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Postbiotics- Functional Food Materials

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Review

Postbiotics- Functional Food Materials

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Abstract: Postbiotics are biologically active probiotic microorganisms that have produced non-viable bacterial products in the host. Because postbiotics are created when bacteria feed on prebiotics, eating a diet rich in probiotic and prebiotic foods may aid in ensuring that the gut has an adequate supply of these vital nutrients. Postbiotics are substances found in cell walls and metabolites created by live bacteria that benefit the host. During the anaerobic fermentation of organic nutrients like prebiotics, postbiotics are useful, bioactive molecules that are created in a matrix. Postbiotics are soluble compounds with low molecular weight that are either created after the lysis of microbial cells or secreted by living microflora as byproducts of this metabolic process. In general, the producer strains from bacterial and fungal species such as *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, *Akkermansia muciniphila*, *Saccharomyces boulardii*, *Eubacterium hallii*, *Faecalibacterium*, etc. When handling and selling food items in an industrial setting, postbiotics can be used as functional components in foods, which has a number of advantages, including the potential to be added to some foods that are known to be harmful to probiotic survival. Postbiotic supplements have grown in popularity among customers because of their numerous health advantages, particularly food, cosmetic and health care industry. Classification of postbiotics are depends various factors including type of microorganism, structural composition and physiological functions. This review present a succinct introduction, history and concept of postbiotics, salient feature of postbiotics, classification, production, purification, characterization, biological functions, and applications of postbiotics in food industry.

Keywords: postbiotics; prebiotics; probiotics; metabolites; lactic acid bacteria; fermentation

1. Introduction

Food is a fundamental human need that must be met in order for all aspects of life to continue to exist. The energy is provided by a variety of nutrients; including lipids, carbohydrates, and proteins, as well as by non-nutrient components like fibre, phytochemicals, antioxidants, vitamins, minerals, probiotics, and prebiotics improve human health by modifying the host physiology and global epigenetic imprints (Bhat & Riar, 2019; Ghadimi et al., 2012; Gul et al., 2016; Sánchez et al., 2017). A vast spectrum of health-promoting bioactive components, including prebiotics, phytochemicals, natural antioxidants, bioactive peptides, etc., have been produced as a result of intense innovation in the functional food industry (Fernandes et al., 2019).

Probiotics are described as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" by the Food and Agriculture Organization of the United Nations - World Health Organisation (FAO-WHO). A defined and constrained list of microbial taxa, primarily lactic acid bacteria (LAB) like *Lactobacillus spp*. and *Bifidobacterium spp*., which are classified as generally recognised as safe (GRAS), are present in the majority of probiotic products (O'Toole et al., 2017). Yoghurt may be the food that contains probiotics most frequently, although other fermented (cheese, yoghurt) or non-fermented (cereal, chocolate bars, fruit juices, smoothies) meals can also contain probiotics. Probiotics may have an impact on the gut microbiota by suppressing and inhibiting infections as well as blocking their adherence to tissue and establishment in the gut (Collado et al., 2009; Bermudez-Brito et al., 2012). Probiotics may also help with immune system development, the production of essential nutrients like vitamins, and the reinforcement of intestinal

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barrier integrity by activating genes linked to tight junction signalling (Bermudez-Brito et al., 2012). According to a consensus statement on the subject by the International Scientific Association of Probiotics and Prebiotics, "Prebiotics are a substrate that is specifically utilized by host microorganisms to provide a health advantage". Prebiotics can change the makeup of the microbiota by promoting the growth of particular species, which will benefit the host's health. These prebiotic effects have been linked to a variety of dietary fibres, phenolics and phytochemicals, conjugated linoleic acid, polyunsaturated fatty acids, human milk oligosaccharides (HMOs), and a wide range of oligosaccharides. These effects have a wide range of health effects that have been elegantly described elsewhere (Vyas and Ranganathan, 2012; Gibson et al., 2017). A common definition of a synbiotic is "synergistic mixtures of probiotics and prebiotics that beneficially affect the host by improving the survival and colonization of live beneficial microorganism in the gastrointestinal tract of the host". Synbiotics can alter the makeup of the gut microbiota and microbial metabolite production (Gurry, 2017; Wegh et al., 2019).

Postbiotics is a term that has recently been developed to describe a wide range of bioactive molecules including non-viable/inactivated microbial cells, cell compounds, and any soluble products or metabolic byproducts resulting from microorganisms (probiotics), which either directly or indirectly mediate beneficial biological activity when administered to consumers (Tsilingiri and Rescigno, 2013; Moradi et al., 2020; Geerlings Wegh et al., 2019; Cuevas-Gonzalez, et al., 2020). Postbiotics are defined as "preparation of inanimate microorganisms and/or their components that confers a health benefit to the host" (Salminen et al., 2021). Postbiotics are produced by a variety of bacterial and fungal species, primarily the strains of *Lactobacillus*, *Bifidobacterium*, *Streptococcus, Eubacterium, Faecalibacterium,* and *Saccharomyces*, can be found naturally in a number of fermented foods like yoghurt, sauerkraut, pickled vegetables, and kombucha (Barros et al., 2020; Aguilar-Toalá et al., 2018; Amores et al., 2018). Currently, there are several commercial postbiotics that are primarily used for treating gastrointestinal or immune-related disorders and are available as supplements or as food matrices (Cuevas-González et al., 2020). Postbiotics are composed of bacterial lysates with cell surface proteins, bacterial enzymes, peptides, metabolites and lower organic acids like lactic acid. The microbial metabolites, proteins, lipids, carbohydrates, vitamins, organic acids, cell wall components, or other complex compounds produced in the fermented matrix provide the basis for postbiotic efficacy (Konstantinov et al., 2013; Aguilar-Toalá et al., 2018). In some circumstances, food processing techniques like heat, sonication, irradiation, and high pressure can affect the postbiotic composition (de Almada et al., 2016). These techniques might have varied effects on the microorganisms engaged in fermentation. For instance, heat-inactivated bacteria-derived proteins may denature, whereas radiation may result in nucleic acid alterations. As a result, the entire food production process has an impact on the postbiotic product's composition and, consequently, the host's reaction to the postbiotic products (de Almada et al., 2016; Taverniti and Guglielmetti, 2011; Amaretti et al., 2013; Choi et al., 2006; Kim et al., 2006; Matsuguchi et al. 2003; Sharma et al., 2011; Shin et al., 2010; Sokol et al., 2008; Tiptiri-Kourpeti et al., 2016). On the other hand, a variety of analytical techniques, such as matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry and HPLC have been suggested for postbiotic identification. For instance, polysaccharide-glycopeptide complexes from Lactobacillus casei YIT9018 were discovered and reported using proton nuclear magnetic resonance spectroscopy (Sawada et al., 1990). Tandem mass spectrometry and Fourier transform ion cyclotron resonance mass spectrometry with direct infusion have both been used to identify and characterise metabolites such as fatty acids, glycerolipids, purines, sphingolipids, and oligosaccharides in biological samples (Antunes et al., 2011; Kok et al., 2013). To assess the potential bioactivity and/or health effects of various postbiotics, including intracellular metabolites and cell wall components, either as isolated structures or mixtures, such as extracts or suspensions, several studies demonstrated the effects of postbiotics both in vitro and in vivo (Robles-Vera et al., 2017). Many dairy-based items naturally include postbiotics, such as kefir, kombucha, yoghurt, and pickled vegetables (Chaluvadi et al., 2015). The majority of the producer strains are *Lactobacillus* and *Bifidobacterium* varieties, but they may also contain *Streptococcus, Akkermansia muciniphila, Eubacaterium hallii, Faecalibacterium,* and *Saccharomyces boulardii*. The producer strains can be employed to extract the postbiotics in situ. Milk products contain exopolysaccharides (EPS) made by lactic acid bacteria (LAB), namely *Lactobacillus rhamnosus*, which

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also improves the physicochemical and sensory properties of food-based products (Aguilar-Toalá et al., 2018; Amores et al., 2019).

