Bacteriocins in Postbiotic Preparations: Antimicrobial Potential, Safety and Translational Challenges

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Abstract

Bacteriocins are ribosomally synthesized antimicrobial peptides or proteins with established value in food bio preservation and growing interest as precision antimicrobials. Their relationship to postbiotics, however, is frequently described incorrectly. Under the International Scientific Association for Probiotics and Prebiotics consensus definition, a postbiotic must contain inanimate microorganisms and/or their components and confer a health benefit; a purified bacteriocin or a cell-free fermentation product is not automatically a postbiotic. This structured narrative review therefore asks where bacteriocins occur across distinct preparation types, how strongly observed effects can be attributed to them, and what evidence supports food, veterinary, or human-health translation. Literature indexed in PubMed and publisher databases was searched through 22 July 2026, with primary studies, consensus statements, and official regulatory evaluations prioritized. Nisin–lipid II binding and mannose-phosphotransferase-system recognition illustrate mechanism-specific activity, while the outer membrane generally restricts direct activity against Gram-negative bacteria. Food applications provide the strongest translational precedent, but performance depends on matrix composition, pH, processing, dose, and hurdle design. Animal studies support microbiome modulation and tolerability for selected molecules; studies of complex cell-free products cannot assign benefits to bacteriocins without chemical quantification or depletion controls. Resistance, cytotoxicity, immunogenicity, pharmacokinetics, delivery, and microbiome disruption require molecule- and route-specific evaluation. Regulatory acceptance of nisin A for defined food uses must not be generalized to other bacteriocins or therapeutic routes. Standardized preparation identity and evidence-linked terminology are prerequisites for credible translation.

Keywords: Bacteriocins, Postbiotics, Antimicrobial Peptides, Food Biopreservation, Safety

1. Introduction

Bacteriocins are ribosomally synthesized antimicrobial peptides or proteins produced by bacteria and archaea. Many lactic acid bacteria make bacteriocins that inhibit competitors occupying the same ecological niche; several also inhibit foodborne or clinically relevant organisms. This diversity has made bacteriocins attractive as food preservatives, microbiome modulators, veterinary interventions, and leads for antimicrobial development (Cotter et al., 2005, 2013; Sugrue et al., 2024). Their appeal is strengthened by sequence programmability, biodegradability, and mechanisms that can differ from those of conventional antibiotics. These features are promising, but they do not establish low toxicity, broad-spectrum activity, resistance-proof efficacy, or clinical usefulness by themselves.

A second literature has developed around postbiotics. The current International Scientific Association for Probiotics and Prebiotics (ISAPP) definition is "a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host" (Salminen et al., 2021). This definition is preparation-based rather than metabolite-based. Deliberately inactivated cells may be delivered with metabolites produced during growth or released during inactivation, but purified metabolites are not postbiotics. A cell-free supernatant that excludes microbial cells and cell structures also does not meet the definition merely because it was produced by a probiotic organism. Consequently, "bacteriocin," "bacteriocin-containing cell-free product," "inactivated-cell preparation," and "live bacteriocin-producing probiotic" are not interchangeable terms.

Conceptual imprecision creates a causal problem. When a complex fermentation product improves an outcome, the effect may reflect organic acids, residual nutrients, exopolysaccharides, cell fragments, multiple peptides, or their interactions. A bacteriocin-specific mechanism requires at least identification and quantification of the molecule and is strengthened by purification, activity-guided fractionation, neutralization or deletion of the structural gene, and add-back experiments. Without such controls, attributing a host or antimicrobial effect to a bacteriocin is a hypothesis rather than a demonstrated conclusion.

This review therefore asks three linked questions: (i) in which preparation types do bacteriocins evidence that bacteriocins cause the reported antimicrobial or host effects; and (iii) what safety, resistance, formulation, and regulatory barriers separate food use from veterinary or human therapeutic translation? The novelty is an evidence-linked framework that treats preparation identity and causal attribution as prerequisites, rather than grouping purified molecules, cell-free products, inactivated cells, and live producers under a single label.

