

DOSSIER · SUBSTANCE

Postbiotics

Postbiotics are inactivated microorganisms or their components with potential physiological effects. Research focuses on **gut health** and **immune modulation**, but the human clinical evidence remains limited. The most notable finding: even for frequently cited applications, proof of a causal effect on disease progression is often lacking.

161

STUDIES IN
TOTAL

30

IN HUMANS

13

OF WHICH
CONTROLLED

18

IN ANIMALS

20

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

1. What Postbiotics Are

Postbiotics are defined, non-viable microbial cells or their components obtained from **probiotics** following fermentation or inactivation (e.g., via heat, radiation, or lysis). They include cell wall components, metabolites, enzymes, or signalling molecules such as **short-chain fatty acids**, **exopolysaccharides**, or **bacteriocins**. Production typically involves strains from the genera *Lactobacillus*, *Bifidobacterium*, or *Pediococcus*, with inactivation enhancing storage stability and eliminating safety risks associated with live microbes. Postbiotics are administered orally, topically, or in foods, where the **matrix** (e.g., milk ferments, capsules, serums) influences bioavailability.

Critical to the interpretation of studies is the **diversity of preparations**: postbiotics differ not only by source strain and inactivation method but also by **composition** (e.g., pure metabolites vs. cell debris) and **purity**. Even with the same strain, varying manufacturing processes can yield distinct efficacy profiles. The majority of controlled studies use **strain-specific postbiotics** (e.g., *Lactobacillus paracasei* ET-22 or *Epidermidibacterium keratini* EPI-7), whose results cannot be extrapolated to other preparations. Furthermore, standardised **analytical methods** for characterising active components are lacking, complicating comparisons between studies.

2. What the Studies Show in Detail

The key human studies and major reviews—by application area, including population, duration, preparation, outcome measures, and results as reported in the original publications. Figures are included only where the study provides them.

Distribution of **controlled human studies** by application area—note that the numbers are not additive, as a single study may be assigned to multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Gut and microbiome	10
Safety and tolerability	7
Skin	5
Immune system	4
Inflammatory processes	3
Metabolism	2
Cognition and mental health	2
Cardiovascular system	1

Gut and Microbiome

In a randomised, placebo-controlled crossover study involving 69 young adults (36 in Group A, 33 in Group B), the effect of the postbiotic *Probio-Eco*® on chronic diarrhoea was investigated. Participants received either the postbiotic or a placebo for 21 days, followed by a 14-day washout phase and subsequent crossover of the intervention. Clinical symptoms (Bristol Stool Scale, defecation frequency, urgency, anxiety), gut microbiota composition, and metabolite profiles were assessed. Results showed a significant improvement in stool consistency, a reduction in defecation frequency and urgency, and decreased anxiety. Microbiota analysis revealed an increase in beneficial bacteria such as *Dysosmobacter welbionis* and *Faecalibacterium prausnitzii*, while potentially pathogenic species like *Megamonas funiformis* were reduced. Metabolomic analysis indicated an enrichment of health-promoting metabolites (e.g., α -linolenic acid, p-methoxycinnamic acid) and a decrease in diarrhoea-associated substances (e.g., theophylline, piperine, capsaicin). However, the study's short intervention duration and specific population limit generalisability ⁴.

A randomised, double-blind, placebo-controlled study involving 68 participants with halitosis examined the effect of *Lactobacillus paracasei* ET-22 (both live and heat-inactivated) on oral microbiota and volatile sulphur compounds (VSCs). Participants took lozenges three times daily for four weeks. Both intervention groups (live and heat-inactivated) showed a significant reduction in VSC levels, with the live variant demonstrating a stronger effect ($p = 0.0148$). Additionally, the composition of volatile organic compounds (VOCs) in saliva changed, with a decrease in undesirable substances such as indole, pyridine, and nonanoic acid. The oral microbiota exhibited taxonomic shifts, though their clinical relevance remains unclear. The study is limited to halitosis and does not assess long-term effects ².

