hussein, L. (2006). Plasma cobalamin and folate and their metabolic markers methylmalonic acid and total homocysteine among Egyptian children before and after nutritional supplementation with the probiotic bacteria Lactobacillus acidophilus in yoghurt matrix. *International journal of food sciences and nutrition*, *57*(7-8), 470-480.

Scarpellini, E., Rinninella, E., Basilico, M., Colomier, E., Rasetti, C., Larussa, T., ... & Abenavoli, L. (2021). From pre-and probiotics to post-biotics: a narrative review. *International journal of environmental research and public health*, *19*(1), 37.

Singh, P., & Saini, P. (2017). Food and health potentials of exopolysaccharides derived from Lactobacilli. *Microbiol. Res. J. Int*, *22*, 1-14.

Thorakkattu, P., Khanashyam, A. C., Shah, K., Babu, K. S., Mundanat, A. S., Deliephan, A., ... & Nirmal, N. P. (2022). Postbiotics: current trends in food and pharmaceutical industry. *Foods*, *11*(19), 3094.

West, C., Stanisz, A. M., Wong, A., & Kunze, W. A. (2016). Effects of Saccharomyces cerevisiae or boulardii yeasts on acute stress induced intestinal dysmotility. *World journal of gastroenterology*, *22*(48), 10532.

Zolkiewicz, J., Marzec, A., Ruszczyński, M., & Feleszko, W. (2020). Postbiotics—a step beyond pre-and probiotics. *Nutrients*, *12*(8), 2189.