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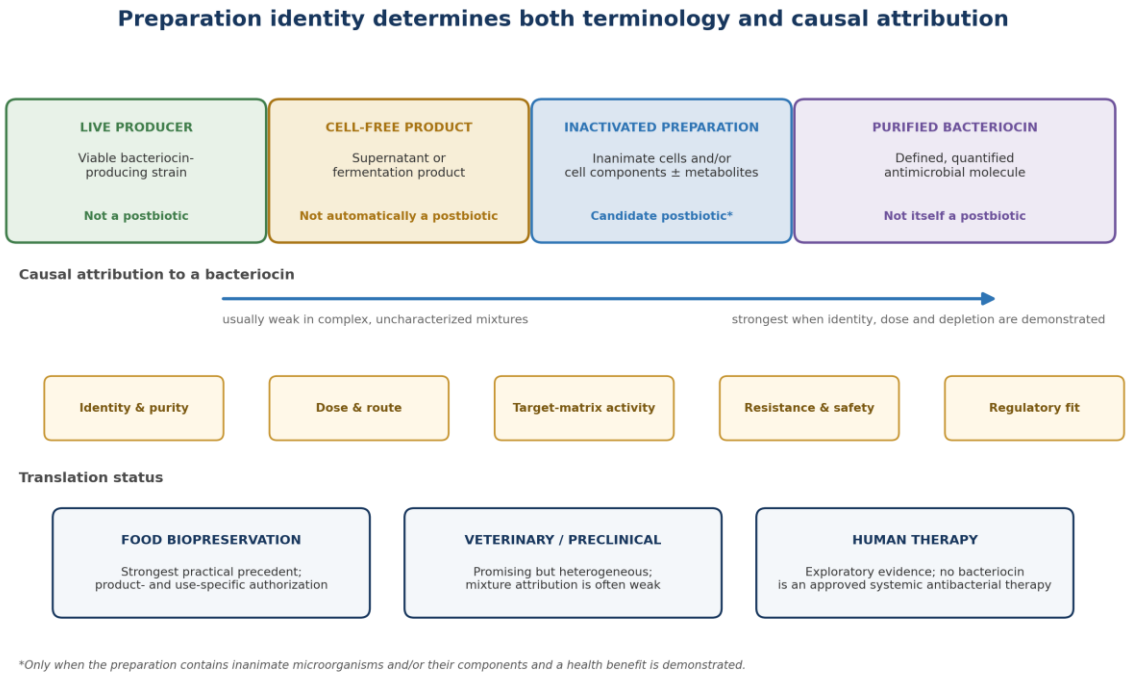

Figure 1. Evidence map linking preparation identity, bacteriocin attribution, development gates, and translation status. The figure was prepared for this review from the ISAPP definition and the evidence appraisal described in Section 2.

2. Literature Search and Evidence Appraisal

Searches combined bacteriocin*, nisin, pediocin, plantaricin, enterocin AS-48, postbiotic*, inactivated microorganism, cell-free supernatant, fermentation product, food preservation, food matrix, toxicity, haemolysis, immunogenicity, resistance, microbiome, pharmacokinetics, animal, clinical trial, and regulation. The principal date range was January 1989 to July 2026; earlier records were eligible when required to establish nomenclature or historical regulatory context. Reference lists of consensus papers, authoritative reviews, and official evaluations were searched backward, and bibliographic details were checked against DOI, PubMed, publisher, or regulatory records.

