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A REVIEW OF POSTBIOTICS AS NEW HEALTH PROMOTERS

Mircea-Cosmin PRISTAVU[1], Camelia DIGUȚĂ[1], Wahauwouélé Hermann COULIBALY[2], Sandrine A. YOUTE FANCHE[3], Getuța DOPCEA[1], Florentina MATEI[1]

[1]University of Agronomic Sciences and Veterinary Medicine of Bucharest, 59 Marasti Blvd, District 1, Bucharest, Romania
[2]Biotechnology and Food Microbiology Laboratory, Food Science and Technology, Formation and Research Unit, University Nangui Abrogoua, 02 BP 801 Abidjan 02, Côte d'Ivoire
[3]University of Yaoundé I, Faculty of Sciences, Department of Microbiology, PO Box 812 Yaounde, Cameroon

Corresponding author email: camifilo@yahoo.com

Abstract

For a long time, probiotics have been widely used as safe microorganisms that can confers a health benefit effects on the host, directly or indirectly. Recently, postbiotics have gained interest as new health promoters. Postbiotics have recently been defined as complex mixture of functional bioactive compounds secreted by probiotics during a fermentation process (such as biosurfactants, proteins, short chain fatty acids, organic acids, bacteriocins, vitamins etc.). According to current data, postbiotics have advantages over live probiotics with regard to: ease extraction, standardization, and storage, availability for industrial-scale-up, specific mechanism of action, impossible to transfer and acquire antibiotic resistance genes and their interaction with the cellular receptors to trigger the targeted responses. However, several aspects related to postbiotics have not been fully elucidated. Here, we provided a critical review of the postbiotic definition, mechanisms of action, underlying their beneficial effects, as well as current trends for applications in foods and pharmaceuticals.

Key words: *probiotics, postbiotics, health benefits, trends.*

INTRODUCTION

In recent years, a trendy concept is "postbiotics" as new health promoters which can mimic the probiotic properties, which demonstrates a growing scientific interest in this topic. However, several aspects related to postbiotics have not been fully elucidated. Here, we provided a critical review of the postbiotic terminology, mechanisms of action, underlying their beneficial effects, as well as current trends for applications in foods and pharmaceuticals. For this reason, a search was performed to identify the most relevant research articles/reviews, available in databases, like Web of Science, PubMed, Google Scholar using different postbiotic terms (such as "paraprobiotics", "inactivated cells", "bacterial lysates" and respectively different probiotic metabolites, cell-free supernatants), without limitation up to 2022.

Postbiotic versus probiotic

Probiotics are defined as "living micro-organisms which, when administered in adequate quantities, confer a health benefit to the host" (WHO/FAO, 2002: Hill et al., 2014). Consumers can purchase their probiotics from dairy products (cheese, yogurt, kefir, etc.), non-dairy products (fermented beverages, sauces, cereals, pickles, Kombucha etc.), as well as pharmaceuticals (in the form of tablets, capsules) used as food supplements (Rivera-Espinoza & Gallardo-Navarro, 2010; Zielinska & Kolożyn-Krajewska, 2018; Diguță et al., 2020). Lactic acid bacterial strains belonging to the genera *Lactobacillus* and *Bifidobacterium* are the most studied and known probiotics. Also, several strains of genera *Enterococcus, Pediococcus, Streptococcus*, *Bacillus* and some yeast (*Saccharomyces boulardii*, *S. cerevisiae*) are reported as probiotic strains (reviewd by Hanson et al., 2016; Górska et al., 2019; Jakubczyk et al., 2020; López-Moreno et al., 2020; Diguță et al., 2020; Yeşilyurt et al., 2021). The beneficial health effects of various types of probiotics have been reported extensively, such as the control of inflammatory bowel diseases (Jakubczyk et al., 2020), modulating the gut microbiota (López-Moreno et al., 2020), prevention of urogenital infections (Hanson et al., 2016), immunomodulating functions (Yeşilyurt et al., 2021), control of serum cholesterol (Ooi et al., 2010) and prevent and therapy certain types of cancer (Górska et al., 2019).

