

Review on the Current Trends and Future Perspectives of Postbiotics for Developing Healthier Foods

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ABSTRACT

It is a known fact that a number of routes explaining the health benefits of beneficial bacterial cells require vitality. However, more recent terms such as the para probiotic and postbiotic have appeared to indicate that, in addition to live cultures, non-viable microbial cells, microbial fractions, or cell lysates also have the ability to benefit the host by boosting bioactivity. According to current scientific research, postbiotics are potentially safer than their parent live cells as alternative agents. Because of their distinct clinical, technological, and economic properties, they can be used as promising tools in the food and drug industries to achieve therapeutic goals and health benefits. The postbiotic theory, proof of their health benefits, probable signaling pathways involved in their protective mechanisms and their potential use as functional foods are all covered in this review.

Keywords: Postbiotics; Bacteria-derived factors; Functional foods; Health benefits

INTRODUCTION

The processes involved in the health benefits of desirable gut bacterial cells include competitive adhesion to mucosa and epithelium [1]. This also deals with alteration of the gut microbiota, enhancement of epithelial lining barrier function, and in addition to the immune system modulation [1]. It is very necessary to observe these systems that are completely dependent on the survival of microorganisms [2]. It was observed from the recent research that not all processes or clinical benefits require living bacteria, and that health-promoting effects may happen without them. Whole-cell, cell free extracts, pure cell wall, and culture supernatant fractions of *Bifidobacterium bifidum* BGN4 have significant immunoregulatory abilities and each fraction showed a variety of immunological reactivity patterns [3]. The microbial carbohydrates from *Bifidobacterium* and *Lactobacillus* species have shown strong tumor-suppressing abilities [4].

The inactivated non-viable microbial cells named as non-viable probiotics, inactivated probiotics, or ghost probiotics, may be beneficial if consumed in sufficient quantities [5]. In addition to that probiotics have been observed to have health advantages, non-viable microbial cells may be safer than probiotics, mainly because they pose minimal threat of microbial translocation, infection, or

tends to increase in inflammatory reactions. This was observed in the users of few probiotics who have unbalanced or compromised immune systems [6]. Bacterial cells can be inactivated physically (by mechanical disruption, heat treatment, UV irradiation high hydrostatic pressure, freeze-drying, or sonication) and chemically (by acid deactivation) or sometimes by both physical and chemical disruption. The bacteria lose their ability to reproduce and retain the health benefits in their viable form [7].

LITERATURE REVIEW

Classes of postbiotics and their characteristics

The nutrients required for gut bacteria to promote the growth of the microbiota are fully provided by their host [8]. Small molecular weight metabolites are produced from bacteria throughout their life cycle and are critical for self-growth, development, reproduction, enhancing the growth of other beneficial species, cell-to-cell communication, and stress resistance [9]. After bacterial lysis, many of these soluble compounds may be generated by living bacteria or discarded into the environment. This results in additional physiological benefits via changing cellular functions and metabolic pathways.

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Postbiotics have a number of desirable qualities, including transparent chemical structures, secure dosage ranges, and a prolonged shelf life (up to 5 years whether employed as a food or beverage ingredient or as a nutritional supplement) [10]. It was found that postbiotics have advantageous absorption, metabolism, distribution, and excretion capacities [11]. This suggests that postbiotics have a significant potential to connect with numerous organs and tissues in the host, inducing a range of biological reactions. In an *ex vivo* assay that some probiotics can cause a local inflammatory response similar to that caused by *Salmonella* [12]. Furthermore, case reports, clinical trials, and experimental models in patients with major and minor have described theoretical concerns associated with the administration of live probiotic bacteria [13]. Because of this, employing postbiotics may be a practical and risk-free substitute for avoiding the dangers of live probiotic bacteria, with the potential to become a popular treatment method for a range of illnesses [14,15].

Methodologies to identify and obtain postbiotics

The acquisition of postbiotics typically involves cell disruption techniques such as heat [3], enzymatic treatments [16], solvent extraction [17], and sonication [18]. Centrifugation, dialysis, freeze-drying, and column purification were additional extraction and cleanup methods that were employed during the operations [19]. Similar to this, different strains of *Bifidobacterium* species, *Lactobacillus* species, *Lactococcus* species and *Streptococcus* species were centrifuged to extract intracellular content [20].