However, Streptococcus and Faecalibacterium species have also been described as a source of postbiotics (Konstantinov et al., 2013; Tsilingiri & Rescigno, 2013). Postbiotics are typically produced from Lactobacillus and Bifidobacterium strains. It has been established that taking postbiotic supplements lowers blood pressure, giving these substances the ability to treat hypertension (Robles-Vera et al., 2017). According to Klemashevich et al. (2014), intestinal microbiota had an impact on a variety of gastrointestinal tract processes, including inflammation, pathogen defence, and immune system development. The crude culture extract and pure EPS from Lactobacillus helveticus MB2-1 show a potent capacity to scavenge three different kinds of free radicals and chelate ferrous ions (Li et al. ., 2014). This review provides a brief history and explanation of the idea of postbiotics, as well as information on the classification, manufacturing, purification, and characterization of postbiotics as well as their biological activities and potential uses in the food industry.

2. History and Concept of Postbiotics

More than 2000 years ago, Hippocrates is said that "all disease begins in the gut." Today, there is no doubt that the intestinal microbiome plays a critical role in the pathogenesis of a number of systemic autoimmune and inflammatory disorders (Lynch and Pedersen, 2016). The emergence of intestinal flora initiated by the Russian microbiologist Elie Metchnikoff started working with Louis Pasteur at the Pasteur Institute in Paris in the early 1900s, Louis Pasteur (1822–1895) made important advancements in the fields of pasteurization, microbial fermentation, and vaccination. During his lifetime, he was able to develop treatments for several of the deadliest diseases in the world, including rabies, anthrax, tuberculosis, cholera, and smallpox. It's been suggested that if one scientist today alone discovered treatments for cancer, heart disease, diabetes, and Alzheimer's disease, that would be the modern-day equivalent of his accomplishments. **Despite Pasteur's amazing achievements, he also contributed to the germ theory of disease by popularizing the idea that germs cause diseases. As a result, antibiotic medications were developed, and a century of bacterial fear ensued. Overuse of antibiotics has damaged immune systems, destroyed the microbiome, and given rise to infectious disease with lethal "superbug" antibiotic resistance over the past several decades.**

Early in the 1900s, Metchnikoff developed a growing interest in the idea of how and why people are getting aged while working at the Pasteur Institute. In the early 1900s, Bulgaria had an extraordinarily long average lifetime of 87 years, and four out of every 1,000 people there were over 100 years old, according to figures he gathered during his study of 36 nations. Metchnikoff thought that "bad" bacteria in the intestinal tract, which create toxins, were to blame for the ageing process. Metchnikoff said that they were to blame for what he termed "intestinal auto-intoxication," which resulted in the aging-related bodily deterioration and breakdown (Ilya Mechnikov, 1908). Finally, Metchnikoff experienced a profound intuitive understanding that paved his status as the "Founding Father of Probiotics." The daily consumption of fermented milk products like yoghurt and kefir, according to Metchnikoff, is what accounts for the long, healthy lives of Bulgarians. He was aware that the lactic acid produced by the bacteria in milk during the fermentation process contributed to the gastrointestinal tract (GI tract's) acidic environment. He postulated that the environment the lactic acid provided prevented the formation of "bad" microorganisms. The end effect was less "intestinal auto-intoxication," which improved health and lengthened lifespan **(Figure 1).**

The current state of microbiome science has considerably benefited the development of postbiotics. The collection of microorganisms, such as bacteria, fungi, and viruses, that dwell inside and on top of our bodies is referred to as the "human microbiome." The first successful sequencing of the human genome was created by the Human Genome Project, which had a budget of $3 billion and lasted for 13 years (1990–2003). This paved the way for the development of cures for many of the chronic degenerative diseases that afflict us today. But the Human Genome Project also led to the creation of amazing technology, which now makes it possible for researchers to sequence genomes at a quick and affordable rate. The Human Microbiome Project led to the publication of more than 350 articles, which are regarded as the "birth" of the modern age of microbiome science.

Our ancestors have known for a very long time how vital fermented foods and bacteria are to health, particularly gut health (Sanlier et al., 2019). The host's health is significantly influenced by the gastrointestinal microbiota (GM) because of the protective roles that microorganisms perform

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(Kranich et al., 2011). Numerous types of diabetes mellitus (DM), inflammatory bowel diseases, cancer, neurological problems, psychological disorders, and even allergies have all been related to dysbiosis. The GM appears to contribute to the onset and course of the disease in these circumstances (Qiu et al., 2021; Sekirov et al., 2010; Tlaskalová-Hogenová et al., 2011). Probiotics and prebiotics are highly beneficial for repairing the intestinal microbial habitat, which benefits the host's health (Vyas et al., 2012; Ojeda et al., 2016). This has been demonstrated in numerous studies that strategies for altering GM composition or activity, such as supplementing with these substances, are very effective in achieving this. The majority of research on GM modulators has unquestionably concentrated on probiotics and prebiotics. Living bacteria known as probiotics support the health of the host in a variety of ways, such as improved intestinal barrier function, infection defence, and immune response modulation (Bermudez-Brito et al., 2012; Gibson et al., 2017). Among bacteria, species from the genera *Lactobacillus, Bifidobacterium, Streptococcus, and Lactococcus*, as well as yeasts from the genus *Saccharomyces*, are most frequently employed (Suez et al., 2019; Martín and Langella, 2019; Sanders et al., 2005). Postbiotics are defined as live microorganisms that, when given to a host in sufficient quantities, impart a health benefit (Hill et al., 2014). According to prebiotics are defined as a substrate that is specifically utilised by host microbes and confers a health advantage on the host (Gibson et al., 2017). A synbiotic defined as combination of live microorganisms and substrate(s) that are only utilised by host microorganisms when they are advantageous to the host's health (Swanson et al 2020). Up until recently, the term was mostly used to refer to indigestible fibres, but the modern meaning now encompasses bioactive substances from many sources, such as polyunsaturated fatty acids and polyphenols.

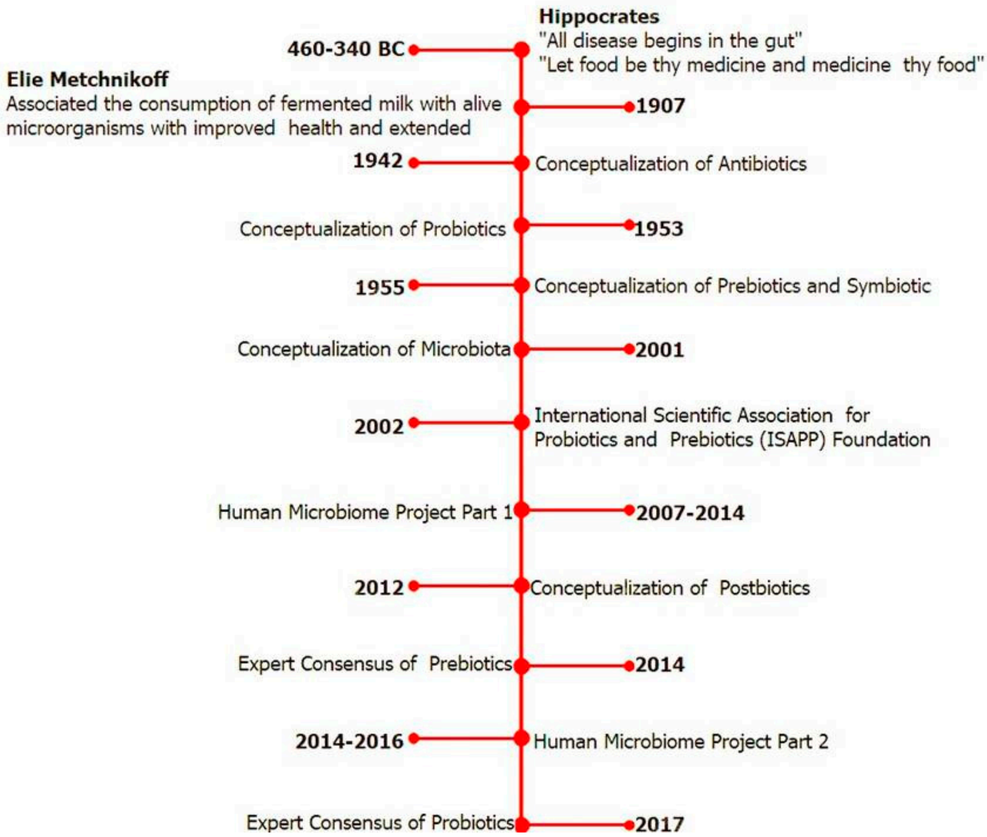

Figure 1. Schematic diagram illustrate major historical milestones in development of the prebiotics, probiotics, synbiotics and postbiotics.

