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REVIEW

Microbial-Derived Bioactive Metabolites as Next-Generation Solutions for Sustainable Food Preservation and Safety

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ABSTRACT

The escalating demand for sustainable and health-conscious food preservation strategies has positioned microbial-derived compounds at the forefront of contemporary food science research. These bioactive metabolites encompassing bacteriocins, antibiotics, antifungal agents, organic acids, and bioactive enzymes demonstrate remarkable efficacy in suppressing foodborne pathogenic microorganisms and minimizing spoilage-related losses. Beyond conventional preservation applications, microbial metabolites serve diverse functions across pharmaceutical, agricultural, and biotechnological sectors, including their roles as natural preservatives, therapeutic agents, fermentation catalysts, and biocontrol agents. Recent advances in strain engineering and synthetic biology have expanded the technological capacity to optimize microbial strains for enhanced metabolite yield, improved stability, and industrial-scale feasibility, thereby presenting economically viable alternatives to synthetic chemical preservatives. The scientific community continues to address critical barriers including production efficiency, regulatory harmonization, consumer perception, and the concerning emergence of antimicrobial resistance. This manuscript synthesizes current knowledge on microbial-derived natural products, elucidating their mechanistic pathways in food preservation and outlining future directions for sustainable food safety innovation. The evidence indicates substantial potential for these eco-friendly bioactive compounds to address multifaceted food security challenges while promoting human and environmental health simultaneously.

1 | Introduction

The study of microorganism-food interactions constitutes a critical discipline within food science, examining the complex relationships between microbial communities and food quality, safety, and long-term preservation [1]. Microorganisms encompassing bacteria, fungi, yeasts, viruses, and parasitic organisms represent the most abundant biological entities encountered throughout food systems, exerting profound effects on product characteristics and consumer safety. These microscopic organisms, ranging from millimeters to nanometers in scale, operate below the threshold of unaided human perception, yet wield considerable influence over food systems [2]. Significantly, microbial populations display dichotomous properties: certain strains promote desirable transformation and preservation outcomes, while pathogenic variants induce severe contamination, spoilage phenomena, and associated health risks. Beneficial microorganisms, specifically lactic acid bacteria, *Bacillus* species, and *Lactococcus lactis*, function as biological guardians within food ecosystems, producing antimicrobial compounds, facilitating preservation through acidification, enhancing sensory attributes, and modulating host immune responses [3]. On the contrary, spoilage-associated microorganisms catalyze undesirable

physicochemical transformations, compromising flavor profiles, textural integrity, olfactory characteristics, and visual appearance, thereby rendering products unsuitable for consumption [4].

Food safety encompasses the comprehensive framework of practices and regulatory measures designed to maintain product integrity from production facilities through consumer acquisition. These protective measures incorporate antimicrobial interventions, equipment sterilization protocols, environmental sanitation procedures, and temperature-humidity management systems. A particularly promising approach involves harnessing microbial natural products, bioactive secondary metabolites synthesized by microorganisms as part of their metabolic repertoire to establish superior preservation outcomes. These compounds demonstrate remarkable antimicrobial potency and represent sustainable alternatives to conventional synthetic preservatives [3, 5].

Microbes function as prolific biofactories, synthesizing diverse metabolite classes that extend far beyond their cellular maintenance requirements. Secondary metabolites, distinct from primary metabolites essential for fundamental cellular operations (nucleotides, amino acids, and carbohydrates), represent the specialized compounds that differentiate microbial species functionally. Examples include bacteriocins, ribosomally synthesized peptides with antimicrobial properties, lactic acid, antibiotics derived from fungi, and enzymatic proteins exhibiting substrate-specific catalytic activities [6]. These compounds address multiple societal challenges: reducing disease burden, improving nutritional status, establishing food preservation mechanisms, and enhancing product quality parameters. The practical applications encompassing antibiotics, antifungal pharmaceuticals, protease inhibitors, antiparasitic agents, and immunosuppressive molecules illustrate the therapeutic and industrial significance of microbial metabolism [7].

Modern food systems face unprecedented challenges threatening security and consumer health. Developing and least-developed nations encounter particularly acute pressures related to food safety, with adequate access to microbiologically safe and nutritionally sufficient provisions remaining aspirational rather than guaranteed [8]. Today's food safety crisis reflects a complex mix of health, environmental, and system-level challenges. Food is increasingly exposed to biological, chemical, and radiological contaminants, leading to repeated outbreaks of foodborne illnesses. At the same time, globalized supply chains spread risk across borders and make food origin and traceability more difficult. These challenges are intensified by food fraud, climate-related disruptions to food production, poor sanitation and storage conditions, and substantial food loss and waste. Limited consumer awareness, fragmented regulatory oversight, the growing threat of antimicrobial-resistant pathogens, and gaps in current detection and control technologies further undermine efforts to ensure safe and secure food systems. Puhač Bogadi et al., [9]. Addressing this complex constellation of challenges necessitates integrative approaches incorporating emerging biotechnologies and naturally derived bioactive compounds. This review synthesizes evidence regarding microbial natural products as promising interventions addressing these multifaceted challenges.

2 | Microbial Natural Products: Origins, Classification, and Biological Properties

2.1 | Biosynthetic Sources and Metabolite Diversity

Microbial organisms synthesize bioactive compounds through sophisticated metabolic pathways operating during both primary and secondary growth phases. The remarkable biosynthetic capacity of individual microorganisms permits synthesis of upwards of 50 distinct secondary metabolites concurrently, each demonstrating specific biological activities [10]. The commercially and scientifically most significant metabolites include antibiotic compounds, antifungal agents, immunosuppressive molecules, antiproliferative agents, enzyme inhibitors, and bioprotective compounds. These molecules exhibit diverse chemical architectures and molecular mechanisms, enabling applications spanning pharmaceutical development, agricultural enhancement, and food preservation technologies [11].

Bioactive compounds of microbial origin constitute low-molecular-weight chemical entities derived from bacterial, fungal, and actinomycete species, synthesized during secondary metabolic phases. Within the food preservation domain, these compounds establish safety through antimicrobial mechanisms specifically, suppression of spoilage organisms and pathogenic bacteria through competitive exclusion and direct inhibition, thereby prolonging shelf stability and reducing contamination-associated losses [12]. The physicochemical characteristics distinguishing microbial metabolites diminished molecular weight, diverse structural configurations, pronounced specificity, elevated catalytic efficiency confer superior functionality in industrial applications. Additionally, these compounds demonstrate biological activity at minimal effective concentrations, rendering them economically viable at scale [12, 13].

2.2 | Principal Microbial Producers and Metabolite Classes

2.2.1 | Bacterial Producers

Bacterial species represent particularly valuable sources of natural product diversity due to their metabolic versatility, ability to adapt to diverse growth conditions, and prolific secondary metabolite synthesis [14]. *Lactobacillus* and related lactic acid bacteria occupy central importance in fermentation industries. These organisms generate various bioactive compounds including bacteriocins (antimicrobial peptides), lactic acid (pH-reducing preservative), enzymatic proteins facilitating biochemical transformations, and probiotic preparations modulating intestinal health. Notably, bacteriocin production occurs in certain species and strains, highlighting strain-dependent variability in their antimicrobial potential [15]. Bacteriocins are ribosomally synthesized proteinaceous antimicrobials produced by diverse bacterial genera, including *Lactobacillus* and *Bacillus*, and can suppress pathogenic bacteria such as *Staphylococcus aureus* via multiple mechanisms. Lactic acid produced during bacterial metabolism functions as a natural preservative in diverse industrial contexts. Additional bacterially-derived products including probiotics improve gastrointestinal health outcomes and prevent disease manifestations, while enzymatic

catalysts (such as lactase) facilitate industrial dairy and food transformation processes [14, 15].

2.2.2 | *Fungal and Filamentous Producers*

Fungal organisms represent major industrial sources of bioactive metabolites. Filamentous fungi such as *Aspergillus, Penicillium*, *Trichoderma*, and *Fusarium* produce diverse secondary metabolites, including antibiotics (e.g., penicillin, cephalosporins, echinocandins), mycotoxins, immunosuppressants (cyclosporine), anticancer agents (e.g., paclitaxel from endophytic taxa), and a wide range of hydrolytic enzymes and organic acids with established roles in food production, pharmaceuticals, agriculture, textiles, and medical therapy [16, 17]. *Penicillium* species, historically renowned for Penicillin, also yield numerous agriculturally and pharmaceutically relevant metabolites and can function as plant-growth-promoting and biocontrol fungi through phosphate solubilization, siderophore and organic acid secretion, and antagonism of phytopathogens [18].

2.2.3 | *Yeast and Other Microbial Sources*

Saccharomyces cerevisiae (commonly designated as baker's yeast) maintains widespread industrial utility in food fermentation, including bread leavening and production of fermented beverages. This organism facilitates insulin synthesis through recombinant technology platforms due to its capacity for rapid proliferation, cost efficiency, and adaptation to large-scale fermentation [19]. Yeast metabolism generates carbon dioxide, ethanol, and ancillary compounds utilized in pharmaceutical, biotechnological, and food production sectors. Additional microorganisms like *cyanobacteria*, *actinomycetes*, and *microalgae* synthesize bioactive metabolites and pigments. *Streptomyces* species demonstrate particular significance, producing antiproliferative compounds, immunosuppressive agents, and diverse antibiotic classes (chloramphenicol, tetracyclines, daptomycin) [19, 20]. Figure 1 depicts a pie chart and bar graph showing principal microbial producers (actinomycetes 42%, fungi 42%, eubacteria 16%) and major metabolite classes like antibiotics, pigments, and antitumor agents from bacteria, fungi, and actinomycetes.