As a result, *Lactobacillus plantarum* K8 (KCTC10887BP) produced Lipoteichoic Acid (LTA), which was identified using Matrix-assisted Laser Desorption/Ionization Time of Flight (MALDI-TOF) mass spectrometry [17]; and *Lactobacillus casei* YIT9018 polysaccharide-glycopeptide complexes, which were identified and characterised using High Performance Liquid Chromatography (HPLC) and proton nuclear magnetic resonance spectroscopy (1 H-NMR) [17]. Furthermore, metabolites (such as fatty acids, glycerolipids, purines, sphingolipids, and oligosaccharides) in biological samples

have been identified and characterised using chromatography in conjunction with tandem mass spectrometry and Fourier transform ion cyclotron resonance mass spectrometry with direct infusion [21,22]. For instance, Ultra-Performance Liquid Chromatography (UPLC) is highly advised because to its high sensitivity and precision, minimal solvent usage, high efficiency, and high resolution [23]. Recent research has demonstrated that UPLC will be recommended due to its superior capacity for postbiotic separation and identification; this technique was used in the profile identification of compounds present in intracellular content of *Lactobacillus plantarum* [24] and the intracellular protein profile in *Lactobacillus mucosae* (e.g., thioredoxin, phosphoglycerate kinase, cysteine synthase) [25]. Similar to this, antifungal metabolites produced by *L. brevis* P68 have been characterised by mass spectrometry, infrared, carbon-13 and 1 H-NMR, and electro-spray ionization [26]. Additionally, when *L. plantarum* 423 was subjected to acidic conditions (pH 2.5), changes in the protein profile of the intracellular content were found utilising a gel-free nano LC-MS/MS proteomics approach [27]. Similar to this, after being exposed to bile salts, the protein content of *Lactobacillus plantarum* was identified by liquid chromatography-mass spectrometry analysis [28].

Although all of these methods can be utilised to detect, additional research is required to enhance media and cultural contexts as well as analytical tools [29]. Once it has been optimised for the laboratory size, it needs to be scaled up and optimised to produce the highest postbiotic yield. It should be noted that clinical trials are necessary to establish the ideal dosage and administration schedule [30].

Postbiotic bioactivity and effects

Numerous studies have been carried out on the health effects and potential bioactivity of postbiotics, such as cell wall components and intracellular metabolites either as isolated structures or mixtures [31-43]. Table 1 shows a summary of the findings (Table 1).

Table 1: *In vitro* and *in vivo* studies of postbiotics, their effects and bioactivity.

Bacteria	Components	Bioactivity or effect	Reference
<i>L. rhamnosus</i> GG	Cell-free supernatants	Anti-inflammatory	[32]
<i>L. casei</i> ATCC 393	Sonicated-cell suspension	Antiproliferative	[18]
<i>L. amylovorus</i> CP1563	Fragmented cells	Anti-obesogenic	[33]
<i>L. plantarum</i> RG11, RG14, RI11, UL4, TL1 and RS5	Cell free supernatants	Antimicrobial	[34]
<i>Enterococcus lactis</i> IITRHR1 and <i>Lactobacillus acidophilus</i> MTCC447	Intracellular content	Hepatoprotective	[34]
7 <i>Bifidobacterium</i> , 11 <i>Lactobacillus</i> , 6 <i>Lactococcus</i> , and 10 <i>Streptococcus thermophilus</i> strains	Intracellular content	Antioxidant	[20]
<i>L. paracasei</i> B21060	Cell-free supernatants	Anti-inflammatory	[12]
<i>L. plantarum</i> K8 (KCTC10887BP)	Lipoteichoic acids	Immunomodulation	[17]
<i>L. casei</i> subspecies <i>casei</i> SY13 and <i>L. delbrueckii</i> subspecies <i>bulgaricus</i> LJJ	Intracellular content	Antioxidant	[16]
<i>L. fermentum</i> BGHV110	Cell lysate suspension	Hepatoprotective	[35]
<i>Bacillus coagulans</i>	Cell wall components	Immunomodulation and anti-inflammatory effect	[36]
<i>B. longum</i> SPM1207	Sonicated-cell suspension	Hypocholesterolemic	[37]
<i>Bifidobacterium</i> species, <i>L. acidophilus</i> , <i>L. casei</i> , <i>L. delbrueckii</i> subspecies <i>bulgaricus</i> , <i>L. gasseri</i> , <i>L. helveticus</i> , <i>L. reuteri</i> , <i>S. thermophilus</i>	Cell wall components and cytoplasmic extract	Immunomodulation	[38]
<i>L. paracasei</i> B21060	Cell-free supernatants	Immunomodulation	[39]
<i>Faecalibacterium prausnitzii</i> A2-165 (DSM 17677)	Cytosolic fraction	Immunomodulation	[40]