The examination, categorization, and characterization of the different probiotic-related concepts have been made possible by technological advances. The International Scientific Association for Probiotics and Prebiotics (ISAPP), which among other things establishes expert consensus, aids in the development of novel concepts. In order to evaluate the definition and use of postbiotics, ISAPP assembled a panel of specialists in 2019 (Yelin et al., 2019; Salminen et al., 2021). These specialists included those with expertise in nutrition, microbial physiology, gastroenterology, paediatrics, food

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science, and microbiology. According to the panel, postbiotic is defined as "the preparation of inanimate microorganisms and/or their components that confer a health benefit on the host." Effective postbiotics must have inactivated microbial cells or cell components, with or without metabolites, in order to contribute to the claimed health benefits (Yelin et al., 2019). The term "postbiotics" was first used in 2012 (Tsilingiri et al., 2012). It is crucial to highlight the most recent changes to the ISAPP consensus statement on the definition and range of postbiotics in addition to the new biotic terminology (Salminen et al., 2021). The concept of postbiotics is relatively recent compared to prebiotics and probiotics. Postbiotic supplements are superior to probiotics despite not being as widely available yet. This is because they are pure, easy to prepare, have a long shelf life, can be produced in large quantities, have precise actions, and can trigger more focused responses through specific ligand-receptor interactions (Nataraj et al., 2020).

According to experimental studies, microbial components are a desirable subject for investigation because they can display a variety of bioactivities that are distinct from those of their live counterparts (probiotics). Postbiotics are a group that has attracted a lot of attention recently (Cuevas-González et al., 2020). Their therapeutic effects should not be restricted to the intestine alone and can be assessed or proven in humans, animals, and other target organs. Additionally, the panel came to the conclusion that postbiotics are intentionally inactivated bacteria that may include metabolites or cell components that have positive health effects. Additionally, the target population, which may include people, pets, cattle, and other targets, must have verified local as well as systemic health advantages. Postbiotics, with the exception of injections, may be injected anywhere on the host surface as long as their safety profile is favorable. Postbiotics were defined to exclude pure microbial metabolites and vaccinations. Probiotics are not always the source of postbiotics.

According to recent studies, postbiotics have been shown to have positive benefits, including immunomodulatory, antibacterial, and anti-cancer action. It lowers blood pressure, cholesterol levels, proliferative qualities, inflammation, oxidative stress, and body weight. Healthy people tolerate postbiotics well. However, some individuals should refrain from consuming probiotic-rich meals to raise their postbiotic levels, such as those who have just undergone surgery, those who have structural heart abnormalities, and those who have digestive tract illnesses, pregnant women, and young children. Due to their weakened immune systems, these groups may be more susceptible to negative reactions. Several foods, including high-fiber meals like oats, flaxseed, and garlic, as well as buttermilk, cottage cheese, fermented pickles, and yoghurt, may help the gut's postbiotics. There have been reports from numerous researchers that postbiotic performance may be influenced by both internal and external influences. Metabolites abilities to function can be inhibited by interactions between their active postbiotic metabolites and internal elements such as the microbiota that is already present, enzymes, and different dietary components (Rad et al., 2020). Proteolytic enzymes are connected to postbiotic dysfunctions (Humam et al., 2021) and Izuddin et al. (2020). The most significant proteolytic enzymes include pepsin, trypsin, chymotrypsin, and others; it has been demonstrated that these enzymes inhibit the activity of postbiotic substances. The antibacterial action of postbiotics is claimed to be most effective between pH 4 and pH 9. External food components like hydrogen ion content of food modify this activity. Pasteurised milk and ground meat are two food kinds that have been employed in postbiotics study because they have an optimal pH and do not interfere with the function of postbiotics (Moradi et al., 2020). Temperature change is another external element that influences the antibacterial action of postbiotics. According to Mirnejad et al. (2013), heat treatment at 30°C for 30 minutes or at 121°C for 15 minutes reduces the antibacterial efficacy of postbiotics. As a result, maintaining a consistent temperature and pH is essential for the formation of postbiotics.

3. Characteristic Feature of Postbiotics

According to ISAPP, postbiotic is defined as "preparation of inanimate microorganisms and/or their components that confers a health benefit on the host", also includes inanimate microorganisms (Salminen et al., 2021). Postbiotic describes compounds created after microbes have been rendered inert, dead, or inactivated. Other hand, postbiotics are probiotic-derived products made from food-grade bacteria that, when taken in sufficient doses, have positive effects on one's health (Maria Carmen et al., 2021). They consist of cellular components as well as secreted substances or metabolic wastes released by living microorganisms or gathered and extracted during cell lysis (Wegh et al.,

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2019). The bacteria that make up a postbiotic can either be whole, inert cells or can be broken down into their structural components, like cell walls. Many postbiotic preparations also contain microbe-produced chemicals like metabolites, proteins, or peptides. These substances may help a postbiotic's overall health benefits, but they are not required. A postbiotic must originate from a specific microorganism or combination of microorganisms whose genomic sequences are known and be created utilizing a well-defined technological process of biomass generation and inactivation that is repeatable (Vinderola et al., 2022). Although postbiotics of fungal origin are also being studied, the majority of postbiotics are formed from bacteria, most frequently from Lactobacilli and Bifidobacterium members. There are currently some commercial postbiotics available as supplements or included in food matrices, most of which are used to treat gastrointestinal or immune system-related disorders (Aguilar-Toalá et al., 2018; Salminen et al., 2021). Lipoteichoic acid extracted from *L. plantarum* exerted a significant attenuation of flexPGN-induced pro-inflammatory signals in human monocytic THP-1 cells (Kim et al., 2011). Oral administration of *Faecalibacterium prausnitzii* supernatant, decreased the severity of 2,4,6-trinitrobenzenesulphonic acid (TNBS)-induced colitis in mice and tended to correct the dysbiosis associated with TNBS colitis, highlighting its potent anti-inflammatory effects (Sokol et al., 2008). *Saccharomyces cerevisiae* is a well-known probiotic producing yeast is used for bioproduction of metabolites which serving as an anti-inflammatory component (Jensen et al., 2007). Human polymorphonuclear (PMN) cells treated with cell wall fragments and metabolite obtained from *Bacillus coagulans* inhibits oxidative stress-induced reactive oxygen species (ROS) formation (Jensen et al., 2010).

Postbiotics have a number of noteworthy characteristics, such as (i) being relatively safe; (ii) being well-tolerated and related with a decreased risk for adverse effects in vulnerable persons (Tsilingiri and Rescigno, 2013; Taverniti and Guglielmetti, 2011; Wang et al., 2020; Toscano et al., 2017); and (iii) being quite safe. According to Zókiewicz et al. (2020), (iii) they don't run the risk of spreading antibiotic-resistant genes to commensal or pathogenic bacteria, and (iv) their efficacy is independent of cell viability, resulting in increased stability and shelf life. (v) They demonstrate a straightforward industrial (large-scale) production (Nataraj et al., 2020); (vi) They exhibit intriguing technological characteristics, such as the rheological properties of exopolysaccharides (EPS) used as a stabiliser in the food industry (Patel and Prajapat, 2013; Nataraj et al., 2020) or the bio-preservative effects of LAB bacteriocins (vii) the broad range of health-promoting effects (Piqué et al., 2019). (viii) as antifungal and antibacterial agents (Cabello-Olmo et al., 2021) **(Figure 2).** Metabolomic techniques are currently widely used to evaluate the metabolic products of bacteria in faeces and serum (Zhao et al., 2017). Many commercial pharmaceutical products, including Cytoflora (cw components of Lactobacillus and Bifidobacterium sp.) and Lacteol (inactivated Lactobacillus sp.), Nyaditum resea (inactivated Mycobacterium), and others, have already been given approval for use as dietary supplements, immunomodulators, and instruments for lowering the risk of infections (Barros et al., 2020).

