

## An Oral Microbiome Perspective: Postbiotics as a Prospective Therapeutic Agents in Dental Medicine (A Short Communication)

Aditya Rediana Friyandika<sup>1\*</sup>, Luthfian Ibnu Afan<sup>2</sup>

Universitas Muhammadiyah Yogyakarta

**Corresponding Author:** Aditya Rediana Friyandika

[aditya.rediana14@gmail.com](mailto:aditya.rediana14@gmail.com)

---

### ARTICLE INFO

*Keywords:* Postbiotics, Oral Microbes, Biofilm, Probiotics, Oral Health

*Received :* 1 September

*Revised :* 17 October

*Accepted:* 18 November

©2024 Friyandika, Afan: This is an open-access article distributed under the terms of the [Creative Commons Attribution 4.0 International](https://creativecommons.org/licenses/by/4.0/).



### ABSTRACT

Recently, there has been an increase in interest in the use of microorganisms that are used as a preventive effort to prevent dental and oral health problems, known as probiotics, prebiotics, synbiotics, and postbiotics. As more and more clinical trials of the use of microorganisms show positive results for certain conditions, Postbiotics have several advantages, including safety, longer shelf life, absence of risk and patentability, which makes them more attractive than probiotics. This review covers a wide range of aspects, starting with an introduction, terminology, role of post biotik, and a brief mechanism of action. The discovery section concludes by highlighting the challenges and future directions to improve postbiotic discovery. The review concludes by highlighting the ongoing applications of postbiotics in expanded clinical trials, providing a comprehensive overview of the current landscape in postbiotic development

## **INTRODUCTION**

In the modern era, medical technology continues to develop, bringing great hope for the prevention and cure of chronic and acute diseases. One of the most dynamic fields is dental medicine, as evidenced by the development of technology and biotechnology that creates innovative solutions to maintain dental and oral health (Salminen et al., 2021). One promising area is the use of microorganism-based products in dental medicine (Kessler et al., 2022). The use of microorganisms as an alternative to conventional methods is believed to bring a new paradigm in medicine, which has been rapidly evolving lately. Conventional methods such as the use of chemicals and physical substances in preventing dental caries are often considered ineffective enough and can even disrupt the balance of microbes (Luo et al., 2024). Therefore, the use of microorganism products continues to be developed as bio-intervention agents that are believed to be able to replace cariogenic microorganisms, even able to colonize in the oral cavity, and proven to be the main choice as prevention and treatment efforts in the world of health (Ma et al., 2023). Probiotics, prebiotics, synbiotics, and postbiotics are terms that are becoming increasingly popular in the world of medicine, especially in the context of modulating the body's microbiome (Liu et al., 2021).

Probiotics have been used to increase the population of good bacteria in the oral cavity. This has been shown to result in a decrease in the production of organic acids that have the potential to damage tooth enamel. However, it should be noted that probiotics have certain limitations, including individual sensitivity and the potential for bacteria to migrate to unwanted locations (Saiz et al., 2021). Therefore, prebiotics are the key factor. Prebiotics serve as substrates for probiotics, thereby facilitating the growth and activity of beneficial bacterial colonies in the oral cavity and increasing the overall efficacy of probiotics (Swanson et al., 2020). The combination of probiotics and prebiotics, known as synbiotics, has shown considerable potential to affect the oral microbiome (Nunpan et al., 2019).

Synbiotics have been shown to increase beneficial bacterial populations, reduce the incidence of pathogenic infections, and facilitate periodontal tissue regeneration (Nunpan et al., 2019). Clinical studies have shown that synbiotics are considered an effective oral biofilm modifier and anti-caries treatment, especially for high-risk patients. This is a promising ecology-based approach to caries prevention (Babu et al., 2023). However, studies in synbiotic research and development have received less attention compared to probiotics, as the concept is relatively newer (Luo et al., 2024).

Postbiotics, a relatively new phenomenon in the field of microbiology, have emerged as a safer alternative to live probiotics. Postbiotics are fermentation byproducts of probiotics that have undergone fermentation and death but still have the capacity to provide direct health benefits to the host (Nataraj et al., 2020). These postbiotics offer a safer alternative to live probiotics because there is no risk of translocation of bacteria into the blood or transfer of antibiotic resistance (Deshpande et al., 2018).