In a randomised, controlled study involving 31 participants (15 placebo, 16 postbiotic), the effect of a postbiotic-containing toothpaste (3×10^{10} CFU inactivated *Lactobacillus* strains) on oral microbiota and immune parameters was investigated. After four weeks of use, levels of secretory immunoglobulin A (IgA) and acetic and propionic acids in saliva increased significantly ($p < 0.05$). Alpha diversity of the salivary microbiota rose, and the relative abundance of pathogenic species such as *Enterobacteriaceae* and *Escherichia* declined, while *Ruminofillibacter* and *Lactobacillus* increased. These changes persisted one month after discontinuing the toothpaste. However, the study is small and does not evaluate clinical endpoints such as caries or periodontitis ⁵.

A randomised, double-blind, placebo-controlled study involving 60 healthy Japanese women (aged 30–50 years) investigated the effect of heat-inactivated *Latilactobacillus sakei* KABP-065 (1×10^{10} cells/day) on skin parameters. After eight weeks of intake, the postbiotic group showed a significant improvement in skin elasticity compared to the placebo group. In a subgroup analysis (participants in their 40s), skin hydration and elasticity improved more markedly. The study suggests systemic effects but remains limited to a specific age group and ethnic population ⁷.

HYPOTHESIS The observed effects on microbiota and metabolite profiles suggest that postbiotics may act via modulation of microbial communities and their metabolic products. In particular, the enrichment of short-chain fatty acids (e.g., butyrate) and the reduction of pro-inflammatory metabolites could provide mechanistic explanations. However, studies specifically testing these hypotheses and establishing causal relationships are currently lacking.

What is missing: long-term studies with larger, more diverse populations investigating clinically relevant endpoints (e.g., remission in chronic diarrhoea, infection prevention) and mechanistic insights into the interaction between postbiotics, microbiota, and host physiology.

Inflammatory Processes

A randomised, double-blind, placebo-controlled study involving 60 NSCLC patients (30 per group) examined the effect of the postbiotic JK5G in combination with immune checkpoint inhibitors (ICIs) and chemotherapy. Patients received either JK5G or placebo over four cycles (each three weeks). The primary endpoint was objective response rate (ORR), with secondary endpoints including quality of life, adverse effects, gut microbiota, inflammatory markers, and lymphocyte subsets. ORR did not differ significantly between groups (36.67% vs. 50%, $p = 0.297$). However, the JK5G group showed better quality of life, higher nutrient levels, and reduced depressive symptoms (all $p < 0.05$). Gut microbiota diversity increased, with a rise in *Bacteroides* and *Faecalibacterium*, while inflammatory markers such as IL-6 and TNF- α were reduced. The study is limited to NSCLC patients and does not assess long-term survival data ³.

A systematic review and meta-analysis of 25 randomised controlled trials (RCTs) analysed the effect of postbiotic-containing interventions on metabolic parameters. The analysis showed a significant reduction in serum insulin ($-2.76 \mu\text{U/mL}$), triglycerides (-8.46 mg/dL), waist circumference (-1.47 cm), and CRP (-0.99 mg/L). No significant effects were observed for fasting blood glucose, HOMA-IR, HbA1c, blood pressure, or BMI. Subgroup analyses suggested stronger effects in younger participants and with longer intervention durations. The meta-analysis aggregates heterogeneous studies, whose results may be influenced by varying strains, dosages, and additional components, and does not isolate the effect of postbiotics alone ⁶.

In a randomised, double-blind, placebo-controlled study involving 60 female patients with vulvar lichen sclerosis (VLS), the effect of a postbiotic derived from *Lactobacillus crispatus* NCU-31 in combination with topical glucocorticoids was investigated. Compared to healthy participants, VLS patients exhibited increased microbial diversity and a reduced prevalence of *Lactobacillus*, while *Prevotella*, *Gardnerella*, and *Streptococcus* were more abundant. The combination therapy resulted in a significant improvement in clinical scores (Cattaneo Clinical Score, IGA) and quality of life (DLQI, VQLI) compared to the placebo group. The study demonstrates promising results but is limited to a specific indication and a small population ⁹.

HYPOTHESIS The observed effects on inflammatory markers and microbiota suggest that postbiotics may exert anti-inflammatory actions through modulation of the immune response and promotion of a healthy microbiota. In particular, the reduction in CRP and pro-inflammatory cytokines indicates a potential systemic effect, though further mechanistic investigation is required.

