Ghost Probiotics in Aquaculture: Mechanisms, Efficacy and Future Prospects

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ABSTRACT

The global surge in seafood demand driven by rising preferences for high protein diets, urbanization, and expanding hospitality networks is directly fuelling growth in the global shrimp/fish farming (aquaculture) industry. Because wild capture fisheries have reached sustainable biological limits, aquaculture now supplies over 55-60% of all shrimp consumed worldwide. However, extending the frontiers of the industry has been a challenge as high stocking density often increases susceptibility to disease and compromises culture species quality. To prevent the diseases aquaculturists use antibiotics. The indiscriminate use of antibiotics leads to development of antibiotic- and drug-resistant pathogens impacting environment and food safety issues. To overcome these issues a new concept of paraprobiotics (ghost probiotics) was introduced. Paraprobiotics also known as ghost probiotics are non-viable microbial cells which when administered in adequate amounts give benefit to the host. The heat killed strains of Lactobacillus sp. probiotics is generally used as paraprobiotics. Paraprobiotics are inactivated therefore they do not carry any risk of systemic infection, sepsis or microbial translocation making them much safer for vulnerable or immunocompromised individuals. There has been a huge adaptation of bacterial derived additives in recent decades particularly in Asia.

INTRODUCTION:

As the global population continues to surge, the demand for affordable, high-quality protein is at an all-time high. With fish and shrimp serving as some of the most accessible and cost-effective protein sources for millions worldwide, the aquaculture industry has rapidly intensified to keep pace. However, this push for higher production has led to increased stocking densities—a practice that inherently carries a heightened risk of disease outbreaks. To combat pathogens and protect yields, the industry has long relied on live probiotics to boost immunity and disease resistance in aquatic species. Yet, live probiotics come with notable drawbacks: they are fragile, sensitive to environmental conditions, struggle with viability during storage, and can occasionally pose infection risks, particularly in sensitive or immunocompromised hosts.

To overcome these hurdles, a promising alternative is transforming modern aquaculture: paraprobiotics, often called "ghost probiotics." These are non-viable, heat-killed microbial cells that retain their key cellular components without the risks associated with live bacteria. By offering the powerful immune-boosting benefits of probiotics (Taverniti & Guglielmetti, 2011) completely free of viability concerns or infection risks, paraprobiotics are paving the way for a safer, more resilient, and sustainable future in aquaculture.

What is paraprobiotics (ghost probiotic)?

Paraprobiotics, often referred to as "ghost probiotics" or "inactivated probiotics," are non-living or inactivated microbial cells, cell fractions, or lysates that provide significant health benefits to the consumer when administered in sufficient amounts. Essentially, they are "dead" probiotic bacteria that still interact positively with your body—a phenomenon researchers call the "probiotic paradox" (Adams, 2010).

Unlike traditional probiotics, which must remain alive to be effective, paraprobiotics are intentionally inactivated using methods like heat treatment, ultraviolet (UV) radiation, or high pressure. The frequent use of antimicrobial drugs has developed drug resistant strains of microbes that require immediate global attention. Random antimicrobial use has impelled microorganisms to adopt and survive by acquiring antimicrobial resistance genes that lead to antimicrobial strains (Imperial & Ibana, 2016).

To overcome this issue of AMR, the best alternative is paraprobiotics even in immunodepressant individuals. Furthermore, these non-viable agents exhibit enhanced stability and reduced regulatory burdens, facilitating their integration into industrial aquaculture practices without the risks of live-cell contamination. Moreover, recent studies indicate that these preparations offer extended shelf lives and provide consistent biological activity, such as immune modulation and pathogen exclusion, without the physiological stresses typically associated with live microbial colonization (Fachri *et al*., 2024).

How dead bacteria can still do good?

Even though bacteria are killed, their outer cell walls, proteins and DNA fragments remain structurally intact. The immune system recognizes these fragments known as microbe associated molecular patterns (MAMPs) (Boller & Felix, 2009) just like it would recognize live bacteria. These bacterial fragments interact with receptors in gut lining helping to stimulate and regulate immune response without causing infection making them safer alternatives. Some cell fragments

directly neutralize toxins or produce condition that inhibit harmful microbes.

