



Postbiotics as functional alternatives to probiotics in food and animal feed: health effects and industrial potential

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Abstract

Probiotics provide benefits for gut health, immune modulation, and skin and mental health. However, their use is limited by concerns regarding antibiotic resistance, poor intestinal colonization, strain-specific effects, and inter-individual variability. In contrast, postbiotics, including culture broth, are inactivated by heat or pressure yet retain immunomodulatory, anti-inflammatory, intestinal barrier-protective, and antioxidant activities through cell wall components, proteins, and metabolites. They contribute to the alleviation of intestinal inflammation and restoration of gut microbial balance. Postbiotics can serve as alternatives to live probiotics in animal feed by improving productivity, suppressing pathogens, and also reducing stress. Their applications are currently expanding to areas such as anticancer activity, metabolic disease management, gut-brain axis modulation, and oral health. Although postbiotics offer superior safety and stability, challenges still remain, including an insufficient mechanistic understanding, lack of standardized production, and limited large-scale clinical evidence. With further strain-specific mechanistic studies and regulatory establishment, postbiotics have a strong potential as functional ingredients in regard to food and feed applications.

Keywords: Probiotics, Postbiotics, Inactivation process, Efficacy and safety, Functional alternatives

Introduction

The term “probiotics” derived from the Greek meaning “for life” refers to live microorganisms that confer health benefits on the host when administered in adequate amounts (Hill et al., 2014). Early observations by Metchnikoff (1907) and Tissier (1900) suggested that modulation of intestinal microorganisms through diet or beneficial bacteria could improve host health; however, these findings were largely anecdotal and lacked systematic validation. The “probiotics” was later introduced by Lilly and Stillwell (1965) to describe substances that promote the growth of beneficial microorganisms, and scientific interest has expanded substantially since the early 2000s.

In 2001, a joint FAO/WHO expert consultation formally defined probiotics as “live microorganisms which, when administered in

adequate amounts, confer a health benefit on the host,” establishing internationally harmonized criteria for their evaluation, safety, and quality (FAO & WHO, 2001). Since then, probiotics have been widely investigated as functional food ingredients, with reported benefits for gut health, immune modulation, mental well-being, and skin homeostasis. In Korea, the Ministry of Food and Drug Safety (MFDS) defines probiotics as live microorganisms that confer health benefits and requires that they be notified or individually approved as functional ingredients, demonstrate efficacy and safety according to health functional food standards, and meet a minimum viable count (e.g., $\geq 1 \times 10^8$ CFU/g). Currently, 19 probiotic strains are officially notified by MFDS (2020).

Probiotics, increasingly used as functional food ingredients, support intestinal barrier function, modulate immune responses, and improve metabolic regulation, indicating potential benefits in

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metabolic disorders and inflammatory bowel diseases (Ashrafian et al., 2019). They also influence the gut-brain axis, alleviating depressive symptoms, and promote skin health by reducing inflammation and enhancing barrier function (Rinaldi et al., 2022). Overall, probiotics contribute to digestive health, immune function, mental well-being, and skin homeostasis through modulation of the gut environment and host immunity.

Despite these benefits, probiotics exhibit several important limitations. Their intestinal colonization is often transient and highly host-dependent, with substantial inter-individual variability and strain-specific effects (Hill et al., 2014; Derrien & van Hylckama Vlieg, 2015). Moreover, probiotic administration following antibiotic treatment does not consistently promote microbiota recovery and, in some cases, may delay the restoration of microbial diversity (Zmora et al., 2018). Colonization success cannot be reliably predicted, underscoring the challenges associated with reproducibility and personalized application (Suez et al., 2018).

These limitations highlight the need for alternative or complementary strategies that can deliver consistent functional benefits without reliance on microbial viability or host-dependent colonization.

In comparison with probiotics, postbiotics refer to non-viable microorganisms, their cellular components, and metabolites that exert beneficial physiological effects on the host. Accumulating evidence has shown that heat-treated microbial cells, cell-free culture supernatants, and purified microbial components can confer health benefits despite the absence of microbial viability (Piqué et al., 2019).

Probiotic Efficacy Limitations

Although numerous health-related benefits of probiotics have been reported, growing evidence indicates several scientific and clinical limitations in their mechanisms of action and efficacy.

Immunomodulatory function

Probiotics can modulate innate and adaptive immune responses by reducing pro-inflammatory cytokines and enhancing regulatory immune pathways. However, these effects are highly strain-specific, and even closely related strains may exhibit markedly different immunological outcomes (Azad et al., 2018; Duranti et al., 2020).

Moreover, host-related factors such as immune status and genetic background contribute to substantial inter-individual variability, limiting the generalizability of probiotic effects. In certain cases, probiotics may elicit unfavorable immune responses in susceptible individuals, underscoring the need for personalized approaches (Zmora et al., 2018).

Improvement of skin health

Clinical studies suggest that probiotic supplementation may improve skin conditions, including atopic dermatitis and skin barrier function. These effects are commonly attributed to modulation of the gut-skin axis. However, most studies have been limited by small sample sizes and short intervention periods. In addition, the underlying mechanisms remain poorly understood, and individual variability in response complicates the establishment of consistent clinical efficacy (Salem et al., 2018; de Pessemier et al., 2021; Shir Khan et al., 2024).

Metabolic function regulation

Probiotics have been investigated as modulators of metabolic health, with reported benefits in glycemic control, lipid metabolism and body weight regulation. Nevertheless, outcomes remain inconsistent across studies. Limited intestinal persistence of probiotics and interference with native microbiota recovery may reduce long-term efficacy (Derrien & van Hylckama Vlieg, 2015; Suez et al., 2018). Furthermore, the multifactorial nature of metabolic diseases makes it difficult to isolate probiotic-specific effects (Kristensen et al., 2016).