The utilization of microorganisms in dentistry has undergone a significant transformation, evolving from the traditional perspective of solely associating diseases with microorganisms to a more contemporary review that recognizes microorganisms as integral contributors to the maintenance of oral health. This perspective offers significant promise in the prevention and treatment of various oral diseases, as well as in improving the quality of life of patients in a more optimal way. Hopefully, this short communication will bring more light on the clinical implications and prospective applications of postbiotics in dentistry, as well as their linkages with other biomedical technologies.

## LITERATURE REVIEW

### Probiotic

Probiotics were first introduced in 1908, and since then, probiotics have continued to be researched and developed gradually. The International Scientific Association of Probiotics and Prebiotics (ISAPP) in 2013 defined probiotics as living microorganisms that, when administered in sufficient amounts, are able to provide health benefits to their hosts (Luo et al., 2024). Previously, Meurman et al. had introduced probiotics for the first time in dentistry; two decades earlier, Meurman et al. introduced *Lactobacillus rhamnosus* GG ATCC 53103, which was proven to colonize the human oral cavity (Luo et al., 2024). Then the development of research and its application continued until probiotics were proven to be able to reduce the level of *S. mutans* in saliva and dental plaque and even restore the balance of the oral microbiota (Luo et al., 2024). Some research has also shown that probiotics are effective in preventing and treating various oral diseases, such as dental caries, oral mucositis, and halitosis (Saiz et al., 2021). Research by Adiningrat et al. showed that *Lactobacillus acidophilus* probiotics are effective in preventing the maturation of biofilms, which are the cause of failure in endodontic treatments (Adiningrat et al., 2023). As a result, probiotics are often applied in several products, such as dairy, food, and even the aquaculture industry (Ma et al., 2023). Probiotic products work in a variety of ways, including those involving immunomodulation, the production of antimicrobial compounds, direct combinations, or competitive inhibition of pathogens (Piqué et al., 2019). Probiotics are made from several other gram-positive bacteria, such as bacteria from the genera *Streptococcus*, *Bacillus*, and *Enterococcus* (McFarland, 2006). Probiotics do have health benefits, but they must weigh storage stability, side effects on immune disorders, antibiotic resistance, and potential transmission. One of the facts is that there are many bacteria that are sensitive to oxygen and heat (Scott et al., 2022). Nowadays, probiotics are increasingly popular in their use. Probiotics have the ability to enhance and control the immune response (Szydłowska & Sionek, 2022). In addition, the use of probiotics has many benefits for human health, including antimicrobials, lactose intolerance, diarrheal diseases, ulcer treatment, immunity enhancement, food preservation, and colon cancer prevention (Luo et al., 2024).

### **Prebiotic**

Prebiotics were first introduced in 1955; then, in 2017, ISAPP defined prebiotics as "substrates used selectively by host microorganisms that provide health benefits" (Gibson et al., 2017). The substrate in question is an original product from within the body that cannot be digested. Prebiotics are a safe and potent alternative to probiotic interventions, as prebiotics are not live bacteria and are not particularly susceptible to environmental factors that affect the survival and efficacy of probiotics (Żółkiewicz et al., 2020). Prebiotic products include sugar, sugar alcohol, oligosaccharides, arginine, urea, and nitrates (Luo et al., 2024).

### **Synbiotic**

Synbiotics were first introduced by Gibson et al. in 1995 as a combination of probiotics and prebiotics; then, in 2020, ISAPP updated its definition of symbiotics as "a mixture consisting of non-host living microorganisms and substrates selectively used by host microorganisms, which provide health benefits to the host (Gibson et al., 2017)." The substrate mentioned is a prebiotic. Two categories of synbiotics are recognized. Complementary synbiotics consist of probiotics and prebiotics that together provide one or more health benefits but do not require interdependent functions. The components should be used at doses that have been shown to be effective for the components themselves. Synergistic synbiotics contain substrates that are selectively used by living microorganisms that are given together (Nunpan et al., 2019). Currently, the use of synbiotics is not fully promising because, according to the effects of synbiotics on metabolic health, it is still unclear (Żółkiewicz et al., 2020).