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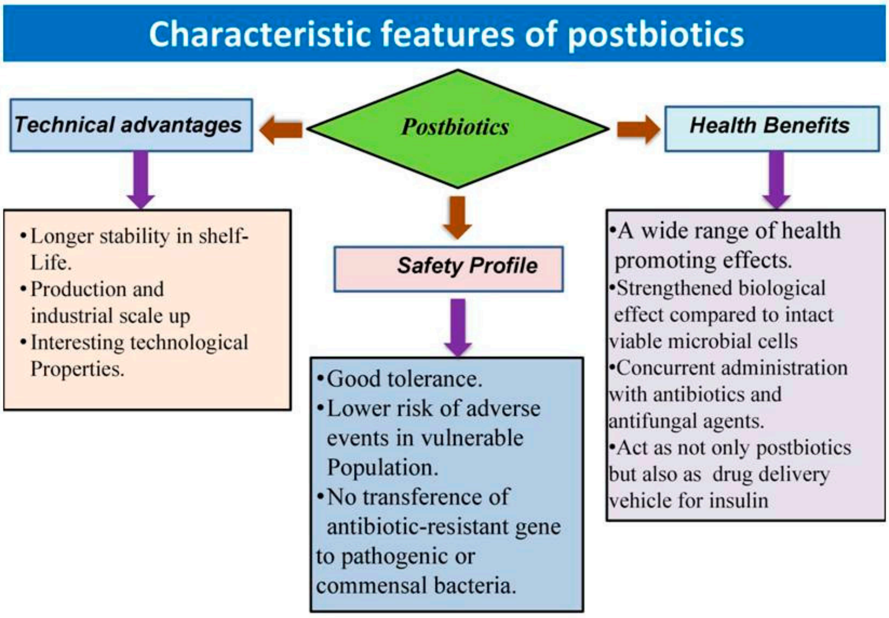

Figure 2. The Scheme illustrate technical advantage, safety profile and health benefits of postbiotcs.

4. Production, Purification and Characterization of Postbiotics

It is believed that billions of bacteria containing more than 3 million genes reside in the human gastrointestinal tract (GI), with the large intestine housing the most metabolically active and varied microbial community (Belizário and Napolitano, 2015). According to Tanaka and Nakayama (2017) and Toda et al. (2019), the human microbiota, which is specific to each individual, appears to begin in the uterus when the foetus consumes amniotic fluid and continues even after delivery. It is essential for human growth and contains more than 1,000 different microbial species (Aggarwal et al., 2022). An individual's gut microbiome contains both beneficial and harmful bacteria and reflects familial inheritance. The balance of both bacterial communities are essential, the imbalance of causes disruption of this regular microflora (dysbiosis) not only affects the GI tract but also has a severe effect on the operation of other organs. According to Carding et al. (2015), this raises the risk of a wide range of infections and chronic disorders, including obesity, autism, psychological abnormalities, gastroenteritis, colon dysfunction, and irritable bowel syndrome. A number of studies have demonstrated that this balance can be restored with the use of postbiotics, which are less risky than pre- and probiotics (De Marco et al., 2018). Numerous studies have suggested that the beneficial effects of probiotics on health may not always be connected to the viability of bacteria. A significant portion of the health advantages of pre-, pro-, and synbiotics appeared to be mediated by different metabolic products, cellular and subcellular structural elements, and intact or ruptured dead microorganisms. Teichoic acid, short chain fatty acids, vitamins, enzymes, exopolysaccharide, different peptides, amino acids, and fermentation by-products are among the postbiotics, which are the structural and metabolic microbial products (Wegh et al., 2019). Probiotics produce these postbiotic components when they feed on prebiotics, during their lengthy storage or processing, such as pasteurization or baking, or during metabolic processes.

There are numerous yeasts and bacteria utilized as probiotics, however their postbiotic usage is unexplored. The focus of postbiotics studies has recently shown immense interest because they offer a secure substitute for live probiotics. Many functional foods, such as dairy products, grains, coffee, fruit juices, etc., include probiotic yeast, *Saccharomyces cerevisiae* var. boulardii. However, in order to potentially increase shelf stability, sensory characteristics, safety, and health advantages, researchers need to create *S. boulardii*-based postbiotic-based functional food preparations (Chan and Liu, 2022). Modern technologies are being used in research to extract, characterize, and examine the bioactivities

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of various postbiotic components in preparation for potential therapeutic applications in the future of medicine (Pyclik et al., 2020). Generally, postbiotics are more stable and don't need cold chains for industrial usage, whereas viable probiotic products need to be stored and transported in cold storage facilities. There is no postbiotic interaction with the food matrix, no possibility of developing antibiotic resistance genes, and no taste or odour modifications that aren't acceptable. Therefore, postbiotics are a secure replacement for those with immunological weaknesses, following transplantation, or for babies. Through the communication axis between the gut and target organs, such as the gut-brain, gut-lung, and gut-liver axes, postbiotics have an impact on other organs both locally and/or systemically (Nataraj et al., 2020).

The bacterial strain, the culturing medium, and how the bacteria are treated after they have multiplied are all important factors that affect the type and quantity of postbiotic products. Food postbiotics are simply soluble components, such as commodities or metabolic byproducts generated into the medium during bacterial growth, and do not undergo any post-propagation processing (Kiewicz et al., 2020). Bacteria may occasionally be subjected to lysis after being multiplied utilising cell fragmentation techniques including thermal, enzymatic, chemical, sonication, hyperbaric, solvent extraction, or a combination of these (Hernández-Granados and Franco-Robles, 2020; Cuevas-González et al., 2020). These mechanisms add various extra intracellular metabolites and components made from cell walls to the postbiotic mixture, enriching it, and provide the ensuing postbiotics new functions. The term "postbiotics" refers to a wide range of substances, such as extracellular vesicles (EVs), bacteriocins, enzymes, proteins, peptides, organic acids, vitamins, and other discharged compounds like EPS, cell wall components, polymers, teichoic acids, peptidoglycans, peptidoglycan-derived muropeptides, pili-type forms, and cell surface fractions, cell free extracts and lysates, culture supernatants, or biosurfactants (Salminen et al., 2021; Tsilingiri and Rescigno, 2013; Taverniti and Guglielmetti, 2011; Wang et al., 2020; Toscano et al., 2017; Zółkiewicz et al., 2020; Nataraj et al., 2020; Patel and Prajapat, 2013).

Additional extraction and purification techniques, such as centrifugation, dialysis, lyophilization, and column purification, were used on the resulting solutions to separate the bacterial cells from the postbiotic metabolites in both treated and untreated postbiotic mixtures (Cuevas-González et al., 2020; de Almada et al., 2016). The microorganisms used as starting points and the inactivation methods or techniques used for their production are generally used to characterise postbiotics because each process affects the quality and quantity of the final postbiotics produced and produces different postbiotics with different effects (Aggarwal et al., 2022). When prebiotics are consumed, stored or processed for an extended period of time, such as during pasteurisation or baking, or when they are metabolised, probiotics produce these postbiotic components. According to Aggarwal et al. (2022), these postbiotics can be created in the lab utilising techniques including radiation (UV/ionizing), high pressure, high temperature, sonication, and formalin inactivation **(Figure 3).** Given the complexity of biological compounds with varying degrees of polymerization and glycosidic bonds, qualitative and quantitative analysis of postbiotics typically requires complicated equipment and numerous concentration/purification steps using well-known techniques like chromatography, spectroscopy such as NMR, Fourier transform infrared absorption spectroscopy, and spectrophotometry (Barros et al., 2020).