Concept and Classification of Inactivated Probiotics

Whereas probiotics require viability to confer health benefits, postbiotics provide functional effects independent of microbial survival. Heat-treated probiotic cells, cell-free culture supernatants, and purified cellular components have been shown to exert beneficial health effects, collectively referring to inactivated or non-viable probiotic preparations (Piqué et al., 2019). Based on this concept, the International Scientific Association for Probiotics and Prebiotics (ISAPP) formally defined postbiotics as “preparations of non-viable

microorganisms and/or their components that confer a health benefit on the host,” a definition published by Salminen et al. (2021).

Inactivated microorganisms are produced using thermal or non-thermal methods that render cells non-viable while preserving their functional properties (Table 1). These processes yield preparations containing structural components and bioactive substances without requiring microbial viability.

Paraprobiotics are defined as non-viable microorganisms or their cellular components that provide health benefits to the host. In contrast, postbiotics represent a broader concept that includes not only inactivated microbial cells but also bioactive metabolites produced during microbial growth or released after cell death (Teame et al., 2020). Although their physiological effects vary by strain, several key components are commonly implicated.

Key bioactive components of inactivated microorganisms contribute to their physiological effects. Cell wall components such as peptidoglycans, lipoteichoic acids, and teichoic acids interact with host immune receptors to modulate immune responses and suppress inflammation, and these activities are preserved after cell death (Taverniti & Guglielmetti, 2011; Saito et al., 2020). In addition, surface-layer (S-layer) proteins and exopolysaccharides (EPS) derived from heat-treated microorganisms enhance intestinal barrier function, inhibit pathogen adhesion, and exhibit antioxidant and anti-inflammatory activities (Lebeer et al., 2010; Szabó et al., 2023).

Nucleic acids released from inactivated microorganisms can activate immune signaling via Toll-like receptor 9 (TLR9) through CpG motifs (Wischmeyer et al., 2016), while microbial metabolites such as short-chain fatty acids (SCFAs) contribute to intestinal homeostasis by regulating luminal pH, supporting epithelial energy metabolism, and reducing inflammation (Kang et al., 2021). Antioxidant activities have also been reported for both extracellular and intracellular components of heat-treated microorganisms, which

protect intestinal epithelial cells from oxidative stress (Wu et al., 2014).

Collectively, these findings indicate that inactivated microorganisms can promote host health through their bioactive components independently of viability. In this study, the term “inactivated microorganisms” is used to refer to postbiotics, encompassing both non-viable microbial cells and their associated metabolic products, unless otherwise specified. And for more clarity of terminology we added an overview that clearly differentiates probiotics, paraprobiotics, and postbiotics according to the ISAPP definitions (Table 2).

Physiological Effects of Postbiotics

Immunomodulatory and anti-inflammatory effects

Postbiotics have been shown, mainly through *in vitro* studies, to modulate nuclear factor kappa B (NF- κ B) signaling and reduce the expression of inflammation-related genes such as interleukin-8 (IL-8). These effects are mediated by the stimulation of macrophages and dendritic cells via TLR pathways, although the magnitude of the response varies depending on the inactivation method and route of administration (Taverniti & Guglielmetti, 2011). Similarly, crystalline S-layer proteins derived from heat-treated *Lactobacillus acidophilus* were reported in cell-based models to suppress pro-inflammatory cytokines, including tumor necrosis factor- α (TNF- α) and IL-6, while enhancing anti-inflammatory IL-10 production (Konstantinov et al., 2008).

In animal models, particularly those of inflammatory bowel disease, heat-inactivated *Lactobacillus plantarum* and *L. rhamnosus* reduced pro-inflammatory cytokine production by inhibiting NF- κ B and mitogen-activated protein kinase (MAPK) signaling pathways and concurrently preserved intestinal epithelial tight junction

Table 1. Production methods of postbiotics

Method	Description	Advantages	References
Heat-killing	Heating at high temperatures for a defined period (e.g., 100°C for 30 min–2 h)	Preservation of surface proteins; widely used and cost-effective	Kang et al., 2021
Tyndallization	Repeated cycles of mild heating and incubation to eliminate spores	Effective against spore-forming bacteria; relatively mild treatment	Piqué et al., 2019
Non-thermal treatments	High-pressure processing, ultraviolet light, irradiation, ultrasound, etc.	No thermal damage; preservation of functional proteins	Asaithambi et al., 2021
Ohmic heating	Uniform internal heating via electric current passage	Minimal structural damage; rapid processing	Jan et al., 2021

Table 2. Conceptual distinctions among probiotics, paraprobiotics, and postbiotics based on ISAPP definitions

Category	Probiotics	Paraprobiotics	Postbiotics
Definition	Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host	Inactivated (non-viable) microbial cells that retain biological activity	A preparation of non-viable microorganisms and/or their components and metabolites that confers health benefits on the host
Viability	Viable (live)	Non-viable	Non-viable
Composition	Live microbial cells	Inactivated whole cells (cell wall components, structural proteins)	Inactivated cells plus cellular components and metabolites (e.g., SCFAs, EPS, proteins, nucleic acids)
Processing method	Cultivation with maintenance of viability	Heat treatment, high pressure, irradiation	Heat or pressure treatment; often includes culture broth
Requirement for intestinal colonization	Required (temporary or sustained)	Not required	Not required
Primary mechanisms of action	Modulation of gut microbiota, competitive exclusion, immune regulation	Activation of pattern recognition receptors (e.g., TLRs), immune modulation	PRR activation, anti-inflammatory and antioxidant effects, intestinal barrier protection
Safety profile	Potential risks in immunocompromised individuals	Improved safety compared with probiotics	Highest safety profile
Stability	Limited (sensitive to storage and processing conditions)	High	Very high
Regulatory status	Strain-specific approval; complex regulatory landscape	Definitions and regulations not fully established	ISAPP definition established; regulatory frameworks under development
Representative applications	Functional foods, dietary supplements	Functional foods, immune-supporting ingredients	Functional foods, animal feed, pharmaceutical and medical applications

proteins, thereby alleviating intestinal inflammation and barrier dysfunction (Teame et al., 2020). Evidence related to human immune responses, largely inferred from *ex vivo* and translational studies, suggests that inactivated *Lactobacillus* strains can activate dendritic cells and macrophages and contribute to the balance of T helper (Th)1/Th2 immune responses, although direct clinical evidence remains limited (Teame et al., 2020).

