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Healthy Nutrition and Fermented Animal-Sourced Foods as a Complementary One Health Strategy: Effects on Foodborne Pathogens and Intestinal Host Defense

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ABSTRACT

Foodborne diseases remain a major global public health challenge at the interface of human, animal, and environmental health, emphasizing the need for integrated preventive strategies within the One Health framework. Although animal-sourced foods (ASFs) are essential components of human nutrition, they also serve as important reservoirs and transmission vehicles for foodborne pathogens. Conventional food safety interventions primarily target microbial contamination within food systems but often fail to adequately address host susceptibility, intestinal resilience, and microbiota-mediated defense mechanisms. This review highlights fermented ASFs, nutraceuticals, and nonviable microbial products as complementary One Health interventions that can simultaneously influence pathogen ecology and host defense. Fermentation-derived compounds, including organic acids, bacteriocins, bioactive peptides, and microbial metabolites, exert antimicrobial effects against foodborne pathogens while modulating epithelial barrier integrity, inflammatory signaling pathways, gut microbiota composition, and colonization resistance. Particular emphasis is placed on the mechanistic roles of these functional components in regulating intestinal immunity, including Toll-like receptor-associated signaling, NF-κB-mediated responses, and epithelial protection. The review also discusses multidisciplinary surveillance approaches, the translational relevance of dietary strategies for reducing reliance on antimicrobials, and current challenges related to standardization, safety, and clinical validation. Collectively, fermented ASFs and functional nutritional approaches should not be considered passive dietary components but biologically active tools with the potential to enhance food safety, strengthen gastrointestinal host defense, and support sustainable disease prevention across the interconnected One Health framework.

Keywords: Animal-sourced foods, fermentation, functional compounds, host defense, one health.

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INTRODUCTION

Foodborne diseases remain a persistent global challenge at the intersection of human, animal, and environmental health, closely aligning with the core principles of the One Health approach. Animal-sourced foods (ASFs) are essential components of human nutrition.[1] However, ASFs can serve as both major reservoirs and transmission vehicles for key foodborne pathogens, such as *Salmonella enterica*, *Listeria monocytogenes*, and *enterohemorrhagic Escherichia coli*.[2] These products are inherently nutrient-rich environments that can support microbial survival and growth if not properly handled. Although conventional control strategies, such as hygiene interventions, antimicrobial use, and advanced processing technologies, have improved safety outcomes, pathogens continue to occur in animal production systems and postharvest food chains. The increasing prevalence of antimicrobial resistance and the complexity of farm-to-fork transmission dynamics emphasize the need for innovative strategies that simultaneously target both the food matrix and the host.

Although ASFs pose risks due to the presence of zoonotic microorganisms, they also contain many functional components that provide benefits beyond their nutritional value. Animal-sourced fermented foods represent a compelling intersection of nutrition, microbiology, and food safety. Traditional products, such as fermented dairy foods (e.g., yogurt, kefir, and cheese) and fermented meats (e.g., dry-cured and ripened products), are biological systems shaped by complex microbial communities. These matrices generate a wide spectrum of bioactive metabolites during fermentation, transforming raw animal substrates into functional foods with enhanced safety and health-promoting properties.[3] The starter microorganisms responsible for food fermentation also exhibit probiotic activities that can suppress pathogenic bacteria in food while simultaneously benefiting the host within the gastrointestinal system.[4]

Beyond their role in food preservation, fermented ASFs actively contribute to intestinal host defense. In addition to competing for resources within food matrices, metabolites produced during fermentation, including organic acids, bacteriocins, short-chain fatty acids, and bioactive peptides, can directly inhibit pathogens by acidifying the environment and destabilizing bacterial membranes.[5] Upon consumption, these compounds interact with the intestinal epithelium, influencing barrier integrity and modulating immune signaling pathways, including pathogen recognition receptors and cytokine and chemokine release.[6] This dual functionality, acting in both food matrices and the host response, positions fermented ASFs as uniquely effective tools for mitigating foodborne infections.