However, the WHO and FAO have warned that probiotics can have some unwanted side effects on safety and technology due to the use of live microbial cells. Numerous clinical studies have reported that the administration of probiotics has led to ambiguous beneficial effects not necessarily due to their viability, but perhaps as a result of the bioactive compounds released by probiotics. However, various studies have shown that survival of an administered probiotic can be affected by various factors in the gastrointestinal tract, and low concentrations of biologically active compounds biosynthesized by probiotics found at specific target sites have been shown to be ineffective *in vivo* (Reid et al., 2011; Shenderov, 2013). The results of studies have also shown that the use of probiotic strains (*Lactobacillus, Bifidobacterium, S. cerevisiae*) has led to safety issues such as horizontal transfer of virulence or antibiotic resistance genes among other intestinal pathogens, the ability to cause opportunistic infections and to stimulate inflammatory responses especially in immunocompromised patients (Mathur & Singh, 2005; Suez et al., 2019). Moreover, from a technological point of view, problems have been reported related to maintaining the viability of probiotics in the final product (up to 10^9 CFU/g or mL), which has proved costly and time consuming, being influenced by many intrinsic and extrinsic factors that related to: 1) the fermentation conditions (optimization of the culture media, temperature, pH, development period); 2) the composition of the food matrix (concentration of carbohydrates, proteins and fats, water activity, presence of preservatives, final acidity, packaging materials); 3) preservation techniques (spray-drying, freeze-drying); 4) storage conditions (oxygen content, temperature, time). In this regard, *in vitro* studies have shown that there is a significant difference between the concentration of live probiotic cells declared and the actual one much lower in the final product, being in fact a mixture of viable and non-viable probiotic cells.

The International Panel of Probiotics Experts clarifies that products that contain ingredients synthesized by probiotics or that contain dead microorganisms are not covered by the definition of probiotics (Hill et al., 2014). According to online consultation of ingredient lists of probiotic products that claim to have beneficial therapeutic effects, they actually include fermentation metabolites obtained through probiotics or inactivated probiotics. Therefore, the industrial applications of metabolites (referred to as postbiotics) and cellular components (referred to as paraprobiotics) derived from probiotics are gaining more and more interest, being considered promising alternative supplements that also have the ability to benefit the host. The benefits of postbiotic versus probiotic use are summarized in Table 1.

Technological process and quantitative control for postbiotics (excluding bacterial lysates) are much faster and more accurate compared to probiotics (Zolkiewicz et al., 2020). In the context of safety, postbiotics avoid problems with the transfer of virulence factors as well as antibiotic resistance genes that may occur with probiotics (Zolkiewicz et al., 2020).

Table 1. The benefits of postbiotics versus probiotics

Criteria	Postbiotics	Probiotics
Technological	High stability, easy to standardize transport and storage	Maintaining viability during the production, transport and storage process is expensive
Safety	No risk of virulence gene transfer and antibiotic resistance	Risk to horizontal transfer of antibiotic resistance and virulence genes to commensal or pathogenic bacteria in the gut
	No risk of translocation from the intestinal lumen to the blood / tissue	Possible risk of bacterial translocation from the intestinal lumen to the blood / tissue especially in vulnerable and immunocompromised patients
Biological	No interference with the beneficial microbiota	Colonization and interference with the host the intestinal microbiota
	Adequate absorption, metabolism and distribution	Biosynthesis of bioactive metabolites takes time

Postbiotics are considered to be an alternative option for therapeutic interventions for a number of allergic disorders, due to their ability to improve the immune system (Imperial & Ibana, 2016).

Postbiotics terminology

Researchers have proposed differently terminology to describe the cellular components and respective metabolites and synthesized and released by probiotics (Figure 1). Most studies reported that postbiotics should provide the host with any physiological benefits, which are sometimes similar to the effects of live probiotics (Malagon-Rojas et al., 2020; Teame et al., 2020). Terms such as "paraprobiotics", "non-viable microbial cells", "phantom probiotics", and "bacterial lysates" have been proposed to indicate the use of inactivated microbial cells or cellular components by heat treatment, enzyme application or ultrasonic processing (de Almada et al., 2016; Barros et al., 2020; Hernandez-Granados & Franco-Robles, 2020; Moradi et al., 2020; Pyclik et al., 2020).

