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Postbiotics as Dynamic Biological Molecules for Antimicrobial Activity: A Mini-Review

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Abstract: Postbiotics, products, or metabolites secreted by living probiotic bacteria like teichoic acids, peptides, enzymes, peptidoglycans, polysaccharides, organic acids, and external cell proteins are said to be produced during the bacterial fermentation process. However, postbiotics may provide immunization, antioxidant, prevents inflammation, low cholesterolemic, antimicrobial, antagonistic obesity, contrast hypertensive, and diabetic retinopathy impacts. In the current review, we attempt to display the antimicrobial performance of postbiotics. In this regard, we considered microbial strains used as postbiotic sources and postbiotics as antimicrobial agents in food products. All databases such as Science Direct, Scopus, Pub Med, and Google Scholar were examined using the following keywords: "postbiotics", "Antimicrobial activity", "Anti-inflammatory", and "Low cholesterolemic". Further studies demonstrated that probiotics are fed special forms of fiber (prebiotic) molecules, indicating substances known as postbiotics. Furthermore, short-chain fatty acids (SCFAs) like acetate, propionate, and butyrate are among the comprehensively investigated postbiotics. The extraction and purification of these compounds are carried out by means of dialysis, centrifugation, and freeze-drying techniques. According to the gained results, postbiotics assist in improving host health by increasing certain physiological functions. Furthermore, postbiotics can be used to increment the useful lifetime of different foods, like dairy products. It has also been shown that manually adding postbiotics to such products prevents the growth and proliferation of molds and thus the spoilage caused by them. This inhibitory effect indicates the antimicrobial properties of these compounds. Finally, we will see significant advances in the biological preservation of products, especially in the food industry.

Keywords: postbiotics; antimicrobial activity; anti-inflammatory; prebiotic; low cholesterolemic; food industry.

1. Introduction

Since postbiotics have been discovered late and investigation has not developed, thus, access to probiotics is not easy. If you seek postbiotic supplements, choose elements that include distinctive kinds of postbiotic, mainly short-chain fatty acids [1], which can be used as a substitute for some nutrients in diets. The human gut is home to many microbiotas, and postbiotic compounds can effectively maintain the balance of this microbiota [2].

Probiotics are beneficial microorganisms that have one or more health effects on the consumer. Most of these health effects can be caused by the production of postbiotics by probiotics in the food product or the host body. However, the molecular mechanisms of probiotic function are complex and remain largely unknown [3]. In addition, despite the protected role of probiotics in the gut, there are problems with uncertainty about bioavailability, risk of infection, and the possibility of antibiotic resistance gene transfer [4]. One of the important goals in maximizing the beneficial effects of probiotics is to increase their survival rate within the fermented products and while passing through the host gastrointestinal tract to reach the main place of activity, the colon, in acceptable numbers (10^7 cfu/g or ml). Probiotics can help keep up stomach-related well-being by controlling destructive microscopic organisms' development and bolsters prebiotics amid a fermentation process, which could be a by-product of postbiotics [5]. Researchers have shown that postbiotics may support forestall total diabetes in individuals with pre-diabetes [6]. Once microbiota is parenthetically out of balance, making affront resistance or pre-diabetes within the person is conceivable [7].

It has been shown that a specific postbiotic named Muramyl Dipeptide (MDP) could diminish affront resistance notwithstanding conditions such as weight misfortune or changes within the intestine microbiome amid corpulence [8]. Schertzer concluded that the imbalance of microbiota and consequently the disruption in the production of postbiotics have a significant effect on the development of diabetes [9]. Therefore, it should be borne in mind that the reduction and imbalance in the number and types of natural microorganisms in the gastrointestinal tract can play a role in developing type 2 diabetes [10]. It is now clear how the gut microbiota sends signals to lower blood sugar [11]. Karim *et al*. (2017) inspected Effects from the distinctive composition of postbiotics and inulin RG14 upon development execution, cecal smaller scale biota, unstable greasy volatile fatty acids, and perfect cytokine explanation at Broilers [12].

