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Nanoparticle-Enhanced Hand Sanitisers for Prolonged Antimicrobial Action: A Comprehensive Review

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Abstract: Background: The global burden of healthcare-associated infections (HCAIs) and the accelerating emergence of multidrug-resistant (MDR) pathogens have created an urgent need for hand hygiene technologies that surpass the capabilities of conventional alcohol-based sanitisers. While ethanol and isopropanol formulations deliver rapid, broad-spectrum microbial kill, their antimicrobial action ceases entirely upon evaporation — typically within 30 seconds of application — leaving hands unprotected against subsequent microbial exposure. Objective: This review critically examines the scientific basis, mechanisms of action, and formulation potential of nanoparticle-enhanced hand sanitisers as a next-generation approach to prolonged antimicrobial hand hygiene. Methods: A comprehensive literature synthesis was conducted covering peer-reviewed studies on antimicrobial nanoparticles — principally silver (AgNPs), zinc oxide (ZnO-NPs), titanium dioxide (TiO_2-NPs), chitosan (CSNPs), and gold (AuNPs) — with specific reference to their physicochemical properties, antimicrobial mechanisms, minimum inhibitory concentrations, and incorporation into topical sanitiser formulations. Results: Nanoparticles exert antimicrobial activity through multiple simultaneous mechanisms including cell membrane disruption, reactive oxygen species (ROS) generation, DNA strand interference, ribosomal denaturation, ATP synthesis inhibition, biofilm penetration, and sustained release of antimicrobial ions. AgNPs in the 9–15 nm range demonstrated the highest bactericidal efficacy, while ZnO-NPs offered photocatalytic activity and GRAS regulatory status. Critically, the sustained-release of Ag^+ and Zn^{2+} ions from nanoparticle reservoirs provides continuous antimicrobial protection for hours to days post-application — a capability entirely absent in conventional formulations. Efficacy against MDR organisms including MRSA was consistently reported across multiple studies. Conclusion: Nanoparticle-enhanced hand sanitisers represent a scientifically robust, multi-mechanistic advancement in infection control. Challenges including cytotoxicity, environmental impact, and regulatory approval require targeted resolution through green synthesis, biocompatible nano-carrier design, and comprehensive clinical safety profiling before widespread deployment.

Keywords: *Nanoparticles; Hand Sanitiser; Antimicrobial; Silver Nanoparticles; Prolonged Action.*

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I. INTRODUCTION

Hand hygiene is universally recognised as the single most effective measure for preventing the transmission of infectious diseases and reducing the burden of healthcare-associated infections (HCAIs).[1] The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) consistently emphasise hand hygiene as the cornerstone of infection prevention programmes across both community and clinical settings. The COVID-19 pandemic significantly amplified global awareness of hand hygiene, accelerating the demand for effective sanitiser products worldwide.

Conventional alcohol-based hand sanitisers containing 60–95% isopropanol or ethanol are widely used due to their rapid and broad-spectrum antimicrobial activity.[2] However, their mechanism of action — protein denaturation through alcohol — is inherently transient. Upon complete evaporation, typically within 15–30 seconds of application, all antimicrobial activity ceases. This leaves hands vulnerable to re-contamination in high-risk environments such as hospitals, clinics, food processing facilities, and public spaces.

The escalating global crisis of multidrug-resistant (MDR) pathogens, including methicillin-resistant Staphylococcus aureus (MRSA), carbapenem-resistant Enterobacteriaceae, and extensively drug-resistant Pseudomonas aeruginosa, demands the development of novel antimicrobial strategies.[3] Nanoparticles (NPs) have emerged as one of the most promising next-generation

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antimicrobial platforms. Defined as materials with at least one dimension in the range of 1–100 nm, nanoparticles possess unique physicochemical properties — including high surface area-to-volume ratio, tunable surface chemistry, and quantum effects — that confer potent and multi-mechanistic antimicrobial activity not observed in bulk materials.[4]