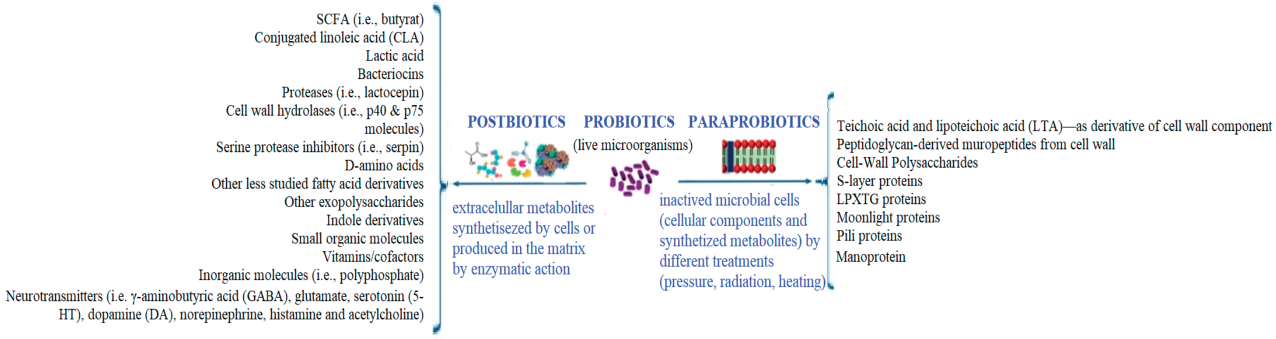

Figure 1. Concepts of probiotic-derived postbiotics (adapted after Siciliano et al., 2021)

An adapted definition of paraprobiotics based on the definition of probiotics with minor modifications and widely accepted by researchers is "non-viable/inactivated/dead microbial cells of probiotics (intact or broken cell components by lysis) or crude cell extracts (with complex chemical composition)", which when administered orally or locally in sufficient quantities determine the benefits to the human or animal consumer (de Almada et al., 2016; Martín & Langella, 2019; Siciliano et al., 2021).

Regarding the use of synthesized probiotic metabolites, the term postbiotic has been proposed. Initially, postbiotics were defined as “soluble products or by-products of metabolic products secreted by probiotics or released after bacterial lysis, capable of conferring beneficial effects on the host directly or indirectly” (de Almada et al., 2016; Aguilar-Toalá et al., 2018; Cuevas-Gonzalez et al., 2020; Zołkiewicz et al., 2020; Siciliano et al., 2021). In addition, postbiotics may be referred to as microbial metabolites and/or cell-free supernatants or extracts. From this perspective, postbiotics obtained from lactic acid bacteria contain numerous metabolites used either as crude extract (or concentrate) or as a semi-purified form.

In its 2021 panel on postbiotics, the International Scientific Association of Probiotics and Prebiotics (ISAPP) proposed a consensus definition that best fits the understanding of the concept of postbiotics, namely “preparations of non-viable microorganisms and/or components that provide health benefits to the host”. Therefore, postbiotics must contain microbial cells or cellular components that have been inactivated with or without metabolites, contributing to the observed health benefits, and to classify a preparation as postbiotic, the microbial composition prior to inactivation must be characterized (Salminen et al., 2021).

In this review we used postbiotic term to indicate all components derived from probiotics with health benefits effects.