The discoveries of inquiring about seem that the appearance of Interleukin 8/Chemokine (C-X-C motif) value was not affected with slim down. Inulin (as a prebiotic) and postbiotics (originated from probiotics)mixture are possible replacements to antimicrobial development boosters within the aviculture industry [13]. Konstantinos *et al.* [14] summarized a part from postbiotics at keeping up colonic's well-being then offered that postbiotics can stand a more secure elective at the analogy to living microbes. Studies have shown that the use of probiotics that produce post-antibiotics such as exopolysaccharides can contribute to gastrointestinal health and prevent diseases such as colon and rectal cancer [15] as Tsilengiri *et al.* suggested usage from postbiotic within therapy and anticipation with gut-relevant illnesses like provocative intestine illness [16].

In 2017, an effective audit was distributed, which checked on randomized, controlled human considers with any clinical endpoint where the mediation was a slaughtered probiotic [17]. Forty ponders were included within the audit. These 40 thinks were heterogeneous with respect to endpoint (avoidance or treatment of a cluster of infections), organism, ponder populace (grown-ups or pediatric). Creators point out, even though that thinks about were likely not fueled to identify a contrast. In two treatment thinks, slaughtered probiotics were way better than live [18]. In one avoidance consider, life was way better than murder. The audit, too, looked for proof of antagonistic impacts of the slaughtered organisms. Tragically, as is regularly the case, most ponders did a destitute work of collecting or detailing antagonistic events so that no conclusion can be made [19].

2. Postbiotics

Postbiotics are useful bioactive complexes produced in a milieu throughout the fermentation process, which can be employed to promote the healthiness of consumers. The more prebiotic carbohydrates available to probiotics, the more diverse postbiotics are produced in the fermentation environment [20]. Some studies have shown that in some cases, probiotics themselves can not play a role in maintaining and promoting intestinal health, but the postbiotics they produce can play an effective role in this regard [21]. Different types of postbiotics, including muramyl dipeptide, teichoic acid, lipopolysaccharide, exopolysaccharides, lactospin, and indole, are produced by probiotics. Short-chain fatty acids, such as acetic acid, butyric acid, and propionic acid, are among the leading largely scrutinized postbiotics [22]. These fatty acids play a major role in the physiological and digestive functions of the intestines. Participating in specific metabolic pathways and digestion and absorption of food play an important role in maintaining intestinal health [23]. Short-chain carbohydrates as probiotic postbiotics are not affected via human stomach-related proteins and advance has well-being by invigorating the development or action of one or a number of intestine microbiota [23-24]. These compounds originated from *Lactobacillus* species play their antimicrobial role in food and the host body as a substitute for live probiotic cells without an adequate number of probiotics [18]. Postbiotic may be a metabolic by-product created by a probiotic microorganism that impacts the host's organic capacities [25].

