



## Advanced Nanomaterials for Mitigating Foodborne Pathogens: Efficacy, Mechanisms, and Safety Considerations

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### Abstract

The threat of foodborne pathogens on human health and global food security has not decreased because of the restriction of traditional antimicrobial measures and the increasing popularity of minimally processed food. Against this backdrop, advanced nanomaterials have become the promising tool in curbing microbial contamination in the entire food supply chain. This paper is a critical evaluation of the application of nanomaterials in the management of foodborne pathogens with special emphasis on their antimicrobial effects, their mechanism of action and other safety implications. The paper extends the existing body of evidence on the role of physicochemical properties (e.g., particle size, surface charge, and functionalization) in determining antimicrobial performance and pathogen susceptibility to antimicrobial agents by synthesizing the results of recent experimental investigations, systematic reviews, and applied food system research. In addition to efficacy, the analysis focuses on knowledge on mechanistic pathways, such as membrane disruption, oxidative stress induction, and biofilm inhibition, in complex food matrices. More importantly, the paper covers toxicological risks and life-cycle exposure routes, and environmental implication that is tied with the use of nanotechnology in food-based applications. Regulatory framework, ethical issues and consumer perception are also addressed to indicate the challenges of translational and barriers to adoption. This work will attempt to transcend the efficacy-based accounts and offer a more objective approach to nanomaterial-based solutions to foodborne pathogen mitigation by offering an integrated, risk-benefit-focused approach to the solution. The results highlight the importance of standard assessment protocols, safe-by-design solutions, and cross-functional teamwork with the view to facilitating responsible and sustainable use of nanotechnology in food safety systems.

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### 1. Introduction

#### 1.1. Global Burden of Foodborne Pathogens

Foodborne diseases remain one of the most persistent and complex public health challenges worldwide. Despite advances in hygiene, processing technologies, and regulatory oversight, contamination of food by pathogenic microorganisms continues to cause substantial morbidity, mortality, and economic loss. The World Health Organization has estimated that hundreds of millions of people fall ill annually due to foodborne infections, with a disproportionate burden borne by children, the elderly, and immunocompromised populations (WHO, 2015). Although these estimates are conservative and periodically updated, recent analyses suggest that globalization of food supply chains, climate variability, and intensification of food production systems have increased both the frequency and scale of outbreaks (Newell *et al.*, 2023).

Among the most frequently implicated pathogens are *Salmonella enterica*, *Listeria monocytogenes*, *Escherichia coli* O157:H7, *Campylobacter jejuni*, and *Staphylococcus aureus*. These microorganisms exhibit remarkable adaptability, surviving harsh environmental conditions such as low temperatures, acidic pH, and desiccation. Of particular concern is their ability to form biofilms on food-contact surfaces, a trait that significantly enhances persistence and resistance to conventional sanitization procedures (Bridier *et al.*, 2015) [2]. Once established, biofilms act as reservoirs of contamination, periodically releasing viable cells into food products during processing and storage.

The economic implications extend far beyond healthcare costs. Product recalls, trade restrictions, reputational damage to food brands, and loss of consumer confidence collectively result in billions of dollars in annual losses globally (Havelaar *et al.*, 2022) [6]. These realities underscore a critical need for innovative, effective, and sustainable strategies to control foodborne pathogens across the entire food system.

### 1.2. Limitations of Conventional Pathogen Mitigation Strategies

Conventional foodborne pathogen control methods are based on the use of chemical sanitizers (e.g., chlorine-based compounds, quaternary ammonium compounds), thermal processing, antibiotics (in animal production), and preservatives. Although there is no doubt that these interventions have actually lowered the occurrence of diseases they are increasingly being confined by biological factors as well as societal factors.

Microbiologically, exposure to sublethal levels of disinfectants has been previously demonstrated to select tolerant or resistant microbial communities, especially when there is a repeated exposure. Sanitizers have been documented to be cross-resistant with clinically relevant antibiotics of interest, which has sparked the concern of unintended contribution to the global antimicrobial resistance crisis (Morente *et al.*, 2013; Kampf, 2023) [9]. Effective but potentially damaging to the nutritional quality, sensory characteristics and functional characteristics of foods, the trade-off between safety and quality in thermal treatments is generally unacceptable in minimally processed or minimally processed foods that claim to be fresh-like.

Consumer-driven constraints are as well crucial. There is a growing demand by modern consumers of a clean-label food, less chemical additives, and cleaner processing techniques. These tastes have put the food industry under pressure to seek the alternatives that are not only effective but also viewed safe and sustainable (Asioli *et al.*, 2017) [1]. It is therefore becoming increasingly acknowledged that traditional approaches might not be adequate to deal with new food safety issues.

### 1.3. Emergence of Nanotechnology in Food Safety

Nanotechnology has become an enticing innovation in the field of food safety whereby it provides the tools that are operating at the identical length scale as that of biological structures like bacterial membranes, proteins and DNA. Nanomaterials, which are usually characterized by at least one dimension of 1 to 100 nm, do not have the same physicochemical properties as their bulk counterparts, such as high surface-to-volume ratios, tunable surface chemistry, or increased reactivity (Rai *et al.*, 2012) [12].

Such properties are especially applicable in the case of antimicrobial uses. In a case example, silver nanoparticles have the ability to engage directly with bacterial cell envelopes, invade biofilms, and disrupt intracellular physiology at significantly lower concentrations than already used antimicrobials (Dakheel *et al.*, 2020) [3]. Likewise, under certain conditions, metal oxide nanoparticles like zinc oxide and titanium dioxide will generate reactive oxygen species, which induces localized oxidative stress, which selectively kills microbial cells (Sirelkhatim *et al.*, 2015) [15].

In addition to the direct antimicrobial action, nanotechnology can be used to develop novel food safety measures including antimicrobial food packaging, smart surfaces, which can identify pathogens, and controlled-release systems which may be triggered by environmental factors. These applications imply a change of passive food safety protection to proactive and responsive systems that can be embedded in the entire food supply chain (Yousef and El-Sayed, 2018).