English-language peer-reviewed primary studies were prioritized when they identified the bacteriocin, described the preparation or inactivation procedure, and reported a relevant food, antimicrobial, safety, animal, or human endpoint. Consensus statements and official regulatory evaluations were included for definitions and legal status. Studies were excluded from bacteriocin-specific conclusions when they evaluated an uncharacterized probiotic, a generic postbiotic product, or a fermentation mixture without evidence that a bacteriocin was present. Reviews were used for scope and cross-checking but not as substitutes for primary toxicology where the original report was available. Evidence was appraised narratively because preparations, organisms, doses, matrices, routes, and endpoints were too heterogeneous for quantitative synthesis. Human controlled evidence was ranked above animal in vivo, ex vivo/in vitro, and mechanistic or indirect evidence. Causal attribution was rated strong when a defined molecule and dose were tested; moderate when a bacteriocin-producing strain or combination was tested with relevant controls; and weak when a complex mixture lacked bacteriocin quantification, depletion, or genetic controls.

3. Conceptual Boundaries: When a Bacteriocin Is—and Is Not—Part of a Postbiotic

Table 1 separates the four preparation types most often conflated in this field. A bacteriocin may be present in all four, but the correct name, safety question, and strength of causal inference differ. The word "postbiotic" is appropriate only for an inactivated-microorganism preparation that contains the required microbial material and for which a health benefit has been demonstrated. Inactivation alone establishes neither benefit nor postbiotic status. Conversely, purification can establish chemical identity and strengthen causal attribution while moving the product outside the postbiotic definition (Salminen et al., 2021).

Table 1. Preparation categories, terminology, and bacteriocin attribution.

Preparation type	What is administered	Postbiotic status	Bacteriocin attribution	Preferred reporting
Purified bacteriocin	Chemically or chromatographically defined peptide/protein; viable cells absent.	Not a postbiotic; it is a microbial metabolite/component tested as a defined molecule.	Potentially strong if identity, purity, activity units or molar dose, and comparator are reported.	Molecule/variant, purity, mass, activity assay, dose, route, formulation, contaminants.
Bacteriocin-containing cell-free supernatant or fermentation product	Soluble fermentation products after centrifugation/filtration; cells and much cell structure removed.	Not automatically a postbiotic under the ISAPP definition.	Usually weak unless the bacteriocin is quantified and depleted, neutralized, or genetically removed.	Producer strain, culture conditions, filtration, pH neutralization, composition, bacteriocin identity/concentration.
Inactivated whole-cell preparation ± metabolites	Inanimate microorganisms and/or cell components, potentially with retained fermentation metabolites.	Candidate postbiotic only after a health benefit is demonstrated.	Mixture-level effect; bacteriocin-specific attribution requires additional controls.	Strain, biomass, inactivation and viability verification, retained components, dose, stability, benefit endpoint.
Live bacteriocin-producing probiotic or protective culture	Viable producer organism, sometimes with in situ bacteriocin production.	Not a postbiotic; may be a probiotic or protective culture if the relevant criteria are met.	Moderate only when bacteriocin-null and complemented strains or direct in situ measurements are used.	Strain identity, viability, colonization/persistence, production in target matrix, genetic controls, dose.

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Figure 1 translates this distinction into a development pathway. Preparation identity comes first; analytical, safety, matrix, and regulatory gates then determine whether evidence can support a food use, a veterinary/preclinical claim, or a human therapeutic claim. The framework deliberately separates regulatory authorization from efficacy: permission to use nisin A in particular foods does not demonstrate that a nisin formulation treats infection.

4. Classification, Biosynthesis, and Mechanisms

4.1 Classification and biosynthesis

Bacteriocin classification has changed as genome mining and structural chemistry have expanded the field. A practical, non-exclusive framework distinguishes post-translationally modified ribosomally synthesized and post-translationally modified peptides (RiPPs; commonly called class I), small largely unmodified peptides (class II), and larger bacteriolytic or non-lytic proteins (class III). Class I includes lanthipeptides such as nisin, whose dehydrated amino acids and lanthionine bridges arise from dedicated maturation enzymes. Class II includes pediocin-like one-peptide bacteriocins, two-peptide systems, leaderless peptides, and circular peptides, although the placement of circular and leaderless bacteriocins differs between schemes. Class III contains larger, often heat-labile proteins. Size cut-offs and subclass labels should therefore be cited to a defined scheme rather than presented as universal facts (Alvarez-Sieiro et al., 2016; Sugrue et al., 2024).