2.3 | Metabolite Categories and Functional Classification

Microbial natural products exhibit heterogeneous biological activities and chemical properties, necessitating systematic classification. Major categories encompass bacteriocins, antibiotic compounds, antifungal agents, organic acids, and bioactive enzymes.

2.3.1 | *Bacteriocins*

Bacteriocins constitute ribosomally synthesized antimicrobial peptides, predominantly produced by gram-positive bacteria such as *Lactobacillus*, *Bacillus*, and *Lactococcus* species. These molecules demonstrate potent suppression of pathogenic bacteria, including *S. aureus* and *Escherichia coli*, establishing food preservation effects and preventing spoilage-associated losses. Bacteriocins manifest either narrow or broad antimicrobial spectra, remain nontoxic to eukaryotic cells, resist proteolytic degradation under certain conditions, and maintain stability under elevated temperatures characteristics rendering them advantageous as food preservatives and probiotic formulation components [21].

2.3.2 | *Antibiotics and Antifungal Agents*

Antibiotic compounds, derived from diverse microbial sources, including penicillins, streptomycins, macrolide compounds, and tetracycline classes, demonstrate substantial clinical utility. These secondary metabolites, exemplified by penicillin from *Penicillium* species, exhibit potent activity against gram-positive bacteria responsible for serious infections (pneumonia, meningitis, diphtheria, gonorrhea). Antibiotic molecules display chemical diversity and diminished molecular weight, functioning through bacteriostatic or bactericidal mechanisms in clinical and veterinary medicine [22]. Antifungal compounds, frequently isolated from fungal and actinomycete sources,

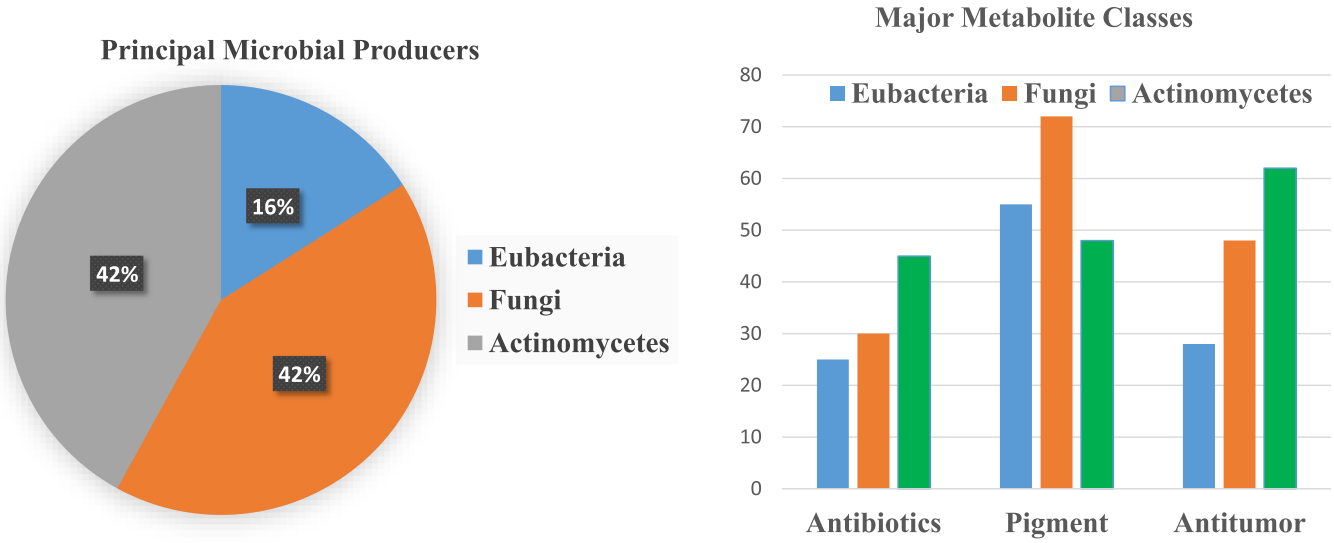

FIGURE 1 | Principal microbial producers and major metabolite classes.

suppress fungal pathogens. Agricultural applications utilize these agents as fungicides, while clinical applications address systemic and superficial mycotic infections. Nystatin exemplifies antifungal efficacy against oral and gastrointestinal *Candida* species infections, while Amphotericin B (derived from *Streptomyces nodosus*) demonstrates superior efficacy in immunocompromised populations (organ transplant recipients, HIV-infected individuals, cancer patients) [23].

2.3.3 | Organic Acids

Organic acid compounds, representing primary metabolites with acidic functional groups, originate during microbial fermentation processes. Bacterial species (*Propionibacterium*, *Lactobacillus*) and fungal organisms (*Aspergillus niger*) synthesize these acids, which function as critical preservation agents and participate in biosynthetic pathways [24].

2.3.4 | Bioactive Enzymes

Bioactive enzymes comprise proteinaceous biological catalysts demonstrating molecular specificity and pronounced capacity to accelerate biochemical reactions. Large-scale fermentation-based synthesis generates industrial quantities supporting textile, leather, food processing, pharmaceutical, diagnostic, biofuel, and detergent manufacturing applications [25].

2.3.5 | Specialized Bioactive Compounds

Additional metabolite categories include antiproliferative agents (mitomycin from *Streptomyces caespitous*, utilized in cancer chemotherapy; Actinomycin D, inhibiting transcriptional processes), toxigenic compounds (aflatoxin from *Aspergillus flavus*), and immunosuppressive molecules (Rapamycin from *Streptomyces hygroscopicus*, preventing organ rejection) [26].

Table 1 presents an overview of major bioactive metabolites derived from microorganisms, highlighting their mechanisms of action, specific food applications, and recommended dosage ranges.

3 | Metabolic Pathways and Genetic Basis of Microbial Natural Product Synthesis

3.1 | Fundamental Metabolic Principles

Microorganisms employ sophisticated metabolic pathways transforming simple precursor molecules into complex bioactive compounds. Anabolic reactions synthesize larger, more structurally complex molecules from simpler precursors, while catabolic reactions dissociate complex molecules into simpler constituents, simultaneously liberating energy. Glucose metabolism exemplifies fundamental catabolic pathways, wherein sequential glycolytic reactions generate pyruvate. Catabolic processes provide carbon skeletons for biosynthetic processes and replenish energy reserves (adenosine triphosphate and related high-energy compounds), sustaining metabolic activities. Anabolic pathways generate cellular constituents' macromolecules essential for cell structure and function [37].

3.2 | Major Biosynthetic Pathways

Polyketide synthase pathways demonstrate particular prevalence in fungal metabolism, with fewer polyketide-producing bacterial species and higher plant sources. These pathways assemble complex molecules from acetyl-Coenzyme A (CoA) and malonyl-CoA units through molecular assembly mechanisms analogous to manufacturing assembly lines [38]. Nonribosomal peptide synthesis generates cyclic compounds (exemplified by cyclosporin, vancomycin) through modular systems initiating and interconnecting amino acid units via mechanisms distinct from classical ribosomal translation. Terpenoid biosynthetic pathways generate terpene compounds (artemisinin precursors, geosmin) derived from isoprenoid building blocks. Shikimate pathways generate aromatic compounds including phenazines, folate precursors, and tryptophan through ribosomal and posttranslational modification processes [39]. Figure 2 categorized microbial metabolites by function: primary (e.g., amino acids, nucleotides via glycolysis, tricarboxylic acid [TCA] cycle) versus secondary (e.g., polyketides, nonribosomal peptides, terpenoids), with examples like bacteriocins for food safety.

3.3 | Genetic Architecture and Gene Regulation

Genetic determinants underlying microbial metabolite synthesis represent subject to mutation and variation, fundamentally affecting biosynthetic capacity and product formation. Genetic information encoding biosynthetic proteins frequently organizes into clustered arrangements incorporating regulatory proteins, operator sequences, and promoter regions governing expression patterns. This sophisticated genetic organization permits coordinated synthesis of pathway components and fine-tuned metabolite production responding to environmental stimuli [40]. Figure 3 shows the metabolic pathways and genetic basis, depicting polyketide synthases, nonribosomal peptide synthetases, and cryptic gene clusters in *Streptomyces*, activated for secondary metabolite production in food preservation contexts.

4 | Mechanistic Pathways: Antimicrobial Actions of Microbial Metabolites

Certain microbial compounds suppress pathogenic organism growth through ribosomial targeting, interfering with protein translation. Streptomycin, derived from *Streptomyces griseus*, exemplifies this mechanism through 30S ribosomal subunit interaction, generating erroneous mRNA reading and consequent translational dysfunction [41]. Microbial metabolites targeting bacterial cell wall components (peptidoglycan layers) induce structural compromise, cellular lysis, and death. This mechanism distinguishes gram-positive from gram-negative organisms based on differential cell wall composition [42]. Compounds suppressing ribonucleic and deoxyribonucleic acid synthesis impede replication and transcriptional processes. Actinomycin D exemplifies this pathway through DNA interaction and RNA synthesis prevention. Certain metabolites destabilize cell membranes, precipitating cell death through apoptotic mechanisms. Amphotericin B exemplifies this action through ergosterol interaction within fungal membranes [43].

TABLE 1 | Bioactive metabolites from microorganisms: Mechanisms of action, food applications, and recommended dosages.