What is lacking: Studies that specifically elucidate the anti-inflammatory mechanisms of postbiotics, particularly regarding their interaction with the immune system and the long-term clinical relevance in chronic inflammatory diseases.

Immune System

A pilot double-blind, randomised, placebo-controlled study involving 41 preterm infants (<36 weeks gestational age) examined the effect of heat-inactivated *Pediococcus acidilactici* K15 on respiratory infections. Participants received K15 or placebo once daily for one year. No significant difference was observed in the number of febrile days (4.5 vs. 6.6 days). However, a subgroup analysis revealed a more pronounced effect in children with older siblings. Faecal microbiota analysis showed an enrichment of *Faecalimonas*, which may promote butyrate production. The study is small and does not investigate specific infectious pathogens or immune parameters ³⁴.

HYPOTHESIS The observed enrichment of butyrate-producing bacteria may indicate an immunomodulatory effect of postbiotics, mediated through the promotion of a healthy gut microbiota. However, direct evidence for a causal role of these microbes in infection prevention is lacking.

What is lacking: Larger studies with specific immune endpoints (e.g., antibody response, cytokine profiles) and longer follow-up periods to investigate the immunomodulatory effects of postbiotics in vulnerable populations such as preterm infants.

Skin

A randomised, double-blind, placebo-controlled study involving 100 healthy adults with periorbital wrinkles investigated the effect of heat-inactivated *Lactobacillus acidophilus* IDCC 3302 (ID-ACT 3302) on skin ageing parameters. Participants received the postbiotic or placebo daily for 12 weeks. The primary endpoint was the change in crow's feet wrinkles, with secondary endpoints including skin hydration, transepidermal water loss (TEWL), skin elasticity, and global improvement scores. The postbiotic group showed no superiority over placebo in wrinkle endpoints but demonstrated a significant improvement in the elasticity index R2. Skin hydration and TEWL improved in both groups.

In a randomised, controlled split-face study involving Asian women, the topical application of a ferment filtrate from *Epidermidibacterium keratini* EPI-7 (a postbiotic) was investigated for its effects on skin ageing parameters. The application led to significant improvements in skin barrier function, elasticity, and dermal density compared to the placebo group. Additionally, the prevalence of commensal skin microbes such as *Cutibacterium*, *Staphylococcus*, and *Lactobacillus* increased, while the diversity of the skin microbiota rose. The study is limited to topical application and a specific population ¹.

HYPOTHESIS The observed effects on skin microbiota and skin parameters may indicate an interaction between postbiotics and the skin barrier, mediated through modulation of the microbiota and the production of antimicrobial metabolites. However, direct evidence for the underlying mechanisms is lacking.

What is lacking: Studies that specifically investigate the systemic and topical mechanisms of action of postbiotics on the skin barrier and skin microbiota, particularly regarding long-term effects and applicability across different skin types and ethnic groups.

Overall Picture

The available studies suggest that postbiotics may influence various applications—from modulating gut microbiota and reducing inflammatory markers in preclinical settings to improving skin parameters in clinical trials. Particularly consistent are the findings on microbiota composition and the enrichment of health-promoting metabolites (e.g., short-chain fatty acids) in animal and cell culture models. Clinical studies demonstrate improvements in chronic diarrhoea, halitosis, skin elasticity, and inflammatory parameters, though often in small, specific populations and with limited duration. The effects on inflammatory markers and metabolites remain preclinical and have not yet been confirmed in human trials.

Evidence for clinically relevant efficacy in controlled human studies is still in its early stages in many areas. In particular, mechanistic links, long-term effects, and the generalisability of results to broader populations stand out as open research questions. Additionally, the postbiotic strains and preparations studied are heterogeneous, complicating the comparability of results.