Biosynthetic loci commonly encode the precursor peptide, modification and export functions, self-immunity, and regulatory machinery. Their location on chromosomes, plasmids, or mobile elements affects stability and transfer. Production is also phenotype-dependent: strain genotype does not establish that an active concentration is reached in a food, intestine, or formulation. Reports should connect genomic prediction to peptide mass, sequence or structural confirmation, and quantitative activity under the intended conditions.

4.2 Mechanism, spectrum, and the Gram-negative barrier

Mechanisms are molecule-specific. Nisin binds the pyrophosphate region of lipid II, thereby sequestering an essential peptidoglycan precursor and organizing membrane pores at low local concentrations (Wiedemann et al., 2001). By contrast, many class IIa pediocin-like bacteriocins recognize the membrane IIC/IID components of a subset of mannose phosphotransferase systems; receptor sequence and expression help define susceptibility (Kjos et al., 2010). Other bacteriocins disrupt membranes without a single known receptor, inhibit enzymes, or degrade cell walls. It is therefore inaccurate to describe every bacteriocin as a nonspecific pore former.

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Spectrum is equally contextual. Many lactic-acid-bacterial bacteriocins are most active against Gram-positive organisms because their cytoplasmic membrane or cognate receptor is accessible. The outer membrane of Gram-negative bacteria impedes many peptides. Activity against Escherichia coli or Salmonella often appears only after membrane permeabilization, high pressure, heating, acidification, chelation, or combination with another antimicrobial. For example, nisin at 10 μM combined with trans-cinnamaldehyde and EDTA delayed growth of porcine E. coli strains in vitro, but the result belongs to the combination and cannot be assigned to nisin alone (Field et al., 2017). Statements of "broad-spectrum" activity must therefore specify strain panel, growth phase, matrix, pH, assay, exposure, and whether a hurdle agent was required.

Potency values are not automatically comparable. Agar diffusion depends on peptide diffusion and indicator physiology; activity units depend on the assay definition; and MICs vary with inoculum, medium, adsorption, and purity. Molar concentration of an identified molecule is preferable for mechanistic comparisons, while food challenge studies should additionally report activity per gram or milliliter, recovery over time, and survivor counts.

5. Food-System Applications and Matrix Performance

5.1 Modes of use

Food biopreservation provides the clearest practical precedent for bacteriocins. Three strategies are distinct: direct addition of a purified or standardized preparation; incorporation into a coating, film, or packaging system; and in situ production by a starter or protective culture (Deegan et al., 2006). Direct addition offers a known input but not necessarily a known active dose after processing. A producer culture may generate activity gradually and locally, yet its performance depends on growth, competition, phage sensitivity, and regulation of the biosynthetic locus. In Cheddar manufacture, a Lactococcus lactis strain producing lacticin 3147 demonstrated the feasibility of integrating a bacteriocinogenic starter into a real fermentation process (Ryan et al., 1996). That is evidence for a live culture strategy, not for a postbiotic. Nisin is particularly useful against susceptible Gram-positive vegetative cells and can inhibit spore outgrowth in some formulations. Nevertheless, attached bacteria and complex surfaces reduce. Nisin is particularly useful against susceptible Gram-positive vegetative cells and can inhibit spore outgrowth in some formulations.

Nevertheless, attached bacteria and complex surfaces reduce predictability; early work on meat showed that nisin delayed growth of susceptible attached bacteria but was insufficient as a stand-alone control across all organisms tested (Chung et al., 1989). Food-safety conclusions should be based on target-pathogen challenge tests in the intended product, not on broth inhibition zones.