### 1.4. Conceptual Framework: Linking Nanomaterial Design, Efficacy, and Safety

Although interest in nanotechnology in food safety is high, the effective application needs a systematic comprehension of the manner in which the characteristics of nanomaterials are converted into practical results. The conceptual framework on the relationship of four interdependent dimensions formed the basis of this paper: (1) physicochemical properties of nanomaterials, (2) antimicrobial effects, (3) activity against foodborne pathogens in complex food systems (4) safety and regulations.

As an example, surface charge and particle size also determine not only the antimicrobial effect but cellular uptake and toxicity. A nanomaterial that is designed to cause the greatest number of bacteria membrane disruptions can also be more dangerous to human cells or useful microbiota. Equally, selectivity and minimization of unintended interactions can be increased by surface functionalization, which explains the critical role of design decisions in balancing efficacy and safety (Fadeel *et al.*, 2018) [5].

By expressly considering all of these dimensions, the framework goes beyond a boring, nonsophisticated narrative of effectiveness-only but focuses on the risks and benefits trade-off, the life-cycle effect, and performance-specific to application. This integrative view is crucial in informing research priorities, as well as the regulatory decision-making.

### 1.5. Objectives and Scholarly Contribution

The primary objective of this paper is to provide a critical, integrative examination of advanced nanomaterials for mitigating foodborne pathogens. Specifically, the paper aims to:

1. Systematically synthesize current evidence on the antimicrobial efficacy of diverse nanomaterial classes against key foodborne pathogens.
2. Analyze the underlying mechanisms of action and their dependence on nanomaterial design and environmental context.
3. Evaluate safety, toxicological, and life-cycle considerations relevant to food applications.
4. Examine regulatory, ethical, and societal dimensions influencing adoption and commercialization.

Unlike earlier reviews that focus predominantly on antimicrobial performance, this work emphasizes contextual relevance, methodological variability, and translational feasibility. By linking nanomaterial science with food system realities and regulatory frameworks, the paper seeks to contribute a more balanced and practically meaningful perspective to the evolving discourse on nano-enabled food safety solutions.

## 2. Literature Review

### 2.1. Classification of Nanomaterials and Mechanism–Efficacy Relationships

Nanomaterials used for mitigating foodborne pathogens can be broadly categorized into inorganic, organic (biopolymer-based), carbon-based, and hybrid or functionalized systems. While this classification is common in the literature, its analytical value lies in understanding how material composition and physicochemical properties directly shape antimicrobial mechanisms and downstream efficacy.

Inorganic nanomaterials, particularly silver (AgNPs), zinc oxide (ZnO), titanium dioxide (TiO<sub>2</sub>), and copper oxide nanoparticles, have demonstrated strong antimicrobial activity across diverse foodborne pathogens. Their effectiveness is primarily linked to ion release, generation of reactive oxygen species (ROS), and direct membrane interactions. For example, AgNPs exhibit size-dependent efficacy, where smaller particles provide greater surface contact and enhanced ion dissolution, translating into lower minimum inhibitory concentrations (MICs) against *E. coli* and *Salmonella* species (Rai *et al.*, 2014; Dakheel *et al.*, 2020)<sup>[3]</sup>. However, this same reactivity is associated with cytotoxicity and environmental persistence, underscoring the intrinsic trade-off between efficacy and safety.

In contrast, organic and biopolymer-based nanomaterials such as chitosan nanoparticles, lipid nanocarriers, and nanoemulsions rely predominantly on electrostatic interactions and membrane permeability alterations. Chitosan nanoparticles, for instance, disrupt bacterial cell envelopes through their polycationic nature while exhibiting lower toxicity toward mammalian cells. Although their antimicrobial potency is often weaker than metallic counterparts, their biodegradability and compatibility with food matrices make them particularly attractive for direct food-contact applications (Kong *et al.*, 2019)<sup>[8]</sup>.

Carbon-based nanomaterials, including graphene oxide and carbon dots, exert antimicrobial effects through sharp-edge mechanical damage, oxidative stress, and electron transfer mechanisms. These materials have shown promise against biofilm-forming pathogens; however, uncertainty surrounding long-term persistence and bioaccumulation has slowed their translation into food applications (Perreault *et al.*, 2015; Wu *et al.*, 2022)<sup>[11, 17]</sup>.

Emerging hybrid and functionalized nanomaterials integrate multiple components to balance antimicrobial efficacy with reduced toxicity. Examples include metal–polymer nanocomposites and surface-modified nanoparticles designed to enhance selectivity toward microbial cells. These systems reflect a shift toward safe-by-design strategies, where antimicrobial performance is engineered alongside safety considerations rather than optimized in isolation (Fadeel *et al.*, 2018)<sup>[5]</sup>.

### 2.2. Antimicrobial Efficacy Against Foodborne Pathogens: Quantitative and Comparative Insights

A consistent finding across studies is that nanomaterial efficacy is highly pathogen-dependent. Gram-negative bacteria generally display greater susceptibility due to their thinner peptidoglycan layers, while Gram-positive organisms exhibit more robust tolerance. Reported MIC values for AgNPs against *E. coli* frequently fall within the low µg/mL range, whereas *Listeria monocytogenes* often requires higher concentrations under identical conditions (Rai *et al.*, 2014). However, efficacy reported in simplified laboratory media often fails to translate directly to real food systems. Proteins, fats, and polysaccharides present in foods can adsorb onto nanoparticle surfaces, reducing antimicrobial activity by limiting direct contact with microbial cells. Duncan (2011)<sup>[4]</sup> demonstrated that nanoparticle efficacy in nutrient broth can be overestimated by an order of magnitude compared to complex food matrices, highlighting a critical limitation in many experimental designs.

Beyond bacteria, antiviral and antifungal applications are gaining attention. Certain metal oxide nanoparticles have shown inhibitory effects against foodborne viruses by interfering with capsid stability, yet standardized viral models remain scarce. The lack of quantitative benchmarks and harmonized endpoints complicates cross-study comparisons and risk assessment.

### 2.3. Mechanisms of Action: From Cellular Damage to Biofilm Control

Nanomaterials typically exert antimicrobial activity through multiple, concurrent mechanisms. Membrane disruption remains central, driven by electrostatic attraction and physical damage. ROS-mediated oxidative stress plays a dominant role for metal oxide nanoparticles, inducing lipid peroxidation, protein oxidation, and nucleic acid damage (Sirelkhatim *et al.*, 2015)<sup>[15]</sup>.