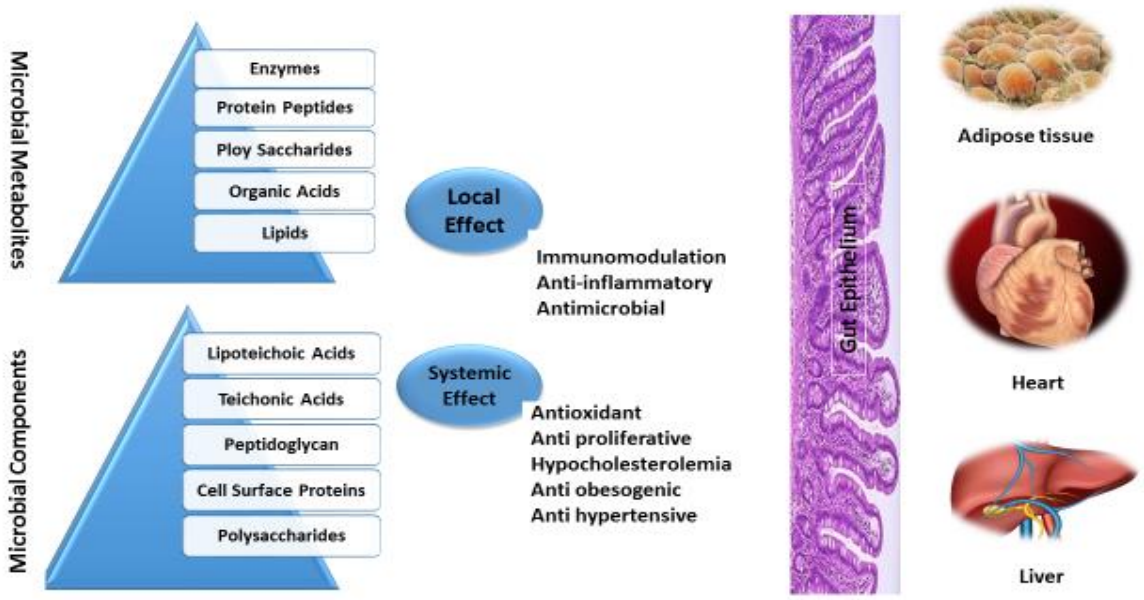

Figure 1. Applications of postbiotics and their potential local.

Bacterial by-products, determined as postbiotics, offer assistance in lowering blood sugar levels in stout individuals with pre-diabetes [26]. Scientists believe that postbiotics can assist overweight individuals with pre-diabetes and prevent them from creating type 2 diabetes [26-27]. Recently, postbiotics have been considered useful prebiotics that, in addition to having beneficial effects on their own, as a rich source of carbohydrates, nourish and increase the effectiveness of probiotics [28]. With the production of postbiotics, especially short-chain fatty acids, the pH is reduced, and the conditions for the growth and activity of pathogenic bacteria are limited [29].

Postbiotics are important for stimulating the growth and activity of *Bifidobacterium* and *Lactobacillus* bacteria [30]. Previously, the presence and activity of bacteria were thought to increase inflammatory reactions and increase blood sugar. Still, today it has been proven that the presence of probiotic bacteria and postbiotic compounds reduces blood sugar and improves insulin function in obese people [31]. In an investigation that researchers were bred to manipulate obese mice genetically, it was found that postbiotics increase the effect of insulin [32-35].

3. Antimicrobial Activity of Postbiotics

Postbiotics have emerged to address the potential bacterial hazards of living cell probiotics, based on the idea that bacterial survival is not essential for human health [36]. Although the postbiotics investigation is still generally later, antimicrobial properties show up to be one of their benefits [37]. Studies have shown that postbiotic compounds have antibacterial (pathogenic and spoiler bacteria) effects, thus preventing infectious diseases and food spoilage. These compounds prevent the colonization of pathogenic bacteria in the intestine and prevent intestinal diseases such as bad-tempered bowel disorder or provocative bowel illness [38]. Postbiotics are unmistakable living beings that apply advantageous impacts on the well-being of the have by influencing the microbial greenery of the body and preventing the replacement of invading bacteria in the gut wall, the production of antimicrobial agents, and changes in environmental acidity [39]. Therefore, by maintaining the balance of intestinal microbiota and establishing the process of fermentation and production of post-antibiotics, the rate of intestinal infections and even other diseases related to the gastrointestinal tract is significantly reduced [40, 41]. By binding to bacterial receptors, postbiotics do not permit pathogenic microorganisms such as toxin-producing *Clostridia*, and *E. coli* and eliminate them from the bowel lumen [42, 43].

Recent development in the understanding of postbiotics natural effects and relevant components uncovered it postbiotics are a proposing compelling prophylactic methodology to anticipate the chance of keeping up alive microorganisms or preterm newborn children that might replace and lead to disease [44, 45].