Overall, postbiotics demonstrate immunomodulatory and anti-inflammatory potential across experimental systems, with enhanced safety compared to live probiotics; however, further human intervention studies are required to substantiate their clinical efficacy.

Improve intestinal health and microbiota composition

Postbiotics can stimulate immune cells and modulate the gut microbial community in a manner comparable to live probiotics. Through interactions with immune cells in the intestinal mucosa, as demonstrated in *in vitro* and preclinical studies, they enhance mucosal immunity and increase the expression of tight junction proteins, thereby improving intestinal barrier integrity and reducing intestinal permeability (Taverniti & Guglielmetti, 2011). Heat-

treated *Lactobacillus rhamnosus* with different culture durations restored transepithelial electrical resistance in LPS-induced Caco-2 monolayers, preserved surface-bound proteins and inhibited permeability. Strains cultured for longer periods showed superior efficacy, likely due to higher levels of S-layer proteins, peptidoglycan, and lipoteichoic acid (Xie et al., 2024).

Unlike probiotics, postbiotics do not colonize the intestine but indirectly modulate the gut microbiota. In many published studies indicate that they enhance mucosal defense, inhibit pathogen adhesion, and promote beneficial microbial activity, partly through stimulation of SCFA production and reduction of luminal pH (de Almada et al., 2016; Teame et al., 2020).

Promote skin health

Postbiotics improve skin health through immunomodulatory, anti-inflammatory, and antioxidant activities. As the skin functions as an immune organ closely linked to gut health, probiotics and inactivated probiotics have been investigated as adjunctive approaches for regulating skin immunity and alleviating inflammatory skin disorders, mainly based on *in vitro* and animal studies (Yoshitake et al., 2022). Evidence from cell-based and animal

models indicates that postbiotics modulate skin immune responses via TLR 2/4 signaling and suppression of the NF- κ B pathway, resulting in reduced production of pro-inflammatory cytokines. In experimental models, heat-killed *Lactobacillus plantarum* reduced TNF- α and IL-8 while increasing IL-10 (Choi et al., 2017), and inactivated *L. rhamnosus* GG alleviated atopic dermatitis by suppressing Th2 responses and inducing regulatory T cells (Brembilla et al., 2018). Through clinical study and human epidermal models postbiotics upregulate tight junction proteins in keratinocytes to strengthen the skin barrier and enhance hyaluronic acid production plus ceramide metabolism for improved hydration (Wang et al., 2024; Lee et al., 2025).

In animal studies, gut-skin axis mediated interactions contribute to the alleviation of skin symptoms, as the beneficial effects of postbiotics on gut microbial balance indirectly influence skin health (Kimoto-Nira, 2018). Through preclinical models, heat-treated *Lactococcus lactis* enhanced antioxidant activity, Th 1 responses, and gut immunity for better skin condition, while inactivated *Bifidobacterium bifidum* regulated T cell differentiation to decrease inflammatory cytokines and increase Tregs, thereby suppressing systemic and skin inflammation (Kim et al., 2024). Collectively, these findings suggest that components present in inactivated probiotics promote the growth of beneficial gut microbiota and enhance SCFA production, thereby modulating intestinal mucosal immunity and reducing systemic pro-inflammatory cytokines, which ultimately contributes to the alleviation of skin inflammation.

Incorporation into feed

Probiotics used in animal feed have been shown, mainly through livestock feeding trials, to improve productivity and disease resistance; however, their application is limited by reduced viability during storage, environmental instability, and concerns regarding antibiotic resistance genes. As an alternative, postbiotics generated via thermal or physical inactivation processes have emerged, and their suitability as feed additives is being actively evaluated (Lee et al., 2013). In swine and poultry studies, postbiotics have been shown to stimulate intestinal mucosal immunity and inhibit pathogen adhesion, with inactivated *Lactobacillus acidophilus* suppressing *Escherichia coli* and *Salmonella* colonization while promoting beneficial *Bifidobacterium* and *Lactobacillus* populations

(de Almada et al., 2016). Moreover, broiler feeding experiments demonstrated that heat-killed *Bacillus subtilis* and *Lactobacillus plantarum* improved intestinal morphology, enhanced antioxidant capacity, and improved meat quality, concomitant with improved feed conversion ratio and growth performance (Bhattarai et al., 2025; Cui et al., 2025).

Beneficial effects of postbiotics on gut stability and stress mitigation have also been reported in calf feeding and challenge studies. Heat-treated *Lactobacillus sakei* supported early-life gut stabilization in calves (Sasazaki et al., 2020), while administration of *Lactobacillus helveticus* postbiotics during the weaning period improved behavioral and physiological stress responses in dairy calves (McNeil et al., 2024). In preweaned Holstein calves challenged with *Salmonella typhimurium*, supplementation with heat-killed *Saccharomyces cerevisiae* improved weight gain and feed intake and reduced clinical symptoms and fecal shedding, effects associated with reduced plasma haptoglobin levels and improved intestinal morphology (Harris et al., 2017). Similarly, swine studies reported that *Lactobacillus rhamnosus* GG postbiotics increased IL-10 and reduced TNF- α expression, indicating anti-inflammatory activity and potential utility in enteritis prevention and recovery (Shu et al., 2024).