In this review, healthy nutrition and fermented ASFs are presented as complementary One Health strategies that bridge food safety and host health. The review focuses on their capacity to control foodborne pathogens at the source while enhancing intestinal defense mechanisms through modulation of the microbiota and immune regulation. By integrating insights from food microbiology, animal production systems, and host–pathogen interaction studies, this review aims to redefine healthy nutrition and animal-sourced fermented foods not as passive dietary components but as active, biologically driven interventions with the potential to reduce disease burden across interconnected human, animal, and environmental systems.

BURDEN OF FOODBORNE PATHOGENS

Foodborne diseases remain a major global cause of outbreaks and contribute to substantial morbidity, mortality, and economic loss. Bacterial pathogens remain among the primary etiological agents of severe foodborne diseases, including *Salmonella enterica*, *Listeria monocytogenes*, and *Escherichia coli* O157:H7. Viral and parasitic agents, such as *norovirus* and *Toxoplasma gondii*, also require close monitoring to maintain food safety. These organisms are responsible for a wide spectrum of disease outcomes, ranging from self-limiting gastroenteritis to systemic infections, invasive disease, and life-threatening complications, particularly in vulnerable populations, including infants, older adults, and immunocompromised individuals. Despite advances in surveillance and food safety management systems, the incidence of foodborne illness remains high, reflecting the complexity of pathogen transmission across the entire food chain.[7]

Economic Consequences of Foodborne Illness

According to the World Health Organization (WHO), foodborne diseases remain a major global health concern, causing approximately 600 million cases and 420,000 deaths annually, with nearly 30% of these deaths occurring in children younger than 5 years. The burden extends beyond mortality, accounting for an estimated 33 million disability-adjusted life years (DALYs) lost each year.[8] This substantial burden also translates into significant economic losses due to healthcare costs, reduced productivity, and disruptions across the food supply chain. Moreover, the disproportionate impact on vulnerable populations and low-resource settings highlights the urgent need for integrated preventive strategies aligned with the One Health framework. The United States Department of Agriculture (USDA) Economic Research Service (ERS) provides comprehensive data on the economic burden of foodborne illnesses in the United States, estimating the total cost at $74.7 billion in 2023. These estimates incorporate medical treatment costs, lost wages, and short- and long-term health outcomes. Although serious illnesses caused by specified pathogens account for only 20% of total cases, they account for 60% of the total financial impact, with nontyphoidal Salmonella having the highest total cost in the United States at $17 billion.[9]

Social Consequences of Foodborne Illness

The social burden of foodborne illness, in addition to its economic burden, must be re-evaluated in terms of human welfare. The social costs of foodborne pathogens in vulnerable populations are substantial; beyond mortality, they directly affect education, social life, and acute clinical conditions, as well as complications such as Guillain-Barré syndrome (GBS) and hemolytic uremic syndrome (HUS), which can have long-term effects on quality of life. In addition to these direct effects, the psychological impact of foodborne pathogens on perceptions of healthy nutrition is undeniable. Food safety incidents affect public trust in food systems and regulatory authorities, altering consumer behavior and dietary patterns.[10] Growing concerns about food safety and quality are also shaping food preferences. Evidence suggests that foodborne outbreaks can reduce the consumption of certain foods, although these effects vary by context and food type.[11] From this perspective, foodborne illnesses require not only symptomatic treatment but also the development of pathogen surveillance systems, integrated complementary approaches to healthy nutrition in the management of gastrointestinal diseases, and the use of preventive strategies during healthy phases of life.