4. Microbial Strains Used as Postbiotic Sources

This can be required utilizing the need to avoid the improvement of safe antimicrobial strains of microbes that will propose at warm to human well-being [46]. *Lactobacillus* strains connected in people have to be utilized as postbiotics in creatures; in any case, Bifidobacterium strains segregated of a human source were utilized as postbiotics in people [47]. Over the last few decades, in most countries, including Europe, *Bacillus* strains are mainly used to produce postbiotics [48]. The main products of postbiotics are related to the production of different types of these compounds in the laboratory, such as the production of short-chain volatile fatty acids and exopolysaccharides. Also, most of the postbiotics employed in living being cultivating are lab resources of these compounds to apply at several animal species of aviculture [49], the pig [50], and likewise ruminants [51]. These compounds may additionally be separated from diverse feces species of animals, such as chicks [52], pig [53], and ruminants [54, 55]. *Bacillus pumilus* Mind 588 separated from ocean water have been inspected at creatures and appear plausibly for developing *E. coli* [56].

Giang *et al*. have separated lactic acid bacteria (LAB) from different materials areas of insides in sound stuffing pigs. These bacterial strains comprised *Enterococcus faecium*, *L. acidophilus*, *L. plantarum,* and *Pediococcus pentosaceus* and were utilized like postbiotics sources of weaned piglets to extend the development [56-57]. LAB strains such as *Pediococcus pentosaceus, P. lolii, L. pentosus, L. plantarum*, *L. buchneri, L. rapi*, and *L. rhamnosus* have been isolated from silages of humid and hot environments [58, 59]. Some studies have shown that LAB separated from youthful fecal calves such as *L. johnsonii*, *L. salivarius*, and *L. murinus*, have a capacity for form such as bacteriocin action versus pathogens [60].

A few inquires have detailed the postbiotics strains, Separate from both new Aquatic and ocean Aquatic creatures [61]. Detailed that *L. salivarius* from bottlenose porpoise can hinder the development of *Salmonella enteritidis* strains that separated both maritime creatures and people [62]. Detailed *Lactobacillus* strains were isolated from the little guts of piglets; most of the strains were of the *L. salivarius* species [63]. These strains appeared hopeful postbiotics virtues, comprising resistor to a pH of 3 and, auto-aggregation impacts and a capacity to appear the pathogen *E. coli* K88 emphatically [64].

Leuconostoc mesenteroides is a species of LAB separated from the bowel of freshwater fishes like snakehead fish [53] and Nile tilapia fish [65]. Employed postbiotics originated from *Leuconostoc cremoris* and *Weissella cibaria* of Atlantic salmon fish and possessed common octopuses [66].

Sarkono *et al*. have shown that *L. paracasei* separated from Normal state have a resistor to bile and acidic situation and have antibacterial activity against some pathogenic bacteria such as *Bacillus cereus, Staphylococcus aureus,* and *E. coli* [67].

Leuconostoc mesenteroides strains have been separated from the guts by new water angles like snakehead fish angle [68] and Nile tilapia angle [69-71].

Table 1. Some bacterial activities species of postbiotics.

Competition with pathogen	References
Lactobacillus plantarum I-UL4	[61]
Lactobacillus rhamnosus	[66]
Lactobacillus paracasei	[68]
Faecalibacterium prausnitzii	[68]
Lactobacillus brevis	[70]
Lactobacillus pentosus	[70]
Lactobacillus gasser	[71]

5. Postbiotics as Antimicrobial Agents in Food Products

LAB are completely affirmed as secure, dynamic, and utilitarian fixings for nourishments have a place in their long foundation of utilization along with aged nourishments [72]. Additionally, their metabolic conclusion items, like lactic acid and bacteriocin, can be utilized like normal perspective and antimicrobial operators against nourishment deterioration and defilement [73].