5.2 Matrix, processing, and hurdle effects

Food composition can help or hinder activity. Low pH often improves nisin solubility and stability, whereas neutral or alkaline conditions can reduce recoverable activity. Proteins, fat droplets, phospholipids, and suspended particles can bind bacteriocins or divert them from bacterial targets. Salt, water activity, indigenous microbiota, bacterial stress state, and proteases further alter efficacy. Thermal processing may preserve many small class I and II peptides while changing the target cell envelope; large class III proteins are generally more heat-sensitive. These interactions explain why a concentration effective in laboratory broth may fail in cheese, meat, or an emulsion.

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Rational hurdles can lower the required bacteriocin dose and broaden coverage. Acidification, mild heat, high pressure, chelators, essential-oil components, or cell-envelope-active antimicrobials may sensitize targets. Hurdles must be evaluated for additive toxicity, sensory acceptability, labelling, and legal status, and synergy should be demonstrated quantitatively rather than inferred from a larger inhibition zone. The nisin–cinnamaldehyde–EDTA example illustrates both the opportunity and the attribution constraint (Field et al., 2017).

Commercial feasibility requires more than killing a challenge organism. Production titre, downstream recovery, purity specification, batch potency, residual culture media, stability during storage, compatibility with the process, flavour or texture effects, and cost per treated unit all matter. A food-grade producer does not make every secreted molecule food-approved, and the safety of the source organism cannot substitute for characterization of the final preparation.

6. Evidence Beyond Food Preservation

6.1 Defined bacteriocins and microbiome modulation

A defined bacteriocin can reshape a microbial community as well as suppress a pathogen. O'Reilly et al. (2023) administered nisin powder or encapsulated nisin to 40 male piglets (10 per group) for four days. Intact, bioactive nisin reached the lower gastrointestinal tract, and treatment produced

reversible changes in community composition and short-chain-fatty-acid profiles. This study provides direct evidence that orally delivered nisin can remain active in vivo, but it also contradicts the assumption that bacteriocins inherently spare commensal microbiota. Whether a change is beneficial depends on indication, duration, baseline ecology, dose, and recovery.

Local human administration has been explored on a small scale. In a four-day plaque-regrowth study, 45 participants were randomized to nisin Z extract, distilled water, or 0.2% chlorhexidine mouthrinse (15 per group). Nisin showed antiplaque activity but was less effective than chlorhexidine (Mitra et al., 2019). The short duration, local route, small sample, and incompletely standardized extract prevent extrapolation to systemic infection or long-term oral health. It is best treated as exploratory human evidence rather than clinical validation of bacteriocins as antibiotic replacements.

6.2 Complex products and veterinary evidence

Complex fermentation products may benefit animal performance or intestinal endpoints, but terminology and attribution require care. Chang et al. (2022) fed 245 broiler chickens one of three Lactiplantibacillus plantarum cell-free fermentation products, a basal diet, or oxytetracycline. The products were produced by centrifugation and 0.22-µm filtration and contained measurable organic acids and antioxidant activity. Improvements were reported in selected growth, barrier, immunological, and microbial outcomes. Because cells were removed, these preparations do not meet the current ISAPP postbiotic definition on the reported processing alone. Moreover, the animal study did not identify a bacteriocin dose or use depletion or gene-knockout controls. The results support the activity of the fermentation products as mixtures, not a bacteriocin-specific mechanism.

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The same caution applies to inflammatory bowel disease, sepsis, obesity, or metabolic claims attributed to generic postbiotics. Evidence that an inactivated preparation or fermentation product modifies inflammation does not establish that its bacteriocin component caused the effect. A defensible chain of evidence requires the molecule to be detected at the administered dose, remain stable or reach the target site, reproduce the effect when purified, lose the effect when selectively removed, and retain an acceptable safety window.

6.3 Representative evidence and attribution

Table 2 compares representative studies using the preparation and attribution framework. It is an evidence map rather than an exhaustive efficacy table. The most informative contrast is between a defined bacteriocin experiment and a complex product for which bacteriocin identity and concentration were not reported.

Table 2. Representative bacteriocin-related evidence, preparation identity, and strength of attribution.