The concept of nanotechnology, introduced by Richard Feynman in his landmark 1959 lecture 'There's Plenty of Room at the Bottom', has since evolved into a mature scientific discipline with widespread biomedical applications.[1] Among these, the incorporation of antimicrobial nanoparticles into hand hygiene products represents a particularly impactful application. Nanoparticles including silver (AgNPs), zinc oxide (ZnO-NPs), titanium dioxide (TiO_2-NPs), chitosan (CSNPs), and gold (AuNPs) have been extensively studied for their ability to disrupt microbial cell membranes, generate reactive oxygen species (ROS), interfere with intracellular components, and release active antimicrobial ions in a sustained manner.[5]

This review comprehensively examines the types, properties, mechanisms of action, and formulation considerations of nanoparticle-enhanced hand sanitisers, with particular emphasis on their ability to provide prolonged antimicrobial protection. The review also addresses current challenges and future research directions necessary for translation into safe, effective, and commercially viable products.

II. HISTORICAL BACKGROUND

➢ *History of Nanotechnology*

Although nanoparticles have existed in nature and been inadvertently used throughout human history — most notably in Lycurgus Cup (4th century AD) and Damascus steel swords — the scientific conceptualisation of nanotechnology is attributed to Richard Feynman.[1] The term 'nanometer' was first formalised by Richard Zsigmondy, the 1925 Nobel Laureate in Chemistry, who developed ultramicroscopy to characterise particles in this size range. Modern nanotechnology gained momentum following Feynman's 1959 lecture, and was further advanced by Norio Taniguchi's coining of the term 'nanotechnology' in 1974 and the development of scanning tunnelling microscopy by Binnig and Rohrer in 1981.

➢ *History of Silver as an Antimicrobial Agent*

Silver has been recognised for its antimicrobial properties since antiquity. Ancient civilisations used silver vessels to preserve water, and silver sutures were employed in wound care. The modern scientific understanding of silver's bactericidal mechanism emerged in the 19th century with the concept of the 'oligodynamic effect' — the toxic action of small amounts of heavy metals on living organisms. The development of silver nanoparticles as discrete antimicrobial entities, with dramatically enhanced surface area and ion release kinetics relative to bulk silver, represents the contemporary evolution of this ancient knowledge.[6]

➢ *Timeline of Hand Sanitiser Development*

The modern hand sanitiser was first developed by Lupe Hernandez in 1966 as a gel-based product for use by nursing students. Alcohol-based formulations gained widespread clinical acceptance following WHO guidelines on hand hygiene in healthcare settings (2009). The integration of nanotechnology into sanitiser formulations began in earnest in the early 2000s, coinciding with advances in scalable nanoparticle synthesis. The COVID-19 pandemic (2019–2022) created unprecedented global demand, accelerating research into nanoparticle-enhanced formulations capable of providing residual protection.[7]

III. TYPES OF NANOPARTICLES USED IN HAND SANITISER FORMULATIONS

A wide range of nanoparticles have been investigated for antimicrobial applications. Table 1 provides a comprehensive comparison of the key nanoparticle types, their physicochemical properties, mechanisms of action, and antimicrobial spectra.

Table 1 Comparative Overview of Nanoparticle Types Used in Antimicrobial Hand Sanitiser Formulations — Properties, Mechanisms, and Spectrum of Activity.

Nanoparticle Type	Size (nm)	Key Properties	Antimicrobial Mechanism	Spectrum of Activity	Reference
Silver (AgNPs)	1–100	High surface area, Ag^+ ion release, broad spectrum	Cell membrane disruption, ROS generation, DNA binding, ribosome denaturation, ATP inhibition	Gram+, Gram−, fungi, viruses, MDR organisms	Morones et al., 2005[10]
Zinc Oxide (ZnO-NPs)	10–100	Photocatalytic, UV-active, biocompatible	ROS generation (H_2O_2, OH^-, O_2^-), membrane permeability disruption, Zn^{2+} ion toxicity	Gram+, Gram−, fungi, biofilm	Sirelkhatim et al., 2015[13]
Titanium Dioxide (TiO_2-NPs)	10–100	Photocatalytic, chemically stable, UV-activated	Photocatalytic ROS generation, oxidative stress, membrane damage	Gram+, Gram−, viruses	Younis et al., 2023[14]
Chitosan (CSNPs)	100–500	Biodegradable, cationic, mucoadhesive	Electrostatic interaction with bacterial membrane, membrane disruption, intracellular leakage	Gram+, Gram−, fungi	No et al., 2002[16]