Metabolite	Producing microorganism(s)	Mechanism of action	Primary food applications	Target pathogens/ Spoilage organisms	Recommended Dosage/Concentration	Regulatory Status
Nisin (Bacteriocin)	*Lactococcus lactis subsp. lactis*	Targets cell membrane through pore formation; inhibits cell wall synthesis (peptidoglycan); ribosomally synthesized and degradable by gastric proteases	Processed cheese, heat-treated meat products, dairy products, and muscle foods	*Listeria monocytogenes, Staphylococcus aureus, Clostridium botulinum, Bacillus cereus*	12–25 mg/kg (cheese); 25 mg/kg (meat); ADI: 1 mg nisin A/kg body weight/day	EFSA E234; FDA GRAS; Codex approved [27].
Pediocin (Bacteriocin)	*Pediococcus acidilactici, Pediococcus pentosaceus*	Targets bacterial cell membrane; bactericidal through membrane depolarization; stable across wide pH range (2.0–7.0) and resistant to heat/freezing	Cottage cheese, cream, cheese sauce, fresh meat, fermented meat products, dairy spreads	*Listeria monocytogenes, Clostridium perfringens, Clostridium botulinum, Staphylococcus aureus*	1350 AU/mL; 10^2–10^3 CFU/mL initial contamination (most effective); commercial formulation ALTA® 2341	Commercial use approved [28].
Reuterin	*Lactobacillus reuteri*	Antimicrobial through metabolite toxicity; active against gram-positive and gram-negative bacteria, fungi, yeasts, and protozoa	Fermented dairy products, probiotic formulations	*Escherichia coli, Listeria monocytogenes, Yersinia enterocolitica, Campylobacter jejuni*	Strain-dependent; 10^7–10^8 CFU/mL inoculation levels	GRAS status in probiotic context [29]
Lactic Acid	*Lactobacillus, Propionibacterium, Lactococcus* species	pH reduction (acidification) inhibits pathogenic metabolism; suppresses *Salmonella*, *Listeria*, and *Clostridium* species through low-pH environment	All fermented foods (yogurt, cheese, kimchi, sauerkraut, fermented vegetables, bread), beverages	*Salmonella* spp., *Listeria monocytogenes, Clostridium* spp., general gram-positive pathogens	0.5%–2.0% (typically achieved through fermentation over 24–48 h); pH target: < 4.5	Generally recognized as safe; approved additive E270 (EU) [30].
Citric Acid	*Aspergillus niger, Yarrowia lipolytica*	pH reduction (acidification); chelation of metal ions; antioxidant activity preventing lipid oxidation	Beverages, pickled products, dairy products, canned foods, fruit products	General pathogen suppression through acidification; anti-spoilage	50–150 g/L (fermentation substrate); final product: 0.2%–1.5% (w/v)	FDA GRAS; Codex approved; EU E330 [31]
Amylase	*Bacillus subtilis, Aspergillus niger, Rhizopus* species	Enzymatic degradation (hydrolysis) of starch molecules into simpler carbohydrate units (glucose, maltose)	Bread manufacturing, brewing, starch processing, industrial fermentation	Prevents starch retrograde degradation; enhances texture and flavor	Bread: 0.5%–2.0% of flour weight; brewing applications: 10–100 U/mL	GRAS status [32]

(Continues)

TABLE 1 | (Continued)

Metabolite	Producing microorganism(s)	Mechanism of action	Primary food applications	Target pathogens/ Spoilage organisms	Recommended Dosage/Concentration	Regulatory Status
Protease	*Bacillus, Aspergillus, Trichoderma* species	Enzymatic proteolysis of food proteins; improves digestibility; degrades surface proteins on pathogenic bacteria	Cheese ripening, meat processing, protein hydrolysates, dairy products	Supportive antimicrobial through protein degradation	Cheese: 1–10 units/mL; meat processing: 0.1%–1.0% (w/w)	GRAS; widely approved in food industry [33]
Penicillin	*Penicillium chrysogenum* (industrial strains)	Beta-lactam antibiotic targeting cell wall peptidoglycan; bactericidal	Pharmaceutical and veterinary applications; historically FDA-approved for food animal treatment	Gram-positive bacteria (e.g., *Staphylococcus, Streptococcus*); restricted in direct food use	300,000–600,000 units/ dose (human); veterinary: strain-specific	Restricted in food (FDA ban on growth promotion in food animals 2023) [34, 35].
Geosmin	*Actinomycetes, Cyanobacteria*	Flavor/aroma compound; potential antimicrobial through biofilm disruption (secondary effect)	Fermented foods, beverages for aroma profiles	General antimicrobial potential (limited direct application)	Trace amounts (ppb levels) in fermented products	Generally used for sensory properties [36]

Metabolic inhibitors obstruct essential biochemical pathways. Sulfonamides exemplify this mechanism through folic acid synthesis inhibition. Antimicrobial compounds suppress biofilm formation through multiple mechanisms: inhibiting biofilm development, disrupting extracellular matrix formation, compromising cellular adhesion mechanisms, and degrading established biofilm components [44]. Microbial producers synthesize compounds enabling competitive dominance, resource acquisition, and growth suppression of competing organisms. These compounds establish niche occupancy through ecological displacement mechanisms [45]. Figure 4 depicts the key antimicrobial mechanisms: cell wall disruption (pradimicins binding D-mannosides), membrane permeabilization by bacteriocins, and enzyme inhibition by secondary metabolites like polyketides from *Streptomyces*.

5 | Control Mechanisms: Pathogen and Spoilage Organism Management

5.1 | Contemporary Control Strategies

Food spoilage represents an acute economic and public health challenge negatively affecting national agricultural productivity, generating food scarcity, and damaging institutional reputation. Effective pathogen and spoilage organism control establishes foundational requirements for ensuring safe, adequate, and nutritionally appropriate food availability for global populations. Pathogenic and spoilage microorganisms synthesize deleterious substances degrading food constituents and inducing life-threatening illness [46]. Multiple control methodologies have achieved implementation: sanitation and hygiene optimization, chemical-based preservation (synthetic preservatives, disinfectants, sanitizing agents), physical interventions (dehydration, membrane filtration, radiative treatment), temperature management (thermal pasteurization, cooking, freezing, refrigeration), and biological control approaches utilizing plant-derived antimicrobial compounds (phenolic constituents, flavonoid derivatives, aromatic hydrocarbons, saponins, organic acids) demonstrating efficacy against *E. coli, S. aureus*, and *Listeria monocytogenes* [47].

Microbial-derived antimicrobial compounds represent particularly promising biocontrol agents. Bacteriocins are widely implemented as food preservatives, suppress pathogenic and spoilage bacteria through multiple mechanisms. Representative bacteriocins (nisin, pediocin, helveticin, acidophilin, diplococcin, lactacin) address spoilage and pathogenic bacteria generating foodborne illness across diverse food industry sectors. Bacteriocins (nisin, pediocin) produced by *Pediococcus* species establish regulatory control over *L. monocytogenes* in meat processing applications, preventing spoilage manifestations [48]. Reuterin is an antimicrobial compound synthesized by *Lactobacillus reuteri,* which suppresses both gram-positive and gram-negative bacteria, fungi, yeast, and protozoan organisms. Reuterin demonstrates particular efficacy against *E. coli*, *L. monocytogenes*, *Yersinia enterocolitica*, and *Campylobacter jejuni*. Lactic acid bacteria synthesize lactic acid during fermentation, reducing pH and establishing antimicrobial effects through acidification. This acidification mechanism suppresses Salmonella and related pathogens, preventing foodborne illness and establishing food safety [49].

