WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 14, Issue 21, 1331-1343. Review Article ISSN 2277–7105

NATURAL ANTIMICROBIAL COMPOUNDS PRODUCED BY FOOD-GRADE MICROBES: A MINI REVIEW ON FUNCTIONAL ROLES AND APPLICATIONS

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Article Received on 07 Oct. 2025,
Article Revised on 27 Oct. 2025,
Article Published on 01 Nov. 2025,

https://doi.org/10.5281/zenodo.17539631

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How to cite this Article: Kusuma, S.A.F. (2025).. Natural Antimicrobial Compounds Produced By Food-Grade Microbes: A Mini Review on Functional Roles And Applications. World Journal of Pharmaceutical Research, 14(21), 1331–1343.

ABSTRACT

Food-grade microorganisms, particularly lactic acid bacteria, Bacillus spp., and certain yeasts, are increasingly recognized as sources of natural antimicrobial compounds that enhance food safety and quality. These microorganisms synthesize diverse bioactive metabolites—including bacteriocins, organic acids, hydrogen peroxide, and biosurfactants—that inhibit foodborne pathogens and extend product shelf life. In recent years, natural antimicrobials from microbial origin have gained attention as sustainable alternatives to synthetic preservatives and antibiotics. Their mechanisms of action involve membrane disruption, cytoplasmic acidification, and oxidative stress induction in target microbes. This review highlights key types of antimicrobial compounds produced by food-grade microbes, their molecular mechanisms, and their practical applications in food preservation and functional food development. Understanding these metabolites provides a foundation for developing eco-friendly biopreservation strategies and supports the global transition toward safer and more natural antimicrobial approaches.

KEYWORDS: Food-grade microorganisms; natural antimicrobials; bacteriocins; lactic acid bacteria; Bacillus; biosurfactants; food preservation; functional foods; bioactive metabolites.

1. INTRODUCTION

Food safety and preservation remain critical challenges in modern food industries, especially as global consumers increasingly demand natural and minimally processed products. The overuse of synthetic preservatives and antibiotics has raised major health concerns, including allergic reactions, carcinogenicity, and the emergence of multidrug-resistant pathogens (O'Sullivan et al., 2020). Consequently, researchers have directed significant attention toward natural antimicrobial alternatives derived from microorganisms that are generally recognized as safe (GRAS). Among these, food-grade microbes such as *Lactobacillus*, *Bacillus*, and certain *Saccharomyces* species represent promising candidates for sustainable biopreservation (Mokoena, 2017).

These microorganisms naturally produce bioactive metabolites—including bacteriocins, organic acids, hydrogen peroxide, and biosurfactants—that inhibit spoilage organisms and foodborne pathogens (Deegan et al., 2006). Unlike synthetic preservatives, these compounds are biodegradable, non-toxic, and compatible with the natural microbiota of food systems. Moreover, the diversity of their antimicrobial mechanisms—ranging from membrane disruption and cytoplasmic acidification to oxidative stress induction—makes them highly effective even at low concentrations (Cotter et al., 2013).

Lactic acid bacteria (LAB) are the most extensively studied producers of bacteriocins and organic acids. Species such as *Lactococcus lactis* and *Lactobacillus plantarum* synthesize nisin and plantaricin, peptides that form pores in bacterial membranes and inhibit Gram-positive bacteria (Papagianni, 2012). Similarly, *Bacillus subtilis* produces lipopeptides such as surfactin, iturin, and fengycin, which show potent activity against bacteria and fungi (Mnif & Ghribi, 2015). Yeasts like *Saccharomyces cerevisiae* also contribute to microbial balance by secreting killer toxins and volatile organic compounds that suppress spoilage yeasts and molds (Passoth et al., 2011).

The application of these natural antimicrobials extends beyond preservation. In functional food development, metabolites from food-grade microbes can enhance gut health, modulate immunity, and prevent intestinal infections (O'Toole & Cooney, 2008). As research advances, their industrial application is expanding into dairy, meat, and beverage sectors where consumer preference strongly favors clean-label formulations. Nonetheless, challenges remain in optimizing large-scale production, improving compound stability, and meeting regulatory standards for safety and labeling (Abee & Kuipers, 2011).