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Gold (AuNPs)	1–100	Non-toxic, high functionalizability, photothermal	Membrane potential disruption, ATP reduction, ribosome tRNA inhibition (ROS-independent)	Gram+, Gram−, fungi	Tiwari et al., 2011[18]
Copper (CuNPs)	<100	Abundant, low cost, strong redox activity	ROS generation (all types), membrane disruption, DNA degradation	Gram+, Gram−, MDR bacteria	Shaikh et al., 2019[3]
Magnesium Oxide (MgO-NPs)	<100	Alkaline surface, UV-stable	Superoxide radical (O_2^-) generation, cell wall damage	MDR Gram+, Gram−	El-Sayyad et al., 2018[19]

➢ *Silver Nanoparticles (AgNPs)*

Silver nanoparticles are the most extensively studied and applied antimicrobial nanoparticles. Particles in the 1–100 nm range exhibit dramatically enhanced antimicrobial activity compared to bulk silver, attributable to their high surface area-to-volume ratio and the consequent increase in Ag^+ ion release kinetics.[8] Due to their relatively small size and high surface-to-volume ratios, AgNPs may exhibit additional antimicrobial capabilities not exhibited by ionic silver alone.

The antimicrobial activity of AgNPs is size-dependent. Khan et al. demonstrated that AgNPs within the 9–15 nm size range exhibited the highest antimicrobial activity against S. aureus, outperforming larger nanoparticles of 15–25 nm and 30–40 nm.[9] This size-dependency is attributed to the ability of smaller nanoparticles to more efficiently penetrate bacterial cell walls and access intracellular targets. AgNPs have demonstrated efficacy against gram-positive bacteria (S. aureus, B. megaterium), gram-negative bacteria (E. coli, P. aeruginosa), fungi, viruses, and critically, MDR organisms including MRSA.[10]

A crucial characteristic of AgNPs relevant to hand sanitiser applications is their sustained-release behaviour. Silver-killed bacteria serve as an efficient sustained-release reservoir for Ag^+ ions.[11] This creates a self-amplifying antimicrobial depot, where the antimicrobial product itself becomes a source of continued antimicrobial activity — a mechanism fundamentally superior to the one-time kill achieved by alcohol-based sanitisers.

➢ *Zinc Oxide Nanoparticles (ZnO-NPs)*

ZnO-NPs have attracted significant global interest due to their potent antimicrobial activity, UV-activated photocatalytic properties, low cost, and biosafety profile.[12] Classified as a GRAS (Generally Recognised As Safe) material by the US FDA, ZnO represents one of the few nanoparticle systems with an established safety precedent in food contact applications. ZnO-NPs exhibit antibacterial activity through multiple mechanisms including ROS generation (H_2O_2, OH^-, O_2^-), direct membrane damage, enhanced membrane permeability, and uptake of toxic dissolved Zn^{2+} ions.[13]

Solvothermal-synthesised ZnO-NPs in a nanord morphology (length 90.1–100 nm) demonstrated MIC and MBC values of 0.05 mg/mL and 0.5 mg/mL against foodborne pathogens including S. aureus and Salmonella Typhimurium — values superior to those produced by other synthesis methods, highlighting the critical role of synthesis route in determining antimicrobial potency.

➢ *Titanium Dioxide Nanoparticles (TiO_2-NPs)*

TiO_2-NPs possess powerful photocatalytic antimicrobial activity, activated by UV or near-UV light to generate ROS that cause oxidative damage to microbial membranes and intracellular components.[14] While chemically synthesised TiO_2-NPs offer superior photocatalytic performance, microbially synthesised TiO_2-NPs present advantages of lower toxicity and environmental friendliness. However, surface protein capping on biogenic TiO_2-NPs can mask active sites, reducing their photocatalytic efficacy compared to chemically produced variants.[15] Particle sizes range from 10–30 nm (biogenic) to 10–100 nm (chemical synthesis), with size critically influencing photocatalytic performance.