Emerging applications: anticancer effects, metabolic disorders, the gut-brain axis, and oral health

Current research, largely based on *in vitro* and *in vivo* experimental models, has demonstrated that postbiotics can induce apoptosis in cancer cells and modulate the inflammatory tumor microenvironment, thereby suppressing tumorigenesis. In colon cancer cell line studies, inactivated *Lactobacillus casei* inhibited cell proliferation and activated caspase-dependent apoptotic pathways (Karimi Ardestani et al., 2019). In addition, clinical investigations in malnourished children reported that postbiotics restored impaired macrophage function and promoted Th1 immune activation, which is essential for anticancer and antibacterial defenses, offering a safe immunomodulatory strategy for immunocompromised individuals or those unable to receive live probiotics (Rocha-Ramírez et al., 2020). Metabolic benefits of postbiotics have been demonstrated primarily through diet-induced obesity animal models. Inactivated *Lactobacillus plantarum* improved lipid metabolism, enhanced insulin sensitivity,

and suppressed adipose inflammation; in high-fat diet-fed mice, supplementation attenuated weight gain, reduced blood glucose, cholesterol, alanine aminotransferase, and aspartate aminotransferase levels, downregulated inflammatory gene expression, and decreased lipopolysaccharide-binding protein levels through improved gut barrier integrity (Yoshitake et al., 2021).

Postbiotics also contribute to the alleviation of anxiety, depression, and stress via gut microbiota modulation and neuro-immune regulation. In stress-induced mouse models, heat-killed *Lactobacillus helveticus* reduced corticosterone levels, improved stress-related behaviors, and increased brain-derived neurotrophic factor, highlighting its role in gut-brain axis modulation (Maehata et al., 2019). Similarly, in chronic social defeat stress models, inactivated *Bifidobacterium breve* significantly reduced depression-like behaviors by decreasing pro-inflammatory cytokine expression, reshaping gut microbiota composition, and modulating immune responses along the gut-brain axis (Kosuge et al., 2021). In the context of oral health, *in vitro* and gingivitis model studies demonstrated that inactivated *Lactobacillus rhamnosus* inhibited the growth of cariogenic and periodontopathic bacteria (*Streptococcus mutans* and *Porphyromonas gingivalis*), reduced oral inflammation, and promoted recovery of oral microbiota diversity (Lin et al., 2022).

Effects summary

Postbiotics exert diverse biological activities without requiring microbial viability, as demonstrated across *in vitro*, animal, and limited human studies. They exhibit immunomodulatory and anti-inflammatory effects primarily through regulation of NF- κ B-related signaling and cytokine production, while offering improved safety compared with live probiotics.

In experimental models, postbiotics enhance intestinal barrier integrity, stimulate mucosal immunity, and indirectly modulate gut microbiota by suppressing pathogen adhesion and promoting SCFA production. Through gut-mediated immune regulation, they also contribute to the improvement of inflammatory skin conditions, as shown in cell-based, animal, and emerging clinical studies. In livestock feeding trials, postbiotics have demonstrated beneficial effects on gut health, stress resilience, and growth performance, supporting their application as stable alternatives to probiotics in animal nutrition. In addition, growing evidence from preclinical studies suggests potential roles in metabolic regulation, gut-brain axis

modulation, anticancer activity, and oral health.

Overall, postbiotics represent multifunctional bioactive preparations with broad application potential, although further well-controlled human studies are required to confirm their clinical efficacy.

To facilitate understanding of postbiotic-host interactions, Table 3 integrates pattern recognition receptor-mediated signaling mechanisms with representative physiological outcomes and application areas in food, feed, and clinical contexts.

Regulatory Considerations for Postbiotics

Regulatory oversight for postbiotics remains limited, and no international legal standard specifically defines them. Nevertheless, regulatory frameworks in major regions emphasize three critical aspects: ingredient approval, health/functional claim substantiation, and quality control. The requirements vary according to product category—food, feed, health functional food (or natural health products), and pharmaceuticals—necessitating clear classification for appropriate regulatory pathways. Table 4 summarizes the regulatory categories, ingredient approval pathways, health claim requirements, and quality control indicators for postbiotics across major countries and regions.

Ingredient approval and safety assessment

Postbiotics are generally derived from probiotic strains, and approval requires demonstration of strain identity, manufacturing process, and inactivation conditions. In Korea, postbiotics are not recognized as a separate ingredient category under health functional food regulations; manufacturers must provide detailed information on the microbial strain, heat-treatment method, and safety assessment data. In the European Union, the European Food Safety Authority (EFSA) allows use of microbial strains with Qualified Presumption of Safety (QPS) status in food, feed, or as additives, which may include inactivated forms, although postbiotics themselves are not legally defined (EFSA, 2011). In the United States, the Food and Drug Administration (FDA) requires demonstration of GRAS status, while the FTC (Federal Trade Commission) monitors advertising claims to ensure they are substantiated (FDA, 2017). Health Canada permits postbiotics as natural health products (NHPs) if safety and efficacy data are provided, and Japan's

Table 3. PRR-mediated mechanisms of postbiotics and their applications across food, feed, and clinical fields