Methodology of the evidence base

['Most controlled studies on postbiotics follow a randomised, double-blind, placebo-controlled design, which strengthens the validity of the results. Typical intervention durations range from four to twelve weeks, with some studies employing crossover designs with washout phases. Primary endpoints often include clinical symptoms (e.g., stool consistency, skin parameters, inflammatory markers), while secondary endpoints encompass microbiota analyses, metabolite profiles, and immune parameters. However, there is a systematic lack of long-term studies with clinically relevant endpoints (e.g., remission in chronic diseases, infection rates), mechanistic investigations into modes of action, and studies involving larger, more diverse populations. Furthermore, many studies are limited to specific strains or preparations, restricting the generalisability of the findings.']

Postbiotics at a glance

ORIGIN:

Postbiotics are defined, non-viable microbial cells or their components, obtained from probiotics through fermentation or inactivation (e.g., heat, radiation, lysis). They include cell wall components, metabolites such as short-chain fatty acids, enzymes, or signalling molecules, and are primarily derived from strains of the genera *Lactobacillus*, *Bifidobacterium*, or *Pediococcus*. Inactivation enhances storage stability and eliminates risks associated with live microbes, while the matrix (e.g., milk ferments, capsules) influences bioavailability.

EVIDENCE BASE:

161 evaluated works · 13 controlled human studies · 17 observational studies · 50 review articles · 18 animal studies · 14 cell culture studies

STRONGEST EVIDENCE:

- **Gut health:** Controlled studies show temporary improvements in diarrhoea (e.g., *Limosilactobacillus fermentum* K8-Lb1) and modulation of oral microbiome dysbiosis (*Lactobacillus paracasei* ET-22), though no lasting colonisation or causal effect on disease progression has been demonstrated.
- **Skin:** Randomised, placebo-controlled studies confirm positive effects on skin parameters such as elasticity and redness (e.g., *Epidermidibacterium keratini* EPI-7, *Lactobacillus acidophilus* IDCC 3302), though effects are strain- and preparation-specific and require further validation.
- **Immunomodulation:** Postbiotics such as JK5G reduced immune-related adverse effects in NSCLC patients undergoing R-CHOP therapy without undesirable interactions, but the causal mechanism remains unclear.
- **Safety:** Controlled studies (e.g., 12-week supplementation with ID-ACT 3302) showed no serious adverse effects, though long-term data on immunogenic reactions to cell components are lacking.
- **Metabolic effects:** A meta-analysis on postbiotic supplementation in obesity provides a hypothesis for potential metabolic benefits, but the heterogeneity of preparations precludes general conclusions.

LIMITATIONS:

- The **diversity of preparations** (strain, inactivation method, purity) complicates comparisons between studies and prevents statements on generic effects. Even identical strains may exhibit different effects.
- **Surrogate markers** (e.g., SCFA concentrations, gene expression patterns) dominate studies, while clinical endpoints (e.g., disease progression) are rarely investigated. The relevance of these markers for clinical outcomes in humans remains unclear.
- **Systemic effects** (e.g., on cognition or metabolism) are hypothetical and not supported by controlled studies. Most effects are limited to local applications (gut, skin, oral cavity).

CLASSIFICATION:

Postbiotics—inactivated microbial cells or their components—show strain- and preparation-specific effects on gut health, skin, and the immune system in early-stage research. Controlled studies provide indications, but causal evidence for systemic effects is not yet established.

3. How Robust the Research Is

The evaluated studies include a subset of human research, among them controlled intervention trials. The research focuses on **gut-associated applications**, followed by **safety assessments**, **skin**, and the **immune system**. The most frequently cited controlled studies investigate **skin ageing**, **halitosis**, **diarrhoea**, and **oncological side effects**, with application forms ranging from oral capsules to cosmetic serums. A notable feature is the **diversity of outcome measures**: while some studies assess clinical symptoms (e.g., skin elasticity, stool frequency), others are limited to **surrogate markers** such as microbiome composition or inflammatory parameters.

The methodological quality of the controlled studies is heterogeneous. Strengths include **randomised, double-blind designs** and the use of **placebo controls**, particularly in topical applications. Weaknesses are evident in **small sample sizes** (often pilot studies) and **short intervention periods**, which preclude conclusions about long-term effects. Furthermore, **dose-finding studies** are frequently lacking, rendering the chosen concentrations appear arbitrary. **Review articles** are dominated by mechanistic hypotheses (e.g., modulation of the **gut-brain axis** or **vagus nerve stimulation**), yet these mechanisms remain unconfirmed in humans. Preclinical studies (animal and cell models) provide only **indications of potential pathways**, such as the regulation of **tight junction proteins** or **cytokine patterns** in vitro or in animals; their relevance for human clinical outcomes is not yet investigated.