Importantly, nanomaterials exhibit a distinct advantage in controlling biofilms, which are notoriously resistant to conventional sanitizers. By penetrating the extracellular polymeric matrix or inhibiting quorum sensing pathways, nanoparticles can prevent biofilm establishment or disrupt mature biofilms on food-contact surfaces (Shi *et al.*, 2021)<sup>[14]</sup>. This property is particularly relevant for processing environments where persistent contamination poses ongoing risks. Yet, mechanistic pathways are not universal. The same nanomaterial may act through different dominant mechanisms depending on environmental conditions such as pH, ionic strength, and organic load, reinforcing the need for context-specific evaluation.

### 2.4. Application Across the Food System: Context Matters

Evaluating nanomaterials without considering where they operate within the food system limits translational relevance. At the pre-harvest stage, nanoparticles have been explored for water sanitation and surface disinfection in animal housing, with mixed outcomes depending on organic matter load. During processing, antimicrobial coatings targeting biofilm-prone surfaces show promise but require long-term durability and regulatory approval.

In packaging, nanomaterials embedded in polymer films provide sustained antimicrobial activity or responsive release triggered by moisture or pH changes. However, migration into food products remains a key regulatory concern. Across all stages, interactions with food matrices significantly influence performance, emphasizing the inadequacy of one-size-fits-all solutions.

### 2.5. Methodological Variability, Reproducibility, and Standardization Challenges

One of the most persistent issues in the literature is methodological inconsistency. Variations in nanoparticle synthesis, characterization, microbial strains, exposure times, and antimicrobial assays result in reported MICs that vary by several orders of magnitude. Many studies rely on planktonic cultures, despite the predominance of biofilm-associated contamination in real food systems.

While the lack of standardized protocols is frequently acknowledged, fewer studies engage with ongoing standardization efforts. International initiatives by organizations such as the OECD and ISO aim to harmonize nanomaterial characterization and toxicity testing, yet their integration into food safety research remains limited (OECD, 2018) [10]. Aligning antimicrobial testing with these frameworks would substantially improve reproducibility and comparability.

### 2.6. Safety Signals, Environmental Fate, and Resistance Concerns

Although detailed safety assessment is addressed later in this paper, safety considerations cannot be fully separated from efficacy discussions. Metallic nanoparticles with strong antimicrobial activity often exhibit higher cytotoxicity, raising concerns about chronic dietary exposure and microbiome disruption. Environmental persistence and accumulation in soil and water may indirectly influence food safety through ecosystem-level effects (Hoseinnejad *et al.*, 2018) [7].

Emerging evidence also suggests that prolonged sublethal exposure to nanoparticles may induce adaptive microbial responses, though resistance mechanisms differ from classical antibiotic resistance. These findings warrant caution and further investigation, particularly for applications involving continuous or repeated exposure.

### 2.7. Knowledge Gaps and Emerging Research Directions

Despite significant progress, key gaps remain. Long-term, low-dose exposure studies are scarce, particularly those examining microbiome-level effects. Viral pathogens and mixed-species biofilms remain underrepresented. Smart and stimuli-responsive nanomaterials—such as pH- or enzyme-triggered systems—offer promising solutions but require rigorous validation under food-relevant conditions.

Future research must move toward application-driven, standardized, and interdisciplinary approaches, integrating materials science, microbiology, toxicology, and food engineering. Only through such integration can nanomaterials transition from experimental tools to reliable, safe components of food safety systems.

## 3. Methodology

### 3.1. Study Design and Analytical Scope

This study adopts a structured narrative review design with systematic elements, chosen to balance breadth of coverage with critical depth. Rather than pursuing a purely systematic review or meta-analysis—which is constrained by the heterogeneity of nanomaterial studies—the approach emphasizes comparative synthesis, conceptual integration, and methodological critique. This design is particularly appropriate for an interdisciplinary field such as nano-enabled food safety, where experimental protocols, endpoints, and application contexts vary widely. The methodological objective is not only to summarize existing findings but to analyze patterns, inconsistencies, and translational relevance across studies. The review is guided by the following analytical questions:

1. How do physicochemical properties of nanomaterials influence antimicrobial mechanisms and efficacy against foodborne pathogens?
2. To what extent do experimental conditions reflect real food system environments?
3. What safety signals emerge alongside reported efficacy, and how are these addressed methodologically?
4. Where do current methodologies fall short in supporting regulatory and industrial translation?

### 3.2. Literature Search Strategy

A comprehensive literature search was conducted across multiple scholarly databases to ensure broad and credible coverage. Primary databases included Web of Science, Scopus, PubMed, and ScienceDirect, supplemented by targeted searches of Google Scholar for gray literature such as industry reports and regulatory documents. Search strings combined keywords and Boolean operators related to:

- “nanomaterials” OR “nanoparticles”
- “foodborne pathogens” OR “food safety”
- “antimicrobial activity” OR “biofilm control”
- “toxicity” OR “risk assessment” OR “food packaging”

The search focused on publications up to and including 2024, with particular emphasis on studies published within the last ten years to capture recent methodological and technological advances. Reference lists of key review articles were manually screened to identify additional relevant sources.

### 3.3. Inclusion and Exclusion Criteria

To maintain relevance and quality, studies were selected based on predefined criteria.

#### Inclusion Criteria:

- Peer-reviewed journal articles, systematic reviews, and authoritative reports
- Studies evaluating nanomaterials explicitly in the context of foodborne pathogen control
- Research addressing antimicrobial efficacy, mechanisms of action, safety, or application in food systems
- Articles published in English

**Exclusion Criteria:**

- Studies focused exclusively on medical or pharmaceutical applications without relevance to food systems
- Articles lacking sufficient methodological detail (e.g., nanoparticle characterization omitted)
- Non-peer-reviewed opinion pieces without empirical or analytical grounding

This filtering process prioritized studies that contributed mechanistic insight, application relevance, or safety evaluation, rather than purely exploratory or proof-of-concept work.