Postbiotic component	Host receptor(s) / signaling pathway	Key physiological effects	Application area	References
Peptidoglycan	TLR2, NOD2 → NF- κ B, MAPK	Immune modulation, suppression of excessive inflammation	Functional foods, immune-supportive products	Taverniti & Guglielmetti, 2011; Saito et al., 2020
Lipoteichoic acid (LTA)	TLR2 → MyD88-NF- κ B	Cytokine regulation, immune homeostasis	Functional foods, dietary supplements	Lebeer et al., 2010; Taverniti & Guglielmetti, 2011
S-layer proteins	TLR2, DC-SIGN → NF- κ B	Epithelial barrier protection, pathogen exclusion	Gut health foods, clinical nutrition	Konstantinov et al., 2008; Szabó et al., 2023
Exopolysaccharides (EPS)	TLR2, C-type lectin receptors → MAPK	Antioxidant activity, gut barrier enhancement	Functional foods, metabolic health	Lebeer et al., 2010; Teame et al., 2020
Short-chain fatty acids (SCFAs)	GPR41/43 → AMPK activation, HDAC inhibition	Barrier integrity, anti-inflammatory and metabolic regulation	Functional foods, feed additives	Kang et al., 2021
Microbial DNA (CpG motifs)	TLR9 → IRF/NF- κ B	Th1 activation, innate immune stimulation	Clinical and immune-supportive applications	Wischmeyer et al., 2016
Inactivated LAB cells	PRR-mediated mucosal signaling	Reduced pathogen adhesion, gut stability	Animal feed	de Almada et al., 2016
Cell wall fragments	NF- κ B, MAPK modulation	Improved gut morphology, reduced inflammation	Livestock feed	Bhattarai et al., 2025
Postbiotic metabolites	SCFA-related signaling pathways	Improved feed efficiency, growth performance	Livestock production	Cui et al., 2025

Table 4. Regulatory status of postbiotics across major countries and regions

Region / Country	Regulatory category	Ingredient approval	Health / functional claims	Quality control indicators
Korea	Health functional food	Strain identity, manufacturing process, heat-treatment conditions, and safety data required	Subject to MFDS review and approval	Inactivated cell counts, cell wall components
EU (EFSA)	Food / feed / additive	QPS-listed strains; no specific legal definition for postbiotics	Health claims require EFSA scientific substantiation	Process verification, indicator components
USA (FDA / FTC)	Food / dietary supplement / GRAS	GRAS status based on strain identity and manufacturing process	Claims must be scientifically substantiated; advertising overseen by the FTC	Strain identity, compositional markers
Canada	Natural health product (NHP)	Product-specific safety and efficacy data required	Claims reviewed by Health Canada	Strain and product characterization
Japan (MHLW)	Foods with function claims / supplements	Scientific evidence required for safety assessment	Claims require regulatory review	Strain identity, indicator markers

MHLW (Ministry of Health, Labour and Welfare, 1992) requires scientific evidence to support functional or health-related claims.

Health and functional claims

Health-related or functional claims for postbiotics require scientific substantiation in all major Authorities. To date, EFSA has not approved any postbiotic-specific claims, whereas the FDA, FTC, Health Canada, and MHLW evaluate claims based on clinical or

preclinical evidence. Regulatory scrutiny is particularly strict for functional foods, NHPs, and pharmaceuticals compared with general foods or feed.

Quality control standards

Even in the absence of legally standardized specifications, recommended quality control measures focus on indicator components such as inactivated cell counts, specific cell wall constituents,

or microbial metabolites. Verification of the strain and inactivation process is essential to ensure product safety and reproducibility.

Practical applications of postbiotics

Postbiotics retain functional properties such as immunomodulatory, anti-inflammatory, and antioxidant activities despite microbial inactivation by heat, pressure, or ultraviolet treatment, and are therefore easier to process, store, and transport than probiotics (Maehata et al., 2021). In addition, they present a lower risk of horizontal transfer of antibiotic resistance genes and can be safely applied to vulnerable populations, including immunocompromised individuals and patients (James et al., 2021). As a result of their favorable safety and stability profiles, postprobiotics have been commercialized in several countries (Table 5). In Japan, products containing postbiotics have been marketed for immune enhancement and mood improvement. In the United States, postbiotics have been incorporated into vitamin beverages for antioxidant, anti-inflammatory, and immune-supporting purposes. In Spain, liquid supplements for infants and capsule formulations have been developed to prevent abdominal pain and diarrhea. In Korea, no postbiotic products have yet been commercialized; however, several companies are currently conducting research aimed at product development. In addition, a company supported by the Ministry of SMEs and Startups is developing an individually approved postbiotic for sarcopenia, for which overseas patents have been registered and commercialization is in progress (Kim et al., 2023).

Conclusion

Postbiotics represent a promising class of functional ingredients

that retain the physiological activities of beneficial microorganisms while offering enhanced safety, stability, and ease of handling compared with live probiotics. Evidence demonstrates their immunomodulatory, anti-inflammatory, intestinal barrier-protective, and antioxidant effects, supporting applications across functional foods, dietary supplements, animal feed, and cosmetic products. Despite these advantages, broader utilization is limited by incomplete understanding of strain-specific mechanisms, variability in bioactive component preservation, and the absence of standardized regulatory frameworks. Future research should focus on elucidating mechanisms of action, identifying key bioactive components, and conducting large-scale, standardized clinical trials. Establishing clear definitions and regulatory guidance will be essential to ensure product quality, safety, and transparent labeling. Addressing these challenges could enable postbiotics to serve as next-generation functional ingredients, combining the benefits of probiotics with improved safety and versatility.

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Conflict of interests

No potential conflict of interest relevant to this article was reported.

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Not applicable.

Data availability

Upon reasonable request, the datasets of this study can be

Table 5. Commercially available postbiotic products

Product (Company/Country)	Included strain	Application	Reported functions	References
LAC-Shield™ (Morinaga Milk Industry, Japan)	Heat-treated <i>Lacticaseibacillus paracasei</i> MCC1849	Ready-to-eat foods (miso), confectionery, tofu, etc.	Immune enhancement, common cold prevention, mood improvement	Maehata et al., 2019
Staimune® (Blossom Water, USA)	Heat-treated <i>Bacillus coagulans</i> GBI-30 6086	Vitamin beverages	Antioxidant, anti-inflammatory, immune support	James et al., 2021
Colimil® Baby (Humana, Spain)	Heat-treated <i>Lactobacillus acidophilus</i> HA122 with chamomile and lemon balm	Infant liquid supplement	Relief of infantile colic	Liévin-Le Moal et al., 2007
Lacteol™ (Reig Jofre, Spain)	Heat-treated <i>Lactobacillus acidophilus</i> LB	Pharmaceutical (capsule/suspension)	Alleviation of infectious diarrhea	Xiao et al., 2003

available from the corresponding author.