Postbiotics: strain-specific or generically effective?

The assumption that postbiotics could exert

GENERIC EFFECTS

is widespread, yet the evidence does not support this. Nearly all controlled studies use **individual, defined strains** (e.g., *Limosilactobacillus fermentum* K8-Lb1 or *Pediococcus acidilactici* K15), whose results are not transferable to other preparations. Even within the same species, differing **inactivation methods** (heat vs. lysis) or **fermentation conditions** can lead to divergent efficacy profiles. The **frequently cited studies** demonstrate positive effects on **skin parameters** or **oral microbiome dysbiosis**, but these are tied to **specific postbiotics** (e.g., EPI-7 from *Epidermidibacterium keratini*). While a **meta-analysis** on metabolic effects summarises several studies, it cannot draw general conclusions due to the **heterogeneity of preparations**.

A further issue is the

LACK OF STANDARDISATION

of outcome measures. While some studies assess **clinical endpoints** (e.g., reduction of diarrhoea or skin redness), others are limited to **surrogate markers** such as **SCFA concentrations** or **gene expression patterns**, whose relevance to disease progression remains unclear. Even in **frequently studied applications** such as **immune modulation** or **metabolic regulation**, it remains uncertain whether the observed effects are **causal** or merely **epiphenomenal**, associated with other processes (e.g., microbiome shifts). While **mechanistic reviews** provide plausible hypotheses (e.g., **TLR4 activation** or **butyrate-mediated histone acetylation**), **evidence for these pathways in humans** is lacking. Without **replication studies** using identical preparations and endpoints, the generalisability of the results remains limited.

4. Common Claims — and What the Data Show

STATEMENT	EVIDENCE
Postbiotics act systemically via the gut	Most studies examine local effects (gut, skin, oral cavity). Systemic effects (e.g., on cognition or metabolism) are hypothesis-driven but not supported by contr
Postbiotics are safer than probiotics	Safety studies show no severe side effects , but long-term data are lacking. Inactivation eliminates risks from live germs, but does not rule out immunogenic rea
Postbiotics can replace probiotics	There are no direct comparative studies . Postbiotics and probiotics operate via different mechanisms (e.g., metabolites vs. colonisation), so substitution is not
Postbiotics sustainably modulate the microbiome	Controlled studies demonstrate temporary shifts in microbiome composition, but no permanent colonisation . The effects typically cease with discontinuation of

5. Profile: Molecule and Charge

Postbiotics are not a single molecule but a **mixture** — there is no empirical formula or fixed molecular mass. What can be described are functional groups, charge behaviour, and redox properties; these are the focus of the next section.

6. Charge, Electrons, Radicals

In cell cultures, the antioxidant effects of postbiotics were demonstrated using radical-scavenging assays such as ABTS (2,2-azinobis(3-ethylbenzothiazoline-6-sulphonic acid))), where free radicals were neutralised ²¹. Further tests included measuring the iron-reducing antioxidant capacity and the reduction of reactive oxygen species (ROS) ²². Postbiotics influenced ROS levels in hydrogen peroxide-induced cells, suggesting modulation of oxidative stress ^{23 24}. In foundational studies, a ROS-dependent bactericidal effect was described, which could be inhibited by radical scavengers such as thiourea ²⁶. Whether these effects are due to charge transfer or cation exchange is not specified in the available studies.

No direct measurements of the electrochemical properties of postbiotics have been conducted in humans. Observations indicate, however, that microbial enzymes during fermentation generate organic acids and bioactive peptides, which could indirectly influence redox-active processes ²⁰. In cell cultures, a significant inhibition of ROS production by postbiotic extracts was demonstrated, suggesting an antioxidant effect. Whether these effects are attributable to electron transfer or radical binding remains to be investigated. Foundational studies describe postbiotics as radical scavengers that reduce oxidative stress ²⁵. However, whether similar mechanisms occur in humans is not supported by electrochemical measurements. Further research on charge distribution or cation exchange capacity would be necessary.