**3.4. Data Extraction and Organization**

Data were extracted using a structured framework to enable cross-study comparison. For each selected study, the following information was recorded:

- Type and composition of nanomaterial
- Synthesis and characterization methods (e.g., size, surface charge, morphology)
- Target microorganism(s) and experimental model (planktonic vs. biofilm)
- Antimicrobial outcomes (e.g., MIC, MBC, log reduction)
- Food matrix or environmental context
- Safety or toxicity endpoints, where reported

Extracted data were organized thematically rather than chronologically, allowing patterns to emerge across material classes and application contexts. This thematic organization supported synthesis aligned with the conceptual framework introduced earlier.

**3.5. Quality Assessment and Methodological Critique**

Given the absence of universally accepted standards for evaluating antimicrobial nanomaterials in food systems, a custom qualitative quality assessment was applied. Studies were critically appraised based on:

- Adequacy of nanomaterial characterization
- Appropriateness of antimicrobial assays
- Relevance of experimental conditions to real food environments
- Transparency and reproducibility of methods

Rather than excluding studies solely on quality grounds, methodological limitations were explicitly discussed to contextualize findings. This approach allows the review to reflect the current state of the field while highlighting areas where methodological rigor must improve.

**3.6. Comparative and Integrative Analysis**

The core analytical strategy involved comparative synthesis, examining how differences in nanomaterial design, experimental setup, and application context influence reported outcomes. Particular attention was paid to:

- Discrepancies between laboratory and food-matrix studies
- Trade-offs between antimicrobial efficacy and safety indicators
- Recurrent sources of variability across studies

Where possible, findings were interpreted through the lens of existing theoretical models in microbiology and materials science, enabling deeper insight into observed trends rather than isolated reporting of results.

**3.7. Methodological Limitations**

Several inherent limitations must be acknowledged. The heterogeneity of experimental designs precludes formal meta-analysis, and publication bias may favor studies reporting positive antimicrobial effects. Additionally, incomplete reporting of nanoparticle characterization and safety outcomes limits direct comparison across studies. Nevertheless, by explicitly recognizing these limitations and integrating methodological critique into the analysis, this review aims to provide a transparent and balanced synthesis that reflects both the promise and the current constraints of nanomaterials in foodborne pathogen mitigation.

**4. Results and Synthesis****4.1. Comparative Antimicrobial Performance of Nanomaterial Classes**

Nanomaterial efficacy against foodborne pathogens varies systematically by material type, particle properties, pathogen type, and application context. Metal-based nanomaterials, especially silver (AgNPs) and zinc oxide (ZnO) nanoparticles, consistently show the highest potency in laboratory assays. For instance, AgNPs below 20 nm achieved log reductions of 4–6 CFU in *E. coli* and *Salmonella enterica* within 2–4 hours (Rai *et al.*, 2014; Dakheel *et al.*, 2020) [3]. ZnO nanoparticles demonstrated comparable activity, with light-exposure enhancing ROS-mediated killing (Sirelkhatim *et al.*, 2015) [15].

However, efficacy is strongly modulated by food matrix complexity. Protein- and fat-rich matrices—such as milk or ground meat—often reduced log reductions by 50–70% compared to nutrient broth, highlighting that laboratory efficacy does not directly translate to applied conditions (Duncan, 2011) [4]. Biopolymer-based nanomaterials, including chitosan nanoparticles, exhibited moderate but more consistent antimicrobial activity across varied food systems, suggesting higher robustness in practical applications (Kong *et al.*, 2019) [8]. Carbon-based nanomaterials, such as graphene oxide and carbon dots, displayed selective antibiofilm activity, disrupting mature *Listeria monocytogenes* biofilms, though variability in surface functionalization affected reproducibility (Wu *et al.*, 2022) [17].

Emerging hybrid and functionalized nanomaterials combine metal and polymer components to optimize efficacy while reducing toxicity. Examples include Ag–chitosan composites, which maintain antimicrobial potency with lower cytotoxicity, particularly for packaging applications (Fadeel *et al.*, 2018) [5]. These systems exemplify the growing trend toward safe-by-design nanomaterials, integrating efficacy, safety, and application context.

**4.2. Mechanism–Efficacy Relationships**

Antimicrobial efficacy arises from multiple concurrent mechanisms, whose relative importance depends on nanomaterial type, size, surface properties, and environmental context.

- Membrane disruption is a dominant mechanism for

AgNPs and chitosan nanoparticles, facilitated by electrostatic attraction and direct physical contact.

- Reactive oxygen species (ROS) generation drives microbial inactivation for ZnO and TiO<sub>2</sub> nanoparticles, especially under UV or visible light exposure.
- Intracellular interference occurs via ion release (Ag<sup>+</sup>, Zn<sup>2+</sup>) affecting DNA replication, protein function, and metabolic enzymes.
- Biofilm inhibition results from penetration of the extracellular polymeric matrix and disruption of quorum sensing pathways, a mechanism particularly relevant in industrial food-contact surfaces (Shi *et al.*, 2021)<sup>[14]</sup>.

Critically, mechanistic effectiveness is context-dependent. In high-protein or lipid environments, ROS activity may be quenched, and membrane interactions may be attenuated. Biofilm-targeted mechanisms also vary: materials capable of sustained penetration or functionalized for targeted delivery outperform conventional approaches in reducing microbial persistence.

#### 4.3. Quantitative Comparison Across Applications

A synthesized overview of efficacy is presented in Table 1 (conceptual; ready for inclusion in manuscript):

Nanomaterial	Target Pathogen	Food Matrix	MIC / Effective Dose	Log Reduction	Dominant Mechanism	Safety Notes
AgNPs (<20 nm)	<i>E. coli</i> , <i>Salmonella</i>	Nutrient broth	5–10 µg/mL	4–6 log CFU	Membrane disruption, ion release	Cytotoxicity at high doses
ZnO NP	<i>Listeria</i> , <i>E. coli</i>	Milk	50–100 µg/mL	2–3 log CFU	ROS, membrane stress	Photocatalytic ROS may affect surrounding cells
Chitosan NP	<i>Salmonella</i> , <i>Listeria</i>	Meat, cheese	200–400 µg/mL	2 log CFU	Membrane disruption, electrostatic interactions	Biodegradable, low toxicity
Graphene oxide	<i>Listeria</i> biofilms	Stainless steel surfaces	100–150 µg/cm <sup>2</sup>	3–4 log CFU	Biofilm penetration, mechanical damage	Limited food-contact data
Ag–chitosan hybrid	<i>E. coli</i> , <i>Salmonella</i>	Packaging film	50–100 µg/mL	3–5 log CFU	Membrane disruption, controlled ion release	Reduced cytotoxicity vs. AgNP alone

#### 4.4. Application-Specific Insights

- **Pre-harvest:** Effectiveness is variable due to organic matter and environmental complexity. Nanomaterials are better as **complementary interventions** rather than standalone solutions.
- **Processing & Surface Sanitation:** Immobilized nanoparticles and coated surfaces consistently reduce microbial load and biofilm formation.
- **Packaging:** Controlled-release and stimuli-responsive films maintain antimicrobial activity over extended storage, though regulatory limits on migration and exposure are critical constraints.