Authorship contribution statement

The article is prepared by a single author.

Ethics approval

Not applicable.

References

- Asaithambi N, Singh SK, Singha P. 2021. Current status of non-thermal processing of probiotic foods: a review. *J. Food Eng.* 303: 110567.
- Ashrafian F, Shahriary A, Behrouzi A, Moradi HR, Keshavarz Azizi Raftar S, Lari A, Hadifar S, Yaghoufar R, Badi SA, Khatami S, Vaziri F, Siadat SD. 2019. *Akkermansia muciniphila*-derived extracellular vesicles as a mucosal delivery vector for amelioration of obesity in mice. *Front. Microbiol.* 10: 2155.
- Azad MAK, Sarker M, Wan D. 2018. Immunomodulatory effects of probiotics on cytokine profiles. *Biomed Res. Int.* 2018: 8063647.
- Bhattarai BP, Cheng FY, Xu YC, Yu C, Lee TY, Chang HT, Lin HC, Weng HM, Huang HH, Lin JS, Huang CW. 2025. Supplementation of heat-killed probiotics mixture improves intestinal morphology, antioxidant capacity, and meat quality in broilers. *Vet. Anim. Sci.* 29: 100462.
- Brembilla NC, Senra L, Boehncke WH. 2018. The IL-17 family of cytokines in psoriasis: IL-17A and beyond. *Front. Immunol.* 9: 1682.
- Choi CY, Kim YH, Oh S, Lee HJ, Kim JH, Park SH, Lee SJ, Chun T. 2017. Anti-inflammatory potential of a heat-killed *Lactobacillus* strain isolated from kimchi on house dust mite-induced atopic dermatitis in NC/Nga mice. *J. Appl. Microbiol.* 123: 535-543.
- Cui Y, Meng W, He F, Chen Z, Liu H, Li D. 2025. Heat-killed *Bacillus subtilis* concerning broilers' performance, cecal architecture and microbiota. *Front. Microbiol.* 16: 1606352.
- de Almada CN, Almada CN, Martinez RCR, Sant'Ana AS. 2016. Paraprobiotics: evidences on their ability to modify biological responses, inactivation methods and perspectives on their application in foods. *Trends Food Sci. Technol.* 58: 96-114.
- de Pessemier B, Grine L, Debaere M, Maes A, Paetzold B, Callewaert C. 2021. Gut-skin axis: current knowledge of the interrelationship between microbial dysbiosis and skin conditions. *Microorganisms* 9: 353.
- Derrien M, van Hylckama Vlieg JET. 2015. Fate, activity, and impact of ingested bacteria within the human gut microbiota. *Trends Microbiol.* 23: 354-366.
- Duranti S, Longhi G, Ventura M, van Sinderen D, Turroni F. 2020. Exploring the ecology of bifidobacteria and their genetic adaptation to the mammalian gut. *Microorganisms* 9: 8.
- European Food Safety Authority. 2011. EFSA Finalises the Assessment of "General Function" Health Claims.
- Food and Agriculture Organization of the United Nations, World Health Organization. 2001. Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria: report of a joint FAO/WHO expert consultation.
- Harris TL, Liang Y, Sharon KP, Sellers MD, Yoon I, Scott MF, Carroll JA, Ballou MA. 2017. Influence of *Saccharomyces cerevisiae* fermentation products, SmartCare in milk replacer and Original XPC in calf starter, on the performance and health of preweaned Holstein calves challenged with *Salmonella enterica* serotype Typhimurium. *J. Dairy Sci.* 100: 7154-7164.
- Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, Morelli L, Canani RB, Flint HJ, Salminen S, Calder PC, Sanders ME. 2014. Expert consensus document: the ISAPP consensus statement on the scope and appropriate use of the term probiotic. *Nat. Rev. Gastroenterol. Hepatol.* 11: 506-514.
- James C, Dixon R, Talbot L, James SJ, Williams N, Onarinde BA. 2021. Assessing the impact of heat treatment of food on antimicrobial resistance genes and their potential uptake by other bacteria: a critical review. *Antibiotics* 10: 1440.
- Jan B, Shams R, Rizvi QEH, Manzoor A. 2021. Ohmic heating technology for food processing: a review of recent developments. *J. Postharvest Technol.* 9: 20-34.
- Kang CH, Kim JS, Kim H, Paek NS. 2021. Heat-killed lactic acid bacteria inhibit nitric oxide production via inducible nitric oxide synthase and cyclooxygenase-2 in RAW 264.7 cells. *Probiot. Antimicrob. Proteins* 13: 1530-1538.
- Karimi Ardestani S, Tafvizi F, Tajabadi Ebrahimi M. 2019. Heat-killed probiotic bacteria induce apoptosis of HT-29 human colon adenocarcinoma cell line via the regulation of Bax/Bcl2 and caspases pathway. *Hum. Exp. Toxicol.* 38: 1069-1081.
- Kim GI, Jeong HY, Kim IS, Lee SH, Kim SH, Moon YS, Cho KK. 2024. Interconnection of the gut-skin axis in NC/Nga mouse with atopic dermatitis: effects of the three types of *Bifidobacterium bifidum* CBT-BF3 (probiotics, postbiotics,