### **Postbiotic**

Postbiotics is a new phenomenon that is increasingly attracting the attention of researchers. Postbiotics are not only metabolites resulting from probiotic fermentation but also the inclusion of microbial cell inactivation and its components that provide direct health benefits to the host. In 2021, the definition has been established by ISAPP (International Scientific Association for Probiotics and Prebiotics), namely "the preparation of non-living microorganisms and/or their components that exert a healthy influence on their hosts" (Salminen et al., 2021). In the sense that a postbiotic is a microbial cell or a component of a cell that is deliberately killed with or without a metabolite process, which contributes to health benefits (Gibson et al., 2017). These postbiotics offer a safer alternative to live probiotics because there is no risk of translocation of bacteria into the blood or transfer of antibiotic resistance (Wegh et al., 2019).

Before the term postbiotic was still not officially stated in some literature, it was called by other terms used, namely, para-probiotics, parapsychobiotics, ghost biotics, metabiotics, tyndallized probiotics, and bacterial lysates (Salminen et al., 2021).

Forms of postbiotics can be of various kinds, including acid metabolites such as peptidoglycans, exopolysaccharides, teichoic acid, bacteriocins, etc. (Salminen et al., 2021). Postbiotic metabolites such as short-chain fatty acids (SCFAs) and biosurfactants can increase local immune activity and reduce oral pathogenic infections. Early studies have shown that postbiotics can be used as a

preventive agent against periodontal infections and gingivitis, as well as improve overall oral health (Wegh et al., 2019).

The three main mechanisms of postbiotic products include modulation of pathogen protection, increased epithelial barrier, and modulation of inflammatory and immune responses (Beattie, 2024). Postbiotics are considered superior to probiotics due to their good acid-base and thermal stability, ease of storage and use, and high safety due to their stability to oxygen and hot temperatures (Scott et al., 2022). In contrast to probiotics, some probiotics may be unstable under certain storage conditions or when combined with medications, as well as pose potential risks to an individual's weakened immune system (McFarland, 2006). Therefore, postbiotics are the right products to complement probiotic products and become a comprehensive bio-intervention (Scott et al., 2022).

Probiotics still need to be considered about the content of different probiotic ingredients as well as strains that exhibit unique characteristics; understanding the specifics of each strain is essential in the prevention and treatment of dental caries. Unlike postbiotics, even if there are no live microorganisms, it is possible to lose the excess of the product. CFS and heat-activated probiotics are two types of postbiotics commonly used in the prevention and treatment of dental caries. However, it should be noted that a wider range of postbiotics – peptidoglycans, lipopolysaccharides, and pili 179 – have been researched in studies outside the oral cavity. Further investigation of different postbiotic mechanisms of action for dental caries could offer innovative methods for preventing and treating this condition (Scott et al., 2022). More research is also needed to evaluate the safety and effectiveness of postbiotics to promote better health outcomes.

One of the promising postbiotics is exosome. Exosomes, also known as intraluminal vesicles (ILVs), are enclosed by a single outer membrane and secreted by all cell types small vesicles that are secreted by cells and function in communication between cells (Qiao et al., 2023). Exosomes have the potential to modulate the immune system and improve oral health by reducing inflammation and improving epithelial integrity. Research shows that exosomes from probiotic bacteria can reduce intestinal permeability and improve epithelial barrier function, which is particularly relevant in the context of dental health (Doyle & Wang, 2019). With their ability to send signals to immune cells, exosomes can contribute to the regulation of local immune responses in the mouth, helping to fight infections and maintain the balance of the oral microbiota.

## Role of Postbiotics

### *Modulation in Microbiota Resident*

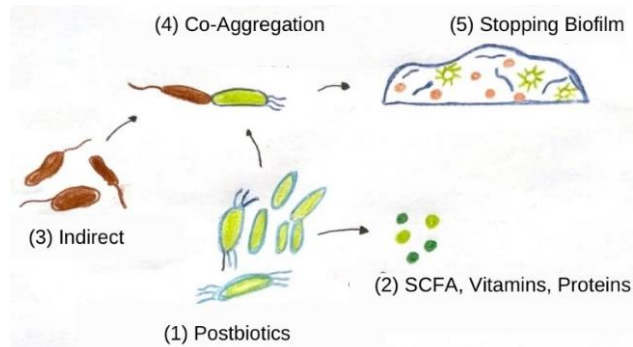


Figure 1. Protective Modulations Against Pathogens. Postbiotics (1), Production of SCFA, Vitamins, Proteins (2), Indirect (3), Co-Aggregation (4), Stopping Biofilm (5)

Mechanisms such as lactic acid transfer, which is consumed by members of the microbiota, modulate the microbiota indirectly by the postbiotic. This results in the production of SCFA and butyrate, which have a positive effect (Laverde Gomez et al., 2019). If the postbiotic provides adhesins such as fimbria and lectins that remain unchanged after processing, the postbiotic can also compete with resident microorganisms for the site of adhesion. Postbiotics stop intestinal pathogens with bacteriocins and metabolites, block the formation of biofilms, and destroy some pathogenic microorganisms (Barcenilla et al., 2000).