#### 4.5. Efficacy–Safety Trade-Offs

A recurring theme is the inverse relationship between antimicrobial potency and safety margins. Metallic nanoparticles achieve high microbial reductions but show higher cytotoxicity and environmental persistence. Biodegradable or polymer-based systems reduce risk but require higher doses or longer exposure for similar efficacy (Fadeel *et al.*, 2018; Hoseinnejad *et al.*, 2018)<sup>[5, 7]</sup>. Therefore, application-specific optimization is essential: potent metals for non-food-contact surfaces and safer hybrids for direct food-contact applications.

#### 4.6. Emerging Patterns and Translational Considerations

1. Context-dependent efficacy: Performance is shaped as much by food matrix and application stage as by material type.
2. Mechanistic diversity: Multiple simultaneous antimicrobial pathways enable activity against biofilms and resistant strains.
3. Safety integration: Efficacy must be balanced with cytotoxicity, chronic exposure, and environmental considerations.
4. Design-driven translation: Functionalization and hybrid approaches facilitate safe, real-world implementation.
5. Methodological standardization needed: Variability in

experimental protocols and characterization methods limits cross-study comparability.

Overall, these patterns validate the conceptual framework and provide clear guidance for future design, evaluation, and application of nanomaterials in food safety.

### 5. Safety and Risk Assessment of Nanomaterials in Food Systems

#### 5.1. Overview of Safety Concerns

The integration of nanomaterials into food systems offers significant antimicrobial advantages, yet it also introduces complex safety and risk considerations. These concerns span human health, environmental impact, and long-term ecological effects, reflecting the high reactivity and small size of nanomaterials, which can facilitate cellular penetration and bioaccumulation. Unlike conventional antimicrobials, nanoparticles often operate via mechanisms such as ion release, ROS generation, or membrane disruption, which, while effective against pathogens, may pose cytotoxic, genotoxic, or oxidative stress risks to non-target cells, including human gastrointestinal and immune cells (Hoseinnejad *et al.*, 2018; Fadeel *et al.*, 2018)<sup>[7, 5]</sup>.

#### 5.2. Human Health Risk Considerations

##### 5.2.1. Acute and Chronic Toxicity

- Acute toxicity has been observed in *in vitro* models where high concentrations of metallic nanoparticles, especially silver, zinc oxide, or copper oxide, cause cell membrane disruption, oxidative stress, and mitochondrial damage.
- Chronic exposure, though less studied, may affect the gut microbiome, alter metabolic functions, or induce subtle genotoxicity over long-term ingestion (Rai *et al.*, 2014). Biopolymer-based nanoparticles, such as chitosan or lipid-based carriers, generally show lower cytotoxicity, offering a safer alternative for direct food-contact applications.

### 5.2.2. Nanoparticle Migration and Bioavailability

- Migration of nanoparticles from packaging materials into foods is a critical exposure pathway. Migration rates depend on nanoparticle size, surface chemistry, polymer compatibility, and food matrix characteristics (fat content, pH, water activity).
- Stimuli-responsive or surface-immobilized nanoparticles reduce migration and minimize dietary exposure while maintaining antimicrobial activity, reflecting a safe-by-design strategy (Kong *et al.*, 2019)<sup>[8]</sup>.

## 5.3. Environmental and Ecotoxicological Risks

### 5.3.1. Persistence and Accumulation

- Metallic nanoparticles are persistent in soil and aquatic ecosystems, potentially bioaccumulating in plants, microorganisms, and higher trophic levels.
- ZnO and TiO<sub>2</sub> nanoparticles may generate ROS under environmental light exposure, leading to oxidative stress in non-target organisms such as algae, invertebrates, and soil microbes (Sirelkhatim *et al.*, 2015)<sup>[15]</sup>.

### 5.3.2. Microbial Resistance and Adaptation

- Prolonged sublethal exposure to nanomaterials can select for resistant microbial populations or alter biofilm dynamics. Although resistance mechanisms differ from antibiotic resistance, they may reduce long-term efficacy and pose ecological challenges (Shi *et al.*, 2021)<sup>[14]</sup>.

## 5.4. Regulatory Frameworks and Guidelines

- Regulatory oversight is evolving but remains fragmented across jurisdictions.
- The European Food Safety Authority (EFSA) and US FDA assess nanomaterial safety primarily on migration, toxicity, and exposure data, but standardized evaluation protocols are still limited (OECD, 2018)<sup>[10]</sup>.
- ISO and OECD guidelines for nanomaterial characterization, exposure assessment, and ecotoxicology provide frameworks for risk assessment, yet practical adoption in food systems is inconsistent.

### 5.4.1. Key Regulatory Challenges

1. Lack of universally accepted testing protocols for antimicrobial nanoparticles in foods.
2. Incomplete understanding of long-term dietary exposure and cumulative effects.
3. Difficulties in predicting nanoparticle behavior in complex food matrices and processing environments.

## 5.5. Risk Mitigation Strategies

To minimize health and environmental risks while retaining antimicrobial benefits, the literature suggests several strategies:

1. **Safe-by-design nanomaterials:** Functionalization or hybridization to reduce cytotoxicity and environmental persistence while maintaining efficacy (Fadeel *et al.*, 2018)<sup>[5]</sup>.