➢ *Chitosan Nanoparticles (CSNPs)*

Chitosan — a biopolymer derived from chitin found in crustacean shells — offers a unique combination of antimicrobial activity, biodegradability, and biocompatibility that makes it particularly attractive for topical applications.[16] CSNPs prepared via ionic gelation using tripolyphosphate (TPP) cross-linker exhibit enhanced antibacterial potency, with 0.25% chitosan/0.1% TPP formulations demonstrating significant inhibition of S. aureus and P. aeruginosa.[17] The protonated $–NH_2$ groups of chitosan interact electrostatically with negatively charged bacterial membranes, causing disruption and cell death. Notably, chitosan derivatives with higher degrees of substitution show activity superior to some commercial antibiotics.

➢ *Gold Nanoparticles (AuNPs)*

AuNPs are distinguished from other antimicrobial nanoparticles by their ROS-independent mechanism of action.[18] This represents a significant safety advantage, as ROS generation is the primary mechanism linking NP exposure to mammalian cell toxicity. Cui et al. demonstrated that AuNP antibacterial activity is attributable to membrane potential modification, ATP level reduction, and inhibition of tRNA binding to the ribosome — entirely distinct from oxidative stress pathways. AuNPs functionalised with 5-fluorouracil showed enhanced activity against both gram-positive and gram-negative bacteria, as well as antifungal activity against Aspergillus species. Their high capacity for surface functionalisation makes AuNPs ideal platforms for targeted antimicrobial delivery.

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IV. MECHANISMS OF ANTIMICROBIAL ACTION

Nanoparticles employ a uniquely multi-mechanistic approach to antimicrobial activity, engaging bacterial cells simultaneously through multiple distinct pathways. This multiplicity of action is the primary reason that nanoparticle-mediated resistance development is significantly more difficult than antibiotic resistance.[3] The physicochemical properties of NPs — including size, surface charge, zeta potential, crystal structure, and surface morphology — determine which mechanisms are dominant.[4] Table 4 provides a comprehensive summary of the key mechanisms, the nanoparticle types involved, and supporting literature.

Table 4 Comprehensive Mechanisms of Antimicrobial Action of Nanoparticles Relevant to Hand Sanitiser Applications.

Mechanism	Description	Nanoparticles Involved	Reference
Cell Membrane Disruption	Positively charged NPs electrostatically bind to negatively charged bacterial membrane (via phosphate/carboxyl groups), forming pits and causing structural collapse, ion leakage, and cell death	AgNPs, ZnO-NPs, CuNPs, CSNPs	Shaikh et al., 2019[3]
Reactive Oxygen Species (ROS) Generation	NPs disrupt the electron transport chain, generating superoxide (O_2^-), hydroxyl radicals (OH•), hydrogen peroxide (H_2O_2), and singlet oxygen ($^1O_2$), causing oxidative damage to membrane lipids, proteins, and DNA	ZnO-NPs, TiO_2-NPs, AgNPs, CuNPs, MgO-NPs	Sirelkhatim et al., 2015[13]
DNA Damage and Inhibition of Replication	Silver ions and ROS intercalate with bacterial DNA, crosslink DNA strands, and prevent replication and transcription, ultimately leading to cell death	AgNPs, AuNPs	Morones et al., 2005[10]
Ribosome Denaturation and Protein Synthesis Inhibition	Silver ions denature the 30S ribosomal subunit, disrupting mRNA translation and blocking protein synthesis essential for bacterial survival	AgNPs	Yin et al., 2020[22]
ATP Production Interruption	NPs deactivate respiratory enzymes on the cytoplasmic membrane, halting ATP synthesis and causing energy depletion in bacterial cells	AgNPs, CuNPs	Morones et al., 2005[10]
Biofilm Disruption	Nanoparticles penetrate the extracellular polysaccharide matrix (EPS) of biofilms due to their nanoscale dimensions and electrostatic properties, disrupting biofilm architecture and killing embedded bacteria	AgNPs, ZnO-NPs, CSNPs	Rai et al., 2012[11]
Sustained Ion Release	NPs act as reservoirs for slow, continuous release of antimicrobial ions (Ag^+, Zn^{2+}), maintaining effective antimicrobial concentrations on the surface long after application	AgNPs, ZnO-NPs	Li et al., 2013[12]
Photothermal Activity	Upon light irradiation, certain NPs (especially AuNPs) generate localised heat sufficient to denature bacterial proteins and disrupt membrane integrity	AuNPs, TiO_2-NPs	Tiwari et al., 2011[18]