Study / setting	Organism or source	Preparation / inactivation	Bacteriocin identity and dose	Model / sample	Comparator	Main outcome
Wiedemann et al. (2001); mechanism	Nisin from Lactococcus lactis	Purified peptide; no cells	Nisin; defined biochemical concentrations	Model membranes and biochemical assays	Membranes with/without lipid II	Lipid II binding combined pore formation with inhibition of cell-wall synthesis.
Ryan et al. (1996); Cheddar cheese	Bacteriocin-producing L. lactis starter	Live producer culture; not inactivated	Lacticin 3147 produced in situ; recovered activity rather than purified dose	Pilot cheese manufacture	Conventional starter/control manufacture	Demonstrated feasibility of a bacteriocinogenic starter in cheese processing.
Field et al. (2017); antimicrobial combination	E. coli strains of swine origin	Purified/standardized nisin in a combination	Nisin 10 µM + trans-cinnamaldehyde 125 µg/mL + EDTA 0.25–2%	In vitro growth assays	Single components and untreated controls	Combination extended growth inhibition, including enterotoxigenic strains.

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O'Reilly et al. (2023); gut microbiome	Nisin; porcine intestinal microbiota	Nisin powder or encapsulated nisin; no cells	150 mg/kg body weight; oral/feed exposure for 4 days	40 male piglets; 10/group	Untreated and encapsulant controls	Active nisin reached faeces; microbiota and SCFA changes were largely reversible after withdrawal.
Chang et al. (2022); broiler gut health	L. plantarum RG11, RI11, RS5	Centrifuged and 0.22-µm-filtered cell-free fermentation products	Bacteriocin identity/concentration not quantified in the feeding study; 0.1% v/w product	245 male Cobb 500 broilers; 5 groups, 7 replicates × 7 birds; 42 days	Basal diet and 0.01% oxytetracycline	Selected growth, barrier, immune and microbial outcomes improved.

7. Resistance and Safety

7.1 Resistance is possible and mechanism-dependent

Bacteriocins should not be described as resistance-proof. Stable or adaptive tolerance can arise through receptor loss or altered expression, cell-envelope charge and fluidity changes, stress responses, proteolysis, efflux, biofilm state, and dedicated immunity determinants. For pediocin-like bacteriocins, reduced or altered mannose phosphotransferase-system function can markedly change susceptibility (Kjos et al., 2011). In Listeria monocytogenes, cell-wall changes associated with pbp2229 expression increased nisin resistance and cross-protection to class IIa bacteriocins (Gravesen et al., 2004). The fitness and virulence effects of resistance may be favourable or unfavourable and must be measured rather than assumed.

Food and clinical development should therefore include spontaneous resistance frequency, serial passage, cross-resistance to other bacteriocins and antibiotics, stability after withdrawal, performance in biofilms, and genomic or transcriptomic characterization. Multi-hurdle design can suppress escape, but sublethal gradients in foods or delivery systems can also select tolerant populations. Surveillance is relevant even for products regarded as natural.

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7.2 Toxicology, host selectivity, pharmacokinetics, and delivery

Safety is molecule-, formulation-, dose-, route-, and population-specific. A peptide tolerated after ingestion may behave differently when inhaled, applied to damaged mucosa, or injected. Food exposure does not establish systemic safety. Development programs should test identity and impurities, cytotoxicity across relevant human cells, haemolysis, local irritation, sensitization and immunogenicity, genotoxicity where indicated, repeated-dose organ toxicity, reproductive or developmental endpoints when exposure warrants them, and effects on the resident microbiome (Soltani et al., 2021). For therapeutic use, absorption, proteolysis, tissue distribution, clearance, anti-drug antibodies, and delivery-site concentrations are central.

Table 3. Representative primary toxicology studies of bacteriocins or bacteriocin preparations.