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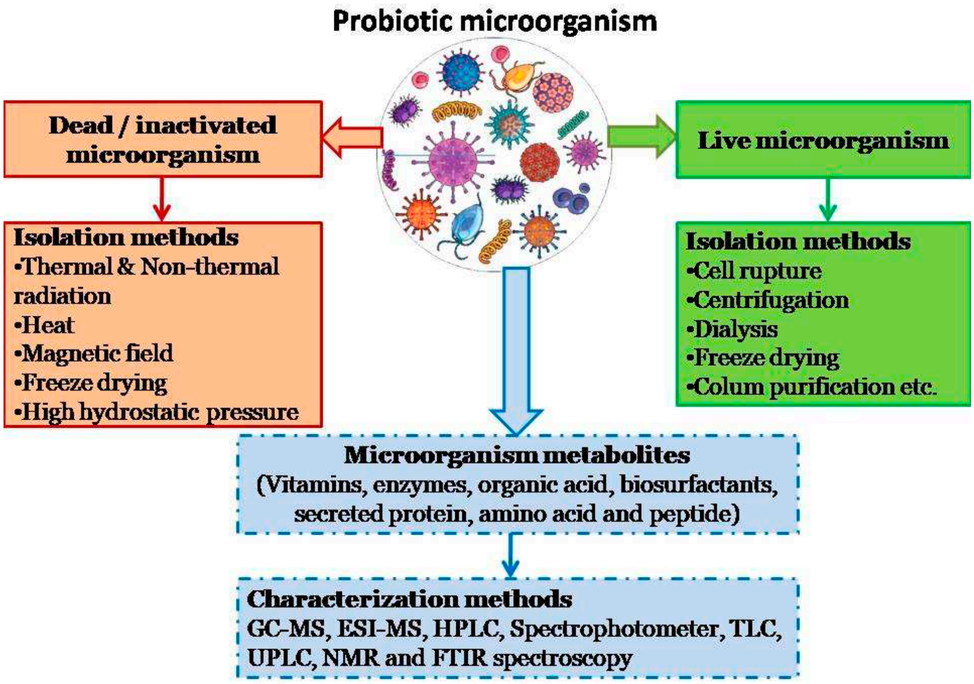

Figure 3. Isolation and characterization of postbiotics from probiotics.

In food, complex microbial cultures, the intestine, or as a result of cell lysis, food-grade bacteria can emit postbiotics. Following the removal of the supernatant, the effects may be immediately examined or specific chemicals may be isolated for further study (Aguilar-Toalá et al., 2018; Cuevas-González et al., 2020; Wegh et al., 2019; ókiewicz et al., 2020). According to the analytical goals and the kind of characterization needed, a suitable technique is commonly selected (Barros et al., 2020). A variety of techniques have been created and are used to evaluate postbiotics qualitatively and/or quantitatively. Depending on the analytical objectives and qualitative and/or quantitative properties of microbial metabolite complexes, many analytical approaches are now being employed to identify postbiotic metabolites (Cuevas-Gonzalez et al., 2020). For the purpose of determining the qualitative and/or quantitative analysis and composition of postbiotics, a number of analytical techniques, including gas chromatography (GC), high-performance liquid chromatography (HPLC), thin-layer chromatography (TLC), and spectroscopic methods, have been reviewed in detail (Ruas-Madiedo et al., 2005; Moradi et al., 2021; Lee et al., 2012; Garnier et al. Because of its high efficiency, resolution, sensitivity, and accuracy as well as its little solvent usage, ultra-performance liquid chromatography offers superior postbiotic separation and identification capabilities (Lin and Pan, 2019; Lim et al., 2018; Wang et al., 2016). Thin layer chromatography has been used to determine that postbiotics contain a variety of compounds (Sharma et al., 2015; Wang et al., 2012). Metabolites in LAB postbiotics have been quantified using colorimetric methods (Ruhmann et al., 2015). Lin and Pan (2019); Arasu et al. (2014) employed nuclear magnetic resonance spectroscopy to comprehend the interactions of postbiotic biological metabolites. The headspace solid-phase microextraction GC-MS method was used to characterise find sixty-two compounds of the volatile profile of postbiotics from *Lactobacillus casei*. Additionally, using GC, the short-chain fatty acid content of postbiotics from four different bacterial strains was studied. One of the most often used analytical techniques for postbiotics analysis, both quantitatively and qualitatively, is HPLC (Ricci et al., 2018). According to Yurdshahi et al. (2020), postbiotics from *Lactobacillus plantarum* were analysed using the Fourier transform infrared spectroscopy method **(Figure 3).**

5. Classification of Postbiotics

Classification of postbiotics are depends on various factors including type of microorganism, structural composition and physiological functions. A variety of postbiotic compounds produced by extracellular and intracellular probiotic bacteria have currently been identified. For example,

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muropeptides derived from peptidoglycans, exopolysaccharide (EPS), teichoic acids, surface protruding molecules like fimbriae, pili, or flagella that make up cell wall components, secreted proteins/peptides, bacteriocins like acidophilin, reuterin, and bifidin, cell-free supernatant, organic acids, neurotransmitters and biosurfactants (Nataraj et al., 2020; Malashree, et al., 2019). Due to their unique physical and chemical properties and functional aspects, postbiotics are classified into different types inactivated and dead probiotics, peptidoglycan, techoic acids, exopolysaccharides, cell free supernatants, short-chain fatty acids, bacteriocins, enzymes, and vitamins and etc.

5.1. Inactivated and Dead Probiotics

Although other techniques, like gamma or UV radiations, tyndallization, sonication, and chemical treatment used for the preparation of postbiotics, heat is the most frequent method used for production of inactivated or dead probiotics. The inactivation process causes differences in the cellular make-up and biological functions (Taverniti and Guglielmetti, 2011). According to studies done on experimental models, the biological characteristics of their viable counterparts, such as the ability to scavenge oxygen radicals, reduce inflammatory indicators, and modify host physiology, are retained by non-viable cells (Sugahara et al., 2017). According to recent studies on eight different strains of *Lactobacillus reuteri*, both live and heat-killed cells of these bacteria adhered to caco 2 cell cultures and prevented enteropathogens like *E. coli*, *Salmonella typhi*, *Listeria monocytogenes*, and *Enterococcus faecalis* from sticking to them (Singh et al., 2017).

5.2. Cell Free Supernatants/Suspensions

Cell-free supernatants (CFS) are a broad category of biomolecular and active metabolites with low or high molecular weights, such as organic acids, diacetylene, carbon dioxide, bacteriocin-like substances, etc., that are typically secreted by lactic acid bacteria and yeasts and may help maintain homeostasis in the body (Kapustian et al., 2018; Siedler et al., 2019). The composition of media influences CFS composition. Cell-free supernatants (CFS) are fluids that include any nutrients from the growth medium that were not absorbed by the microbes as well as any metabolites left over from microbial development. CFS, which are produced when microbes are fermented, have antibacterial, antibiofilm, anti-inflammatory, antioxidant, and anticancer activities and are also used to treat diarrhea (Lee et al., 2022). Generally, CFS is produced by safe bacteria, and these bioactive materials can be used as an alternative to common antimicrobials. These metabolites can be isolated from the microorganism's cells by centrifugation, and it has been discovered that they are highly abundant in anti-inflammatory, anti-cancer, antioxidant, phenolic, and flavonoid chemicals. These metabolites are potentially increasing the expression of anti-inflammatory cytokines like IL-10 and suppress pro-inflammatory cytokines like TNF α and IL-1β. Due to organic acids, proteinaceous compounds, and fatty acids, CFS generated by LAB may have an antimicrobial impact. Lactic and acetic acid, together with other substances, are principally in charge of the antibacterial action of CFS from LAB (Mani-López et al., 2022). The anti-proliferative effects of the cell-free culture filtrate from *Lactobacillus fermentum* were also reported by Lee et al. (2020), who looked at the anti-cancer capabilities of this substance. They used 3D spheroid cultures of colorectal cancer cells as a model for their research. According to a different study, cell-free Lactobacillus reuten supernatant, which is likely to contain carbohydrates and fatty acid metabolites, has the potential to be used in the prevention and treatment of dental caries and periodontal diseases.