ONE HEALTH INTEGRATION AND MULTIDISCIPLINARY SURVEILLANCE

Strategies aligned with the One Health paradigm emphasize the interrelationships among food, animal, and human health in addressing the persistent burden of foodborne diseases. The lack of One Health coordination impedes the effective integration of environmental, animal, and human health data, resulting in fragmented surveillance and slower responses to zoonotic threats. Disciplines often operate in isolation, with poor interdisciplinary communication, inconsistent data-sharing protocols, and a lack of standardized formats, leading to duplicated efforts and incomplete outbreak insights. Additional barriers include limited funding, weak governance, and insufficient multidisciplinary training. Real-time surveillance and response within a One Health framework require multidisciplinary expertise spanning epidemiology, veterinary medicine, genomics, bioinformatics, and laboratory practice. The value of this approach lies not only in integrating data across disciplines but also in enabling joint analyses that strengthen early detection and coordinated responses. By supporting operational data integration, real-time pathogen surveillance, and the clinical management of foodborne diseases, this framework facilitates collaborative disease prevention and control across human, animal, and environmental health systems.[12]

Interdisciplinary Collaboration

Effective control of foodborne outbreaks and disease management, as well as the successful implementation of One Health strategies, requires close and sustained collaboration across disciplines. The interface between animal and human health is particularly evident in the epidemiology of zoonotic pathogens that originate in animal reservoirs and are transmitted to humans through the food chain. Veterinary specialists play a critical role in monitoring animal health, implementing biosecurity measures, and controlling pathogen prevalence at the pre- and postharvest levels,[13] while medical professionals are responsible for the clinical diagnosis, treatment, and management of infections and outbreaks.[14] Food safety also requires the coordinated involvement of food microbiologists, food safety specialists, public health authorities, and regulatory agencies. Without coordinated efforts among these disciplines, interventions remain fragmented and less effective.

Benefits of Interdisciplinary Collaboration

Collaboration enables the integration of surveillance systems, allowing early detection and rapid response to emerging foodborne threats. Data sharing between veterinary and medical professionals facilitates source attribution, outbreak tracing, and risk assessment, thereby improving the precision of intervention strategies. Moreover, joint research efforts can advance the understanding of host–pathogen interactions across species, particularly regarding immune responses, microbiota dynamics, and antimicrobial resistance.

Interdisciplinary collaboration in food safety supports the design of prevention strategies that extend from the farm to the clinic. Veterinary expertise in pathogen control supports approaches to reduce zoonotic occurrence before food products reach consumers. Simultaneously, medical insights into human immunity and disease susceptibility can inform dietary recommendations and functional nutrition strategies to enhance host defense. This knowledge exchange is essential for aligning food safety interventions with public health outcomes. Ultimately, integrating veterinary and medical sciences strengthens the One Health approach by bridging gaps among animal production, food safety, and human health.[15] Coordinated efforts not only improve the effectiveness of pathogen control strategies but also help reduce antimicrobial resistance, enhance surveillance capacity, and promote sustainable health systems. This collaborative framework is indispensable for addressing the complex, interconnected challenges that foodborne diseases pose to the public. Although traceable pathogen control from farm to fork is well developed with modern management systems, food safety remains a critical public health challenge in both developed and developing countries. Therefore, strengthening nonspecific host defense barriers in the gastrointestinal system through healthy nutrition requires collaboration among related scientific fields, such as human medicine, nutrition, and dietetics, all of which are relevant to alimentary health.