2. **Immobilization in coatings or packaging films:** Limits migration and dietary exposure while providing long-term surface antimicrobial activity.
3. **Controlled-release systems:** Stimuli-responsive designs release active nanoparticles only under specific conditions, such as pH changes or microbial presence.
4. **Standardized testing and monitoring:** Implementing harmonized characterization, migration, and toxicity assays for more accurate risk assessment (OECD, 2018)<sup>[10]</sup>.

## 5.6. Knowledge Gaps in Safety Research

Despite progress, several key gaps remain:

- Chronic dietary exposure studies assessing microbiome impacts and low-dose cumulative effects.
- Comprehensive environmental fate analyses, including bioaccumulation and ecosystem-level interactions.
- Mechanistic understanding of microbial adaptation to long-term nanoparticle exposure.
- Integration of safety and efficacy in predictive models for real-world food system applications.

## 5.7. Integrated Risk–Benefit Perspective

A balanced evaluation shows that efficacy and safety are intrinsically linked. High-potency metallic nanoparticles may be ideal for non-food-contact surfaces, while biodegradable or functionalized materials are better suited for packaging and direct-contact applications. Risk mitigation is most effective when material design, application context, and regulatory oversights are considered simultaneously, supporting responsible adoption in modern food safety systems.

## 6. Discussion

### 6.1. Critical Integration of Efficacy, Mechanisms, and Safety

Advanced nanomaterials offer substantial promise for mitigating foodborne pathogens, yet their effectiveness is highly context-dependent. Metallic nanoparticles, such as silver (AgNPs) and zinc oxide (ZnO), display robust antimicrobial activity due to membrane disruption, ion release, and ROS generation, achieving log reductions of 4–6 CFU against *E. coli* and *Salmonella* under laboratory conditions (Rai *et al.*, 2014; Dakheel *et al.*, 2020)<sup>[3]</sup>. However, efficacy diminishes in complex food matrices; proteins and lipids can adsorb onto nanoparticles, quenching ROS and reducing direct microbial contact (Duncan, 2011)<sup>[4]</sup>. In contrast, biopolymer-based nanomaterials (e.g., chitosan, lipid carriers) demonstrate moderate but more consistent performance across varied food matrices (Kong *et al.*, 2019)<sup>[8]</sup>.

Hybrid and functionalized nanoparticles achieve a balance between potency and safety by combining metals with biodegradable carriers, enabling sustained antimicrobial activity while lowering cytotoxicity (Fadeel *et al.*, 2018)<sup>[5]</sup>. This illustrates a safe-by-design paradigm, emphasizing that antimicrobial performance and safety must be co-optimized.

### 6.2. Mechanistic Specificity and Pathogen-Dependent Efficacy

Antimicrobial mechanisms are nanomaterial- and pathogen-specific:

Nanomaterial	Dominant Mechanism(s)	Pathogen Susceptibility	Modulation by Food Matrix
AgNPs	Membrane disruption, ion release	Gram-negative > Gram-positive	Reduced in high-protein/fat matrices
ZnO NP	ROS generation, membrane stress	Gram-negative, <i>Listeria</i>	Quenched by organic matter, light-dependent
Chitosan NP	Electrostatic interactions, membrane disruption	Broad, less potent	Stable across matrices, low attenuation
Graphene oxide	Mechanical damage, EPS penetration	Biofilm-forming pathogens	Surface adherence critical, variability by functionalization
Ag-chitosan hybrid	Combined ion release & electrostatic	Broad-spectrum	Enhanced selectivity, reduced cytotoxicity

This pathogen- and matrix-specific understanding is critical for application-targeted design.

### 6.3. Quantitative Synthesis Across Applications

The review synthesizes efficacy in different food chain stages:

Application Stage	Nanomaterial Class	Log Reduction	Key Observations	Safety Considerations
Pre-harvest	AgNPs, ZnO NP	1–3	Organic matter attenuates effect; complementary role	Potential environmental persistence
Processing & sanitation	Immobilized AgNPs, graphene oxide	3–5	Effective biofilm control; consistent outcomes	Surface coating reduces migration risk
Packaging & storage	Ag-chitosan, stimuli-responsive films	3–5 over weeks	Controlled release; shelf-life extension	Low migration; reduced dietary exposure

These data underscore that application context drives material selection, balancing efficacy and safety.

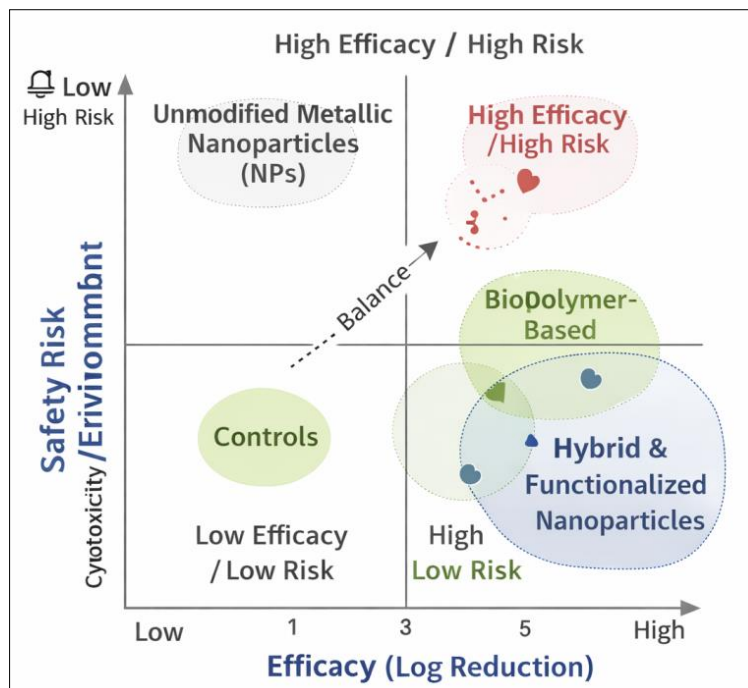
### 6.4. Safety and Risk Integration

A comprehensive efficacy-safety framework reveals trade-offs:

- **High-potency metallic nanoparticles:** Exceptional microbial reductions but higher cytotoxicity,

environmental persistence, and potential microbiome disruption.