Bacteriocin / preparation	Study design and sample	Exposure	Reported findings
Nisin A commercial preparation Hagiwara et al. (2010)	F344 rats; 10 males and 10 females/group; 90-day dietary study; NaCl reference group	0, 0.2, 1.0, or 5.0% commercial preparation; highest intake ≈2,996 mg/kg/day males and 3,187 mg/kg/day females; ≈224.7 and 239 mg active nisin A/kg/day	No toxicologically significant treatment-related changes; highest dose was the study NOAEL.
Enterocin AS-48 Baños et al. (2019)	BALB/c mice; 90-day dietary study; nisin comparator	50, 100, or 200 mg/kg diet	No deaths or major clinical/biochemical toxicity; focal hepatocyte vacuolar degeneration occurred in some animals at 100–200 mg/kg.
Enterocin AS-48 Cebrián et al. (2019)	Human-cell and blood assays; mouse skin sensitization; zebrafish embryos	In vitro concentrations up to 27 µM; topical sensitization	Low haemolysis/cytotoxicity at proposed antimicrobial concentrations and

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		doses 1, 10, 20 µg/5 µL	little pro-inflammatory activity; zebrafish embryos were more sensitive.
P34 preparation (Vaucher et al., 2011)	BALB/c mice; acute oral and 21-day repeated exposure; nisin comparator	Acute 82.5–330 mg/kg; repeated 0.825 mg/kg/day	No mortality; estimated LD50 above the highest tested dose; limited serum changes, with histological findings reported.
TSU4 Sahoo et al. (2017)	Male BALB/c mice; immunogenicity, acute oral and 21-day repeated exposure	Acute 50, 100, 200 mg/kg; repeated 0.5 mg/kg/day	No mortality and no major serum-biochemical or histological abnormalities; LD50 reported above 200 mg/kg.
Pediocin N6 powder Ketaren et al. (2016)	Male Swiss mice; n=5/dose; single-dose study with 15-day observation	5,000, 10,000, 15,000, or 20,000 mg powder/kg	No deaths; LD50 could not be calculated and was inferred to exceed 20,000 mg powder/kg.

Table 3 reconstructs representative primary toxicology evidence. Acute LD50 limits, repeated-dose NOAELs, and absence of observed mortality answer different questions and are not interchangeable. Nominal doses of commercial preparations also must not be reported as active-peptide doses. For example, Hagiwara et al. (2010) tested a commercial nisin preparation containing approximately 7.5% active nisin A; the highest preparation intake was about 3,000 mg/kg body weight/day, corresponding to approximately 225–239 mg active nisin A/kg body weight/day.That repeated-dose NOAEL is not an LD50 and does not define safety for parenteral nisin.

8. Regulatory Status and Commercial Translation

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Regulation follows the product, jurisdiction, intended use, dose, and route—not the general word bacteriocin. In the United States, 21 CFR §184.1538 addresses a defined nisin preparation for specified food uses and manufacturing conditions (U.S. Food and Drug Administration, 2026). This is a food-ingredient provision, not approval of nisin as a drug or of every bacteriocin-producing organism. The European Food Safety Authority likewise evaluated nisin (E 234) for food-additive exposure rather than therapeutic use (EFSA Panel on Food Additives and Nutrient Sources Added to Food, 2017). The Joint FAO/WHO Expert Committee on Food Additives evaluation applies specifically to nisin A and reports an acceptable daily intake of 0–2 mg/kg body weight expressed as nisin A (JECFA, 2024). That value should not be transferred to pediocin, plantaricin, AS-48, a crude supernatant, or a parenteral product.

Regulatory submissions for a purified molecule generally require structural identity, purity and impurity profiles, validated potency, manufacturing controls, stability, exposure, and indication-specific safety and efficacy. A complex inactivated-cell preparation requires strain-level identity, absence of viable cells, inactivation validation, composition, batch consistency, and evidence for the claimed health benefit. A live producer introduces additional questions of viability, genetic stability, antimicrobial-resistance genes, environmental release, and in situ production. These paths may fall under food additive, feed additive, novel food, dietary supplement, veterinary medicinal product, drug, or biologic frameworks depending on jurisdiction and claim.