Sources, types of postbiotics and their characteristics

In general, lactic acid bacteria (mainly the genera *Lactobacillus, Bifidobacterium*) (Tsilingiri & Rescigno, 2013; Moradi et al., 2020; Pyclik et al., 2020) but also bacterial species of *Bacillus* (Jensen et al., 2010; Majeed et al., 2020) or yeasts *Saccharomyces* (Mei Zhi & Shao-Quan, 2022) with proven probiotic properties, are used to obtain postbiotics. Probiotic bacteria produce metabolites during their development, playing a key role in regulating the development of their own cells, encouraging the growth of other beneficial organisms, providing protection against stressors (Hibbing et al. 2010). In general, postbiotics can be differentiated either by their

composition, i.e. by lipids (i.e., butyrate, propionate), proteins (i.e., p40 molecule), vitamins (i.e., B vitamins), carbohydrates (i.e., teichoic acids, galactose-rich polysaccharides), and complex molecules such as lipoteic acids, peptidoglycan-derived muropeptides etc. (Tsilingiri & Rescigno, 2013). Bacteriocins are the most studied antimicrobial agents against various pathogens, i.e., *Listeria* sp., *Salmonella* sp. And *Escherichia coli* (Hartmann et al., 2011; O'Bryan et al., 2018; Fernandes & Jobby, 2022). Postbiotics have several important properties, such as clear chemical structures, easy production, ideal dose, safe profile and long shelf-life, which are highly sought after (Shigwedha et al., 2014). In addition, it has been shown that postbiotics can have equivalent health beneficial effects as that of probiotics, such as antimicrobial, immunomodulatory, anti-inflammatory, hypocholesterolemic, hepatoprotective, anti-proliferative, antioxidant properties (Figure 3) (Sawada et al., 1990; Shin et al., 2010; Tsilingiri & Rescigno, 2013; Nakamura et al., 2016; De Marco et al., 2018; Aguilar-Toalá et al., 2018; Chuah et al., 2019). Bacteriocins, organic acids, short-chain fatty acids, enzymes, alcohols and other low molecular weight metabolites are the main metabolites responsible for the antimicrobial action of lactic acid bacteria. Cell-derived ingredients generally exhibit immunomodulation and antiproliferative activities (Hernandez-Granados & Franco-Robles, 2020).
Therefore, the use of postbiotics may be a valid and safer alternative to avoid the risks associated with live probiotic bacteria, which gives postbiotics some practical applicability and functionality to become an important strategy for treating many diseases (Tsilingiri & Rescigno, 2013).

Methods used to obtain postbiotics

At the laboratory and industrial level, there are several important conditions that need to be considered in order to optimize the production of postbiotics (regardless of the type of preparation - inactivated cells or metabolites), such as: 1) microorganisms used; 2) culture media; 3) extraction step; 4) preservation methods and 5) method of application (Figure 2).
Lactic bacteria are grown mainly in De Man, Rogosa and Sharpe (MRS) broth medium.

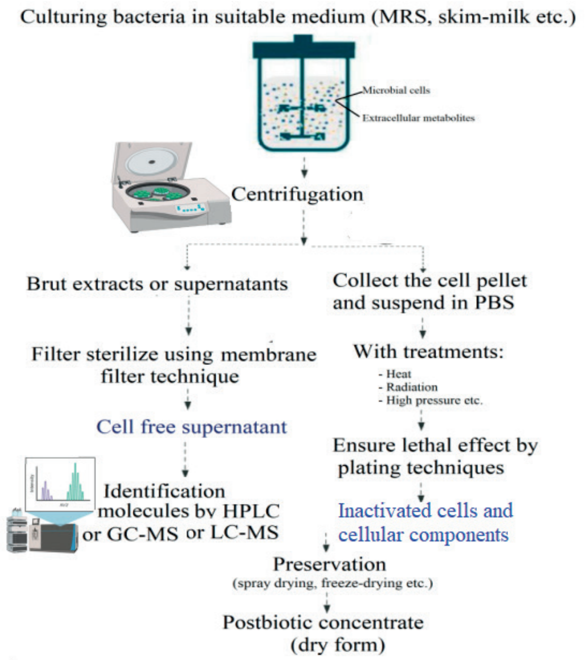

Figure 2. Workflow of production and characterization of the probiotic-derived postbiotics (adapted after Moradi et al., 2021; Nataraj et al., 2020)