7. Interactions with Other Substances

Substances with which this compound has been **jointly** investigated or discussed in human studies and review articles on this platform — whether in combination, comparison, or via shared mechanisms. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Gut microbiome	683	33
Butyrate (butyric acid)	120	5
Probiotics	118	22
Chronic inflammation	48	3
Stress, cortisol, and inflammation	24	3
Spermidine	12	0
Green tea and EGCG	10	0
Dietary fibre and psyllium husk	7	1
Urolithin A	6	0
Therapeutic fasting and intermittent fasting	6	2

Data on interactions between postbiotics and medications or nutrients are limited. One human observation describes the combination of postbiotics (JK5G, JK21) with R-CHOP in high-risk DLBCL (IPI score 4), with no evidence of adverse interactions ²⁷. In vitro studies using human intestinal cell lines (Caco-2, HT-29) show no cytotoxicity or genotoxicity with formulations derived from cell-free supernatant and heat-inactivated bacteria. Animal studies suggest synergistic effects: postbiotics (0.30%) enhanced growth and immune response in broilers when combined with inulin (1.0%) ³⁰. Additionally, an interaction with nutrients was observed, where fish oil (enriched with docosahexaenoate) and medium-chain triglycerides altered the plasma lipidomes of cats and reduced putrefactive postbiotics in the bloodstream ³³.

Direct evidence of effects on enzymes or metabolic pathways is lacking, but indirect indications exist. Postbiotics modulate host metabolism and immune responses via microbial metabolites that interact with signalling pathways ^{12 29}. In vitro data show that certain postbiotics (e.g., from *A. muciniphila*, *F. prausnitzii*) can reduce the expression of ACE, ATR1, and ACE2 in human tissue, suggesting an influence on renin-angiotensin system-related genes ²⁸. Cell culture studies demonstrate synergistic antibacterial effects of postbiotics (*L. paracasei* SD1, *L. rhamnosus* SD11) in combination with glycerol monolaurate or poly-L-lysine against *H. pylori* ^{31 31}. Nutrient-dependent metabolic shifts were observed in consortia under rumen-like conditions, where nitrogen enrichment and carbon limitation promoted the production of branched short-chain fatty acids ³².

8. Overdose, Tolerability, and Limits

No specific dosage thresholds or systematic investigations regarding overdose, toxicity, or upper limits of postbiotics are available. In controlled human studies, no severe adverse effects were observed, even with prolonged use. For example, a 12-week supplementation with ID-ACT 3302 showed no serious side effects, and safety was comparable to placebo ¹¹. A four-week study with KABP-065 postbiotics demonstrated no worsening of gastrointestinal symptoms; the frequency of adverse events did not differ from the placebo group ⁷. Similarly, no associated side effects were reported with K15 intake in preterm infants ³⁴.

Contraindications are not explicitly established due to a lack of clinical data on at-risk groups. Postbiotics are considered safer than live microorganisms, though evidence remains limited ^{5 10}. Observational studies suggest that microbiota interventions—including postbiotics—may influence the tolerability of therapies such as chemotherapy or immune checkpoint blockade, without identifying specific dose-response relationships or contraindications ¹⁷. Adverse effects in controlled studies were not systematically linked to particular dosages. Long-term effects, interactions with medications, and individual factors such as immune status or pre-existing conditions warrant further investigation. No animal or tissue studies on toxicity or upper limits are available.

9. The Most Robust Studies

Ranked by evidential strength, not by prominence. The full evaluation includes significantly more studies; only the most reliable are listed here.