### *Improved Epithelial Barrier Function*

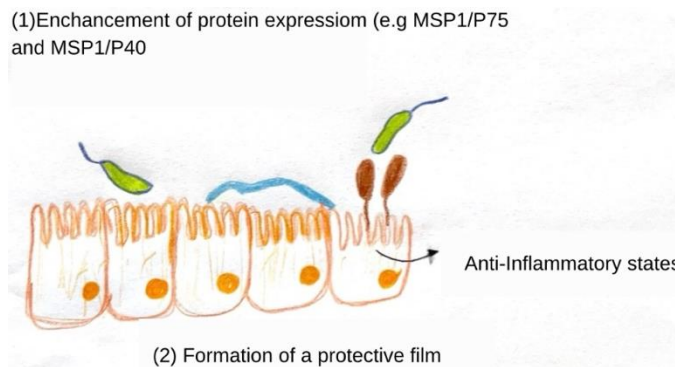


Figure 2. Improved Epithelial Barrier Function. Enhancement of Protein Expression (E.G MSP1/P75 And MSP1/P40) (1), Formation of a Protective Film(2)

The main proteins secreted Msp1/p75 and Msp1/p40 or a new protein named HM0539 from the probiotic model *L. Rhamnosus* GG can improve epithelial barrier function (Yan et al., 2013). In addition, surface-associated exopolysaccharides (sPEC) of *Bifido* bacteria species (*B. long*) can improve barrier function by reducing inflammation and preventing abnormal inflammatory reactions. It is possible that short-chain fatty acids can control the epithelial barrier function and protect the epithelium from damage caused by lipopolysaccharides (Elson & Cong, 2012).

*Modulation of Local and Systemic Immune Responses*

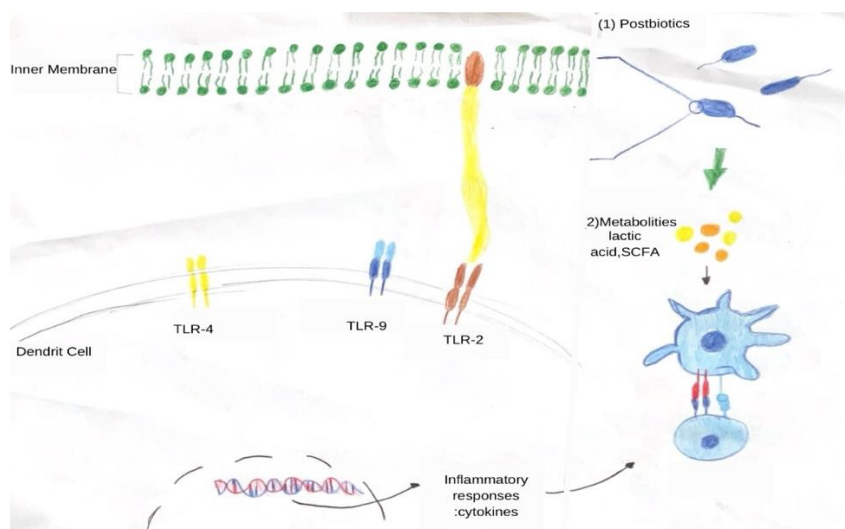


Figure 3. Modulation of Local and Systemic Immune Responses. Postbiotics (1), Metabolites Lactic such as Acid, SCFA (2), Inflammatory Responses such as Cytokines (3)

Microorganism-associated molecular patterns (MAMPs) perform immunomodulatory functions by interacting with specific immune cell pattern recognition (PRR) receptors, such as toll-like receptors (TLRs), nucleotide-binding oligomerization domain receptors (NODs), and type C lectins (Chung et al., 2019). These interactions result in the manufacture of various cytokines and immune modulators at both the local and systemic levels. If these MAMPs are not destroyed or altered, microbial metabolites present in postbiotic formulations, such as lactic acid, indole tryptophan derivatives, histamine, and branched-chain fatty acids and SCFAs, can affect the systemic immune response (Lemoine et al., 2023).