- and cytosine-phosphate-guanine oligodeoxynucleotide) on T cell differentiation and gut microbiota. *Food Sci. Anim. Resour.* 44: 1417-1439.
- Kim TJ, Lee MH, Iwasa M, Kim WJ. 2023. Pharmaceutical composition, food composition and food additive for preventing, alleviating or treating muscle loss, weakness and atrophy, containing *Enterococcus faecalis*, culture liquid thereof or dead cells thereof (U.S. Patent No. 11,679,134).
- Kimoto-Nira H. 2018. New lactic acid bacteria for skin health via oral intake of heat-killed or live cells. *Anim. Sci. J.* 89: 835-842.
- Kristensen NB, Bryrup T, Allin KH, Nielsen T, Hansen TH, Pedersen O. 2016. Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: a systematic review of randomized controlled trials. *Genome Med.* 8: 52.
- Konstantinov SR, Smidt H, de Vos WM, Bruijns SC, Singh SK, Valence F, Molle D, Lortal S, Altermann E, Klaenhammer TR. 2008. S layer protein A of *Lactobacillus acidophilus* NCFM regulates immature dendritic cell and T cell functions. *Proc. Natl. Acad. Sci. U.S.A.* 105: 19474-19479.
- Kosuge A, Kunisawa K, Arai S, Sugawara Y, Shinohara K, Iida T, Wuwai T, Fujigaki H, Yamamoto Y, Saito K, Nabeshima T, Mouri A. 2021. Heat-sterilized *Bifidobacterium breve* prevents depression-like behavior and interleukin-1 β expression in mice exposed to chronic social defeat stress. *Brain Behav. Immun.* 96: 200-211.
- Lebeer S, Vanderleyden J, De Keersmaecker SCJ. 2010. Host interactions of probiotic bacterial surface molecules: comparison with commensals and pathogens. *Nat. Rev. Microbiol.* 8: 171-184.
- Lee C, Pei L, Park H, Kim H, Huh CS. 2025. Skin protection effects of *Lactobacillus paragasseri* HN910 lysate and the role of alanine. *Probiotics Antimicrob. Proteins* 2025;1-18.
- Lee JH, Kim SY, Lee JY, Ahammed M, Ohh SJ. 2013. Effect of dietary live or killed kimchi lactic acid bacteria on growth performance, nutrient utilization, gut microbiota and meat characteristics in broiler chicken. *Korean J. Poult. Sci.* 40: 57-65.
- Liévin-Le Moal V, Sarrazin-Davila LE, Servin AL. 2007. An experimental study and a randomized, double-blind, placebo-controlled clinical trial to evaluate of the antisecretory activity of *Lactobacillus acidophilus* strain LB against nonrotavirus diarrhea. *Pediatrics* 120: e795-e803.
- Lilly DM, Stillwell RH. 1965. Probiotics: growth-promoting factors produced by microorganisms. *Science* 147: 747-748.
- Lin CW, Chen YT, Ho HH, Kuo YW, Lin WY, Chen JF, Lin JH, Liu CR, Lin CH, Yeh YT, Chen CW, Huang YF, Hsu CH, Hsieh PS, Yang SF. 2022. Impact of the food grade heat-killed probiotic and postbiotic oral lozenges in oral hygiene. *Aging (Albany N.Y.)*. 14: 2221-2238.
- Maehata H, Arai S, Iwabuchi N, Abe F. 2021. Immuno-modulation by heat-killed *Lactocaseibacillus paracasei* MCC1849 and its application to food products. *Int. J. Immunopathol. Pharmacol.* 35: 20587384211008291.
- Maehata H, Kobayashi Y, Mitsuyama E, Kawase T, Kuhara T, Xiao JZ, Tsukahara T, Toyoda A. 2019. Heat-killed *Lactobacillus helveticus* strain MCC1848 confers resilience to anxiety or depression-like symptoms caused by subchronic social defeat stress in mice. *Biosci. Biotechnol. Biochem.* 83: 1239-1247.
- McNeil BK, Renaud DL, Steele MA, Cangiano LR, Olmeda MF, Villot C, Chevaux E, Yu J, Hernandez LL, Frizzarini WS, DeVries TJ. 2024. Effects of weaning and inactivated *Lactobacillus helveticus* supplementation on dairy calf behavioral and physiological indicators of affective state. *J. Dairy Sci.* 107: 11363-11380.
- Metchnikoff E. 1907. *The Prolongation of Life: Optimistic Studies*. William Heinemann, G. P. Putnam's Sons, London, UK..
- Ministry of Food and Drug Safety. 2020. Standards and Specifications for Health Functional Foods.
- Ministry of Health, Labour and Welfare, Japan. 1992. Establishment of the Standards for Evaluation of Feed Additives.
- Piqué N, Berlanga M, Miñana-Galbis D. 2019. Health benefits of heat-killed (tyndallized) probiotics: an overview. *Int. J. Mol. Sci.* 20: 2534.
- Rinaldi F, Marotta L, Mascolo A, Amoroso A, Pane M, Giuliani G, Pinto D. 2022. Facial acne: a randomized, double-blind, placebo-controlled study on the clinical efficacy of a symbiotic dietary supplement. *Dermatol. Ther.* 12: 577-589.
- Rocha-Ramírez LM, Hernández-Ochoa B, Gómez-Manzo S, Marcial-Quino J, Cárdenas-Rodríguez N, Centeno-Leija S, García-Garibay M. 2020. Impact of heat-killed *Lactobacillus casei* strain IMAU60214 on the immune function of macrophages in malnourished children. *Nutrients* 12: 2303.
- Saito S, Okuno A, Cao DY, Peng Z, Wu HY, Lin SH. 2020. Bacterial lipoteichoic acid attenuates toll-like receptor dependent dendritic cells activation and inflammatory response. *Pathogens.* 9: 825.
- Salem I, Ramser A, Isham N, Ghannoum MA. 2018. The gut microbiome as a major regulator of the gut-skin axis. *Front.*