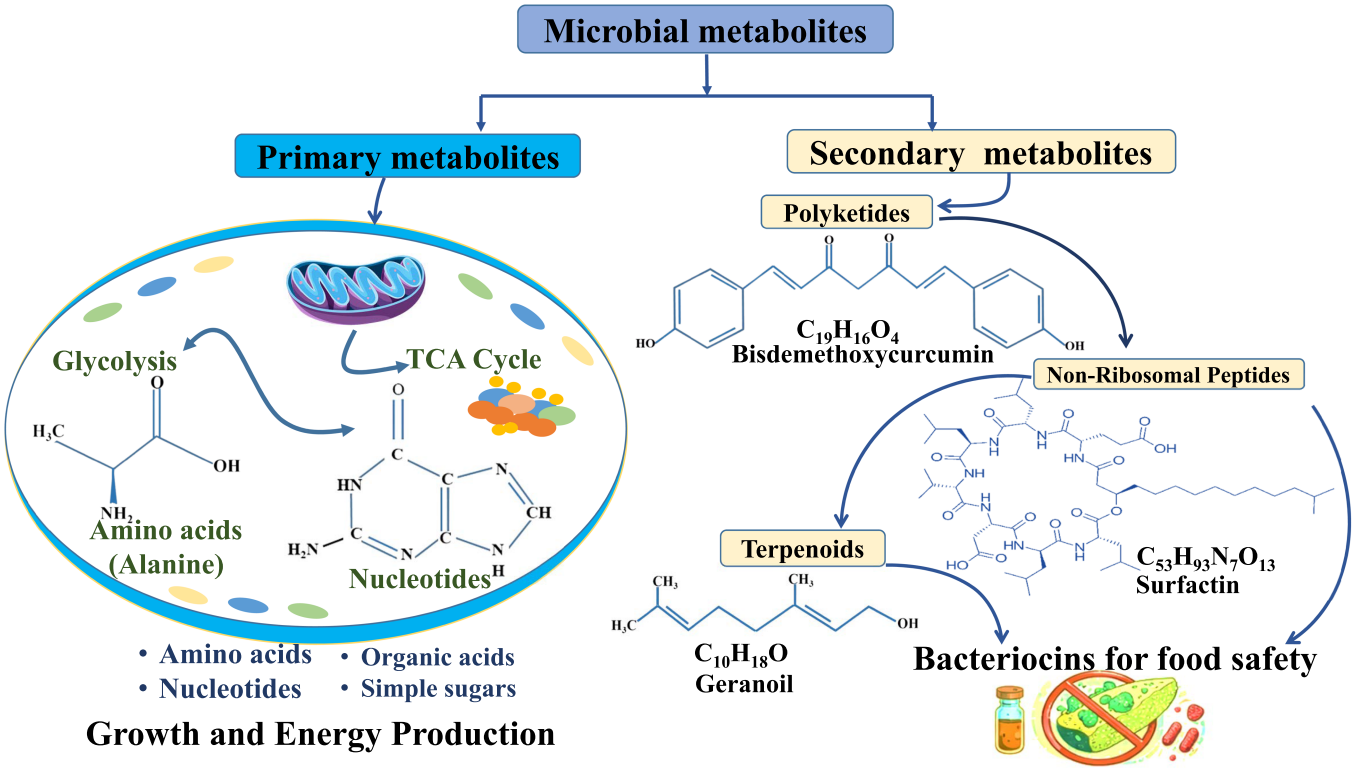

FIGURE 2 | Microbial metabolites flowchart (created in https://freepik.com).

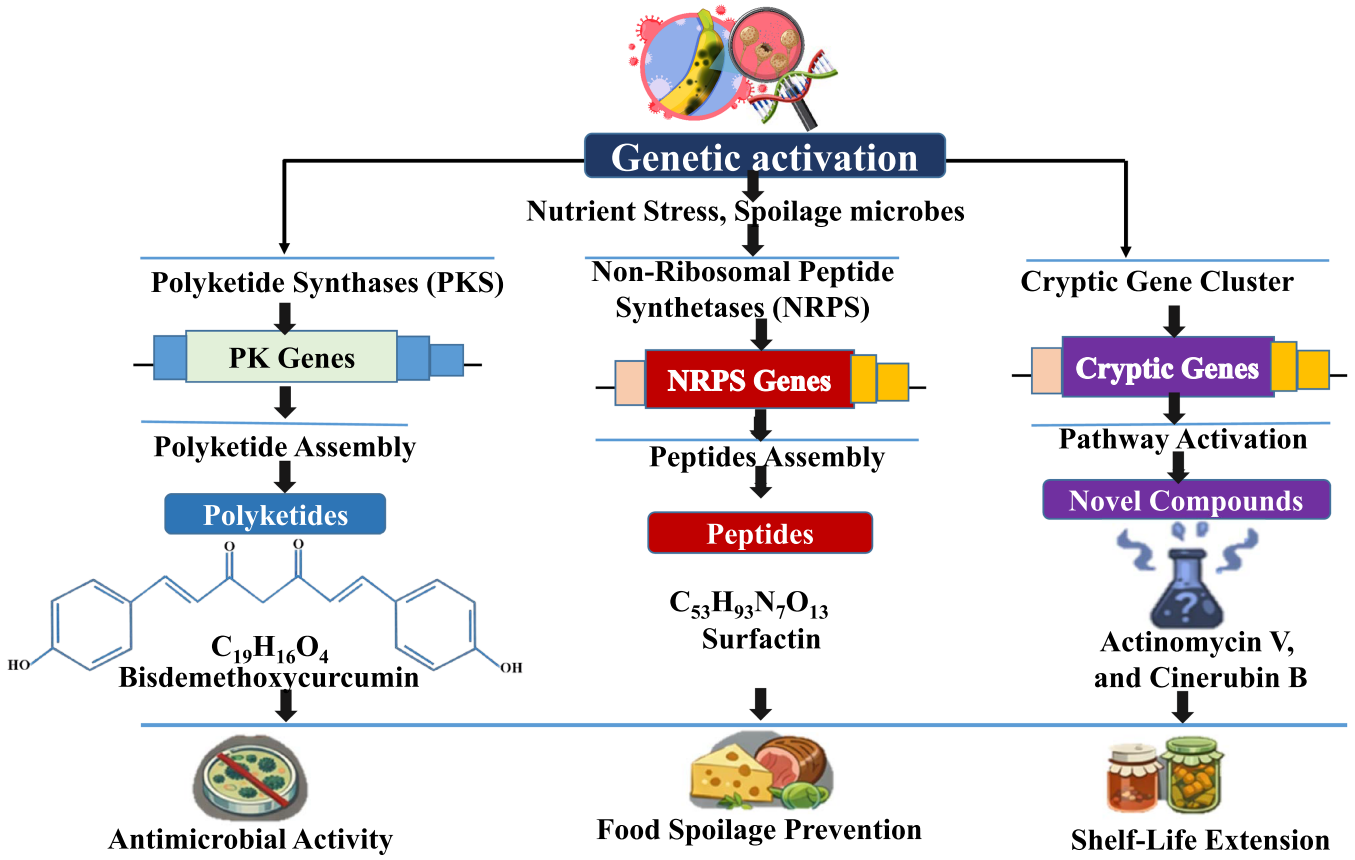

FIGURE 3 | Secondary metabolites in *Streptomyces* sp. for food preservation (created in https://freepik.com).

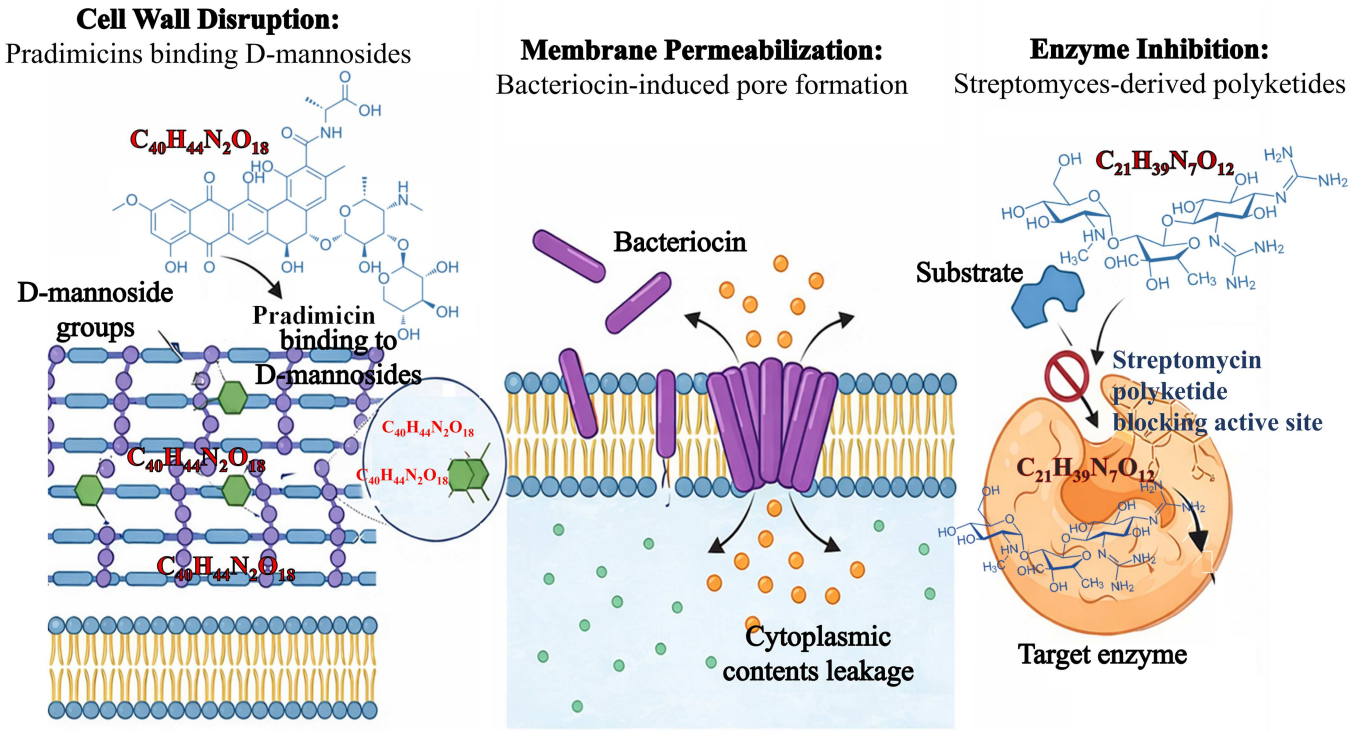

FIGURE 4 | Key antimicrobial mechanisms (created in https://biorender.com).