## METHODOLOGY

We conducted a narrative literature review using the PubMed database, a platform for medical literature. The searching process began with the identification of relevant keywords, including "postbiotics," "microbiota," "biofilm," "probiotics," and "oral health." These keywords and combinations were used to narrow down the search results and ensure that the sorted articles were related to the topic at hand.

After entering the keywords into the PubMed search platform, we used Boolean operators (AND, OR, NOT) to optimize the search results. For example, searching with the phrase "oral microbiome AND postbiotics" allowed us to find articles that specifically addressed the interaction between the oral microbiome and postbiotics.

The initial search results yielded a large number of articles, we proceeded to filter the information further. To further filter the information, we applied several parameters provided by PubMed, including publication type, publication date, and language. We focused on articles published within the last twenty-five years to ensure that the information was current and relevant.

After focusing on articles published within the last twenty-five years, we saved the relevant articles in PDF format and made brief notes on the research objectives, methodology, and main results of each article.

## **RESULT**

According to our literature study, we found 75 articles. We set the inclusion criteria to include articles that explicitly addressed the effects of postbiotics on oral health and the oral microbiome. However, articles that were not peer-reviewed or irrelevant to our research topic were excluded from the list. After applying the inclusion and exclusion criteria, the number was reduced to 54. We conducted a thorough review of the selected articles, noting the methodology, results, and conclusions of each study. This process further narrowed the selection to a limited number of articles. In the end, 36 articles were chosen as primary literature sources. They were selected based on their relevance, quality, and contribution to understanding the role of postbiotics in the oral microbiome and dentistry. These chosen articles not only adhere to academic standards but also offer valuable insights into this topic.

## **DISCUSSION**

Postbiotic usage can decrease the growth of pathogenic bacteria such as *Veillonella* spp., *Actinomyces graevenitzii*, *Prevotella* spp., and *Selenomonas* spp., as well as the quantity of oral pathogens like *Streptococcus mutans*, the primary bacterium that causes dental caries (Lin et al., 2022). Furthermore, postbiotics have antioxidant qualities that might aid in lowering the inflammatory response in periodontal tissue, which is valuable for treating periodontitis (Butera et al., 2022). The potential of postbiotics to assist the regeneration of periodontal tissue and to repair and remineralize the radicular surface of teeth is another advantage of their usage (Van Holm et al., 2023). Peptides, teichoic acids, and polysaccharides are examples of bioactive metabolites that can break down pathogen membranes and lessen their capacity to colonize (Xie et al., 2024). Furthermore, postbiotics have the ability to prevent the development of biofilms, which provide the perfect environment for bacteria to proliferate and develop antibiotic resistance (Homayouni Rad et al., 2020). In addition, postbiotics have a strong immunomodulatory impact. Cytokines are chemical mediators that contribute to the body's inflammatory response, and SCFA compounds have the ability to increase their synthesis (Xie et al., 2024). Because of their qualities that promote food safety, postbiotics can potentially be utilized as an alternative food preservative. Because they prolong food's shelf life and prevent food from spoiling, these items are crucial for maintaining food safety and fostering health (Vera-Santander et al., 2023). Additionally, postbiotics may improve food's nutritional content and other health advantages (Wegh et al., 2019). By lowering the risk of some foodborne infections, fermented foods containing postbiotics may

also enhance gut health (Wegh et al., 2019). Researchers' attention has been drawn to the direction of postbiotic research in recent years, and it has steadily grown into a popular area of study. Since many probiotics are susceptible to heat and oxygen, postbiotics are thought to be safer than probiotics because of their high safety, simplicity of use and storage, and good acid-base and thermal stability (Maleki et al., 2021). These possibilities point to a bright future for postbiotics in dentistry, both in terms of treating and preventing a range of oral diseases. Confirmation of the safety and efficacy of postbiotic usage in clinical dental applications requires more investigation.

## CONCLUSION AND RECOMMENDATION

A paradigm change toward more efficient and comprehensive methods of managing oral health is represented by the incorporation of postbiotics into daily practice in the dental treatment. Optimizing postbiotic formulations and investigating their long-term impacts in a variety of groups should be the main goals of the future studies. Dental medicine transformation may greatly enhance treatment modalities and preventative approaches by implementing these cutting edge therapeutic agents, which will eventually improve the holistic outcome and the patient's quality of life.