This mini review summarizes recent advances in the discovery and application of antimicrobial compounds produced by food-grade microorganisms. It highlights key metabolite classes, their mechanisms of action, and their current and potential uses in food preservation and health promotion. By compiling current insights, this review aims to support the shift toward safe, sustainable, and naturally derived antimicrobials that meet the dual demands of efficacy and consumer acceptance.

2. CLASSES OF NATURAL ANTIMICROBIAL COMPOUNDS

Food-grade microorganisms produce several types of antimicrobial metabolites with distinct chemical natures and biological roles. the major classes include bacteriocins, organic acids, hydrogen peroxide and volatile metabolites, biosurfactants/lipopeptides, and aldehydes such as reuterin. These compounds not only ensure food safety by inhibiting pathogens but also contribute to sensory and nutritional properties of fermented foods.

2.1 Bacteriocins

Bacteriocins are ribosomally synthesized antimicrobial peptides secreted mainly by lactic acid bacteria (lab). They act by forming pores in the cytoplasmic membrane of target bacteria, causing ion leakage and cell death. Nisin from *Lactococcus lactis* is the most characterized example, approved by the fao/who for use as a food preservative. other notable bacteriocins include pediocin pa-1, plantaricin, and enterocin, effective against *Listeria monocytogenes* and *Staphylococcus aureus* (cotter et al., 2013). Their stability at low ph and moderate heat makes them ideal for dairy and meat preservation.

2.2 Organic Acids

LAB produce lactic, acetic, and propionic acids during carbohydrate fermentation. These acids lower the environmental pH, inhibit enzymatic activity, and disrupt membrane potential of spoilage bacteria. Lactic acid also enhances flavor and texture in fermented foods. Combined with bacteriocins, organic acids exert a synergistic inhibitory effect (Papagianni, 2012).

2.3 Hydrogen Peroxide and Volatile Compounds

Hydrogen peroxide (H_2O_2) is a by-product of flavoprotein oxidases in aerobic LAB. It causes oxidative stress and damages cell membranes, DNA, and proteins in competing microbes. LAB also generate volatile antimicrobials like diacetyl and acetoin, which inhibit Gram-negative bacteria (Parente & Ricciardi, 1999).

2.4 Biosurfactants and Lipopeptides (Bacillus spp.)

Species of *Bacillus* secrete amphiphilic lipopeptides—surfactin, iturin, and fengycin—that disrupt microbial membranes and inhibit fungal spore germination. These biosurfactants reduce surface tension, facilitate biofilm removal, and show potential as eco-friendly food sanitizers (Mnif & Ghribi, 2015; Antonioli Júnior et al., 2023).

2.5 Reuterin and Other Secondary Metabolites

Lactobacillus reuteri produces reuterin (3-hydroxypropionaldehyde) from glycerol via glycerol dehydratase. Reuterin exhibits broad-spectrum activity against bacteria, yeasts, and protozoa by interfering with thiol-dependent enzymes (Cleusix et al., 2007). It is considered one of the most versatile antimicrobial aldehydes of microbial origin.

3. MECHANISMS OF ANTIMICROBIAL ACTION

Natural antimicrobial compounds produced by food-grade microorganisms exhibit multiple mechanisms of action that collectively inhibit or kill pathogenic and spoilage microbes. Their activity is not limited to a single cellular target but involves a combination of physical, chemical, and biochemical disruptions, including membrane permeabilization, enzyme inhibition, intracellular acidification, and oxidative stress induction. Each compound class displays unique molecular mechanisms that reflect its structure and biosynthetic origin. Representative antimicrobial metabolites produced by lactic acid bacteria, *Bacillus* species, and yeasts are summarized in Table 1, highlighting their molecular mechanisms and industrial applications in food preservation and probiotic development.

3.1 Bacteriocins

Bacteriocins are ribosomally synthesized antimicrobial peptides that mainly target Gram-positive bacteria by disrupting the integrity of the cytoplasmic membrane. The most extensively studied bacteriocin, nisin, interacts with the cell wall precursor lipid II, forming transmembrane pores that cause potassium ion efflux and depletion of the proton motive force (Cotter et al., 2013). This dual action — inhibition of cell wall synthesis and pore formation — results in rapid cell death.

In contrast, class II bacteriocins such as pediocin PA-1 and plantaricin act without extensive post-translational modification. They form voltage-dependent pores that alter membrane potential and lead to leakage of essential ions and metabolites (Simons et al., 2020). These bacteriocins are highly specific, thermostable, and active at acidic pH, making them particularly useful for the preservation of dairy and meat products. In mixed microbial systems, their selective inhibition of pathogens also supports the dominance of beneficial starter cultures.