5.2 | Bio-Preservation Principles and Implementation

Bio-preservation encompasses the application of microbial organisms or their bioactive metabolites to extend food shelf stability through suppression of spoilage microorganisms. Bio-preservative approaches represent sustainable alternatives to chemical preservatives, particularly given mounting evidence regarding potential health concerns associated with long-term synthetic preservative consumption and documented food quality degradation [50]. Fermentation, a fundamentally important bio-preservation strategy, involves microbial-catalyzed degradation of complex organic molecules, generating organic acids, alcoholic compounds, and ancillary substances enhancing aroma and flavor characteristics. Lactic acid bacteria synthesize organic acids during fermentation, establishing conditions inhibiting pathogenic metabolism, suppressing spoilage-associated growth, extending shelf stability, and enhancing safety profiles [51]. Bacteriocins from lactic acid bacteria demonstrate antimicrobial effects against both gram-positive and gram-negative organisms, establishing bio-preservation benefits across food categories. Diverse LAB strains (*L. lactis*, *Pediococcus acidilactici*, *Pediococcus pentosaceus*, *Enterococcus faecalis, Enterococcus faecium, Streptococcus thermophilus*) produce bacteriocins, demonstrating effectiveness against *L. monocytogenes* in meat products, facilitating preservation and extending shelf stability while improving product quality parameters [52]. Figure 5 depicts the principles across food categories, meat (LAB bacteriocins vs. Listeria), dairy (nisin for shelf life), and vegetables (essential oil synergies) with arrows to pathogen inhibition and quality metrics like reduced spoilage.

5.3 | Natural Preservation Applications in Specific Food Categories

Contemporary meat preservation encompasses bio-preservation techniques employing beneficial microorganisms and their antimicrobial metabolites, establishing antagonistic effects against pathogenic and spoilage populations. This approach prioritizes lactic acid bacteria species (*Lactobacillus, Leuconostoc, Pediococcus, Lactococcus*) designated as "Generally Recognized as Safe" (GRAS), actively contributing to fermentation processes and generating diverse antimicrobial compounds (organic acids, hydrogen peroxide, and bacteriocins). Bio-preservation implementation in meat products involves purified bacteriocin application, inoculation with antimicrobial metabolite-producing strains, and direct introduction of lactic acid bacteria suppressing pathogenic and spoilage organisms [53, 54].

Dairy products demonstrate particular susceptibility to microbial spoilage due to favorable growth conditions (nutrient-rich environment including proteins and lipids). Common spoilage organisms (*L. monocytogenes, E. coli*, *S. aureus*, *Pseudomonas* species) substantially reduce dairy product quality and shelf stability. LAB-treated milk for cheese production generates increased exopolysaccharide quantities, enhancing textural properties. LAB produces organic and carbonyl compounds elevating sensory characteristics [53, 55]. Bacteriocins from LAB organisms (Lactococcin BZ, Enterocin KP combinations) inhibit *L. monocytogenes* in full-fat, reduced-fat, and skim milk products. *Lactobacillus plantarum* strains and derived plantaricin compounds demonstrate particular utility in cheese applications due to bacteriostatic capacity, especially under acidic pH conditions. Yogurt bio-preservation utilizing *Lactobacillus pentosus* prevents fungal spoilage manifestations. Bacteriocins,

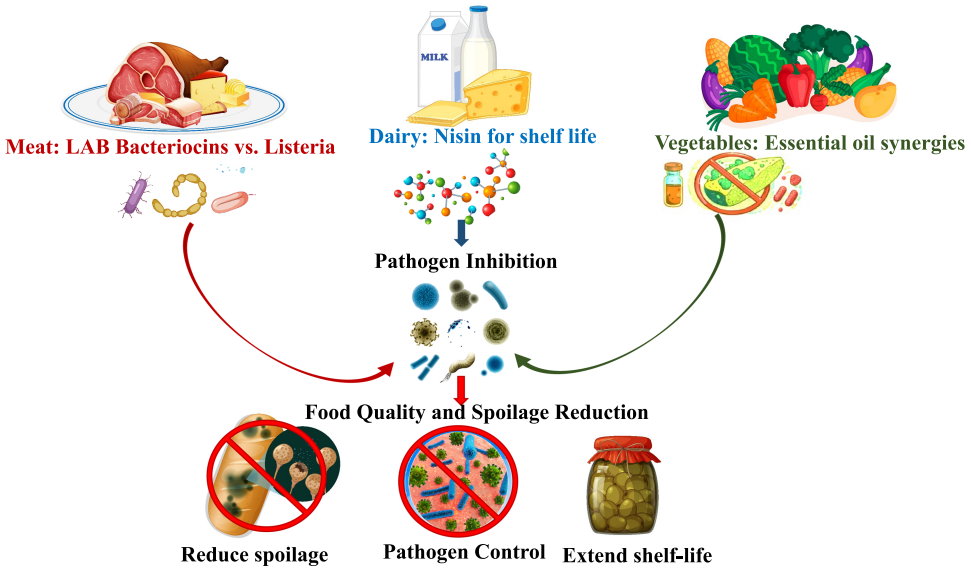

FIGURE 5 | Biopreservation principles across food categories (created in https://freepik.com).

as natural antimicrobial peptides from bacterial sources including lactic acid bacteria establish safety through inhibition of harmful pathogens (*Listeria, Staphylococcus, E. coli*) while maintaining host safety. These compounds extend shelf stability through natural preservation mechanisms [55, 56].

Enzymatic browning, textural degradation, and microbial spoilage represent primary deterioration mechanisms in vegetable and plant-based products. Microbial-derived enzyme inhibitors and antimicrobial compounds address these preservation challenges, while novel delivery systems enhance antimicrobial stability and efficacy in plant-based food matrices [57].

5.4 | Shelf-Life Extension and Quality Maintenance

Bacteriocins function as proteinaceous antimicrobial agents targeting spoilage and pathogenic microbes. These compounds suppress foodborne pathogens (*Clostridium botulinum*, *E. faecalis, L. monocytogenes*) while maintaining safety through proteolytic degradation by host enzymes, establishing biopreservation efficacy [58]. Nisin, produced by *L. lactis*, demonstrates widespread utility in cheese and processed meat production due to its unique amino acid composition (*lanthionine, dehydroalanine*). Nisin application in cheese production inhibits *S. aureus* contamination from raw milk sources. Lactic acid bacteria extend shelf stability of perishable products through dual functions as antimicrobial agents and probiotic supplements. LAB produces diverse antimicrobial substances: hydrogen peroxide, organic acids, bacteriocins, ethanol. Additional LAB-produced compounds (diacetyl, acetaldehyde) contribute antimicrobial effects, although diacetyl applications require limitation due to organoleptic intensity and required effective concentrations [59].

Contemporary consumer preferences emphasize foods promoting general health and wellness beyond minimal nutritional requirements. Functional foods and products delivering health advantages exceeding inherent nutritional contributions have achieved increased prominence. Food nutritional quality and functional benefit enhancement have become essential, particularly addressing public health challenges and improving population health outcomes. Microbial-derived compounds including probiotics and postbiotics function as food supplements, providing nutritional benefits, enhancing gastrointestinal health, modulating immune responses, preventing disease manifestations, and meeting consumer preferences. Representative probiotic organisms (*Lactobacillus species, E. coli*, certain *Saccharomyces* species, *Bifidobacteria* genera) demonstrate potential as health-promoting agents for diverse applications [58, 60]. Table 2 focuses on the application of biopreservation strategies across different food categories.

6 | Industrial Applications and Emerging Challenges

6.1 | Contemporary Industrial Implementation

Diverse microbial strains generate fermented dairy products through enzymatic and fermentative processes. Principal lactic acid bacteria genera, which are *Lactobacillus*, *Leuconostoc*, *Lactococcus*, *Pediococcus*, *Streptococcus*, comprise the foundational microbial communities establishing dairy product characteristics. Microbial fermentation of milk carbohydrates (predominantly lactose) generates lactic acid and related by-products. Protein precipitation through acidification generates textural modification in fermented products compared to unfermented milk. Low pH and elevated acidity suppress pathogenic organism growth and microbiological proliferation. The fermentation process establishes straightforward mechanisms extending milk shelf stability and enhancing safety profiles. Dairy products provide substantial nutritional contributions: vitamin D, calcium, vitamin B12, vitamin A, riboflavin, potassium, phosphorus, and magnesium [53].

Cereal foods incorporate probiotic organisms conferring human health benefits. Representative microorganisms (*Bifidobacterium, Saccharomyces, Streptococcus, Enterococcus, Escherichia, Bacillus* species) facilitate gastrointestinal digestion and enhance intestinal health through microbiota modulation and

TABLE 2 | Biopreservation applications by food category, metabolites, target pathogens, implementation strategies, and documented results.