Commercial food use of nisin therefore demonstrates that a bacteriocin can be manufactured, standardized, and regulated for a circumscribed purpose. It does not validate “bacteriocins as therapeutic proteins” as a class. As of the search date, the peer-reviewed landscape remains dominated by in vitro and animal studies, and no bacteriocin discussed here is established as an approved systemic antibacterial therapy for humans (Sugrue et al., 2024).

9. Production, Standardization, and Research Priorities

Translation is most likely when discovery and product design are linked from the outset. High titre alone is insufficient if a peptide is unstable, adsorbs to biomass, is costly to purify, or loses activity in the target matrix. Fermentation optimization should report producer strain, medium, pH, temperature, aeration, induction, growth phase, volumetric activity, peptide concentration, and recovery yield. Downstream processing should distinguish crude activity units from mass of active peptide and document residual solvents, media components, endotoxin where relevant, and congeners.

For inactivated-cell preparations, standardization must extend beyond the bacteriocin. Thermal, pressure, irradiation, or chemical inactivation can change cell-wall architecture, release intracellular material, degrade peptides, and alter immunological activity. Viability should be assessed with methods capable of detecting injured survivors, and the retained biomass and metabolite profile should be quantified. Batch release criteria should connect chemical identity to a validated biological assay.

Six priorities would make the field more reproducible and clinically credible:

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- Use evidence-linked terminology: state whether the test article is a purified molecule, cell-free product, inactivated-cell preparation, or live producer, and reserve "postbiotic" for preparations meeting the consensus definition and benefit criterion.
- Establish causality in mixtures using targeted quantification, activity-guided fractionation, immunoneutralization, bacteriocin-null mutants, selective depletion, and add-back controls.
- Report concentration in interpretable units, including molar or mass dose of active peptide, purity, activity-unit definition, formulation, route, and recovered activity at the target site.
- Use target-matrix and target-population models: food challenge tests, polymicrobial biofilms, relevant animal disease models, and adequately powered human trials with pre-specified endpoints.
- Build resistance and microbiome endpoints into efficacy studies rather than treating them as afterthoughts; include recovery after exposure and cross-resistance testing.
- Develop route-specific safety and pharmacokinetic packages and avoid extrapolating food authorization or acute oral tolerability to chronic or invasive therapeutic use.

A minimum evidence package for a bacteriocin-containing postbiotic should therefore include: confirmed strain identity; validated inactivation and absence of viable cells; quantitative biomass and composition; bacteriocin identity, concentration and stability; a demonstrated health benefit of the complete preparation; and bacteriocin-specific controls if the molecule is claimed as the active principle. This package would allow reviewers and regulators to distinguish a credible mechanism from attractive but untested labelling.

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Conclusion

Bacteriocins are a diverse antimicrobial class with a strong food-biopreservation precedent and important mechanistic and preclinical potential. Their value is diminished, not enhanced, when purified bacteriocins, cell-free fermentation products, inactivated-cell preparations, and live producer strains are collapsed into the single term postbiotic. Under the current consensus definition, a purified bacteriocin is not itself a postbiotic, and a cell-free product is not automatically one.

The strongest evidence supports defined mechanisms, selected food applications, and molecule-specific oral or local preclinical studies. Human therapeutic evidence remains limited, and complex-product studies usually cannot assign host benefits to bacteriocins without analytical and causal controls. Resistance can emerge; microbiomes can be altered; and safety depends on the molecule, formulation, dose, route, duration, and population. Nisin A's food regulatory status is an important precedent but cannot be generalized to other bacteriocins or therapeutic indications.

Future progress depends on precise preparation identity, quantitative reporting, target-matrix validation, resistance surveillance, route-specific toxicology, and controlled clinical evaluation. With those standards, bacteriocins may become useful components of postbiotic preparations or independent antimicrobial products—two related but scientifically and regulatorily distinct development paths.

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