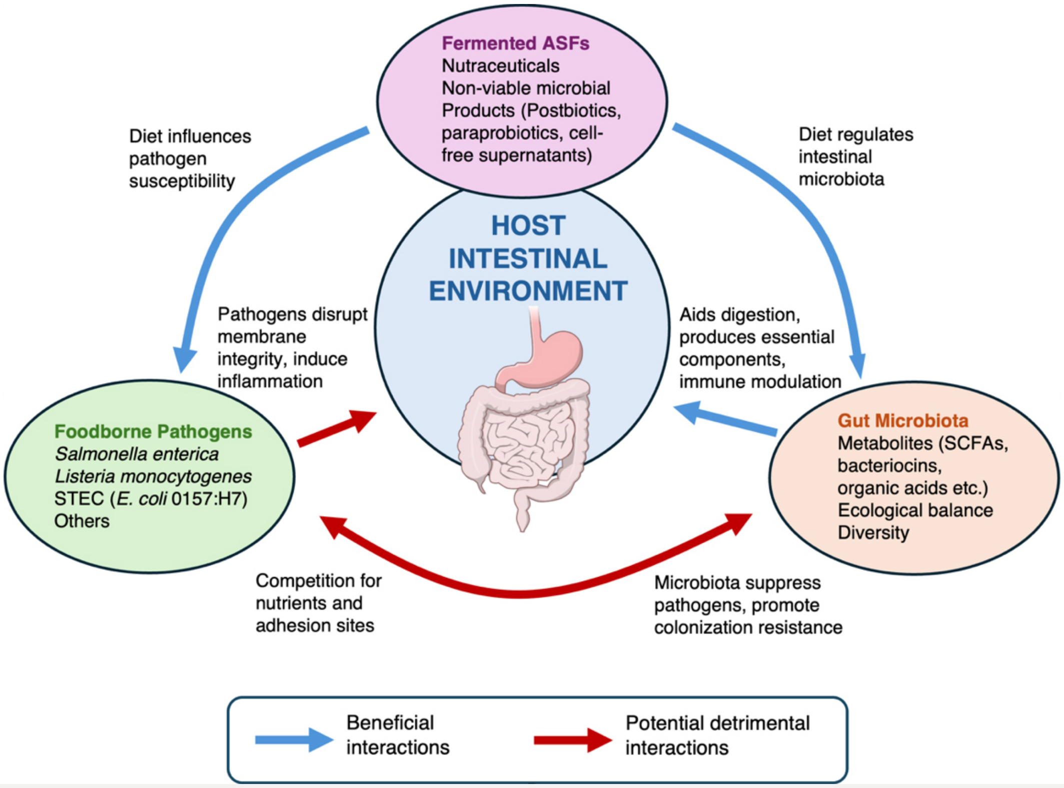

Figure 1. Interactions among fermented animal-sourced foods, gut microbiota, foodborne pathogens, and the host intestinal environment.

ASF: Animal-sourced food; SCFA: Short-chain fatty acid; STEC: Shigatoxigenic *Escherichia coli*. (Gastrointestinal illustration was supplied from BioArt (https://bioart.niaid.nih.gov/)).

ROLE OF DIETARY COMPOUNDS IN MODULATING GASTROINTESTINAL DISEASE

Diet is a primary ecological determinant of host–microbe interactions and exerts system-wide effects that directly influence disease susceptibility across human, animal, and environmental niches. Beyond its fundamental role in energy provision, diet regulates the composition and metabolic activity of the gut microbiota, thereby enhancing colonization resistance against enteric pathogens. Nutrient availability and substrate diversity selectively shape microbial communities, influencing the production of metabolites such as short-chain fatty acids (SCFAs), secondary bile acids, and antimicrobial peptides. These metabolites act as key signaling molecules that reinforce epithelial barrier integrity, regulate mucosal immunity, and suppress pathogen growth.[16] Consequently, dietary patterns rich in bioactive and fermentable substrates can shift the intestinal ecosystem toward a protective state, whereas nutrient imbalances or highly processed diets may predispose hosts to dysbiosis and increased infection risk. Integrating functional nutrition, fermented foods, nutraceuticals, and nonviable microbial products into human dietary practices represents a rational pathway for reducing the burden of infectious diseases while promoting sustainable health across interconnected biological systems. Interactions among fermented ASFs, gut microbiota, foodborne pathogens, and the host intestinal environment are shown in Figure 1.