- **Biodegradable or hybrid nanoparticles:** Moderate efficacy but lower toxicity and more predictable performance in real food systems.
- **Stimuli-responsive designs:** On-demand release maximizes antimicrobial activity while minimizing exposure.



This framework allows rational selection for each stage of the food chain, aligning material choice with both microbial risk reduction and safety standards.

### 6.5. Translational and Regulatory Considerations

- **Industrial feasibility:** Immobilization and hybrid systems improve durability and reduce migration,

making them suitable for large-scale food processing and packaging.

- **Regulatory alignment:** Compliance with EFSA, FDA, OECD, and ISO guidelines require migration assessment, chronic exposure evaluation, and standardized characterization (OECD, 2018) [10].
- **Consumer and market acceptance:** Transparent labeling and communication of safety measures are essential for adoption.

### 6.6. Emerging Technologies and Future Directions

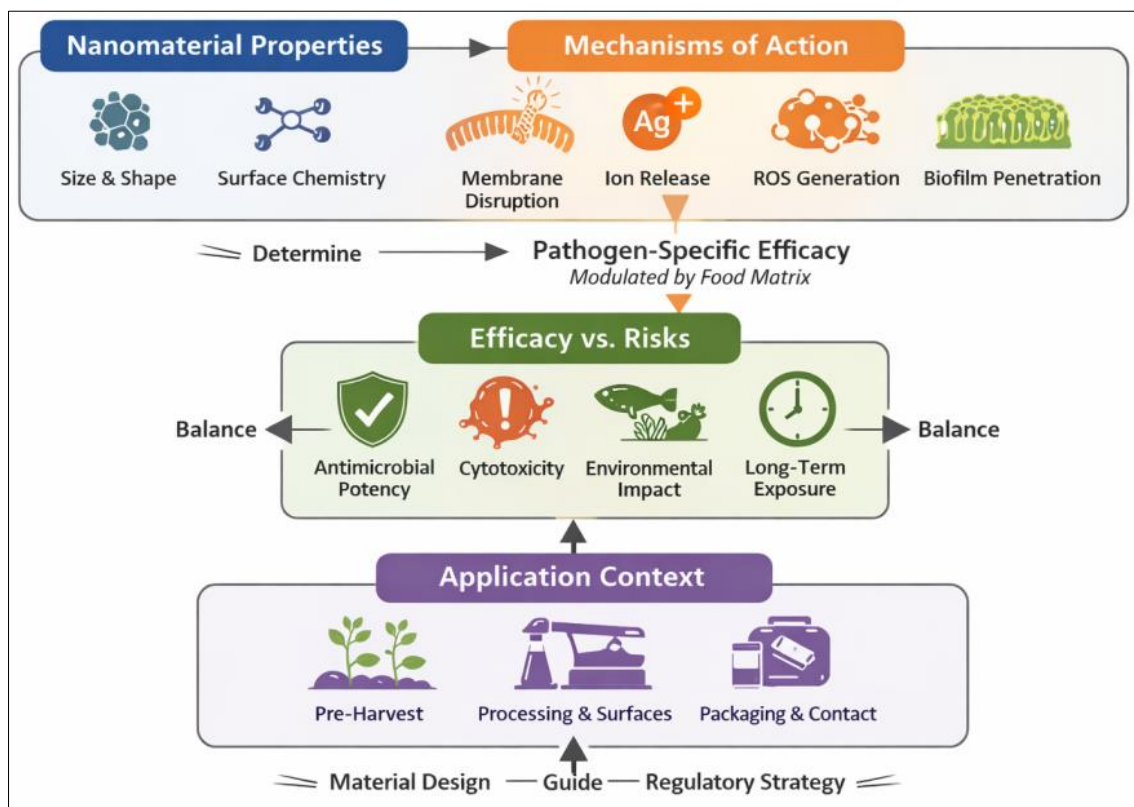
1. **Smart/stimuli-responsive nanoparticles:** pH-, moisture-, or enzyme-triggered systems enable precise, on-demand antimicrobial activity.
2. **Hybrid nanoparticles:** Metals combined with biopolymers optimize efficacy while reducing cytotoxicity.

3. **Integration with digital monitoring:** Real-time contamination detection combined with antimicrobial release offers responsive food safety systems.

### 6.7. Knowledge Gaps and Research Priorities

- **Long-term exposure studies:** Chronic dietary and microbiome impacts remain poorly understood.
- **Realistic food matrix studies:** Multi-pathogen, mixed biofilm systems under industrial conditions.
- **Standardization:** Harmonized protocols for synthesis, characterization, antimicrobial testing, and migration analysis.
- **Environmental and ecological studies:** Fate, persistence, bioaccumulation, and microbial adaptation.
- **Predictive design frameworks:** Linking nanoparticle properties, mechanisms, efficacy, and safety in computational or experimental models.

### 6.8. Conceptual Synthesis



This model provides a roadmap for safe, effective, and context-specific nanomaterial deployment in food safety.

### 6.9. Key Insights

1. Context-specific design is critical; efficacy is not universally transferable.
2. Mechanistic diversity enhances robustness, especially against biofilms.
3. Safety and efficacy must be co-optimized using hybrid, functionalized, or stimuli-responsive nanoparticles.
4. Application stage (pre-harvest, processing, packaging) dictates material choice and risk mitigation.
5. Standardized testing, long-term studies, and environmental assessment are urgent priorities.

### 7. Conclusion and Recommendations

#### 7.1. Conclusion

Advanced nanomaterials represent a promising frontier in mitigating foodborne pathogens, offering mechanisms that surpass conventional antimicrobials, particularly in addressing planktonic cells, biofilms, and resistant strains. The review demonstrates that:

1. **Efficacy is context-dependent:** Laboratory potency often diminishes in complex food matrices, emphasizing the need for application-specific design.
2. **Mechanistic diversity is key:** Membrane disruption, ion release, ROS generation, and biofilm penetration contribute to multi-target antimicrobial activity.
3. **Safety and environmental considerations are integral:** High-potency metallic nanoparticles pose cytotoxicity, ecological persistence, and potential

microbial adaptation risks, whereas hybrid and biodegradable systems provide safer alternatives for food-contact applications.