3.2 Organic Acids

Lactic, acetic, and propionic acids produced by lactic acid bacteria play crucial roles in maintaining the safety and stability of fermented foods. Their antimicrobial activity arises primarily from their ability to penetrate microbial cell membranes in their undissociated form (HA). Once inside the cytoplasm, the acids dissociate into protons (H^+) and conjugate bases (A^-), resulting in a significant drop in intracellular pH (Papagianni, 2012).

This acidification disrupts enzyme activities, impairs nutrient transport, and causes accumulation of toxic anions, eventually leading to cell death. Additionally, organic acids contribute to flavor development and enhance bacteriocin activity through synergistic pH effects, where lower pH values favor bacteriocin stability and diffusion.

3.3 Hydrogen Peroxide and Volatile Compounds

Hydrogen peroxide (H_2O_2) is another major antimicrobial metabolite generated by lactic acid bacteria under aerobic or microaerophilic conditions. Produced by flavoprotein oxidases during carbohydrate metabolism, H_2O_2 acts as an oxidizing agent that generates hydroxyl radicals, damaging lipids, nucleic acids, and proteins of target microorganisms (Parente & Ricciardi, 1999). The oxidative stress induced by these radicals leads to irreversible cellular damage.

In addition, volatile metabolites such as diacetyl and acetoin interfere with sulfhydryl (–SH) groups of bacterial enzymes, causing enzyme inactivation and metabolic arrest. These volatiles are especially effective against Gram-negative bacteria, which are less sensitive to bacteriocins, thus expanding the antimicrobial spectrum of lactic acid bacteria.

3.4 Biosurfactants and Lipopeptides

Members of the *Bacillus* genus produce amphiphilic molecules known as lipopeptides — primarily surfactin, iturin, and fengycin — which exhibit strong antibacterial and antifungal properties. These biosurfactants insert into microbial membranes and alter lipid packing, leading to membrane thinning, increased permeability, and subsequent leakage of intracellular contents (Mnif & Ghribi, 2015).

Surfactin, one of the most potent natural biosurfactants, reduces surface tension to as low as 27 mN/m and disrupts biofilms by interfering with cell adhesion processes (Antonioli Júnior et al., 2023). Iturin and fengycin, on the other hand, specifically inhibit fungal growth by binding to sterols in the fungal membrane, causing cytoplasmic leakage and mitochondrial dysfunction. The ability of lipopeptides to inhibit both bacteria and fungi makes them highly valuable in food sanitation and preservation applications.

3.5 Reuterin

Reuterin, a multifunctional aldehyde (3-hydroxypropionaldehyde) produced by *Lactobacillus reuteri* during glycerol fermentation, exerts a broad spectrum of antimicrobial activity against bacteria, yeasts, and protozoa. Its mechanism is based on the reactivity of the aldehyde group, which forms covalent adducts with free thiol groups of cysteine residues in enzymes, leading to irreversible inhibition of essential metabolic processes (Cleusix et al., 2007).

This thiol-reactive nature results in oxidative imbalance within the cell and the accumulation of reactive oxygen species (ROS). Reuterin is unique because of its stability across a wide pH range and its reversible equilibrium with acrolein, which enhances its antimicrobial potency. Its compatibility with probiotic strains also makes it a promising compound for inclusion in functional foods targeting gastrointestinal pathogens.

Collectively, these mechanisms reveal that natural antimicrobials from food-grade microbes act through multifaceted pathways that combine physical disruption and biochemical inhibition. Their synergistic interactions—such as the combined effect of bacteriocins and organic acids—can significantly enhance antimicrobial efficiency without relying on synthetic preservatives. Understanding these molecular actions is critical for designing next-generation biopreservation systems that are both safe and sustainable for global food industries.

Table 1: Major classes of antimicrobial compounds synthesized by food-grade microorganisms and their mechanisms of antimicrobial activity.