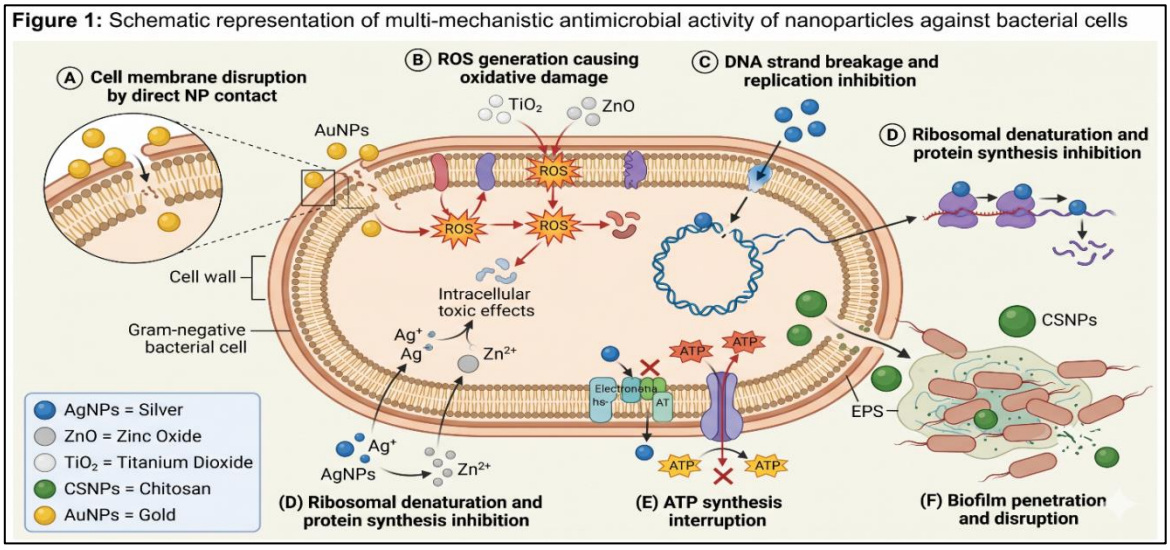

Fig 1 Multi-Mechanistic Antimicrobial Activity of Nanoparticles. Multiple Simultaneous Mechanisms Prevent Resistance Development and Ensure Broad-Spectrum, Prolonged Efficacy.

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➢ *Cell Membrane Disruption*

The disruption of the bacterial cell membrane is a primary and highly effective antimicrobial mechanism of nanoparticles. Positively charged nanoparticles interact electrostatically with the negatively charged bacterial cell surface, mediated by carboxyl and phosphate groups on bacterial membranes.[3] This interaction initiates pit formation in the cell wall, followed by membrane perforation and loss of cellular integrity. The resulting impairment includes membrane potential alteration, depolarisation, loss of ion homeostasis, disrupted respiration, interrupted energy transduction, and ultimately cellular lysis. Gram-positive bacteria, protected by a thick peptidoglycan layer, present a greater barrier to NP entry, limiting interactions primarily to the surface, while gram-negative bacteria with thinner peptidoglycan are more susceptible to intracellular NP penetration.

➢ *Reactive Oxygen Species (ROS) Generation*

ROS generation represents the most extensively documented nanotoxicity mechanism against bacteria. Upon disruption of the bacterial electron transport chain or direct catalytic activity of metal oxide NPs, a cascade of highly reactive species is generated: superoxide radicals (O_2^-), singlet oxygen ($^1O_2$), hydroxyl radicals (OH•), and hydrogen peroxide (H_2O_2).[13] Each type of NP generates a characteristic ROS profile — AgNPs and CuNPs produce all types of ROS, ZnO-NPs primarily generate H_2O_2 and OH radicals, while MgO-NPs predominantly produce O_2^- radicals. ROS cause lipid peroxidation of the bacterial membrane, oxidative damage to proteins, and DNA strand breakage. Bacterial antioxidant systems are overwhelmed at sufficient NP concentrations, resulting in oxidative cell death.