Food category	Primary bioactive metabolites used	Producing strain(s)	Target pathogens/ Spoilage organisms	Implementation method	Key Results/Efficacy	Storage conditions	Shelf life extension
Meat and Meat Products	Nisin (12–25 mg/kg), Pediocin (1,350 AU/mL), Lactic acid (via LAB fermentation)	*Lactococcus lactis* (nisin), *Pediococcus* spp. (pediocin), *Lactobacillus*, *Pediococcus*, *Enterococcus* (lactic acid)	*Listeria monocytogenes*, *Clostridium botulinum*, *Clostridium perfringens*, *Staphylococcus aureus*	Direct nisin/pediocin addition; LAB inoculation (10^7–10^8 CFU/mL); fermentation co-culture	1–2.5 log CFU/g reduction of *L. monocytogenes* after 28 days at 5°C; pediocin residual activity detected for ≥ 28 days on meat surface; 0.5–2.2 log reduction at 2-min exposure with pediocin.	4°C–5°C refrigeration; aerobic or vacuum packaging	28–45 days (vs. 7–14 days control) [61].
Dairy Products (Cheese)	Nisin (12 mg/kg), Pediocin (10^7 CFU/mL), LAB-derived bacteriocins (Lactococcin BZ, Enterocin KP), Lactic acid	*Lactococcus lactis* (nisin); *Pediococcus* spp.; *Enterococcus faecium*, *Staphylococcus equorum*, *Lactobacillus plantarum*	*Listeria monocytogenes*, *Bacillus cereus*, *Staphylococcus aureus*	Nisin in cheese curd/whey; LAB as adjunct cultures or starter cultures; protective cultures co-inoculation	Nisin: 2 log reduction of *L. monocytogenes* after 7 days at 4°C; Adjunct S. equorum SE3: 7 log unit inhibition of *L. monocytogenes* within 24 h; *E. faecium* KE82: 4–5 log reduction of *L. monocytogenes* after 72 h at 22°C; *B. cereus* reduced to nondetectable levels after 30 days	4°C; vacuum-packaged or controlled atmosphere	30–45 days (vs. 14–21 days control) [21].
Dairy Products (Yogurt)	Lactic acid (0.8–1.2% through fermentation), *Lactobacillus pentosus* (probiotic + antimicrobial), LAB bacteriocins	*Lactobacillus bulgaricus, Streptococcus thermophilus, Lactobacillus pentosus, Lactobacillus acidophilus*	*Candida* spp. (fungal spoilage), *Listeria monocytogenes, Staphylococcus aureus*	Co-fermentation with LAB; L. pentosus inoculation prevents fungal spoilage; LAB-derived bacteriocins	*L. pentosus* prevents fungal spoilage manifestations; pH reduction to 3.8–4.2 suppresses pathogenic growth; lactic acid acts as natural preservative without additives	4°C; sealed container	21–28 days shelf life (vs. 14 days without protective cultures) [62].
Fermented Vegetables	Lactic acid (via LAB fermentation 0.5–1.5%), bacteriocins (from	*Lactobacillus plantarum, Lactobacillus brevis, Lactobacillus*	General gram-positive spoilage bacteria, *Salmonella, Listeria*	LAB inoculation (10^7–10^8 CFU/mL); natural spontaneous fermentation; co-culture with protective strains	2–3 log CFU/mL reduction of spoilage organisms; lactic acid accumulation inhibits gram-negative pathogen	Room temperature (18°C–22°C) for controlled fermentation; final storage at 4°C	30–60 days (room temp fermented products show excellent stability

(Continues)

TABLE 2 | (Continued)

Food category	Primary bioactive metabolites used	Producing strain(s)	Target pathogens/ Spoilage organisms	Implementation method	Key Results/Efficacy	Storage conditions	Shelf life extension
	LAB), hydrogen peroxide	*pentosus, Pediococcus cerevisiae*			growth; fermentation over 48–72 h achieves preservation		at cool storage) [63].
Bread and Cereals	Enzymes (amylase, protease: 0.5–2.0% flour weight), *Saccharomyces cerevisiae* (fermentation CO_2 generation, enzyme production)	*Bacillus subtilis, Aspergillus niger* (amylase); *Saccharomyces cerevisiae*	Mold spoilage (*Aspergillus*, *Penicillium*), *Bacillus* species (rope spoilage)	Enzyme addition during dough preparation; LAB fermentation (natural sourdough using *Lactobacillus plantarum, Lactobacillus brevis*)	Enzymatic supplementation enhances flavor, volume, texture; fermentation with LAB (pH ≤ 3.5) prevents *Bacillus* spore germination and mold growth; lactic acid production inhibits spoilage	Room temperature; reduced water activity (moisture < 35% in finished loaf)	5–7 days (vs. 2–3 days control bread); sourdough extends to 10–14 days without preservatives [64].
Processed Meat Products (Sausages)	Pediocin (10^3–10^4 AU/mL through producer strain inoculation), lactic acid, nitrite (synergistic), spice-derived compounds	*Pediococcus pentosaceus, Lactobacillus plantarum, Pediococcus acidilactici*	*Listeria monocytogenes, Clostridium botulinum*, *Staphylococcus aureus*, spoilage *lactobacilli*	Bacteriocin-producing starter culture inoculation; co-fermentation with protective cultures; direct pediocin addition (purified)	Pediocin-producing strains reduce *L. monocytogenes* by 1–4 log within 48–72 h fermentation; residual antimicrobial activity maintained throughout storage; synergy with reduced nitrite levels	4°C; vacuum or controlled atmosphere packaging	45–60 days (vs. 21–30 days control) [54].
Beverages	Lactic acid (0.3–0.8% from LAB fermentation), organic acids (citric acid: 0.2–1.5%), antimicrobial peptides	*Lactobacillus*, species (kefir, kombucha-associated LAB)	Gram-positive spoilage bacteria, mold (xerophilic species)	Fermentation with LAB (24–48 h); acidification to pH < 4.0; pasteurization combined with LAB	Fermented beverages (kefir, kombucha): LAB + acetic acid bacteria produce bacteriocins and organic acids preventing pathogen growth; pH reduction and residual antimicrobial compounds suppress mold	Refrigeration (4°C) or room temperature for shelf-stable products	14–30 days refrigerated; 3–6 months shelf-stable (pH-dependent) [3].

immune system enhancement. Cereal grains function as fermentable substrates supporting probiotic microorganism proliferation. Critical considerations encompassing cereal grain composition, processing parameters, substrate formulation, starter culture performance, probiotic strain viability during preservation, organoleptic characteristics, and nutritional value influence product efficacy [65]. Additionally, cereals provide nondigestible carbohydrates functioning as prebiotic substrates, selectively stimulating beneficial colonic microorganisms and establishing advantageous physiological effects. Fermented grain-based foods deliver documented health benefits from nutrient-dense composition (carbohydrates, proteins, dietary fiber, vitamins, minerals). Probiotic and lactic acid bacteria fermentation enhances nutritional profiles. Multiple probiotic bacterial genera (*Lactobacillus, Bifidobacterium, Saccharomyces, Leuconostoc, Enterococcus, Pediococcus*) establish utility in nondairy probiotic products, improving nutritional quality [65, 66].

Fermented meat product development requires consideration of intrinsic meat microbiota, salt content, nitrite preservation, reduced water activity, and diminished carbohydrate availability establishing optimal conditions for probiotic bacterial proliferation. Environmental factors influence meat microbial communities, affecting microbial populations from primary sources or secondary contamination-derived origins. Biological preservation is alternatively designated as biological protection, which involves preserving food through microbial organism or metabolite application [67]. Lactic acid bacteria establish substantial promise for biological preservation applications due to consumer safety, growth suppression of competing organisms, and documented safety history. These microorganisms undergo enzymatic degradation via host proteases, with minimal impact on intestinal microbial ecology. LAB development in meat represents "cryptic fermentation" wherein flesh buffering capacity and diminished carbohydrate content restrict LAB-mediated flavor profile modification. Lactic acid bacteria function protectively against spoilage and pathogenic microbes through competitive mechanisms and antimicrobial substance synthesis (bacteriocins, enzymes, organic acids) [3].

Microbial organisms synthesize diverse pigments; scientists endeavor to identify industrially viable options. Green algae, fungi, and bacterial species generate color compounds; representative organisms (*Dunaliella*, *Haematococcus*, *Penicillium*, *Monascus*) have achieved commercial production with industrial pigment applications. Numerous industries, including food, textiles, cosmetics, and pharmaceuticals, depend substantially on colorant substances. Synthetic dye toxicity concerns have stimulated substantial research investigating natural dye alternatives. Microbial-derived pigments represent promising natural color sources [68]. Microbial fermentation products serve as food supplements and additives: antioxidants, flavoring agents, pigments, preservatives, and amino acids. Microorganisms produce substantial proportions of food flavoring compounds, establishing flavors for meat, soybean, milk, vinegar, beer, and fermented vegetables. Consumer preference strongly favors natural food additives derived from microorganisms compared to synthetic chemical alternatives. Multiple microorganisms demonstrate potential as food additive synthesis sources [69].

Microbial enzymes demonstrate remarkable activity and diverse applications. Plant and animal-derived materials undergo gradual replacement through enzymatic applications, achieving widespread industrial utility. Bread mold amylase finds application in bread manufacturing, industrial alcohol synthesis, and brewing. Enzymatic supplementation during bread production facilitates desired product generation through complex starch molecule degradation into simpler carbohydrate units [70]. Enzymatic bread supplementation enhances flavor, volume, and textural characteristics. Bacterial organisms contain abundant metabolically essential enzymes (hydrolases, transferases, oxidative enzymes, isomerases). These enzymes contribute significantly to pathogenic properties across pathogenic bacterial populations. *Clostridium* collagenases represent the historically first-identified and characterized reference enzymes for collagenolytic enzyme comparison [71]. Bacterial collagenase research remains limited; nevertheless, these enzymes demonstrate diverse applications and benefit numerous fields. Amylases achieve large-scale bacterial and fungal production. Hydrolytic bacterial enzymes (*Bacillus subtilis*) and fungal sources (*Rhizopus* species) produce amylases. Fungal amylases separate starch from fruits. Industrial baking and brewing industries have replaced traditional enzyme sources (yeast, barley, wheat) with *Bacillus* and *Aspergillus* amylases. Multiple microorganisms represent viable options for large-scale enzyme synthesis [72].