The brown to yellow-brown color of postbiotics prepared with MRS broth may limit the use of the postbiotic mixture in some foods or pharmaceutical products. Alternatively, the production of postbiotics by lactic acid bacteria and on fermentation media using renewable sources (i.e. cheese whey) would be an interesting choice (Amiri et al., 2021). After the fermentation period, the microbial cultures are subjected to additional extraction processes, such as centrifugation, sterile filtration (with 0.22 or 0.45 μm pore size filters), column purification or dialysis in order to separate biosynthesized metabolites from bacterial cells (Sawada et al., 1990; Vidal et al., 2002; Matsuguchi et al., 2003; Amaretti et al., 2013, Nataraj et al., 2020; Moradi et al., 2021).
In order to obtain a postbiotic mixture, in most cases, the researchers prepared cell free supernatants, with or without cell lysis, which may contain 1) metabolites synthesized in the environment during bacterial growth or 2) structural substances produced by lactic acid bacteria. In some studies, after propagation, bacterial cells have undergone cell lysis treatments, which include heat (Lee et al., 2002), extraction with solvent (Kim et al., 2011), enzymatic treatments (Li et al., 2012), sonication (Matsuguchi et al., 2003; Choi et al., 2006; Kim et al., 2006; Shin et al., 2010;

Amaretti et al., 2013; Tiptiri-Kourpeti et al., 2016). These treatments supplemented with some additional intracellular metabolites and cell wall-derived ingredients into the postbiotic mixture, provide new functionality to the obtained postbiotics.

Postbiotics can be stored in both liquid and dry form (by spray-drying or freeze-drying).

It is therefore necessary to analyze the technological and industrial processes that can be used to expand the production of postbiotics for functional purposes at cost-effective levels. Dunand et al. (2019) reported an increasing protective effect of the postbiotics of fermented milk produced at laboratory and industrially scale against *Salmonella enterica* serovar *typhimurium* infection in mice, after 20 days of exposure. Puccetti et al. (2018) developed gastro-resistant spray-dried microparticles loaded with postbiotics (indole-3-aldehyde) for localized delivery in the small intestine.

Even if the production of postbiotics is possible on a laboratory scale or in small-scale production, the constraints could arise at the industrial level due to the changing conditions of processing or scaling which may lead to structural changes and variations in the physiological function of postbiotics.

Identification and characterization of postbiotics

The different analytical approaches have been proposed for the identification and characterization (qualitative and/or quantitative) of postbiotics, the exploration of a wide range of microbial complexes and molecules (de Almada et al., 2016; Aguilar-Toalá et al., 2018; Shenderov et al., 2020).

Consequently, matrix-assisted laser desorption/ionization mass spectrometry (MALDI-TOF) was used to identify lipoteichoic acids produced by *L. plantarum* K8 (KCTC10887BP) (Kim et al., 2011) and HPLC and proton spectroscopy. Polysaccharide-glycopeptide complexes of *Lactobacillus casei* YIT9018 were identified and characterized by nuclear magnetic resonance imaging (1 H NMR) (Sawada et al., 1990). In addition, chromatography coupled with tandem mass spectrometry and Fourier transform ion cyclotron resonance mass spectrometry were used to identify and characterize metabolites such as fatty acids, sphingolipids, purines, glycerolipids, oligosaccharides. However, ultra-performance liquid chromatography (UPLC) are highly preferred to identify the profile of compounds, because of low usage of solvent, high separation, high sensitivity and precision capacity (Choi et al., 2006; Kim et al., 2011; Dong & Guillarme, 2013). It is important to note that clinical trials are needed to define the appropriate dose and the optimal frequency of administration (Patel & Denning, 2013). In a study by Chamberlain et al. (2019), 97 metabolites and 71 lipids of the probiotics *Lactobacillus acidophilus* ATCC 4357 and *Lactobacillus gasseri* ATCC 33323 were identified using ultra-HPLC high-resolution mass spectrometry (MS). On the other hand, Moradi et al. (2019) identified, by gas chromatography coupled with mass spectrometry (GC-MS), almost fifty metabolites released in an average of three *Lactobacillus* strains.

In the future, the metabolic assessment profile is intended to provide new techniques for more accurate and complex identification of postbiotics, which may be helpful in explaining possible modulation of signaling pathways associated with biological activities.