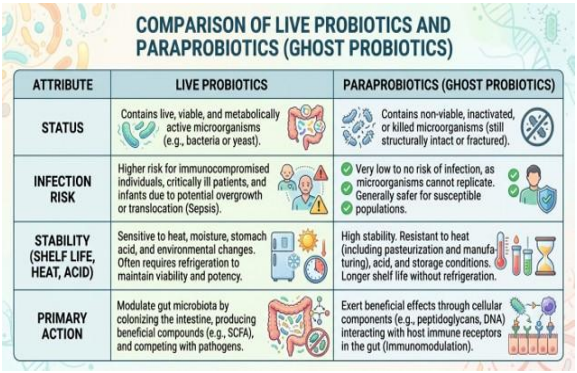


Fig.1: Difference between probiotics and paraprobiotics (ghost probiotics)

MECHANISMS OF PARAPROBIOTICS

1. Cellular Recognition: Activating the Immune "Radar"

Even after bacteria are inactivated, key structural components embedded in their cell walls—such as peptidoglycans, teichoic acids, lipoteichoic acids, exopolysaccharides, and surface proteins—remain completely intact. Host immune cells are equipped with special sensors called Pattern Recognition Receptors (PRRs), such as Toll-like receptors (TLR2) and NOD-like receptors. When these receptors spot the cell wall fragments of paraprobiotics, they recognize them as harmless signals. This harmless interaction keeps the immune system alert and prepared without triggering a false alarm or an active infection.

2. Immunomodulation: Balancing the Inflammatory Response

Paraprobiotics do not just wake up the immune system; they help train it to respond appropriately. By interacting directly with key immune managers like dendritic cells and macrophages, paraprobiotics help steer immune responses toward a calm, regulated state.

- T-Cell Training: They encourage naive T-cells to turn into helper T-cells (Th1) or Regulatory T-cells (Tregs), which keep overall inflammation in check. This regulatory mechanism facilitates the suppression of excessive pro-inflammatory cytokines, thereby mitigating tissue damage and enhancing the overall resilience of the host under immunological stress (Siciliano *et al*., 2021; Taverniti & Guglielmetti, 2011).

- Cytokine Control: They help block pro-inflammatory signaling pathways (such as suppressing LPS-induced NF-κB pathways), which reduces the production of inflammatory signals like Interleukin-8 (IL-8).

- Antibody Transport: They upregulate protective proteins like the polymeric immunoglobulin receptor (pIgR), (Johansen & Kaetzel, 2011) boosting the delivery of protective antibodies into the gut.

3. Barrier Enhancement: Strengthening the Gut Lining

A healthy gut relies on a strong physical barrier to keep harmful microbes and toxins out of the bloodstream. Paraprobiotic fragments actively support this barrier in two key ways:

- Tightening the Seals: They stimulate the expression of tight-junction proteins—the "cellular glue" that holds the lining of your intestines closely together.

- Mucus Production: They encourage intestinal cells to produce mucin, creating a thick protective coating over the gut wall.

By keeping the gut barrier strong and intact, paraprobiotics help reduce "leaky gut" conditions and prevent bacterial translocation—the unwanted movement of microbes into circulation.

4. Pathogen Antagonism: Blocking Out Harmful Microbes

Bad bacteria need to attach to the intestinal lining to cause trouble. Paraprobiotics combat this through physical competition and microbial balancing:

- Competitive Binding: Even in their non-viable state, paraprobiotics and their cell-wall fractions can physically bind or clump together with harmful pathogens. This neutralizes the bad microbes and prevents them from anchoring to intestinal receptors.
- Shifting the Microbiome: Regular presence of paraprobiotics helps cultivate an environment that favors beneficial groups (like Lactobacillales and Bifidobacteriales) while keeping potential pathogens (like Escherichia-Shigella) in check.

5. Toxin Sequestration: Soaking Up Harmful Compounds

Paraprobiotic cells possess passive binding properties that allow them to absorb and neutralize environmental and dietary toxins. For instance, both live and heat-killed strains can physically bind to endocrine-disrupting plasticizers like bis(2-ethylhexyl) phthalate (DEHP), helping to reduce the body's absorption of these harmful chemicals.

How ghost probiotics works in aquaculture?