Compound Class	Producing Microorganism	Representative Compound	Mechanism of Action	Primary Target Microorganisms	Main Applications	Ref
Bacteriocins	*Lactococcus lactis*	Nisin A/Z	Binds to lipid II → pore formation & inhibition of peptidoglycan synthesis	*Listeria monocytogenes*, *Clostridium botulinum*	Processed cheese, canned food	Cotter et al., 2013
	Lactobacillus plantarum	Plantaricin EF	Disrupts membrane potential; induces potassium leakage	*S. aureus*, *L. monocytogenes*	Fermented vegetables, meat	Simons et al., 2020
	Pediococcus acidilactici	Pediocin PA-1	Voltage-dependent pore formation via Man-PTS receptor binding	*Listeria*, *Enterococcus*	Sausages, meat preservation	Deegan et al., 2006
	Enterococcus faecium	Enterocin AS-48	Circular peptide; inserts into membrane bilayer forming toroidal pores	*Bacillus cereus*, *Listeria*	Dairy and fish products	Abriouel et al., 2010
Organic Acids	*Lactobacillus casei*	Lactic acid	Passive diffusion → cytoplasmic acidification & enzyme inhibition	Gram-negatives (*E. coli*, *Salmonella*)	Yogurt, kefir	Papagianni, 2012
	Propionibacterium freudenreichii	Propionic acid	Acid stress and anion accumulation → energy depletion	*Pseudomonas*, *Molds*	Cheese ripening	Mokoena, 2017
Hydrogen Peroxide & Volatiles	*Leuconostoc mesenteroides*	H_2O_2	Generates hydroxyl radicals → oxidative damage to DNA and proteins	*Enterobacter*, *E. coli*	Fermented vegetables	Parente & Ricciardi, 1999
	Lactobacillus delbrueckii	Diacetyl	Reacts with –SH groups on bacterial enzymes → enzyme inactivation	*S. aureus*, *Candida*	Yogurt, butter flavor fermentation	De Vuyst & Leroy, 2020
Biosurfactants / Lipopeptides	*Bacillus subtilis*	Surfactin	Amphiphilic insertion → membrane disruption and biofilm inhibition	*Listeria*, *Candida albicans*	Bakery, fruit coating	Ali et al., 2022
	B.	Iturin A/C	Binds fungal sterols → increases	*Aspergillus*,	Bakery, soy	Antonioli

	amyloliquefaciens		permeability and causes leakage	*Penicillium*	fermentation	Júnior et al., 2023
	B. velezensis	Fengycin	Inhibits phospholipid bilayer synthesis and mitochondrial respiration	*Fusarium, Aspergillus*	Fruit and grain protection	Dias & Nitschke, 2023
Reuterin (Aldehyde)	*Lactobacillus reuteri*	3-Hydroxypropionaldehyde (Reuterin)	Thiol oxidation → enzyme inactivation, ROS accumulation	*E. coli, Candida, H. pylori*	Functional foods, probiotics	Cleusix et al., 2007
Other Secondary Metabolites	*Saccharomyces cerevisiae*	Killer toxin (K1)	Forms ion channels in yeast membranes → K^+ efflux & apoptosis	*Candida, Rhodotorula*	Wine, fermented beverages	Grande Burgos et al., 2014
	Propionibacterium freudenreichii	CO_2 and formic acid	Depletion of oxygen tension; inhibition of aerobic spoilage bacteria	*Pseudomonas, Bacillus*	Cheese maturation	Johansen & Jespersen, 2019

4. APPLICATIONS AND FUTURE PROSPECTS

The growing consumer preference for clean-label and preservative-free products has accelerated the use of natural antimicrobial compounds derived from food-grade microbes in food systems. These bioactive metabolites—such as bacteriocins, organic acids, reuterin, and biosurfactants—provide an eco-friendly alternative to chemical preservatives. Their applications extend from traditional food preservation to the development of functional foods, probiotic formulations, and active packaging materials.

4.1 Food Preservation and Biopreservation

Bacteriocins, particularly nisin and pediocin, are among the most widely applied natural preservatives in dairy, meat, and fish products. Nisin is commercially approved in over 50 countries as a natural food preservative (E234) due to its effectiveness against *Listeria monocytogenes*, *Clostridium botulinum*, and *Staphylococcus aureus* (Cotter et al., 2013). It is used in pasteurized milk, processed cheese, and canned foods to inhibit spore germination and post-processing contamination. Pediocin PA-1, produced by *Pediococcus acidilactici*, is commonly applied in fermented sausages and ready-to-eat meats to extend shelf life without altering sensory quality.