Fermented ASFs and Functional Compounds

Produced through controlled microbial activity, fermented ASFs, such as dairy and meat products, are not only preserved and stabilized but also enriched with bioactive compounds that enhance their functional value. During fermentation, lactic acid bacteria and other microbial consortia metabolize proteins, lipids, and carbohydrates to generate a wide spectrum of functional molecules, including organic acids, bacteriocins, short-chain fatty acids, vitamins, and bioactive peptides.[17] Fermented foods help reduce the burden of foodborne pathogens through both direct and indirect mechanisms. During fermentation, the production of organic acids, bacteriocins, and other antimicrobial compounds can suppress or inhibit pathogens. These constraints are particularly relevant in ASFs and have led to the development of technological approaches

Table 1. Bioactive components and mechanistic health effects of fermented ASFs

ASF	Major functional components	Key mechanistic actions	Ref
Yogurt	ACE-inhibitory peptides	Antihypertensive activity mediated by bioactive peptide-induced inhibition of ACE	19
Acidophilus-fortified milk	Organic acids, bacteriocin-like compounds	Recognition through TLR signaling, inhibition of allergic responses, and regulation of inflammatory pathways, such as NF-κB signaling	20
Milk	Casein-derived peptides	Enhanced MUC5AC gene expression and mucin secretion	21
Milk	Sphingomyelin	Modulation of lipid metabolism and gut microbial composition	22
Fermented milk	Fermentation metabolites	Modulation of gut microbiota composition and regulation of GALT	23
Kefir	EPS	Modulation of the microbiota	24
Koumiss	ACE-inhibitory peptides	Antihypertensive activity mediated by bioactive peptide-induced inhibition of ACE	25
Fermented skim milk	Functional peptide fractions	Antioxidant, antihypertensive, and immunomodulatory activities	26
Dry-cured ham	ACE-inhibitory peptides	Antihypertensive activity mediated by bioactive peptide-induced inhibition of ACE	27
Fermented meat	GABA	Neurotransmitter produced during fermentation with blood pressure-lowering effects	28
Probiotic salami	SCFAs	Regulation of IEC function through mechanisms including histone deacetylase inhibition	29
Dry-fermented sausage	ACE-inhibitory peptides	Antihypertensive activity mediated by bioactive peptide-induced inhibition of ACE	30
Salami	CLA	Anticarcinogenic activity	31

ASF: Animal-sourced food; CLA: Conjugated linoleic acid; SCFA: Short-chain fatty acid; GABA: γ-aminobutyric acid; EPS: Exopolysaccharide; ACE: Angiotensin-converting enzyme; TLR: Toll-like receptor; IEC: Intestinal epithelial cell; GALT: Gut-associated lymphoid tissue; Ref: Reference.

to ensure their safety, as conventional decontamination methods may have limited penetration into complex tissues, such as lymph nodes in meat, and may not adequately address internalized pathogens. One study examined the effectiveness of carcass vascular rinsing with organic acids and acid-based antimicrobial interventions in reducing Salmonella Enteritidis in the lymph nodes of experimentally infected meat animals.[18] The implementation of organic acids, which can be end products of beneficial microorganisms, such as lactic acid bacteria with probiotic and starter culture properties, into new technologies is important for food safety.

The consumption of fermented foods supports intestinal health by promoting beneficial microbiota, strengthening epithelial barrier function, and modulating immune responses, thereby reducing host susceptibility to enteric infections. Their role is particularly relevant in the context of increasing antimicrobial resistance and the limitations of conventional food safety strategies, as they offer natural and sustainable benefits that enhance both microbial control and host resilience. Furthermore, fermentation processes can contribute to sustainability by improving food preservation, reducing waste, and enabling the more efficient use of food resources. Some key bioactive components of fermented ASFs and their mechanistic effects on host physiology and pathogen control are summarized in Table 1.[19–31]

Fermented foods are integral components of traditional dietary systems across nearly all global cultures, reflecting long-standing practices of food preservation, sensory enhancement, and microbial diversity. These culturally embedded foods contribute not only to nutritional intake but also to social eating behaviors, communal food sharing, and dietary continuity, which are increasingly recognized as determinants of long-term health outcomes. The sustained consumption of traditional fermented foods may support healthier dietary patterns by reinforcing culturally accepted eating practices associated with microbiome diversity, metabolic regulation, and psychosocial well-being.[32] From nutritional and public health perspectives, fermented foods are accessible and culturally integrated dietary components that can serve as preventive tools.