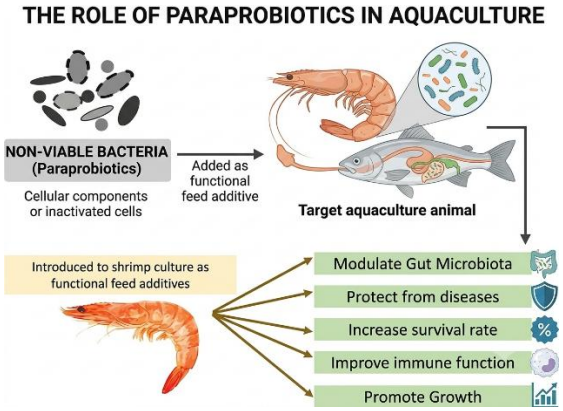


Fig.2: Role of paraprobiotics in aquaculture

Advantages of paraprobiotics

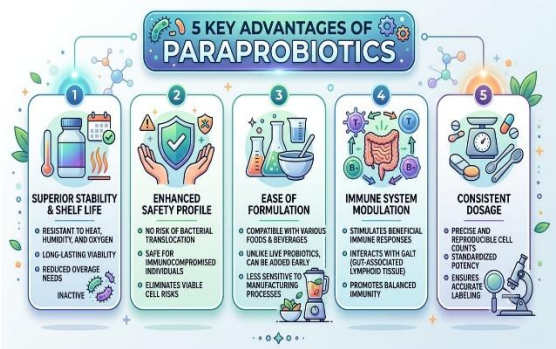


Fig.3: Advantages of paraprobiotics

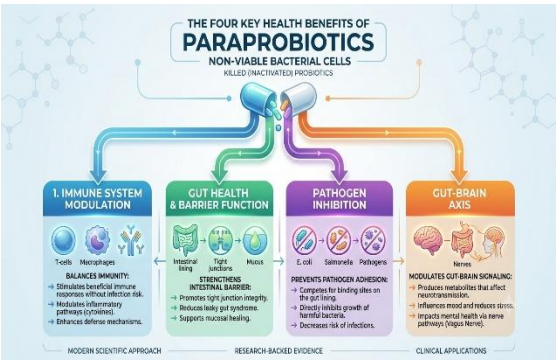


Fig .4: Efficacy of using Paraprobiotics

Future prospectus of paraprobiotics

Sector	Emerging Applications & Future Scope
Functional Foods & Beverages	Fortification of shelf-stable products like baked goods, canned drinks, chocolates, cereal bars, and ambient dairy.
Dermatology & Cosmetics	Integration into topical skincare, anti-acne formulations, and treatments for atopic dermatitis to support the skin microbe.
Clinical Pharmaceuticals	Targeted therapies for inflammatory bowel diseases (IBD), IBS, respiratory tract infections, and post-antibiotic recovery.
Nutraceuticals & Oral Health	Microencapsulated oral supplements, lozenges, and toothpastes targeting oral pathogens and dental health.
Animal Health & Agriculture	Usage in antibiotic-free animal feed to prevent pathogen outbreaks and improve livestock gut health.

CONCLUSION

Ghost probiotics, or paraprobiotics, represent a major shift in how we approach gut health and preventative care. For years, live cultures were considered the gold standard, but keeping them alive through heat, shelf storage, and stomach acid posed constant challenges. Paraprobiotics prove that bacteria do not need to be alive to deliver powerful health benefits. By utilizing inactivated cellular structures, ghost probiotics interact directly with human immune receptors, reinforce the gut barrier, lock out harmful pathogens, and even support mental wellness via the gut-brain axis. Crucially, they achieve this with remarkable stability and safety. They eliminate the risk of bacterial translocation in vulnerable or immunocompromised individuals and thrive in everyday ambient foods, cosmetics, and medical therapies where live strains simply cannot survive. Looking ahead, the future of ghost probiotics lies in refining inactivation techniques and conducting broader clinical trials to fine-tune dosages for specific conditions. As research advances and clear regulatory frameworks emerge, these non-viable microbes are set to transform the functional food, pharmaceutical, and wellness industries—making effective microbiome support safer, more accessible, and easier to integrate into daily life.

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