<i>L. acidophilus</i> (ATCC 43121, ATCC 4356, 606), <i>L. brevis</i> ATCC 8287, <i>L. casei</i> (YIT 9029, ATCC 393), <i>L. rhamnosus</i> GG	Intracellular content	Antiproliferative	[41]
<i>Streptococcus salivarius</i> subspecies <i>thermophilus</i> ATCC 19258 and <i>L. delbrueckii</i> species <i>bulgaricus</i> ATCC 11842	Intracellular content	Antioxidant	[42]
<i>L. acidophilus</i> KCTC 3111, <i>L. jonsonnii</i> KCTC 3141, <i>L. acidophilus</i> KCTC 3151, <i>L. brevis</i> KCTC 3498	Intracellular content	Antioxidant	[42]
<i>L. casei</i> YIT 9029, <i>L. fermentum</i> YIT 0159	Lipoteichoic acids	Immunomodulation	[19]

The most prevalent sources of postbiotics are *Lactobacillus* and *Bifidobacterium* strains, however postbiotics from *Streptococcus* and *Faecalibacterium* species have also been documented [43]. Postbiotics have been proven to reduce blood pressure, giving them the ability to act as an antihypertensive. According to study, the gut microbiota affects a number of bodily functions, such as inflammation, pathogen defence, and immune system development [44]. The argument that these positive benefits might be based on chemicals secreted-derived is being supported by increasing evidence, mostly acquired from the analysis of *Lactobacilli* strains, as demonstrated by the recent development of the postbiotic concept [45].

Using *L. reuteri* 17938, mucosal-like dendritic cells stimulated by retinoic acid regulate immunomodulation through their effects on regulatory T-cells by secreting the anti-inflammatory cytokine IL-10. Superoxide Dismutase (SOD), Nicotinamide Adenine Dinucleotide (NADH)-oxidase, and Nicotinamide Adenine Dinucleotide (NADH)-peroxidase are a few examples of intracellular bacterial enzymes that have been shown to have positive health effects (e.g., antioxidant) [46].

DISCUSSION

Potential food applications of postbiotics

In contrast to the use of probiotics, postbiotics are expected to be more stable than the living bacteria from which they are manufactured (Venema). Bacilysin and chlorotetaine are two antimicrobial peptides produced by *Bacillus* species strain CS93 that have been discovered to be water soluble and active over a broad pH range by Phister, O'Sullivan, and McKay (2004). This suggests that a variety of food products may benefit from their use. Additionally, it has been suggested that using certain phytase-producing lactic acid bacteria as bread starters is a good substitute for generating low-phytate whole wheat bread [47]. Previous studies have demonstrated that prolonging the fermentation process and/or lowering the pH during the fermentation of whole wheat dough can lead to advanced phytate hydrolysis. These conditions may have an impact on the sensory qualities of the finished products as well as the microbial production of phytate-degrading enzymes.

Despite the fact that many foods already contain postbiotics or their precursors (such as kombucha, kefir, yoghurt, and pickled vegetables) [48], there are certain postbiotics that have been added to foods rather than being created naturally by the producer strain. For instance, *Lactobacillus plantarum* cell-free supernatant has been investigated as a bio preservative for soybean grains [49]. Nisin, a lantibiotic produced by specific *Lactococcus lactis* subspecies. *Lactis* strains, is the only bacteriocin that is allowed for use as a food preservative. Nisin is found in foods like canned soups, ice for storing fresh fish, baby food, baked goods, mayonnaise, and dairy products, especially cheeses [50]. In light of the aforementioned, it appears that the use of foods as a delivery system for postbiotics is a sector with many opportunities, as well as substantial challenges.

Enhancing animal health is another potential application because postbiotics have been found to affect how quickly hens, broilers, and piglets grow [51]. The broilers fed *Lactobacillus plantarum* postbiotics gained greater overall weight and ultimate body weight than broilers that were fed with a standard diet without postbiotics. In a related study, Loh et al. found that more eggs were laid by the chickens fed with postbiotics supplement. In the future, postbiotics may be employed as microbial-free food supplements, fermented functional foods, and preventive drugs for a range of diseases [52-54].

CONCLUSION

Postbiotics, which have been demonstrated to have favourable effects on the host, are cell-wall components secreted by living bacteria that are released after lysis of bacteria. Anti-inflammatory, anti-proliferative immunomodulatory, antioxidant, anti-obesogenic and anti-hypertensive qualities are induced by postbiotics. Even though the exact mechanism is still unknown, the above qualities show that postbiotics contribute to the improvement of host health. To enable the discovery and characterization of new postbiotics, which could help with the comprehension of signaling pathway alteration, more work is required. A novel study will make it possible to gather thorough information to guarantee the production process stability and effectiveness of postbiotic products. Due to the ease with which uncontrolled environmental factors can alter metabolism and experience unexpected short-term variability, special attention should be paid to the development of uniform and strictly defined culture processes in order to avoid potential variability in the generation of postbiotics. Additionally, to support the health benefits of postbiotic supplementation, well-designed randomised placebo-controlled human/clinical intervention trials and metabolomics studies are required.

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