The antibacterial ability of culture suspensions produced from four probiotic strains, *Lactobacillus rhamnosus*, *L. fermentum*, *L. delbrueckii* subsp. lactis, and *Pediococcus acidilactici* against Clostridium perfringens was reported by Hamad et al. in 2020. The growth of *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus niger*, and *Aspergillus flavus* was significantly suppressed by the lactic acid, hydrogen peroxide, protein, and diacetyl generated from Lactobacillus and Pediococcus species culture filtrate (George-Okafor et al., 2020). According to Oscáriz and Pisabarro (2001), the mechanism of inhibition appears to be the creation of pores in cell membranes and cell lysis caused by lactic acid, followed by the actions of diacetyl and bacteriocins. Hydrogen peroxide, fatty acids, secreted proteins, and organic acids were discovered in the culture suspension of the dental health probiotic *Weissella cibaria* strain CMU. Organic acid, secreted proteins and hydrogen peroxide have all been shown to have antibacterial activity against periodontal pathogens by disrupting cell membranes, lowering the pH of the cytosol, producing hydroxyl radicals, and interfering with

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cellular metabolic function (Lim et al., 2018). As several biomolecules, CFS seems to have superior biological impacts on host health than pure bio molecules (Hartmann et al., 2011). Pyrrolo [1,2-a] pyrazine-1,4-dione was observed in the CSF of the several examined species of lactobacilli using GC-MS analysis. Strain specific substances was observed such as butyric acid, benzoic acid, biosurfactants (laurostearic acid), different peptides, fatty acids, ethanol, phenol, cyclopentanes, esters, and aldehydes are also present in strain-specific ways. Numerous of these substances exhibit antioxidant activity, biofilm removal capability, and antagonistic activity against *L. monocytogenes*, indicating their potential application as food additives, particularly for *L. salivarius* (Moradi et al., 2020). *Enterococcus faecalis* CFS's antibacterial activity was thermostable and peaked at neutral pH 7.0, supporting its use in food preservation (de Las M Cardoso et al., 2012). CFS is produced by various cultures or strains of bacteria exhibited differential functions. A CFS derived from *Lactobacillus acidophillus* and *Lactobacillus casei* was found to have antioxidant and anti-inflammatory effects (De Marco et al., 2018). Lactobacillus and Bifidobacterium were also found to have antibacterial activity by inhibiting *E. coli* strains (Khodaii et al., 2017). It has been postulated that the antioxidant capacity of diverse intracellular fractions formed from Lactobacillus strains mediates the rise in glutathione cellular concentration, a significant non-enzymatic antioxidant that is essential for maintaining the intracellular redox state. On the other hand, such non-enzymatic postbiotics antioxidant properties may also have a scavenging effect on ROS and reactive nitrogen species (Yoon et al., 2004; Amaretti et al., 2013; Zhang et al., 2011).

5.3. Cell Wall Fragments

Cell wall contains various components including teichoic acids, lipoteichoic acids, and other compounds. Among the immunogenic components of bacterial cell walls, teichoic acids, lipoteichoic acids, and other compounds are potential to elicit an immune response (van der Es et al., 2017). A Gram-positive bacterium's cell wall is mostly made up of lipoteichoic and teichoic acids, which account for around 60% of the cell wall mass (Saeui et al., 2015). Different lipoteichoic acid structures among the four strains of *Lactobacillus plantarum* led to various immunological reactions from immune cells, as evidenced by the lipoteichoic acid recovered from the K8, K88, K5-5, and K55-5 strains of *L. plantarum* (Jung et al., 2022). Teichoic acids are essential for pathophysiology and the development of antibiotic resistance (Brown et al., 2013). According to Lebeer et al (2012), teichoic and lipoteichoic acids both exhibit a variety of bioactivities, such as anticancer, immunomodulatory, and antioxidant characteristics.

5.4. Exopolysaccharides

According to Caggianiello et al. (2016), Lactobacilli and other bacteria produce a variety of homo- and hetero-polysaccharides, including kefricin, glucans, uronic acid, etc. These are collectively referred to as exopolysaccharides, and they can be released extracellularly, cling to the surface of the microbial cell as a slime layer, or remain firmly attached as a capsule. These macromolecules have the power to defend against phages, phagocytes, and toxic substances, but they also have an impact on the immune system, physiological processes, lipid metabolism, and pathogen colonisation in hosts. According to research by Dinic et al. (2018), using EPS from Lactobacillus paraplantarum BGCG11 decreased proinflammatory (IL-I, TNF, iNOS) and concurrently elevated antiinflammatory (IL-6, IL-10) cytokines, hence reducing inflammation in rats. According to Liu et al. (2010) and Wang et al. (2020), the EPS generated from the probiotics Lactobacillus fermentum and Paenibacillus polymyxa cultures shown antioxidant activity and may thus have therapeutic effects in illnesses like diabetes, arthrosclerosis, and rheumatoid arthritis. Additionally, EPS extracted from pathogenic E. coli and S. aureus prevented them from developing biofilms and suppressed tumour growth and inflammation (Wang et al., 2020). The bioremediation, pharmaceutical, food, and textile industries all show significant applications for EPS derived from various bacteria (Angelin and Kavitha, 2020). Examples of food additives include xanthan, alginate, gellen, levan, and pullulan (Moscovici, 2015). Centrifugation is the first stage in a multi-phase method to extract EPS, which also includes acid protein removal, cold ethanol precipitation, filtration to remove small molecules, and lastly dialysis and lyophilization (Juráková et al., 2022). EPS are essential for cell adhesion and defence. The structural diversity of EPS produced by lactic acid bacteria (LAB) enables the polymers to have a range of bioactivities, including immunomodulatory, antitumor and antimutagenicity, antioxidant,

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anti-inflammatory, antihypertensive activity, antibacterial and antiviral, cholesterol-lowering, and anti-gastrointestinal activity (Gezginç et al., 2022). According to Khalil et al. (2018), EPS generated from Lactobacillus strains showed antibacterial and antioxidant activities and improved lipid metabolism by inhibiting cholesterol absorption. By increasing the activities of antioxidant enzymes such catalase, glutathione peroxidase, and superoxide dismutase and lowering the levels of lipid peroxidation in serum and mouse livers, EPS generated from Lactococcus lactis subsp. lactis displayed antioxidant activity (Gao et al., 2019). The food industry currently uses EPS as an emulsifier, stabiliser, and water-binding agents.

5.5. Enzymes

Enzymes are proteins which catalyse biological reactions. According to their activity or function, enzymes can be classified into six primary groups: oxidoreductases, transferases, hydrolases, lyases, isomerases, and ligases (Singhania et al., 2017; Kumar et al., 2017). A small number of bacterial strains, primarily Bacillus subtilis and Bacillus licheniformis, as well as a few fungal strains, notably Aspergillus niger and Aspergillus oryzae, are the primary sources of enzymes, which are used in a variety of physiological, metabolic, and regulatory processes. A significant amount of glutathione peroxidase was detected in two strains of Lactobacillus fermentum, and it was later discovered to possess strong in vitro antioxidant capabilities. Under difficult conditions like temperature, pH, organic solvents, oxidising agents, and detergents, the Bacillus genus is able to produce proteolytic enzymes in large yields that are remarkably stable. It has been demonstrated that the catalase of a genetically modified strain of Lactobacillus lactis can protect mice from chemically induced colon cancer (Kim et al., 2005; Contesini et al., 2018; de LeBlanc et al., 2008).