Postbiotic bioactivity

Most *in vitro* and *in vivo* studies focus on postbiotics (metabolites and cell derived ingredients) obtained from different strains of *Lactobacillus* and *Bifidobacterium* and, to a lesser extent, *Saccharomyces* species. Despite the fact that the mechanisms involved in most postbiotic activities are not yet clearly defined, scientific evidence suggests that postbiotics have directly and indirectly a wide range of beneficial properties to health, such as antioxidant, antimicrobial and immunomodulatory activities (Shenderov, 2013; de Almada et al., 2016; Aguilar-Toalá et al., 2018). The main results obtained are listed in Table 2.

Preclinical studies should be performed to select of the best postbiotic candidate. In recent years, animal studies, in some conditions, have shown that postbiotics have health benefits. Guo et al. (2013) found that selenium exopolysaccharide isolated from *Lactococcus lactis* subsp. *lactis* exhibited a stronger antioxidant activity than non-selenated polysaccharides, which was identified by measuring the antioxidant enzymes, while decreasing lipid peroxidation levels in the serum and liver of mice. Postbiotics have been reported to have an impact on behavior in animal models. For example, the administration of heat-killed fermentate (ADR-159) obtained from *Lactobacillus fermentum* and *Lactobacillus delbrueckii* had an impact on the both microbiota and composition in mice model (Warda et al., 2019). The sociability of animals fed with ADR-159 was measured by a three-chamber social test, in which treated animals showed a higher preference in the room containing a new (unknown) mouse with the variant in which he is in a room with a familiar mouse, based on the paradigm of the preference of social novelty described by Warda et al. (2019).

Table 2. *In vitro* and *in vivo studies* of probiotic - derived postbiotics and their effects

Lactic acid bacteria	Postbiotic component	*In vitro* and *in vivo* studies	Effect	Reference
3 *Lactobacillus acidophilus*, 1 *L. brevis*, 2 *L. casei*, 1 *L. rhamnosus* GG	Intracellular content	HeLa, MCF7, U-87, Hep G2, U2OS, PANC-1, HT-29, WiDr, DLD-1 and CX-1 cells	Antiproliferative	Choi et al., 2006
1 *L. acidophilus*, 1 *L. jonsonnii*, 1 *L. acidophilus*, 1 *L. brevis*	Intracellular content	*In vitro*	Antioxidants	Kim et al., 2006
7 *Bifidobacterium*, 11 *Lactobacillus*, 6 *Lactococcus,* and 10 *S. thermophilus*	Intracellular content	*In vitro*	Antioxidants	Amaretti et al., 2013
L. johnsonni La1, *L. acidophilus* La10	Lipoteic acids	HT29 human cell line	Immunomodulation	Vidal et al., 2002
L. casei YIT 9029, *L. fermentum* YIT 0159	Lipoteic acids	RAW macrophages 264.7	Immunomodulation	Matsuguchi et al., 2003
Bifidobacterium longum SPM1207	Sonicated cell suspension	Rats model with high cholesterol	Hypocholesteroloma	Shin et al., 2010
L. amylovorus CP1563	Fragmented cells	Obese mouse models	Antiobezogen	Nakamura et al., 2016
L. casei YIT9018	Polysaccharide -glycopeptide complexes	Models of spontaneous hypertensive mice and renal hypertensive mice	Anti-hypertensive	Sawada et al., 1990
L. casei ATCC 393	Sonicated cell suspension	Murine CT26 and HT29 human colon cancer cell line	Antiproliferative	Tiptiri-Kourpeti et al., 2016
L. fermentum BGHV110	Cell lysate suspension	Human hepatoma HepG2 cells	Hepatoprotective	Dinić et al., 2017
L. rhamnosus GG	Cell-free supernatants	Smooth muscle cells of the human colon	Anti-inflammatory	Cicenia et al., 2016
L. rhamnosus CRL1505	Peptidoglycan	Swiss albino males and females infected with *Strept. pneumoniae* serotype 6B	Increasing the immune response. A decrease in inflammatory tissue damage	Kolling et al., 2015
L. rhamnosus GG	Soluble proteins	Newborn rats infected with *E. coli* K1 C57BL / 6 mice with induced colitis	Beneficial effects on the functioning of the intestinal barrier	Gao et al., 2019
L. plantarum K8, KCTC10887BP	Lipoteic acids	Human monocyte cells THP-1	Immunomodulation	Kim et al., 2011
Lactococcus lactis subsp. *lactis*	Exopolysaccha ride	Immunocompromised mice	Antioxidant and immunomodulatory	Guo et al., 2013
Bacillus coagulans	Cell-free supernatants	Human polymorphonuclear cells	Immunomodulatory and anti-inflammatory	Jensen et al., 2010