Organic acids such as lactic and acetic acids act synergistically with bacteriocins by maintaining acidic environments that favor their stability and diffusion (Papagianni, 2012). In fish and seafood products, the incorporation of *Lactobacillus*-derived reuterin effectively reduces the load of spoilage bacteria while maintaining freshness and texture (Cleusix et al., 2007). Moreover, biosurfactants from *Bacillus subtilis*—notably surfactin and fengycin—are increasingly used to prevent fungal contamination in cereals and bakery goods, as well as to control biofilms in food-contact surfaces (Mnif & Ghribi, 2015).

4.2 Functional Foods and Probiotic Development

Beyond preservation, antimicrobial metabolites play important roles in developing functional foods with health-promoting properties. Probiotic strains capable of producing bacteriocins or reuterin can colonize the intestinal mucosa, competitively exclude pathogens, and modulate immune responses (O'Toole & Cooney, 2008). *Lactobacillus reuteri* strains used in yogurt and infant formula, for example, produce reuterin that suppresses *Escherichia coli* and *Candida albicans* in the gut (Spinler et al., 2017). Similarly, biosurfactants from probiotic *Bacillus* species exhibit antimicrobial, anti-adhesive, and anti-inflammatory effects, contributing to gut and skin health (Antonioli Júnior et al., 2023). These findings have opened opportunities for the design of "next-generation probiotics" with dual functionalities — health modulation and natural pathogen control.

4.3 Industrial and Environmental Applications

The amphiphilic nature of microbial biosurfactants provides diverse industrial and environmental benefits. In food processing plants, surfactin-based formulations are employed as bio-cleaners to remove biofilms and prevent cross-contamination (Ali et al., 2022; Dias & Nitschke, 2023; Gayathiri et al., 2022). Their biodegradability and low toxicity make them safer than synthetic surfactants for cleaning food-contact surfaces.

In packaging technology, antimicrobial peptides and biosurfactants can be incorporated into biopolymer films to create *active packaging* systems that inhibit surface contamination during storage (Ribeiro et al., 2022). Moreover, the combination of natural antimicrobials with nanomaterials—such as chitosan nanoparticles or silver nanocomposites—enhances stability and controlled release, expanding their usability in modern food supply chains.

4.4 Future Prospects

The future of microbial-derived antimicrobials lies in optimizing production efficiency and ensuring regulatory acceptance. Co-culture fermentation and metabolic engineering approaches can enhance metabolite yield while preserving microbial viability. Advanced encapsulation techniques, such as spray-drying and microencapsulation, are being developed to improve compound stability during food processing and storage.

Multi-omics technologies—genomics, proteomics, and metabolomics—offer new insights into biosynthetic pathways and regulation of antimicrobial production (Yang et al., 2022). This knowledge can accelerate strain improvement and enable the design of tailor-made microbial consortia for specific food applications. In addition, integrating predictive modeling and artificial intelligence for fermentation control can ensure consistent product quality at industrial scales.

Ultimately, the application of natural antimicrobials from food-grade microbes represents a sustainable step toward cleaner, safer, and more resilient food systems. Continued interdisciplinary collaboration between microbiologists, food technologists, and bioprocess engineers will be essential to translate these bioactive compounds from laboratory innovation into large-scale industrial reality.

CONCLUSION

Food-grade microorganisms constitute a sustainable and versatile source of natural antimicrobial compounds that can enhance both food safety and human health. These microbes—particularly lactic acid bacteria, Bacillus species, and certain yeasts—produce a wide range of bioactive metabolites such as bacteriocins, organic acids, reuterin, hydrogen peroxide, and biosurfactants. Each compound class exhibits distinct biochemical mechanisms, including pore formation, intracellular acidification, oxidative stress, and disruption of membrane integrity, providing broad and complementary antimicrobial coverage.

The integration of these natural antimicrobials into food systems offers promising alternatives to synthetic preservatives, reducing chemical additives while maintaining product quality and stability. In addition to their preservative functions, many of these metabolites possess probiotic and immunomodulatory properties, positioning them as dual-purpose agents for both food preservation and functional health promotion.

Future research should focus on optimizing production yield through metabolic engineering, improving compound stability via encapsulation technologies, and elucidating synergistic interactions among different microbial metabolites. The continued exploration of molecular mechanisms, strain diversity, and application strategies will accelerate the development of safe, natural, and eco-friendly biopreservation technologies, advancing the global transition toward cleaner and more sustainable food systems.

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