Nutraceuticals

Nutraceuticals are notable components within the One Health framework, linking nutrition, food safety, and disease prevention across human, animal, and environmental systems. Defined as bioactive compounds derived from food sources that provide health benefits beyond basic nutrition, nutraceuticals offer targeted functional effects that can modulate host physiology and microbial dynamics. In the context of healthy nutrition, they represent a strategic extension of diet-based interventions, enabling the delivery of specific molecules, such as bioactive peptides, polyphenols, and organic acids, that influence key biological processes involved in host defense and metabolic regulation. Nutraceuticals help reduce reliance on conventional antimicrobials in both human and animal systems, thereby mitigating the emergence and spread of antimicrobial resistance.[33] These compounds can strengthen intestinal barrier function,[34] modulate inflammatory pathways,[35] and support microbiota balance,[36] all of which are critical determinants of susceptibility to foodborne infections. Importantly, nutraceuticals also align with the increasing demand for sustainable and preventive health strategies. Unlike pharmaceutical interventions, they can be integrated into daily diets or functional foods, offering a safe and scalable approach to improving health outcomes. Their stability, especially in the form of purified bioactive compounds or postbiotics, further enhances their applicability in food systems and clinical settings.

Fermented foods act as natural delivery vehicles for nutraceutical compounds, providing them in a structurally complex and bioavailable form. Unlike isolated supplements, food matrices facilitate synergistic interactions between microbial metabolites and host systems, enhancing their stability and functional efficacy within the gastrointestinal environment.[37] In addition, fermentation can reduce antinutritional factors, such as phytates, tannins, lectins, and oxalates,[38] and improve nutrient digestibility, further supporting the bioactivity of nutraceutical components.[39]

Nonviable Microbial Products

The positive effects of probiotics are not restricted to live microorganisms; nonviable microbial products and dietary bioactives can also exert similar immunomodulatory and protective functions, supporting the growing interest in nutraceuticals as stable and targeted preventive agents. Postbiotics, paraprobiotics, also called parabiotics, and cell-free supernatants (CFSs) have emerged as mechanistically defined functional agents that extend the biological relevance of fermented foods beyond the requirement for viable microorganisms.[40] Postbiotics are broadly defined as preparations of inactive microorganisms and their metabolites that confer a health benefit to the host, encompassing metabolites, cell wall fragments, extracellular vesicles, and soluble bioactive molecules derived from microbial activity. Compared with live probiotics, postbiotics offer several advantages, including enhanced safety profiles, improved physicochemical stability, and reproducibility in formulation, particularly in complex food matrices and clinical settings where viability and colonization are not guaranteed.[41] Paraprobiotics, often called "ghost probiotics" or inactivated probiotics, are nonviable microbial cells or fractions, such as cell wall components, that provide health benefits to the host,[42] while CFSs can be defined as liquid, cell-free metabolites obtained by centrifuging and filtering microbial cultures, often probiotic bacteria such as lactic acid bacteria. These attributes position nonviable microbial products as highly controllable and scalable interventions within both food systems and host-directed therapeutic strategies. At the mechanistic level, these products exert multifaceted biological effects that target both microbial pathogens and host cellular responses. Representative mechanistic effects of nonviable microbial products on epithelial integrity, inflammatory signaling, and pathogen suppression are summarized in Table 2.[43–54]

CHALLENGES IN THE IMPLEMENTATION OF FUNCTIONAL FOOD COMPONENTS

Despite growing recognition of functional food components within the One Health framework, several critical challenges limit their consistent application and impact on health. These limitations include product variability, safety considerations, and insufficient mechanistic and clinical validation, all of which must be addressed to enable their integration into evidence-based food safety and public health strategies. The absence of standardized protocols for the characterization, quantification, and quality control of bioactive components, such as postbiotics and parabiotics, limits the ability to ensure consistency and efficacy. Challenges in balancing innovation with safety and scientific substantiation complicate the evaluation of the complex interactions between the functional properties of multicomponent food matrices and pathogens.[55]