Beneficial effects of LAB have been determined exactly, for example, the prevention from urogenital infections [74], control from inflammatory intestine diseases [75], immunomodulation action [76], control of serum cholesterol [77], and hamper specific kinds of cancer [78]. Cell-free supernatant from *L. plantarum* YML 007 having a bio-preserving impact on soybeans caused enhanced shelf life of unshelled soybeans up to 2 months [79]. Exopolysaccharide from *L. rhamnosus* showed an 8.2% increase in Cheddar cheese yield with

L. lactis [68]. Bifidin from *Bifidobacterium lactis* Bb-12 resulted in increasing the shelf life of minced meat up to 3 months at -18˚C by 100 % reduction of *E. coli* O157:H7 [80].

Numerous components intervening in the well-being benefits of advantageous bacterial cells do vital practicality [81]. In any case, unused terms like postbiotic or paraprobiotic have developed to indicate that dead microbial cells, microbial divisions, or cell lysates are possible to propose physiological preferences for making extra bioactivity [82]. Postbiotics derived from LAB have been extensively studied, and it has been proven that each specific genus and species of this family produce specific postbiotics that have the property of dissolving. Also, the colonies of these bacteria are mucoid form in the culture medium and, in many cases, produce a film [83]. *L. plantarum*, as a primary strain of LAB can make PM with unmistakable postbiotics impacts detailed [84]. In addition to the developing reports of anticancer highlights of LAB, much-districted knowledge is available on the anti-proliferative and cytotoxic activity of PM produced via *L. plantarum*. Consequently, the cytotoxicity from PM discharged via 6 strains of *L. plantarum* on various cancer and normal cells has been explored [85].

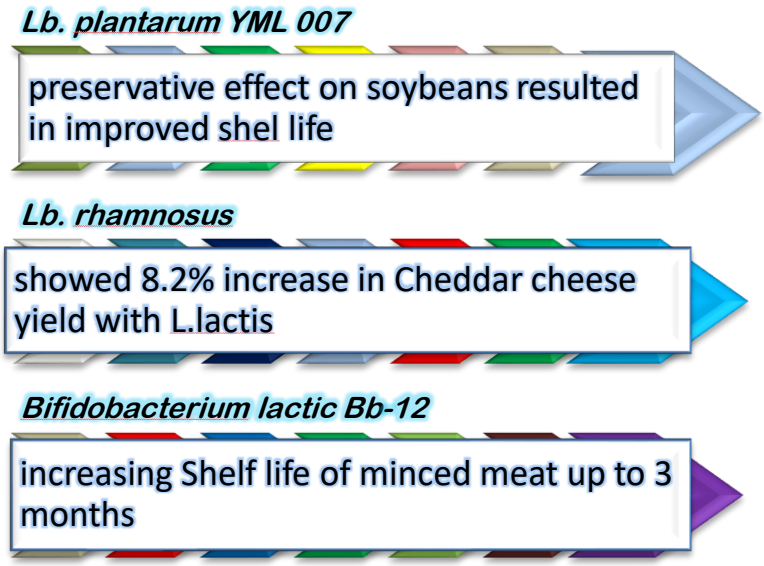

Figure 2. Postbiotic pathogens in the food industry.

6. Antimicrobial mechanisms of postbiotics

The potential utilization of postbiotic metabolites as a replacement for in-feed antimicrobials in animals has been inspected and demonstrated to be valuable [86]. Postbiotics propose to imitate the viable restorative impacts, anticipating the hazard of keeping up live microorganisms to preterm newborn children with youthful intestinal boundaries or disabled resistant protections [87]. Inside the gastrointestinal tract, many microorganisms can catabolize indigestible carbohydrates to produce large amounts of butyrate and volatile short-chain fatty acids [89].

Here are some of the health-promoting effects of postbiotics:

Impact on constipation: Existence and incomplete fermentation of carbohydrates in the gastrointestinal tract causes water to be trapped inside and, as a result, causes constipation. Also, fermentation of fibrous food products in the colon enhances microbiota capacity and amount of stool [90]. In a study of the elderly, it was shown that feeding on inulin (as an indigestible carbohydrate/prebiotic) relieves constipation and increases the amount of feces [91]. Postbiotics such as exopolysaccharides, which have a carbohydrate structure, have similar effects.