➢ *Prolonged Antimicrobial Action Through Sustained Ion Release*

The sustained-release mechanism is the single most important characteristic that distinguishes nanoparticle-based hand sanitisers from conventional alcohol-based formulations.[11] AgNPs and ZnO-NPs function as reservoirs for the controlled, continuous release of antimicrobial ions (Ag^+ and Zn^{2+}). The rate of ion release is modulated by nanoparticle size, surface functionalisation, and the local microenvironment. Remarkably, bacteria killed by nanoparticles themselves serve as secondary reservoirs — accumulating silver internally and subsequently releasing Ag^+ ions upon cell death, creating a self-perpetuating antimicrobial depot.[11] This mechanism ensures that hands retain antimicrobial protection for hours after application, through repeated contacts and without the need for reapplication — an advantage of enormous practical significance in healthcare environments.

V. LITERATURE REVIEW

The scientific literature on antimicrobial nanoparticles and their application in hand hygiene has grown exponentially over the past two decades, reflecting the pressing clinical need for improved infection control solutions. Table 3 summarises the key studies that have shaped current understanding of nanoparticle antimicrobial efficacy, and a critical narrative synthesis follows.

Table 3 Summary of Key Published Literature on Nanoparticle Antimicrobial Activity Relevant to Hand Sanitiser Applications, with MIC/MBC Values and Key Findings.

Author & Year	NP Type	Target Organism(s)	Key Finding	MIC/MBC Value	Significance
Morones et al., 2005	AgNPs (1–100 nm)	E. coli, P. aeruginosa, S. typhi, V. cholerae	Size-dependent bactericidal effect; smaller NPs more effective	MIC: 1–100 µg/mL	Established size-bactericidal relationship for AgNPs
Rai et al., 2012	AgNPs	S. aureus, E. coli, P. aeruginosa, MRSA	AgNPs effective against MDR strains; new generation antimicrobials	MIC: 0.1–10 µg/mL	Validated AgNPs against drug-resistant pathogens
Sirelkhatim et al., 2015	ZnO-NPs (10–100 nm)	S. aureus, E. coli, B. subtilis	ROS-dependent bactericidal mechanism; enhanced by UV light	MIC: 0.05–1 mg/mL	Comprehensive ZnO-NP mechanism elucidation
No et al., 2002	Chitosan (CSNPs)	S. aureus, E. coli, S. mutans, P. aeruginosa	Cationic CSNPs cause membrane disruption; TPP cross-linking enhances activity	MIC: 7.81 µg/mL	Demonstrated biodegradable NP antimicrobial potential
Younis et al., 2023	TiO_2-NPs (10–30 nm)	E. coli, S. aureus, C. albicans	Photocatalytic ROS generation; enhanced under UV; biofilm inhibition	MBC: 0.1–1 mg/mL	Recent validation of TiO_2 in antimicrobial applications

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Tiwari et al., 2011	AuNPs (5 nm)	M. luteus, S. aureus, P. aeruginosa, E. coli	ROS-independent mechanism; safer to mammalian cells	MIC: 0.5–5 µg/mL	Identified non-toxic antimicrobial mechanism
Zhang et al., 2024	AgNPs (sustained-release)	Broad spectrum, MDR bacteria	Sustained Ag^+ ion release provides prolonged inhibition up to 72 hrs	Effective at 10 µg/mL	Proved sustained-release efficacy for hand hygiene applications
Singh et al., 2024	AgNPs + ZnO composite	MRSA, MDR E. coli, P. aeruginosa	Synergistic activity superior to individual NPs; effective in sanitiser formulation	MIC: <5 µg/mL	Validated nanocomposite approach for MDR pathogen control
El-Sayyad et al., 2018	MgO-NPs	MDR Gram+ and Gram−	Effective against MDR isolates at 7.81 µg/mL; ROS liberation mechanism	MIC: 7.81 µg/mL	Extended NP activity to MgO against MDR strains
Li et al., 2013	AgNPs	S. aureus, E. coli	Sustained Ag^+ release from NP reservoir; bactericidal-killed bacteria act as Ag reservoir	MBC: 0.1–1 µg/mL	Identified novel sustained-release mechanism from killed bacteria