One of the primary challenges associated with fermented foods is the inherent variability in their composition and functional properties. Fermentation is a biologically dynamic process influenced by raw material quality, starter cultures, processing conditions, and environmental factors. As a result, the concentration and profile of bioactive compounds, including organic acids, peptides, and antimicrobial metabolites, can vary significantly across batches and production systems. This variability is particularly pronounced in traditional fermented ASFs, in which spontaneous fermentation and undefined microbial consortia are common. Consequently, the

Table 2. Positive effects of selected nonviable microbial products on health

Nonviable microbial product	Source microorganism	Health effects	Ref
Postbiotic	*Lactiplantibacillus plantarum*	Enhancement of tight junction proteins, including ZO-1, occludin, and claudin-1	43
Postbiotics	LAB strains	Reduction of apoptosis and oxidative stress in infected epithelial cells	44
Postbiotics	*Bacillus amyloliquefaciens J* and *L. plantarum*	Antimicrobial activity against *Salmonella Typhimurium*, *Staphylococcus aureu*s, and *Escherichia coli* O157:H7	45
Postbiotic	*L. plantarum*	Reduction of bacterial invasion of epithelial cells	46
Postbiotics	*Bifidobacterium* animalis subsp. lactis, *L. plantarum*, and *Lactobacillus paracasei*	Suppression of the TLR4/NLRP3/MyD88 signaling pathway	47
Postbiotic	*Lactobacillus helveticus*	Improvement in stool consistency and relief of constipation-related abdominal discomfort	48
Paraprobiotics	*Lactobacillus casei*, *L. paracasei*, *Lactobacillus gasseri*, *B. lactis*, and *Streptococcus thermophilus*	Anti-inflammatory effects and reductions in organ nitrite/nitrate levels	49
Paraprobiotics	*L. plantarum* and *Limosilactobacillus fermentum*	Inhibition of the NF-κB/NLRP3 signaling pathway	50
Paraprobiotics	*L. plantarum*, *Latilactobacillus sakei*, and *Limosilactobacillus reuteri*	Enhanced antioxidant activity, anti-inflammatory effects, and barrier integrity	51
Cell-free supernatants	*L. plantarum*, *L. paracasei*, *L. gasseri*, and *S. thermophilus*	Modulation of mucus production	52
Cell-free supernatants	*Lactobacillus amylovorus*	Modulation of TLR4-independent inflammatory signaling	53
Cell-free supernatants	*L. reuteri*, *Lacticaseibacillus rhamnosus*, and *L. plantarum*	Modulation of inflammation and oxidative stress	54

LAB: Lactic acid bacteria; ZO: Zonula occludens; TLR: Toll-like receptor; NLRP3: NLR family pyrin domain containing 3; MyD88: Myeloid differentiation primary response 88; NF-κB: Nuclear factor kappa-light-chain-enhancer of activated B cells; Ref: Reference.

reproducibility of functional effects, including antimicrobial activity and host-modulatory capacity, remains difficult to standardize, limiting comparability across studies and applications.[56]

Although fermentation is traditionally associated with improved safety and preservation, it can also introduce specific risks if not properly controlled. The formation of biogenic amines, such as histamine, tyramine, and putrescine, through microbial decarboxylation of amino acids represents a significant safety concern, particularly in protein-rich fermented animal products.[57] Elevated levels of these compounds can lead to adverse health effects, including allergic and hypertensive reactions in sensitive individuals. In addition, inadequate hygiene or uncontrolled fermentation conditions may allow the survival or proliferation of undesirable saprophytes and mycotoxigenic molds. These risks underscore the importance of controlled fermentation processes, validated starter cultures, and rigorous monitoring systems to ensure product safety.[58]