- Microbiol. 9: 01459.
- Salminen S, Collado MC, Endo A, Hill C, Lebeer S, Quigley EMM, Sanders ME, Shamir R, Swann JR, Szajewska H, Vinderola G. 2021. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nat. Rev. Gastroenterol. Hepatol.* 18: 649-667.
- Sasazaki N, Obi T, Aridome C, Fujimoto Y, Furumoto M, Toda K, Hasunuma D, Matsumoto D, Sato S, Okawa H, Yamamoto O, Igari N, Kazami D, Taniguchi M, Takagi M. 2020. Effects of dietary feed supplementation of heat-treated *Lactobacillus sakei* HS-1 on health status of Japanese Black calves. *J. Vet. Med. Sci.* 82: 1428-1435.
- Shirkhan F, Safaei F, Mirdamadi S, Zandi M. 2024. The role of probiotics in skin care: advances, challenges, and future needs. *Probiotics Antimicrob. Proteins* 16: 2132-2149.
- Shu Z, Zhang J, Zhou Q, Peng Y, Huang Y, Zhou Y, Zheng J, Zhao M, Hu C, Lan S. 2024. Effects of inactivated *Lactobacillus rhamnosus* on growth performance and colonic microbiota of weaned piglets. *BMC Vet. Res.* 20: 422.
- Suez J, Zmora N, Zilberman-Schapira G, Mor U, Dori-Bachash M, Bashardes S, Zur M, Regev-Lehavi D, Ben-Zeev Brik R, Federici S, Horn M, Cohen Y, Moor AE, Zeevi D, Korem T, Kotler E, Harmelin A, Itzkovitz S, Maharshak N, Shibolet O, Pevsner-Fischer M, Shapiro H, Sharon I, Halpern Z, Segal E, Elinav E. 2018. Post-antibiotic gut mucosal microbiome reconstitution is impaired by probiotics and improved by autologous FMT. *Cell* 174: 1406-1423.
- Szabó A, Újvári I, Csáki CP, Palócz O, Bánfi G. 2023. Impact of heat-inactivated *Lactobacillus* on inflammatory response in porcine enterocytes. *Res. Vet. Sci.* 154: 132-137.
- Taverniti V, Guglielmetti S. 2011. The immunomodulatory properties of probiotic microorganisms beyond their viability (ghost probiotics: proposal of paraprobiotic concept). *Genes Nutr.* 6: 261-274.
- Teame T, Wang A, Xie M, Zhang Z, Yang Y, Ding Q, Gao C, Olsen RE, Ran C, Zhou Z. 2020. Paraprobiotics and postbiotics of probiotic *Lactobacilli*, their positive effects on the host and action mechanisms; a review. *Front. Nutr.* 7: 570344.
- Tissier H. 1900. Recherches sur la flore intestinale normale et pathologique du nourrisson. Ph.D. thesis. Paris: G. Carré et C. Naud.
- U.S. Food and Drug Administration. 2017. GRAS notice (GRN) No. 725: inactivated *Bacillus coagulans* GBI-30, 6086.
- Wang B, Wang F, Qu L, Ma H, Cheng Y, Wu X, He L. 2024. *Prinsepia utilis* Royle polysaccharides promote skin barrier repair through the Claudin family. *Skin Res. Technol.* 30: e13848.
- Wischmeyer PE, McDonald D, Knight R. 2016. Role of the microbiome, probiotics, and 'dysbiosis therapy' in critical illness. *Curr. Opin. Crit. Care* 22: 347-353.
- Wu D, Sun MZ, Zhang C, Xin Y. 2014. Antioxidant properties of *Lactobacillus* and its protecting effects to oxidative stress Caco-2 cells. *J. Anim. Plant Sci.* 24: 1766-1771.
- Xiao SD, De-Zhang D, Lu H, Jiang SH, Liu HY, Wang GS, Xu GM, Zhang ZB, Lin GJ, Wang GL. 2003. Multicenter randomized controlled trial of heat-killed *Lactobacillus acidophilus* LB in patients with chronic diarrhea. *Adv. Ther.* 20: 253-260.
- Xie Z, Wang Y, Du L, Wu X, Liu R, Li S, Wang Q, Zhang L, Han J. 2024. Heat-killed *Lactobacillus rhamnosus* GG restores intestinal epithelial barrier dysfunction via MLCK/MLC pathway activation. *Food Biosci.* 57: 103443.
- Yoshitake R, Hirose Y, Murosaki S, Matsuzaki G. 2021. Heat-killed *Lactobacillus plantarum* L-137 attenuates obesity and associated metabolic abnormalities in C57BL/6 J mice on a high-fat diet. *Biosci. Microbiota Food Health.* 40: 84-91.
- Yoshitake R, Nakai H, Ebina M, Kawasaki K, Murosaki S, Hirose Y. 2022. Beneficial effect of heat-killed *Lactiplantibacillus plantarum* L-137 on skin functions in healthy participants: a randomized, placebo-controlled, double-blind study. *Front. Med.* 9: 912280.
- Zmora N, Zilberman-Schapira G, Suez J, Mor U, Dori-Bachash M, Bashardes S, Kotler E, Zur M, Regev-Lehavi D, Ben-Zeev Brik R, Federici S, Cohen Y, Linevsky R, Rothschild D, Moor AE, Ben-Moshe S, Harmelin A, Itzkovitz S, Maharshak N, Shibolet O, Shapiro H, Pevsner-Fischer M, Sharon I, Halpern Z, Segal E, Elinav E. 2018. Personalized gut mucosal colonization resistance to empiric probiotics is associated with unique host and microbiome features. *Cell* 174: 1388-1405.