5.6. Short Chain Fatty Acids (SCFAs)

An important class of compounds known as SCFAs are produced when gut bacteria like Bacteroides and Firmicutes ferment plant polysaccharides (Kim et al., 2018). Inulin and fructooligosaccharides, two prebiotics, are fermented to produce SCFAs, primarily acetate, propionate, and butyrate, which are found in the colon and faeces in an estimated 60:20:20 molar ratio and aid in the regeneration of the intestinal epithelium (Takagi et al., 2016; Zolkiewicz et al., 2020). In addition, it suppresses the production of pro-inflammatory cytokines, which prevents nuclear factor-kappa B (NF-B) from activating. The reduction of atherogenesis in a mouse model was demonstrated using an in vivo model of butyrate (Kasahara et al., 2018). Acetate and lactate are produced by bifidobacteria when there are too many carbs for it to develop. Inhibiting the growth of Klebsiella oxytoca, for instance, Lactobacillus acidophilus, Lactobacillus fermentum, Lactobacillus paracasei ATCC 335, and Lactobacillus brevis produced SCFAs by lysing the cell wall (Higashi et al., 2020). SCFs have several positive health effects. In addition to improving colon function and lowering pH, they also encourage the proliferation of epithelial cells and blood flow in the colon (Topping, 1996). Bird et al. (2010) found that SCFs significantly lower the prevalence of colo-rectal diseases. When colonic bacteria ferment undigested carbohydrates, they mostly produce acetate, propionate, and butyrate, in ratios that normally vary from 3:1:1 to 10:2:1. Acetate aids in cholesterol regulation and is used as a growth factor by other bacteria. Propionate and butyrate, play a part in gluconeogenesis, provide colonocytes and epithelial cells with their main source of energy, and promote the apoptosis of colon cancer cells (Rowland et al. (2017).

5.7. Bacteriocins

Lactic acid (LAB), as well as other eubacteria and archaebacteria, produce ribosomally synthesized tiny peptides or proteins known as bacteriocins that have the ability to either kill or impede the growth of other bacteria. According to Soltani et al. (2021), the therapeutic utility of bacteriocin as next-generation antimicrobials in reducing the threat posed by drug-resistant pathogenic organisms is highlighted by its restricted to broad-spectrum inhibitory effect against bacterial growth. Examples include nisin, subtilosin, lactococcin G&Q, enterocin, lactocyclicin, bovicin, plantaricin, and lacticin, among others (Perez et al., 2014). Bacteriocins demonstrate their potential for food preservation. Nisin was the first bacteriocin to receive regulatory approval for commercial use as a food preservative from organizations like the European Food Safety Authority (EFSA), the FDA, and Health Canada. It is now used as a food additive in more than 80 nations.

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Bacteriocins prevent pathogen growth in the GI tract by creating pores in cell membranes, preventing the proper construction of cell walls, and preventing enzyme and protein functions. The multi-bacteriocinogenic strains of *Lactobacillus paracasei* and *Lactobacillus taiwanensis* showed antibacterial activity against *E. coli* and *Salmonella gallinarum*& enteropathogenic *E. coli* (Belguesmia et al., 2020; Kim et al., 2020 respectively. Due to various qualities of bacteriocins, it has been widely used in various applications including medicine, cancer therapy, food, cosmetics, and veterinary use.

5.8. Vitamins

Vitamins are chemical substances that are thermosensitive and necessary for the body to carry out a number of physiological processes, including DNA replication, repair, and methylation. Since humans lack the biological processes to synthesise vitamins, they must be obtained from external sources. Vitamins play a crucial role in many physiological processes, such as bone health, brain function, blood clotting, and riboflavin's role as a hydrogen carrier in redox reactions. Vitamin K also plays a role as a cofactor of gamma carboxylase activity in blood clotting. various critical vitamins, such as vitamin K and various B group vitamins like folate, riboflavin, cobalamin, pyridoxine, thymine, niacin, and nicotinic acid, are produced by lactic acid bacteria and Bifidobacterium sp. (Hill, 1997; LeBlanc et al., 2013). Numerous fermented foods, including fermented milk, yoghurt, and cheese, are great suppliers of these vitamins, which help our bodies' digestive systems. In addition to being essential for producing energy, controlling genes, and changing intestinal immunity, B group vitamins including B12, B2, B6, B9, and vitamin K may all be synthesised by gut microbiomes on their own. Vitamin B is also known to have anticancer properties. Cobalamin, generally known as vitamin B12 (B12), is a water-soluble vitamin that is essential for maintaining hematopoiesis and the health of neurons. It is an essential nutrient found in animal products. Probiotics like L. sanfranciscensis, L. reuteri, L. rossiae, and L. fermentum, which have been shown to synthesise vitamin B12 and could be useful substitutes for industrial production, have recently been found to contain genes encoding the enzymes necessary for cobalamin (B12) synthesis (Masuda et al., 2012; Martín et al., 2005; De Angelis et al., 2014). In contrast to MK-6, MK-8, and MK-9, which are produced by Bacteroides fragilis, MK-10, MK-11, and MK-12 are produced by Eubacterium lentum, Lactococcus lactisssp. lactis, and Lactococcus lactis.cremoris (Camelo-Castillo et al., 2021). Cortés-Martn et al. (2020) found that the gut microbiota also produces dietary polyphenols. To function as bioactive molecules in the circulatory, renal, and brain systems, aromatic amino acids are generated and metabolised in the gut (Liu et al., 2020).

5.9. Neurotransmitters

Neurotransmitters like serotonin, dopamine, norepinephrine, catecholamines, and acetylcholines are produced by gut bacteria such Bifidobacterium, Lactobacillus plantarum, Lactobacillus brevis, and Bacillus subtilis. These neurotransmitters plays major part in the brain function via gut brain axis through modulation of enteric nerves signaling. Tryptophan is an amino acid that is transformed into serotonin, which is in charge of improving mood. Inhibiting neurotransmission is what gamma amino butyric acid does, and when it doesn't work, anxiety and depression result. While acetylcholine and catecholamines are essential for CNS activities like emotion, memory and learning, and motor control. According to Patterson et al. (2014), microbiome management can cure mental conditions that are linked to depression and that these compounds appear to have antidepressant potential.

5.10. Extracellular Vesicles

Extracellular vesicles (EVs) are spherical, lipid bilayer membrane-bound particles that commensal bacteria like E. coli and Akkermansia muciniphila release into the environment. These are engaged in the horizontal transfer of genetic material across bacterial species and contain a variety of substances including proteins, DNA, RNA, glycolipids, polysaccharides, enzymes, toxins, etc. According to studies by Ahmadi Badi et al. (2017) and Chelakkot et al. (2018), these substances are thought to regulate the permeability of the gut barrier, signalling pathways, maintain intestinal homeostasis, improve lipid profiles, and facilitate communication between the gut and the brain. Survival, competitiveness, pathogenesis, and immunomodulation are a few of the ways that bacterial EVs can regulate. They can also swiftly cross the mucus barrier and interact with the host, which

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lowers the risk of sepsis. In earlier investigations, there was an association between obesity and reduced barrier integrity. Increased intestinal barrier permeability causes metabolic endotoxemia, which is regarded to be the primary contributing factor to obesity-related metabolic diseases (de et al., 2020; Molina-Tijeras et al., 2019; Damms-Machado et al., 2017). EVs derived from *Akkermansia muciniphila* reduced fat accumulation, body weight gain, and pathological abnormalities in HFD-fed mice; the tested EVs had the most significant effects on adipocyte size, eWAT weight, lipid balance, and expression of inflammatory cytokines in the adipose tissue and glucose tolerance in diabetic mice. EVs derived from *Propionibacterium freudenreichii* reduced inflammation through modulation of the NF-B pathway (de et al., 2020; Everard et al., 2013; Ashrafian et al., 2019; Ashrafian et al., 2021; Keshavarz Azizi Raftar et al., 2021).