Certain fungi (*A. flavus*, *Aspergillus parasiticus*) synthesize mycotoxins, toxic and carcinogenic secondary metabolites. Representative mycotoxins demonstrate mutagenic effects (aflatoxin, ochratoxin A), teratogenic consequences (patulin, aflatoxin B1, ochratoxin A), carcinogenic properties (aflatoxin B1, ochratoxin A), and additional hepatotoxic, nephrotoxic, and endocrine-disrupting effects (zearalenone). Mycotoxin food contamination poses substantial threats to human and animal health. Hepatic and renal cancer in human and animal populations has been linked to mycotoxin-contaminated food consumption [73]. Aflatoxin, the predominant mycotoxin, contributes to malignant transformation and congenital abnormalities. Mycotoxin contamination threatens food quality, necessitating detoxification to reduce contamination and enhance safety and quality. Microbial utilization for mycotoxin elimination represents a relatively contemporary detoxification approach, demonstrating effectiveness and environmental compatibility while maintaining food nutritional value. Multiple microorganisms exhibit robust mycotoxin detoxification capacity (*L. plantarum*, *Lactobacillus acidophilus*, *B. subtilis*). Microbial detoxification demonstrates substantial promise for comprehensive and efficient food detoxification [74].

6.2 | Production, Preservation, and Application Strategies

Fermentation represents the primary pathway through which microbes generate diverse food products. Fermentation implements multiple metabolic pathways biochemically transforming simple carbohydrates into valuable chemicals (carbon dioxide, alcohol, acids). Microbial application for food product generation and quality enhancement has achieved widespread prevalence, with biotechnologists developing novel products through beneficial microbial metabolite utilization [75]. Bacterial

organisms establish diverse beneficial functions in food processing substantially affecting food quality and quantity. Microbial food processing techniques have achieved increased international attention as viable preservation methodologies and essential nutrient sources. Representative examples include *Streptococcus* and *Lactobacillus* species fermenting lactose into lactic acid during dairy product synthesis [3]. Numerous organisms including bacteria, fungi, and yeasts provide human health benefits through substantial food industry contributions. Yeast and bacterial organisms achieve most widespread absorption in food and feed processing. Microbes provide products desirable physicochemical and biological properties at minimal cost, simultaneously enhancing flavor, aroma, and shelf stability. Microbial-based processes simultaneously generate income and reduce operational costs [76].

Probiotics are living beneficial bacteria, which establish health effects through gastrointestinal tract colonization and harmful bacterial replacement. Nondairy probiotic foods have achieved heightened demand due to dietary allergies, lactose intolerance, vegetarian preferences, and vegan dietary choices. Traditional probiotic introduction involved fermented dairy products (yogurt, cheese, and fermented beverages); contemporary nondairy options provide alternative delivery vehicles. Probiotic delivery encompasses both fermented and nonfermented nondairy products [77]. Probiotic bacteria frequently undergo microencapsulation for functional food production: yogurt, cheese, ice cream, cereals, chocolate, confections, and processed meat products. Probiotics establish particular importance in food industries, predominantly within dairy sectors. The most frequently utilized probiotics are *Lactobacillus* and *Bifidobacterium* strains, demonstrated widespread adoption. Emerging genera (*Propionibacterium*, *Peptostreptococcus*, *Pediococcus*, *Leuconostoc*, *Enterococcus*, *Saccharomyces*, *Streptococcus*) are progressively establishing application within probiotic food and beverage domains [78]. Contemporary studies exemplify probiotic beverage development utilizing *L. acidophilus* LA-5 enhanced with mango juice. Mango juice enhancement improved probiotic viability. This formulation enhanced probiotic tolerance during in vitro gastrointestinal simulation. Beverage sensory analysis revealed increasing sensory scores correlating with heightened mango juice concentration [77, 78].

Food safety authorities, industrial manufacturers, and consumers prioritize food-borne illness prevention. Natural preservatives provide essential shelf life and safety enhancement. Microbial organisms generate numerous chemicals suppressing other microorganisms. Bacterial-derived compounds establish antimicrobial opposition to competing bacteria. Active bacteria suppress microorganism growth that deteriorates food [79] Bacteriocin, a proteinaceous antimicrobial agent functions as an antibacterial substance against microbial pathogens and spoilage organisms. Gram-positive and gram-negative bacteria produce bacteriocins. Bacteriocins inhibit foodborne pathogens (*L. monocytogenes, C. botulinum*, *E. faecalis*). Protease-degradable bacteriocins establish safe bio-preservation utilization [21]. Nisin comprised of amino acids (lanthionine, dehydroalanine, aminobutyric acid) derives from *L. lactis*. Nisin inhibits numerous gram-positive bacteria. Cheese manufacturing utilizes nisin for *S. aureus* inhibition in raw milk. Lactic acid bacteria serve as primary biocontrol agents extending perishable product shelf stability through dual antimicrobial and probiotic functions. LAB antimicrobial properties result from diverse antimicrobial substance synthesis: hydrogen peroxide, organic acids, carbon dioxide, bacteriocins, reuterin, and ethanol. *Pediococcus* species generate heat-stable bacteriocins (*P. pentosaceus*, *P. acidilactici*). Pediocin application in cheese and meat-based products demonstrates preservation efficacy [59].

6.3 | Advanced Delivery System Implementation

Contemporary food safety and shelf-life enhancement strategies employ novel delivery systems for microbial natural products, incorporating antimicrobial agents (bacteriocins, essential oils) within food-grade carriers (nanoparticles, liposomes, emulsions). These systems enhance antimicrobial stability, solubility, and release control. These approaches simultaneously preserve sensory qualities and prevent degradation while satisfying consumer demand for sustainable, natural food-processing and packaging methodologies [80].

Microorganisms produce bioactive natural products subsequently converted into pharmaceutical agents treating immune disorders, malignancies, and infections. Traditional microbial product application approaches (spraying, food mixing) frequently yield suboptimal outcomes: diminished bioactivity, reduced environmental stability, minimal consumer acceptance, heterogeneous distribution. Innovative delivery systems establish improved bioavailability, heightened antimicrobial activity, controlled or sustained release, active compound protection from degradation, and sustainability through minimized synthetic packaging [81]. Edible films, thin biopolymer layers incorporating microbial natural products establish edible, consumable delivery vehicles. Representative antimicrobial film applications utilize bacteriocins (nisin, pediocin) establishing food protection. Lactic acid films establish pH reduction and spoilage prevention. Enzymatic films target particular spoilage organisms. Edible films incorporating diverse extracts and essential oils demonstrate documented efficacy against foodborne pathogens (*Salmonella, L. monocytogenes, E. coli*) [82]. Exemplary strawberry edible films incorporating grapefruit seed extract (10%) demonstrated aerobic bacterial, yeast, and fungal population reduction during 14-day storage, with *E. coli* and *L. monocytogenes* growth inhibition. Edible films establish utility for fruit and vegetable wrapping, meat and cheese protection against *Salmonella* and *Listeria*, and oral enzyme/probiotic delivery. Edible film advantages: palatability, safety, biodegradability, shelf life extension, environmental sustainability [83]. Edible coatings are applied as liquids establishing protective surface layers, incorporate microbiological agents (probiotics like *Lactobacillus* species) and antifungal compounds (natamycin from fungi). Coating applications encompass meat, cheese, vegetables, cut fruits, and functional foods delivering probiotics. Coating benefits: moisture loss prevention, flavor/texture improvement, controlled antimicrobial release [84]. Packaging material embedment of microbial natural products incorporates bioactive compounds within biodegradable materials (polylactic acid, starch-based packaging), establishing intelligent packaging interacting with food beyond passive wrapping, preventing spoilage, and signaling freshness. Bioactive packaging contains substances actively suppressing microorganism growth (organic acids, antimicrobial peptides) [85]. Representative products: essential

oils, microbial biosurfactants (antifungal, antioxidant effects), antimicrobial peptides (nisin, reuterin, lactic acid, acetic acid from *Lactobacillus*). Packaging applications encompass meat, dairy, ready-to-eat foods, and pharmaceutical containment. Packaging benefits: chemical preservative reduction, extended shelf stability, enhanced safety, diminished environmental impact [86].

6.4 | Safety, Regulatory Framework, and Consumer Perspectives

Consumed contaminated foods expose populations to microbial pathogenic illness. Comprehensive food preservation techniques maintain microbiological safety alongside nutritional value and sensory attributes. Health concerns escalate natural antimicrobial agent demand. Beyond quality and stability improvement, microbial natural products demonstrate efficacy against diverse pathogenic and spoilage organisms (*Salmonella, E. coli, L. monocytogenes*, *Campylobacter* species, *S. aureus*). These antimicrobials prevent microorganism surface growth and establish food product preservation, functioning alongside edible food coatings [87]. Food ingredients achieve classification as GRAS ("generally recognized as safe") substances or "food additives" requiring FDA approval for particular applications. GRAS classification requires expert consensus supporting ingredient safety recognition. GRAS status derives from scientific evidence demonstrating safety equivalent to food additive regulation requirements or documented safe utilization history predating 1958 [88]. Representative microbial-derived food additives appearing in federal regulations (21CFR sections 172 and 173) include: Natamycin (*Streptomyces natalensis, Streptomyces chattanoogensis*), Yeast protein (*S. cerevisiae*), Yeast-malt sprout extract (*S. cerevisiae, Saccharomyces fragilis*, *Candida utilis*), Xanthan Gum (*Xanthomonas campestris*), Gibberellic acid (*Fusarium moniliforme*), dried yeasts (*S. cerevisiae, S. fragilis, C. utilis*) [89].