In another study, the heat-killed *Lactobacillus helveticus* strain MCC1848 conferred anxiolytic or antidepressant effects in model mice (Maehata et al., 2019). Despite their effectiveness in animal studies, they may not necessarily be transferred to human studies.

Application of postbiotics in the food, feed and pharmaceutical industries

In last years, functional foods supplemented with probiotics, prebiotics and postbiotics have gained a lot of attention from scientists, producers and consumers.

In the case of postbiotics, survival is not the main factor and the proper amount of it can be controlled during production and storage conditions, therefore its applications in a delivery system, such as functional foods and/or pharmaceuticals may require some technical and economic privileges for producers (Barros et al., 2019) (Figure 3).

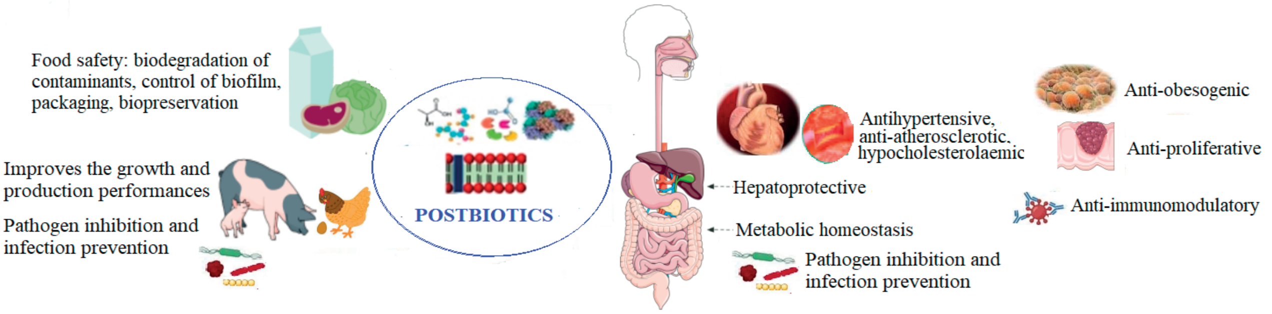

Figure 3. Potential application of probiotic-derived postbiotics. Graphical illustration was created partially using https://smart.servier.com/

On the other hand, postbiotics can be intentionally added to a wide range of foods (fermented and/or unfermented) for various purposes (Chaluvadi et al., 2015). In addition, other research has shown that the postbiotic supernatant derived from *L. plantarum* YML007 may be a potential bio-preservative, which has a positive effect on soybeans and has improved its lifespan by up to 2 months. Post-biotic exopolysaccharides from lactic acid bacteria such as *L. rhamnosus* indicate a key role in the food industry, which can improve the physicochemical and sensory properties of food (Aguilar-Toalá et al., 2018).

Another biological role of postbiotics is the detoxifying function against toxic metabolites, which in recent years have gained much attention from scientists. In most investigations, the main mechanisms of action of various postbiotics are referred to as surface adsorption by cell wall components and/or degradation of toxic substances by various metabolites, such as enzymes. Also, adding postbiotic yeast cell wall extract (0.2%) to food/feed can significantly prevent zearalenone-induced reproductive toxicity of 0.4 mg/L (Wang et al., 2019).