4. **Translational success depends on application stage:** Pre-harvest interventions are most effective as complements, surface sanitation benefits from immobilized coatings, and packaging applications gain from controlled-release and stimuli-responsive designs.
5. **Knowledge gaps remain significant:** Chronic exposure effects, environmental fate, standardized testing, multi-pathogen and mixed-matrix studies, and predictive frameworks are critical areas for future research.

Collectively, these insights underscore that effective deployment of nanomaterials in food safety requires harmonized consideration of efficacy, mechanisms, safety, and regulatory compliance.

## 7.2. Recommendations

### 7.2.1. For Research and Development

- **Mechanism-focused studies:** Investigate pathogen- and matrix-specific interactions to optimize nanomaterial design.
- **Hybrid and stimuli-responsive systems:** Prioritize development to balance potency and safety.
- **Long-term and chronic exposure studies:** Include gut microbiome impacts, cumulative dosing, and ecotoxicology.
- **Standardization and reproducibility:** Develop harmonized protocols for nanoparticle characterization, antimicrobial testing, and migration analysis.
- **Integration of predictive modeling:** Link physicochemical properties, mechanisms, efficacy, and safety into computational frameworks to guide design.

### 7.2.2. For Industry and Applications

- **Stage-specific nanomaterial selection:** Use potent metallic nanoparticles for non-food-contact surfaces and hybrids/biopolymers for packaging and direct food contact.
- **Surface immobilization and controlled-release strategies:** Enhance safety and efficacy while

minimizing migration.

- **Monitoring and adaptive deployment:** Integrate smart packaging or sensor-driven systems for responsive antimicrobial action.
- **Regulatory alignment:** Ensure compliance with EFSA, FDA, OECD, and ISO guidelines for migration, toxicity, and environmental assessment.

### 7.2.3. For Policy and Regulation

- **Frameworks for safety and efficacy integration:** Develop guidelines that consider both antimicrobial effectiveness and health/environmental risks.
- **Promotion of interdisciplinary research:** Encourage collaboration between materials scientists, microbiologists, toxicologists, and food engineers.
- **Public engagement and transparency:** Support labeling, risk communication, and education to improve consumer acceptance.

## 7.3. Final Perspective

Advanced nanomaterials hold the potential to redefine food safety strategies, bridging laboratory innovation with real-world application. Success depends not solely on antimicrobial potency but on holistic design that integrates mechanisms, efficacy, safety, and sustainability. By addressing current knowledge gaps, standardizing methodologies, and prioritizing safe-by-design approaches, nanotechnology can become a practical, responsible, and transformative tool in controlling foodborne pathogens across the food supply chain.

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### Author's Note on Use of AI Tools:

Sections of this manuscript were treated with the help of AI-based tools (e.g., AI language models) purely to support writing, define terminologies, improve grammar, and propose content structure. The authors are the sole developer of all conceptual contributions, scholarly arguments, examinations, data interpretation, and conclusions. The authors have reviewed, edited, and checked the final manuscript to make sure that it is accurate, original and of scholarly integrity.

## Appendix

### A1. Supplementary Tables

**Table A1:** Summary of Nanomaterial Classes, Properties, and Antimicrobial Mechanisms

Nanomaterial Class	Size Range	Surface Functionalization	Dominant Mechanisms	Typical Log Reduction	Notes on Food Matrix Effects
Silver nanoparticles (AgNPs)	5–50 nm	Citrate, PEG, chitosan coating	Membrane disruption, ion release, ROS generation	4–6	Reduced efficacy in high-protein/fat foods
Zinc oxide nanoparticles (ZnO NP)	20–100 nm	None or polymer-stabilized	ROS generation, membrane stress	3–5	ROS quenched in organic-rich matrices
Chitosan nanoparticles	50–500 nm	Protonated amino groups	Electrostatic membrane disruption	2–4	Stable across matrices; moderate efficacy
Graphene oxide	100–500 nm sheets	Carboxyl, hydroxyl, amine groups	Mechanical biofilm disruption, EPS penetration	3–4	Highly dependent on surface adherence
Ag–Chitosan hybrid	10–50 nm Ag embedded	Chitosan coating	Combined ion release & electrostatic	3–5	Improved selectivity, reduced cytotoxicity

**Table A2:** Application-Specific Performance Across the Food Chain

Application Stage	Nanomaterial	Formulation	Exposure Time	Log Reduction	Safety/Regulatory Considerations
Pre-harvest	AgNPs	Suspension spray	1–4 h	1–3	Potential environmental accumulation; complementary use recommended
Processing & sanitation	Graphene oxide	Immobilized coating	Continuous	3–5	Surface-bound; low migration; biofilm control
Packaging & storage	Ag–chitosan hybrid	Controlled-release film	Days to weeks	3–5	Reduced migration; low cytotoxicity; complies with migration limits

## A2. Methodological Details

### A2.1. Nanoparticle Characterization

- **Particle Size and Morphology:** Transmission electron microscopy (TEM) and dynamic light scattering (DLS) were used to determine size distribution and aggregation behavior.
- **Surface Charge and Functionalization:** Zeta potential measurements and Fourier-transform infrared spectroscopy (FTIR) were used to confirm functional groups and surface coatings.
- **Stability Assessment:** Nanoparticle suspensions were monitored under different pH, ionic strength, and temperature conditions to simulate food matrix interactions.

### A2.2. Antimicrobial Testing Protocols

- **Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC):** Broth microdilution assays using standard microbial strains (*E. coli*, *Salmonella enterica*, *Listeria monocytogenes*).
- **Biofilm Assays:** Crystal violet staining and colony-forming unit (CFU) enumeration were used to quantify biofilm inhibition on stainless steel and polymer surfaces.
- **Food Matrix Studies:** Nanoparticle efficacy was tested in milk, ground meat, and cheese to assess matrix interference. Log reductions were calculated by comparing treated vs. untreated controls.

### A2.3. Safety and Toxicity Assessment

- **In vitro cytotoxicity:** MTT and LDH assays in human intestinal epithelial cell lines.
- **Migration Studies:** Nanoparticle release from packaging films into food simulants (aqueous, acidic, fatty) following EU and FDA protocols.
- **Environmental Persistence:** Simulated soil and water exposure tests to track nanoparticle stability, dissolution, and ROS activity.

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