Market development proceeds through multiple influential factors. Heightened environmental impact awareness generates increasing preference for sustainable substitutes including microbial-based products. Microbial products establish expanding agricultural applications as soil conditioners, biofertilizers, and biopesticides, improving crop yield while reducing artificial chemical dependency [90]. Growing consumer preference for natural, health-promoting products drives probiotic and microbial therapeutic demand within healthcare sectors. This preference constitutes a primary force propelling microbial product market expansion within food, beverage, and healthcare industries. Consumer preference for general wellness-supporting products lacking artificial additives escalates demand. Similarly, microbial products establish food industry applications: preservation, fermentation, and nutritional enhancement [91].

6.5 | Technological and Economic Barriers

Microorganisms' distinctive characteristics and inherent biosynthetic capacities establish promising technologies addressing contemporary challenges. They participate in scientific investigation across diverse exploration domains, particularly within specific cultural and environmental contexts. Microbial technology demonstrates effectiveness when deployed under optimized culture conditions, producing desired metabolites [91]. Contemporary market supply of microbial inoculants has expanded substantially through emerging biotechnologies. Most substantial advancements occur where metabolite marketing effectively supports microbial technology. Microbial technology implementation presents significant opportunity replacing fertilizer and chemical pesticide utilization with extensively employed contemporary organic agriculture biopesticides [92].

Natural product efficacy and commercial viability within food industries depend substantially upon stability, production expenses, and scalability. Stability describes bioactive compound capacity, maintaining biological activity and functional properties across diverse food processing and preservation conditions. Representative examples include bacteriocins, organic acids, enzymes, and natural pigments [93]. Multiple variables influence stability: pH, temperature, light exposure, oxidative processes, and food ingredient contact. Nisin exemplifies stability advantages, remaining stable in acidic environments and tolerating moderate heat, rendering it suitable for processed foods (cheese, canned vegetables). Conversely, certain enzymes and pigments degrade rapidly with heat or light exposure, necessitating protective strategies (microencapsulation, stabilizer formulation) extending shelf stability [94].

Production expenses substantially impact microbial natural product adoption within food industries. Cost components encompass energy expenditure, fermentation infrastructure, raw materials (carbohydrates, nitrogen sources for microbial growth), and particularly downstream processing (extraction, purification). Food-grade purification frequently represents the most expensive manufacturing process [95]. Expense reduction through diminished-cost substrates (agricultural or food industry waste) and genetically engineered high-yield strains offers potential. Complex manufacturing procedures maintain certain natural compounds at elevated costs. For instance, bacteriocins such as nisin demonstrate substantial efficacy at minimal concentrations; nevertheless, extensive purification costs challenge widespread preservation utilization economic viability [96].

Scalability is the capacity for straightforward production scale-up from laboratory or pilot operations to full industrial dimensions without efficiency, quality, or safety compromise, and represents a critical parameter. Fermentation complexity and microorganism sensitivity present scalability obstacles. Elevated volumes complicate management of oxygen transfer, pH maintenance, nutrient distribution, and contamination prevention [93]. Downstream processing requires modification for elevated volumes while maintaining consistent quality. Contemporary biotechnological progress has improved bioreactor designs, continuous fermentation systems, and real-time monitoring, increasingly facilitate production scaling. Industrial-scale enzyme synthesis (amylases, proteases) through optimized bioprocesses exemplifies scalability feasibility with appropriately engineered systems. Notwithstanding substantial potential, successful industrial implementation requires conscientious scalability, stability, and production cost evaluation [95].

6.6 | Biotechnological Progress and Synthetic Biology Advancement

Microbial biotechnology deploys microorganisms for diverse applications, revolutionized industries from environmental restoration through food production to pharmaceutical manufacturing. Contemporary synthetic biology and synthetic ecology developments provide novel methodologies enabling microorganism engineering and system management for advantageous objectives [97]. Synthetic biology encompasses generating novel biological systems or repurposing preexisting systems for particular applications. Genetic microorganism modification for industrial chemical, pharmaceutical, and biofuel production has become progressively sustainable and efficient. Genome editing instruments (CRISPR-Cas9 and related technologies) have facilitated precise microbial genetic manipulation and genetic circuit and metabolic pathway alteration. These engineered organisms demonstrate substantial promise addressing global food production, health, and energy challenges while establishing sustainable alternatives to conventional chemical synthesis methodologies [98]. Additionally, synthetic biology presents environmental remediation opportunities through engineered microorganism deployment as inventive pollutant degradation, contaminant detoxification, and ecosystem restoration catalysts. Multiple applications concentrate on pure cultures, representing minimal microbial world components. Microbial community intricacy produces individual microorganism behavioral divergence from community context due to component interactions. These constraints may complicate synthetic biology natural environment implementation [99].

Multiple engineered platforms have synthesized and produced high-value compounds. Liu and collaborators summarized the microbial framework for fatty acid-derived compound production. Heterotrophic organisms (*E. coli, S. cerevisiae*, *Yarrowia lipolytica*, *Aureobasidium*) have undergone engineering for fatty acid-derived compound synthesis from organic carbon sources, whereas autotrophic organisms (*Cupriavidus necator, Rhodococcus opacus, Synechococcus* PCC 7002, *Nostoc punctiforme*) synthesize compounds from CO_2 utilizing chemical sources, light, and electrical energy [100] Sajid et al. [101]. elucidated engineered *E. coli* and *S. cerevisiae* currently producing isoflavonoids through artificial biosynthesis pathways, Yuan et al. [102]. examined fermentation processes in microbial cell factories for fat-soluble vitamin production (vitamins A/D/E and K) and water-soluble vitamin synthesis (vitamins B_1, B_2, B_3, B_5, B_6, B_7, B_9, B_{12}, and C).

Microbial strain improvement represents a fundamental industrial microbiology and biotechnology procedure targeting enhanced metabolite, enzyme, or biomass synthesis capacity. This encompasses deliberate, calculated modifications, genetic, biochemical, or physiological optimizing of microorganism performance within industrial environments. These modifications guarantee high yield, productivity, stability, and cost-effectiveness in industrial bioprocesses [103]. Industrial fermentation and biotechnology predominantly utilize microorganisms derived from natural isolates, microbes obtained directly from natural habitats (soil, water, plant matter). Although wild-type strains possess fundamental metabolite, enzyme, or bioactive compound synthesis capacity, their inherent production levels, proliferation rates, and metabolic effectiveness frequently fall beneath large-scale industrial application requirements [104]. This intrinsic limitation establishes substantial obstacles to sustainable, economically viable bioprocesses. Contemporary biotechnology has revolutionized microorganism applications, including bacteria in dairy production and yeast in baking. Wild microbial strain utilization presents biotechnologists substantial challenges [105]. Predetermined consistency and quality timeframe achievement proves difficult due to frequent natural population instability and unpredictability in consistent food product generation capacity. These microorganisms frequently struggle surviving fermentation conditions; fermenter interiors interfere with regular operations, generating potentially harmful metabolite production. Diminished proliferation rates commonly reduce food processing industry productivity, escalating production expenses and economic viability detriment. This emphasizes the necessity for robust microbes tolerating fermentation conditions while enhancing yield efficiency [106]. Genetic modification research demonstrates modified microorganism capacity for harsh fermentation condition tolerance. Representative examples include microorganism genetic modification for elevated temperature proliferation within fermenters through heat-tolerance gene introduction [107]. This capacity enables robust, stable, rapid-growth microbial strain establishment, rendering them appropriate for diverse biotechnological applications. Representative engineered strains and derived food products include *S. cerevisiae* and multiple yeast strains used in baguette production, *L. lactis* subsp. *cremoris* employed in fermented dairy products such as yogurt and cheese, and *A. niger* widely applied in enzyme and organic acid production for the food industry [108].

7 | Future Perspectives and Research Directions

The expanding scientific understanding of microbial natural products highlights substantial potential for addressing global food security challenges while promoting environmental sustainability. Future advancement necessitates: intensified research establishing novel natural product sources and production methodologies, biotechnological innovation optimizing yield and stability, rigorous regulatory harmonization facilitating international product standardization, consumer education programs promoting natural alternative acceptance, and comprehensive antimicrobial resistance surveillance. These coordinated efforts will establish microbial natural products as fundamental components of contemporary food safety and preservation systems [109, 110].

8 | Conclusion

Microbial natural products demonstrate remarkable capacity to enhance food safety through quality improvement, pathogen reduction, and spoilage prevention. Bio-preservation may represent the biological alternative to conventional physical and chemical preservation methodologies, generally regarded as compromising product quality and, in certain instances, posing health hazards. Comprehensive food bio-preservation employing bacteriocins, bacteriophages, and bacterial endolysins can substantially enhance food processing, preservation, and safety.

Food production and processing industry expansion has heightened awareness of microbe importance. Due to genetic modification accessibility for superior product quality and large-scale production, microbial process-based food and associated product manufacturing demonstrates reduced expense and enhanced simplicity. Microorganism food processing utilization yields time and energy conservation plus enhanced commercial-scale system reproducibility. Escalating demand for processed foods reflects contemporary lifestyles necessitating convenient nutrition, mandating affordable, shelf-stable products at substantial volumes. Technological advancement facilitates beneficial microorganism identification; consequently, investigation should concentrate on establishing novel microbial manufacturing natural sources, improving extant procedures, and generating innovative production methodologies for health and nutritional advantage foods at commercial scale. Most significant microorganism food industry applications encompass: microbial organism, particularly probiotic, utilization in dairy, grain, meat, and associated industry sectors; metabolite application extending shelf stability and preserving food product quality; microorganism utilization for food-produced mycotoxin elimination; and ultimately microorganism application for food industry waste reduction.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The article describes entirely thermotical research.

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