Controlled Human Studies

- ¹ Efficacy and Safety of Epidermidibacterium Keratini EPI-7 Derived Postbiotics in Skin Aging: A Prospective Clinical Study (2023)
- ² *Lactobacillus paracasei* ET-22 and derived postbiotics reduce halitosis and modulate oral microbiome dysregulation: a randomised, double-blind, placebo-controlled study (2023)
- ³ JK5G postbiotics attenuate immune-related adverse events in NSCLC patients by regulating gut microbiota: a randomised controlled trial in China (2023)
- ⁴ Effects of postbiotics on chronic diarrhoea in young adults: a randomised, double-blind, placebo-controlled crossover trial assessing clinical symptoms (2024)
- ⁵ Evaluating the Role of Postbiotics in the Modulation of Human Oral Microbiota: A Randomised Controlled Clinical Trial (2025)
- ⁶ The effect of postbiotics supplementation on obesity and metabolic health: a systematic review and meta-analysis of randomised controlled trials (2025)
- The Effectiveness of Heat-Killed *Pediococcus acidilactici* K15 in Preventing Respiratory Tract Infections in Preterm Infants: A Pilot Study (2024)
- ⁷ Novel Application of Oral Postbiotics for Skin Condition in Healthy Middle-Aged Women: A Randomised, Double-Blind, and Placebo-Controlled Study (2025)
- ⁸ Pilot Study on the Effects of a Cosmetic Serum Containing Niacinamide, Postbiotics and Peptides on Facial Skin in Healthy Participants: A Randomised Controlled Trial (2024)
- A Randomised, Double-Blind, Placebo-Controlled Study to Evaluate the Effect of *Limosilactobacillus fermentum* K8-Lb1 Postbiotic on Weight Management (2026)
- ⁹ Postbiotics originated from *Lactobacillus crispatus* NCU-31 improves vulvar lichen sclerosis: a randomised, double-blind controlled trial (2026)
- ¹⁰ A Heat-Inactivated Two-Strain *Lactocaseibacillus paracasei* Fermented Milk as a Postbiotic for Functional Constipation: A Randomised Controlled Trial (2026)
- ¹¹ Effects of Heat-Killed *Lactobacillus acidophilus* IDCC 3302 on Skin Ageing Parameters: A Randomised, Double-Blind, Placebo-Controlled Trial (2026)

Observational Studies in Humans

- Gut Microbiota Metabolites in Major Depressive Disorder—Deep Insights into Their Pathophysiological Role and Potential Translational Applications (2022)
- ¹² Roles of the Intestinal Microbiota and Microbial Metabolites in Acute GVHD (2021)
- ¹³ Pre-, Pro-, Syn-, and Postbiotics in Infant Formulas: What Are the Immune Benefits for Infants? (2023)
- ¹⁴ Effect of Gut Microbiota-Derived Metabolites on Immune Checkpoint Inhibitor Therapy: Enemy or Friend? (2022)
- ¹⁵ Gut Microbiome Modulation in Hepatocellular Carcinoma: Preventive Role in NAFLD/NASH Progression and Potential Applications in Immunotherapy-Based Strategies (2025)
- ¹⁶ The Modulation Effect of a Fermented Bee Pollen Postbiotic on Cardiovascular Microbiota and Therapeutic Perspectives (2023)
- ¹⁷ The Emerging Role of Microbiota in Lung Cancer: A New Perspective on Lung Cancer Development and Treatment (2025)
- ¹⁸ Dysbiosis–NK Cell Crosstalk in Pancreatic Cancer: Toward a Unified Biomarker Signature for Improved Clinical Outcomes (2025)
- The Microbiome and Uremic Solutes (2022)
- ¹⁹ The Role of Postbiotics in Asthma Treatment (2024)
- Critical Role of Reproductive Tract Microbiota and Derived Metabolites in Inflammation, Tumour Immunity, and Tumourigenesis of Gynaecological Cancers: A Review (2026)

10. Summary

Postbiotics represent an emerging field of research with findings on **gut-associated applications**, **skin**, and **immune modulation** from controlled human studies. These studies suggest strain- and preparation-specific effects, such as in diarrhoea, skin ageing, or immune-related adverse effects of oncological therapies. The methodological quality of these studies is heterogeneous: while randomised, double-blind designs with placebo controls (particularly in topical applications) are convincing, small sample sizes, short intervention periods, and the absence of dose-finding studies limit their validity. The observed effects are often transient and cease upon discontinuation, suggesting no sustained modulation of the microbiome or systemic effects. Nevertheless, the data indicate a favourable safety profile, as even with prolonged use, no severe adverse effects have been documented.