## FURTHER STUDY

This study may exhibit several limitations in the literature deep exploration, details mechanism in the underlying molecular mechanisms and also the clinical validated evidence in proposing this idea. A more comprehensive understanding is required to support postbiotic promotion for dental medicine in the future.

## ACKNOWLEDGMENT

Thank you to the Faculty of Dentistry and the Molecular Medicine and Therapy Research Laboratory RIC, Universitas Muhammadiyah Yogyakarta, for supporting this study.

## REFERENCES

- Adiningrat, A., Kusnadi, R. A., Allam, A. S., Sofiani, E., Maulana, I., & Yumoto, H. (2023). The Effect of Probiotic *Lactobacillus acidophilus* and Ethanolic Propolis Compound toward Nucleic Acid Deposition in the Extracellular Polymeric Substance of Root Canal Bacteria. *European Journal of Dentistry*, 17(02), 418–423. <https://doi.org/10.1055/s-0042-1750771>
- Babu, A. S., Guruprasath, N., Adeyeye, S. A. O., Sankarganesh, P., Kumar, A. G., & Sivapriya, T. (2023). A Critical Analysis of Postbiotics: Exploring their Potential Impact on the Health and Food Industries. *Journal of Pure and Applied Microbiology*, 17(4), 2041–2059. <https://doi.org/10.22207/JPAM.17.4.18>
- Barcenilla, A., Pryde, S. E., Martin, J. C., Duncan, S. H., Stewart, C. S., Henderson, C., & Flint, H. J. (2000). Phylogenetic Relationships of Butyrate-Producing Bacteria from the Human Gut. *Applied and Environmental Microbiology*, 66(4), 1654–1661. <https://doi.org/10.1128/AEM.66.4.1654-1661.2000>

- Beattie, R. E. (2024). Probiotics for oral health: A critical evaluation of bacterial strains. *Frontiers in Microbiology*, 15, 1430810. <https://doi.org/10.3389/fmicb.2024.1430810>
- Butera, A., Gallo, S., Pascadopoli, M., Taccardi, D., & Scribante, A. (2022). Home Oral Care of Periodontal Patients Using Antimicrobial Gel with Postbiotics, Lactoferrin, and Aloe Barbadensis Leaf Juice Powder vs. Conventional Chlorhexidine Gel: A Split-Mouth Randomized Clinical Trial. *Antibiotics*, 11(1), 118. <https://doi.org/10.3390/antibiotics11010118>
- Chung, I.-C., OuYang, C.-N., Yuan, S.-N., Lin, H.-C., Huang, K.-Y., Wu, P.-S., Liu, C.-Y., Tsai, K.-J., Loi, L.-K., Chen, Y.-J., Chung, A.-K., Ojcius, D. M., Chang, Y.-S., & Chen, L.-C. (2019). Pretreatment with a Heat-Killed Probiotic Modulates the NLRP3 Inflammasome and Attenuates Colitis-Associated Colorectal Cancer in Mice. *Nutrients*, 11(3), 516. <https://doi.org/10.3390/nu11030516>
- Deshpande, G., Athalye-Jape, G., & Patole, S. (2018). Para-probiotics for Preterm Neonates-The Next Frontier. *Nutrients*, 10(7), 871. <https://doi.org/10.3390/nu10070871>
- Doyle, L., & Wang, M. (2019). Overview of Extracellular Vesicles, Their Origin, Composition, Purpose, and Methods for Exosome Isolation and Analysis. *Cells*, 8(7), 727. <https://doi.org/10.3390/cells8070727>
- Elson, C. O., & Cong, Y. (2012). Host-microbiota interactions in inflammatory bowel disease. *Gut Microbes*, 3(4), 332–344. <https://doi.org/10.4161/gmic.20228>
- Gibson, G. R., Hutkins, R., Sanders, M. E., Prescott, S. L., Reimer, R. A., Salminen, S. J., Scott, K., Stanton, C., Swanson, K. S., Cani, P. D., Verbeke, K., & Reid, G. (2017). Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nature Reviews Gastroenterology & Hepatology*, 14(8), 491–502. <https://doi.org/10.1038/nrgastro.2017.75>
- Homayouni Rad, A., Aghebati Maleki, L., Samadi Kafil, H., Fathi Zavoshti, H., & Abbasi, A. (2020). Postbiotics as novel health-promoting ingredients in functional foods. *Health Promotion Perspectives*, 10(1), 3–4. <https://doi.org/10.15171/hpp.2020.02>
- Kessler, S. Q. S., Lang, P. M., Dal-Pizzol, T. S., & Montagner, F. (2022). Resistance profiles to antifungal agents in *Candida albicans* isolated from human oral cavities: Systematic review and meta-analysis. *Clinical Oral Investigations*, 26(11), 6479–6489. <https://doi.org/10.1007/s00784-022-04716-2>
- Laverde Gomez, J. A., Mukhopadhyay, I., Duncan, S. H., Louis, P., Shaw, S., Collie-Duguid, E., Crost, E., Juge, N., & Flint, H. J. (2019). Formate cross-feeding and cooperative metabolic interactions revealed by transcriptomics in co-cultures of acetogenic and amyolytic human colonic bacteria. *Environmental Microbiology*, 21(1), 259–271. <https://doi.org/10.1111/1462-2920.14454>
- Lemoine, A., Tounian, P., Adel-Patient, K., & Thomas, M. (2023). Pre-, pro-, syn-, and Postbiotics in Infant Formulas: What Are the Immune Benefits for Infants? *Nutrients*, 15(5), 1231. <https://doi.org/10.3390/nu15051231>