6. Applications of Postbiotics in Food Industry

Functional foods that are probiotic, prebiotic, and postbiotic have received a lot of attention recently from researchers, manufacturers, and consumers. The development of innovative functional foods and preventative medicine formulations for improving host health, as well as accurately characterising their mechanisms of action, are currently the focus of a sizable section of postbiotic research (Rad et al., 2020). A variety of food products with bioactive ingredients, such as probiotics, dairy, and non-dairy products, are already available on the market to meet the nutritional needs of consumers with various dietary preferences, such as those who are allergic to milk proteins, lactose intolerant, and vegetarians (Rad et al., 2020; Thorakkattu et al., 2022). Postbiotics are stable over a wide range of temperatures and pH levels, making it easy to add meals and components before thermal processing without affecting their effectiveness. Both technically and financially, producers might gain from this. They can be employed in delivery systems like pharmaceutical goods and/or functional meals since the right amount of postbiotics can be managed under manufacturing and storage conditions when survival is not the main determining factor (Rad et al., 2020). Bacterial lysates with cell surface proteins, bacterial enzymes, peptides, metabolites, neuropeptides, and lower organic acids like lactic acid are examples of postbiotics. Fermentation is the most prevalent postbiotic source in the food industry. Postbiotics are naturally present in many dairy-based products, such as kefir, kombucha, yoghurt, and pickled vegetables. Generally, Lactobacillus sps, Bifidobacterium, Saccharomyces, Bacillus, Streptococcus, or Faecalibacterium genera are highly effective postbiotics producing microorganisms in the form of cytoplasmic extracts and cell wall components (Tejada-Simon et al., 1999; Sokol et al. 2008; Jensen et al., 2010; Arshad et al., 2018). According to several studies (Vidal et al., 2002; Matsuguchi et al., 2003; Choi et al., 2006; Kim et al., 2011; Tiptiri-Kourpeti et al., 2016), several Lactobacilli species, including L. rhamnosus, L. bulgaricus, L. acidophilus, L. reuteri, L. casei, L. fermentum, L. On the other hand, the most prevalent probiotics producers of postbiotics are Bifidobacterium sps, including B. bifidum, B. longum, B. breve, and B. longum. According to an in vivo investigation, mice that were injected with B. longum showed a strong antibody response, but the cell-wall and cytoplasmic fractions had little effect on the immune system (Takahashi et al., 1998). Additionally, L. plantarum species are thought to be potential food bio-preservatives and to benefit animal gut health since they create metabolites with high levels of mixed organic acids and bacteriocin. Nisin, a type of bacteriocins produced by Lactococcus lactis subsp. lactis, is used as a preservative in many foods, including dairy products, infant formula, and canned soups (Chen and Hoover, 2003). EPS produced by LAB, such as Lactobacillus rhamnosus, which is important in dairy products, might enhance the physicochemical and sensory qualities of food-based products (Aguilar-Toalá et al., 2018). Thanks to the postbiotic of supernatant from Lactobacillus plantarum YML007, the shelf life of soybeans was extended by up to two months (Rather et al., 2013). Postbiotic enzymes, including purified phytases from the microorganisms Bifidobacterium pseudocatenulatum and Bifidobacterium longum spp. infantis, raised the amounts of myoinositol triphosphate while lowering the amount of phytates in cereal combinations (Tomasik et al., 2020). Cereals lost some of their vitamin B content when they were heated or ground. Vitamin B1, B2, B3, B9, B11, and B12 can be created by additional bacteria as a result of grain fermentation and LAB pre-treatment, which can compensate for these vitamin losses. Cereals that had undergone LAB fermentation had considerably greater levels of total lysine, protein fractions, sugars, soluble dietary fibre, and Ca, Fe, and Zn bioavailability. Wheat may also produce antioxidant peptides, -aminobutyric acid, and angiotensin I-converting enzyme inhibitory peptides via LAB fermentation

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(Arora et al., 2011; Capozzi et al., 2012; Ayyash et al., 2019). Postbiotics are chemicals obtained from specific bacteria that prevent microbiological food degradation and increase the shelf life of foods. Because they exhibit anti-microbial activity on both pathogenic and spoilage microorganisms through a variety of mechanisms, such as by creating cavities in CM, changing the proteins in cell walls, and lowering the pH of bacteria cytoplasm, postbiotics are highly significant in the food industry (Rad et al., 2021). The nutritional value and organoleptic changes of non-vegetarian food can be preserved by directly applying the postbiotic coating (for example, to fish fillets and slices of meat) or by spraying it (for example, on ground fish and meat), depending on the type of meat and the postbiotic. Postbiotics comprised of Pediococcus acidilactici, Latilactobacillus sakei, and Staphylococcus xylosus flavonoids and phenolics reduce Salmonella typhimurium in chicken drumsticks (Incili et al., 2022). By consuming products made from the fermentation of Saccharomyces cerevisiae, it may be possible to limit the amount of Salmonella enterica contamination in poultry products (Chaney et al., 2022). Postbiotic-containing preservatives were found to be equally as effective as frequently used commercial preservatives in preserving vacuum-packaged cooked sausages in order to provide natural preservation technologies (de Lima et al., 2022). Postbiotics can be used as an alternative to biocontrol to make dairy products, fruits, and vegetables safe. For instance, it has been discovered that a number of bacteriocins and the LABs that make them have a role in controlling cheese blowing errors. Postbiotics can be used as sanitizers in the food business (Moradi et al., 2020).

7. Conclusion and Future Perspectives

Hippocrates declared that "all disease begins in the gut" more than 2,000 years ago, but research into the complex, nuanced, and dynamic link between the intestinal microbiota, health, and disease aetiology is still in its infancy. Intestinal microbiome abnormalities affect immune function and pathogenesis and are critical to gut homeostasis. Postbiotics, which have been demonstrated to benefit the host, are made up of metabolites and/or fragments of cell walls secreted by living bacteria or released after bacterial lysis. Postbiotics may contribute to the improvement of host health by having specific physiological effects because of their many health benefits. To confirm the clinical advantages of postbiotics, more randomized, placebo-controlled clinical trials are required. Considering all the literature into account, this review discusses various aspects of postbiotics including history and concepts, major historical milestones in development of the postbiotics and salient features of postbiotics. Further we discuss production, purification and characterization of postbiotics and also discuss classification of postbiotics and role of postbiotics in food industry. Although postbiotics shows various beneficial activities including antibacterial, anti-cancer, antiobesogenic, anti-inflammatory, antiproliferative, hypocholesterolemic, antioxidant, and immunomodulatory effects, composition and their bioactivity are essential and the degree of efficacy need to be investigated. Postbiotics have become the subject of an increasing number of international research projects since 2013. However, compared to probiotics and prebiotics, postbiotics have significantly fewer research projects because of their later start. Postbiotics will be the subject of more research, which will lead to fresh discoveries and a number of positive outcomes that will enhance their application in the food and pharmaceutical industries. The factors, such as eating habits, which may influence the utilization of these advantageous chemicals in functional foods should be assessed in further research. More research should be done in order to better understand how they affect the host. Additionally, because postbiotics are used widely in the food and pharmaceutical industries, it is essential that they be manufactured under ideal industrial conditions and with strict adherence to quality control standards. Additional consortium oriented research and initiatives will support the creation of safe, all-natural clean-label products that are also residue-free, preserving human health. Therefore, the quality of novel postbiotic components must be thoroughly assessed in order to achieve the additional health benefits. To ensure that the food and pharmaceutical sectors are successful and viable, it is also necessary to consider the long-term health benefits of taking these supplements. As a result, postbiotics are continually changing, and future study should focus on the effects of postbiotics on health to their specific processes. Further in-depth investigation into the biological response of the metabolites and host postbiotic interactions utilising different omic approaches suggests that postbiotics may have further applications in the clinical as well as non-clinical sectors. The main dietary sources where the effects of postbiotic supplementation have been studied are fermented baby formula and bacterial lysates. Overall, there is scant data to back up the assertion that these products are better for kids' health than postbiotic-free formulas.

Postbiotics have more pronounced effects on the food and health industries, hence research is needed to develop more standardised ways for evaluating the quantitative-effects link in a way that is more reasonable, scientific, and accurate. This will increase backing for the postbiotic preparations' wholesome and long-term growth. Despite the paucity of study on postbiotics' applications in the food industry and in medicine, studies are still required to address larger, better-quality, and more rigorous trial data to demonstrate the benefits of postbiotics. Additionally, several countries have incorporated postbiotics in their national legislation and made their goods available to the general public despite the lack of defined global regulatory standards for postbiotics. The definition, mechanism, efficacy, and safety of postbiotics are all being studied, and this study will provide producers and regulatory authorities with useful standards for evaluation. Postbiotic therapy' safety and potential hazards haven't been thoroughly studied or understood. More multicenter research is required to establish the outcomes and safety of different postbiotics.

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