In this regard, a new approach is the use of postbiotics as safe additive in food (Moradi et al., 2020). Moradi et al. (2019) investigated the potential of three different postbiotics *Lactobacillus* spp. in minced meat and whole milk. However, the antimicrobial activity depended on the type of postbiotics and the contact time (Moradi et al., 2019). Another innovative approach is the incorporation of postbiotics into polymeric film. Beristain-Bauza et al. (2016; 2017) investigated *in vitro* the antimicrobial activity of protein films supplemented with cell-free supernatants of *Lactobacillus rhamnosus* or *Lactobacillus sakei* to control some gram-positive and negative bacteria. For the wide application of postbiotics in the human food, feed and pharmaceutical industries, it is required to create a bridge between science knowledge, industry and informing the consumer about their beneficial effects. Commercial products based probiotic-derived postbiotics, are currently available on the market. Pro-Symbioflor® (SymbioPharm GmbH, Herborn, Germany) is an autolysate of cells and cell fragments of *Enterococcus faecalis* (DSM 16440) and *Escherichia coli* (DSM 17252) which help alleviate disturbance of the gastrointestinal function, irritable bowel syndrome, improve the immune system and reduce the incidence of atopic dermatitis (Lau et al., 2012).

Hylak® Forte (Ratiopharm/Merckle GmbH, Germany) is a postbiotic liquid containing active metabolites (e.g., such as short-chain fatty acids, amino acids and vitamins) derived from *Lactobacillus acidophilus* DSM 414, *L. helveticus* DS 4183, *Escherichia coli* DSM 4087 and *Streptococcus faecalis* DSM 4086, used to relieve bacterial imbalance in the gastrointestinal tract and associated symptoms as bloating, diarrhea, and constipation (Omarov et al., 2014; Patil et al., 2019). CytoFlora® (BioRay Inc., Laguna Hills, CA, USA) is a cell wall lysate without microbes from various strains of

Lactobacillus, Bifidobacterium, Streptococcus, used to correct intestinal dysbiosis, promote a balanced immune response, and relieves symptoms in children with autism (Ray et al., 2010). West et al. (2013) reported an improvement of behavior of the children with autism spectrum disorder when received a blend of Del-Immune V® (Pure Research Products, LLC, Boulder, CO, USA) (which contains derived from cell wall fragments from *Lacticasei bacillus rhamnosus*) plus probiotics.

LactoSporin®, a purified extracellular metabolite from fermented broth *Bacillus coagulans* MTCC 5856 has been shown to treat acne vulgaris (Majeeed et al., 2020). The potential mechanism of LactoSporin® as an antimicrobial agent is by lowering the pH, inhibiting the microbial biofilm, and draining ions from the target cells (Majeed et al., 2020). Other skin care products combine postbiotics with plant extracts - a vaginal cream (Marcale Seroyal Genestra) based on fermented *Lactobacillus* (*Lactobacillus acidophilus* (CUL-60) and *Lactobacillus gasseri* (CUL-09) with a plant support *Bulb Allium sativum* Extract (Garlic) and *Rosa damascena* flower oil) used to relieve fungal infections; Payot Crème N°2 Nuage (based on extracts of Boswellia and Jasmine with lysate fermented bifida and alpha-glucan oligosaccharide).

Furthermore, supplementation of *L. plantarum* postbiotics in feed, significantly improves the growth performance of livestock (Loh et al., 2013, 2014; Kareem et al., 2016; Danladi et al., 2022), laying performance (Loh et al. (2013), antioxidant activity in the blood (Izuddin et al., 2020), immune response (Danladi et al., 2022). Currently, much of the research on postbiotics is dedicated not only to the precise identification of their mechanisms of action, but also to the development of new functional food formulations and prophylactic drugs to improve host health (Aguilar-Toalá et al., 2018).

CONCLUSIONS

According to current data, postbiotics are characterized by their specific chemical structure, easy production, ideal dose, safe profile and long shelf-life, thereby facilitating transfer from labo to industrial level and wide commercialization. As discussed in this review, the postbiotics represent an important opportunity for the development of the innovative functional ingredients as new health promoters due its immunomodulatory, antihypertensive, antimicrobial and antioxidative properties. Consequently, postbiotics can be widely used in the future in food, feed and pharmaceutical industries.

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