- Lin, C.-W., Chen, Y.-T., Ho, H.-H., Kuo, Y.-W., Lin, W.-Y., Chen, J.-F., Lin, J.-H., Liu, C.-R., Lin, C.-H., Yeh, Y.-T., Chen, C.-W., Huang, Y.-F., Hsu, C.-H., Hsieh, P.-S., & Yang, S.-F. (2022). Impact of the food grade heat-killed probiotic and postbiotic oral lozenges in oral hygiene. *Aging*, 14(5), 2221–2238. <https://doi.org/10.18632/aging.203923>
- Liu, Y., Wang, J., & Wu, C. (2021). Modulation of Gut Microbiota and Immune System by Probiotics, Pre-biotics, and Post-biotics. *Frontiers in Nutrition*, 8, 634897. <https://doi.org/10.3389/fnut.2021.634897>
- Luo, S.-C., Wei, S.-M., Luo, X.-T., Yang, Q.-Q., Wong, K.-H., Cheung, P. C. K., & Zhang, B.-B. (2024). How probiotics, prebiotics, synbiotics, and postbiotics prevent dental caries: An oral microbiota perspective. *NPJ Biofilms and Microbiomes*, 10(1), 14. <https://doi.org/10.1038/s41522-024-00488-7>
- Ma, L., Tu, H., & Chen, T. (2023). Postbiotics in Human Health: A Narrative Review. *Nutrients*, 15(2), 291. <https://doi.org/10.3390/nu15020291>
- Maleki, A., Hasannezhad, P., Abbasi, A., & Khani. (2021). Antibacterial, Antiviral, Antioxidant, and Anticancer Activities of Postbiotics: A review of Mechanisms and Therapeutic Perspectives. *Biointerface Research in Applied Chemistry*, 12(2), 2629–2645. <https://doi.org/10.33263/BRIAC122.26292645>
- McFarland, L. V. (2006). Meta-Analysis of Probiotics for the Prevention of Antibiotic Associated Diarrhea and the Treatment of Clostridium difficile Disease. *The American Journal of Gastroenterology*, 101(4), 812–822. <https://doi.org/10.1111/j.1572-0241.2006.00465.x>
- Nataraj, B. H., Ali, S. A., Behare, P. V., & Yadav, H. (2020). Postbiotics-parabiotics: The new horizons in microbial biotherapy and functional foods. *Microbial Cell Factories*, 19(1), 168. <https://doi.org/10.1186/s12934-020-01426-w>
- Nunpan, S., Suwannachart, C., & Wayakanon, K. (2019). Effect of Prebiotics-Enhanced Probiotics on the Growth of Streptococcus mutans. *International Journal of Microbiology*, 2019, 4623807. <https://doi.org/10.1155/2019/4623807>
- Piqué, N., Berlanga, M., & Miñana-Galbis, D. (2019). Health Benefits of Heat-Killed (Tyndallized) Probiotics: An Overview. *International Journal of Molecular Sciences*, 20(10), 2534. <https://doi.org/10.3390/ijms20102534>
- Qiao, X., Tang, J., Dou, L., Yang, S., Sun, Y., Mao, H., & Yang, D. (2023). Dental Pulp Stem Cell-Derived Exosomes Regulate Anti-Inflammatory and Osteogenesis in Periodontal Ligament Stem Cells and Promote the Repair of Experimental Periodontitis in Rats. *International Journal of Nanomedicine*, Volume 18, 4683–4703. <https://doi.org/10.2147/IJN.S420967>
- Saiz, P., Taveira, N., & Alves, R. (2021). Probiotics in Oral Health and Disease: A Systematic Review. *Applied Sciences*, 11(17), 8070. <https://doi.org/10.3390/app11178070>
- Salminen, S., Collado, M. C., Endo, A., Hill, C., Lebeer, S., Quigley, E. M. M., Sanders, M. E., Shamir, R., Swann, J. R., Szajewska, H., & Vinderola, G. (2021). The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics.