HYPOTHESIS The mechanistic hypotheses regarding postbiotics—such as modulation of the gut-brain axis, TLR4 activation, or butyrate-mediated histone acetylation—are plausible, yet causal evidence in humans is lacking. Preclinical studies (animal and cell models) provide indications of potential mechanisms, such as the regulation of tight junction proteins or cytokine patterns, but these findings remain preclinical and do not confirm such effects in humans. Should the local effects be confirmed in larger, long-term human studies, postbiotics could establish themselves as a safe alternative or adjunct to probiotics—particularly in areas where live microbes pose risks (e.g., immunosuppression). Furthermore, they may play a role in personalised medicine if strain- and preparation-specific efficacy profiles can be standardised. **Hypothesis:** The antioxidant properties of postbiotics, demonstrated in cell cultures via radical-scavenging assays, suggest a potential modulation of oxidative stress in preclinical settings, but whether these effects translate to humans remains unclear. Electrochemical measurements of charge distribution or cation exchange capacity could provide further insights.

To clarify the clinical relevance of postbiotics, **replication studies** using identical preparations, standardised endpoints, and adequately powered sample sizes are essential. **Dose-finding studies** should be prioritised to define effective concentrations and avoid arbitrary dosing. Additionally, **long-term studies** are needed to assess the safety and sustainability of effects, particularly regarding immunogenic reactions. For systemic applications (e.g., cognition,

metabolism), robust data are currently lacking—controlled studies with clinical endpoints would be necessary to validate the hypothetical effects. Further research is also required in **standardising analytical methods** to characterise the active components of postbiotics and enable comparisons between studies. Finally, **direct comparative studies** between postbiotics and probiotics should be conducted to determine whether substitution or combination is beneficial. Without such studies, the generalisability of findings remains limited, and postbiotics remain a promising but insufficiently validated field of research.

11. Unresolved Questions

- **Dose-response relationship:** What concentrations are optimal for which applications? Systematic dose-finding studies are currently lacking.
- **Long-term effects:** Most studies last only weeks. It remains unclear whether effects persist after discontinuation or if continuous administration is required.
- **Mechanistic validation:** The postulated mechanisms (e.g., **vagus nerve stimulation**, **SCFA signalling**) have not been confirmed in humans.

12. Further Paths

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

- Interaction network

Frequently Asked Questions

Can postbiotics be used in inflammatory bowel disease?

There are **no controlled studies** on **Crohn's disease** or **ulcerative colitis**. Existing research on **chronic diarrhoea** or **irritable bowel syndrome** shows **symptomatic effects**, but no impact on the **underlying disease**. Research in this area is still in its early stages, with **strain-specific postbiotics** (e.g., derived from *Lactobacillus* species) under investigation. Any use should be **adjunctive** and under **medical supervision**, as interactions with **immunosuppressants** cannot be ruled out.

Are postbiotics suitable for skincare?

Controlled studies have examined certain preparations for improvements in **skin elasticity**, **moisture content**, and **wrinkle formation**; however, results are inconsistent and apply only to **specific preparations** (e.g., EPI-7 from *Epidermidibacterium keratini* or heat-inactivated *Lactobacillus acidophilus*). Effects are **locally limited** and typically observed after **several weeks of use**. Whether postbiotics are superior to **conventional active ingredients** (e.g., retinoids, hyaluronic acid) has not been investigated. The evidence base is **emerging**, so no conclusions can be drawn regarding **long-term effects** or **risks** (e.g., sensitisation).

Can postbiotics strengthen the immune system?

Some controlled studies have assessed the modulation of **immune parameters** (e.g., **cytokine profiles**, **IgA levels**) or **infection frequency** (e.g., in preterm infants); however, results are inconsistent and **strain-dependent**. Furthermore, studies on **clinically relevant endpoints**, such as **disease duration** or **complication rates**, are lacking. **Mechanistic hypotheses** (e.g., **TLR activation**, **dendritic cell maturation**) are based on **cell and animal studies**, the applicability of which to humans remains unclear. An **immunostimulatory effect** in terms of **vaccine enhancement** or **cancer prevention** has not been investigated.

Sources

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