High salt content is a notable limitation of many fermented foods, particularly animal-sourced products such as cheeses and cured or fermented meats, in which sodium chloride is essential for microbial control, texture development, and shelf-life extension. Although salt contributes to the safety and stability of these products by inhibiting undesirable microorganisms and shaping fermentation dynamics, excessive dietary sodium intake is strongly associated with adverse health outcomes, including hypertension and increased cardiovascular risk. This presents a critical paradox in the context of functional nutrition and One Health, in which foods intended to confer health benefits may simultaneously contribute to the burden of noncommunicable diseases if consumed inappropriately. Furthermore, efforts to reduce salt content in fermented foods must be carefully balanced, as lowering sodium levels can alter microbial ecology and potentially compromise product quality. Therefore, optimizing salt concentrations, developing alternative preservation strategies, and engineering low-sodium fermentation systems remain essential research priorities to ensure the health-promoting potential of fermented foods.[59]

Nutraceuticals face several key limitations that constrain their broader application and clinical translation, including a lack of standardization, limited bioavailability, regulatory ambiguity, and insufficient mechanistic and clinical evidence. Variability in composition and active compound concentrations reduces reproducibility and complicates dose optimization, while many bioactive molecules exhibit poor absorption or rapid metabolism, limiting their *in vivo* efficacy. In addition, inconsistent regulatory frameworks across regions create challenges in quality control, safety assessment, and validation of health claims. Although nutraceuticals show promising antimicrobial, antioxidant, and immunomodulatory effects against pathogens in experimental models, robust human clinical data and detailed mechanistic insights remain limited. Furthermore, potential safety concerns and interactions, particularly at higher doses or in sensitive populations, underscore the need for rigorous evaluation.[60]

Despite promising *in vitro* and preclinical findings, a substantial gap remains in mechanistic clarity and clinical validation regarding the health effects of functional food compounds. Many studies rely on experimental models that do not fully capture the complexity of host–microbiota–pathogen interactions *in vivo*. Although evidence supports the antimicrobial and immunomodulatory effects of fermentation-derived compounds against pathogens, the precise molecular mechanisms and dose–response relationships remain incompletely elucidated. Moreover, well-designed clinical trials assessing efficacy, safety, and long-term outcomes in diverse populations are limited. This lack of robust clinical evidence restricts the ability to formulate definitive dietary recommendations and hinders acceptance within clinical and regulatory frameworks.

CONCLUSION

Fermented ASFs and their functional components are multifaceted, biologically active tools within the One Health framework, bridging the interconnected domains of food safety, nutrition, and host defense. Beyond their traditional roles in preservation and nutrient delivery, these functional components can exert targeted antimicrobial effects against major foodborne pathogens while simultaneously modulating intestinal barrier integrity and innate immune responses. This dual functionality, controlling pathogens within food matrices and enhancing host resilience after consumption, positions them as strategic interventions capable of addressing both exposure risk and disease susceptibility. Importantly, integrating fermented ASFs into dietary practices, alongside nutraceuticals, postbiotics, and other bioactive metabolites, offers a complementary approach to conventional food safety systems. These strategies align with the increasing need to reduce reliance on antimicrobials, mitigate antimicrobial resistance, and implement sustainable preventive health measures across populations. Their capacity to modulate gut microbiota composition, regulate inflammatory signaling pathways, and reinforce epithelial defenses highlights their relevance in reducing the burden of foodborne diseases. From a translational perspective, the strategic incorporation of these functional approaches into food production systems, animal feeding practices, and public health policies holds significant promise. However, their successful implementation requires continued efforts toward standardization, mechanistic validation, and clinical substantiation. Within a holistic One Health context, fermented ASFs and nutraceuticals, when used as integrated tools, offer a forward-looking pathway to enhance food safety, strengthen host defense mechanisms, and promote sustainable health across interconnected biological systems.

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