- Nature Reviews. Gastroenterology & Hepatology, 18(9), 649–667.  
<https://doi.org/10.1038/s41575-021-00440-6>
- Scott, E., De Paepe, K., & Van De Wiele, T. (2022). Postbiotics and Their Health Modulatory Biomolecules. *Biomolecules*, 12(11), 1640.  
<https://doi.org/10.3390/biom12111640>
- Swanson, K. S., Gibson, G. R., Hutkins, R., Reimer, R. A., Reid, G., Verbeke, K., Scott, K. P., Holscher, H. D., Azad, M. B., Delzenne, N. M., & Sanders, M. E. (2020). The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of synbiotics. *Nature Reviews Gastroenterology & Hepatology*, 17(11), 687–701.  
<https://doi.org/10.1038/s41575-020-0344-2>
- Szydłowska, A., & Sionek, B. (2022). Probiotics and Postbiotics as the Functional Food Components Affecting the Immune Response. *Microorganisms*, 11(1), 104. <https://doi.org/10.3390/microorganisms11010104>
- Van Holm, W., Lauwens, K., De Wever, P., Schuermans, A., Zayed, N., Pamuk, F., Saghi, M., Fardim, P., Bernaerts, K., Boon, N., & Teughels, W. (2023). Probiotics for oral health: Do they deliver what they promise? *Frontiers in Microbiology*, 14, 1219692. <https://doi.org/10.3389/fmicb.2023.1219692>
- Vera-Santander, V. E., Hernández-Figueroa, R. H., Jiménez-Munguía, M. T., Mani-López, E., & López-Malo, A. (2023). Health Benefits of Consuming Foods with Bacterial Probiotics, Postbiotics, and Their Metabolites: A Review. *Molecules*, 28(3), 1230.  
<https://doi.org/10.3390/molecules28031230>
- Wegh, C. A. M., Geerlings, S. Y., Knol, J., Roeselers, G., & Belzer, C. (2019). Postbiotics and Their Potential Applications in Early Life Nutrition and Beyond. *International Journal of Molecular Sciences*, 20(19), 4673.  
<https://doi.org/10.3390/ijms20194673>
- Xie, W., Zhong, Y.-S., Li, X.-J., Kang, Y.-K., Peng, Q.-Y., & Ying, H.-Z. (2024). Postbiotics in colorectal cancer: Intervention mechanisms and perspectives. *Frontiers in Microbiology*, 15, 1360225.  
<https://doi.org/10.3389/fmicb.2024.1360225>
- Yan, F., Liu, L., Dempsey, P. J., Tsai, Y.-H., Raines, E. W., Wilson, C. L., Cao, H., Cao, Z., Liu, L., & Polk, D. B. (2013). A *Lactobacillus rhamnosus* GG-derived Soluble Protein, p40, Stimulates Ligand Release from Intestinal Epithelial Cells to Transactivate Epidermal Growth Factor Receptor. *Journal of Biological Chemistry*, 288(42), 30742–30751.  
<https://doi.org/10.1074/jbc.M113.492397>
- Żółkiewicz, J., Marzec, A., Ruszczyński, M., & Feleszko, W. (2020). Postbiotics – A Step Beyond Pre- and Probiotics. *Nutrients*, 12(8), 2189.  
<https://doi.org/10.3390/nu1208218>