Impact on blood lipid-lowering: Studies have shown that postbiotics reduce the amount of lipids in the blood of animals. However, confirmation of this effect on humans requires further studies [92]. It has also been shown that postbiotics affect the activity of triglycerides and reduce the synthesis of fatty acids, which again has not been proven in humans [93].

Impact on inflammatory diseases: Postbiotics can strengthen the immune system of the body and the immune system of the gastrointestinal tract by strengthening and changing the flora of the intestinal tract, and as a result, prevent the occurrence of inflammatory diseases, especially intestinal inflammation [94].

Impact on the absorption of beneficial elements: investigations conducted on animal and human models have shown the helpful activity of postbiotics in the uptake of calcium, magnesium, zinc, and iron elements [95]. Human studies have indicated that digestible oligosaccharides positively affect calcium absorption when needed, especially during puberty and menstruation. Enhancing the amount of calcium, potassium, and magnesium ions in the intestinal lumen controls and prevents cellular transformation [96].

Impact on cancer lessening: Studies have shown that with an increasing amount of probiotics in the gastrointestinal tract, the production of postbiotics such as oligosaccharides and butyrate is increasing that these compounds play an important role in controlling preventing cell deformation and cancer [97]. Also, it has been shown that postbiotics can increase the activity of *Lactobacillus* and *Bifidobacteria*, causing these bacteria to join with certain carcinogens and neutralizing them [98]. Indeed, the ideal generation of inhibitory action of postbiotic highlights is crucial, agreeing to its improving mechanical capacities. Consider in past decades has highlighted the improvement of bacitracin generation beneath controlled aging circumstances [99].

7. Future Perspectives of Postbiotics

This article reviews the antimicrobial properties of postbiotics and highlights aspects of overcoming microbial resistance. With enhancing impacts of antibiotics, it gives the impression that co-administration of antibiotics and postbiotics can be a proper way to overwhelm the problem of microbial resistance. However, proof of this theory requires extensive laboratory and clinical animal and human studies [100, 101]. The most refinement between a postbiotic and a probiotic is that a probiotic must be an alive organism when managed [102]. Postbiotics refer to different parts of a dead and broken cell or to the extracellular secretions of living bacteria. The most intrigued in postbiotics stems from the viable reality that after you don't get to stress approximately keeping the organism lively, fabricate, bundling, capacity, transport, and all taking care of for all intents and purposes are enormously simplified. Because of its activity, the structure of a probiotic may raise concerns about a possible infection; inactive and dead organisms are a safer alternative to probiotics. Already, a series of studies are proving the effects of post-biotics on human health. One of the applications to increase the effectiveness of postbiotics can be microencapsulation of these compounds, as probiotics are microencapsulated to increase the viability and targeted release [103, 104].

Figure 3. Future trends of postbiotic applications.

4. Conclusions

Nowadays, there is increasing attention to probiotic impacts determined using microbial metabolites considered like bioactive postbiotic metabolites. Postbiotics are considered dissolvable agents (items or metabolic by-products), created using live microorganisms, or discharged then bacterial lysis, like as proteins, teichoic acids, peptides peptidoglycan is taken peptidoglycans, cell surface proteins, polysaccharides, and natural acids. These postbiotic have fallen intrigued according to their self-evident chemical features, security dosage items, long rack life, and the substance of diverse signaling particles that will have anti (inflammatory obesogenic, immunomodulatory, hypertensive, proliferative, oxidant) hypocholesterolemia applications. These focused favors which postbiotics may chip into the advancement of having well-being with raising certain physiological needs implementation, in spite of the fact that the proper items have not been completely clarified.

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Conflicts of Interest

The authors declare no conflict of interest.

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