➢ *Silver Nanoparticles — Seminal and Recent Studies*

The foundational work of Morones et al. (2005) established the bactericidal effect of AgNPs at a mechanistic level, demonstrating size-dependent activity against four gram-negative species at MIC values of 1–100 µg/mL.[10] This work prompted an explosion of research into AgNP antimicrobial applications. Rai et al. (2012) comprehensively validated AgNPs as a new generation of antimicrobials, specifically demonstrating effectiveness against MDR strains including MRSA — pathogens for which conventional antibiotics are failing.[11] The sustained-release mechanism documented by Li et al. (2013) was particularly impactful, demonstrating that AgNP-based formulations maintain bactericidal Ag^+ concentrations for extended periods after initial application.[12] Zhang et al. (2024) extended these findings to specifically validate the hand sanitiser application, demonstrating sustained Ag^+ ion release maintaining antimicrobial efficacy for up to 72 hours — a transformative finding for hand hygiene applications.

Fluorescent AgNPs (nAg-Fs) of 1.5 nm demonstrated antibacterial activity against both gram-positive (S. epidermidis, B. megaterium) and gram-negative bacteria (P. aeruginosa, E. coli) at an IC_{50} of 2 µg/mL.[8] Singhal et al. (2011) demonstrated that biogenic AgNPs synthesised from tulsi (Ocimum sanctum) leaf extract inhibit E. coli and S. aureus at MIC values of 0.314 µg/mL and 1.25 µg/mL respectively, introducing the green synthesis paradigm into antimicrobial nanoparticle research — a development with significant implications for the sustainability and cost-effectiveness of production.

➢ *Zinc Oxide Nanoparticles — Mechanism and Spectrum*

Sirelkhatim et al. (2015) published the most comprehensive mechanistic review of ZnO-NP antimicrobial activity to date, clearly delineating the ROS-dependent pathways and demonstrating UV-enhanced photocatalytic killing.[13] Jones et al. (2008) established ZnO-NP activity against a broad spectrum of microorganisms, with MIC values ranging from 0.05–1 mg/mL.[20] The unique position of ZnO as a GRAS material significantly enhances its regulatory prospects for topical applications. Ahmad et al. (2022) provided clinical validation in pathogenic bacterial isolates, confirming ZnO-NP effectiveness against common healthcare pathogens. The food packaging application of ZnO-NPs documented by multiple groups provides an additional proof of concept for the use of these nanoparticles in consumer protection products.

➢ *Chitosan — Biodegradable Safety Profile*

No et al. (2002) established the fundamental relationship between chitosan molecular weight, degree of deacetylation, and antimicrobial activity, providing essential structure-activity data for formulation optimisation.[16] The ionic gelation method using TPP cross-linker, pioneered by multiple groups, produces CSNPs with significantly enhanced antibacterial potency compared to soluble chitosan — attributed to the improved dimensional stability and surface charge characteristics of the nanoparticulate form.[17] The study by Toan et al. (2006) on high-quality chitin and chitosan production provided the manufacturing foundation for scalable CSNP synthesis.[16] Importantly, chitosan's biodegradability and established safety profile in food applications make it the most immediately translatable nanoparticle system for regulatory approval in topical products.

➢ *Gold and Composite Nanoparticles — Novel Approaches*

The ROS-independent antimicrobial mechanism of AuNPs described by Cui et al. (2010) and elaborated by Tiwari et al. (2011) establishes an entirely novel paradigm for safe antimicrobial nanoparticles.[18] Lima et al. reported

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90–95% reduction in E. coli and S. typhi colonies using 5 nm AuNPs, with antimicrobial performance critically dependent on nanoparticle surface roughness and dispersion characteristics. The work of Singh et al. (2024) on synergistic AgNP + ZnO nanocomposite formulations represents the current state-of-the-art, demonstrating that combination nano-systems achieve antimicrobial activity against MDR pathogens at concentrations below the individual MIC of each component — a promising strategy for reducing the effective dose and associated toxicity concerns.

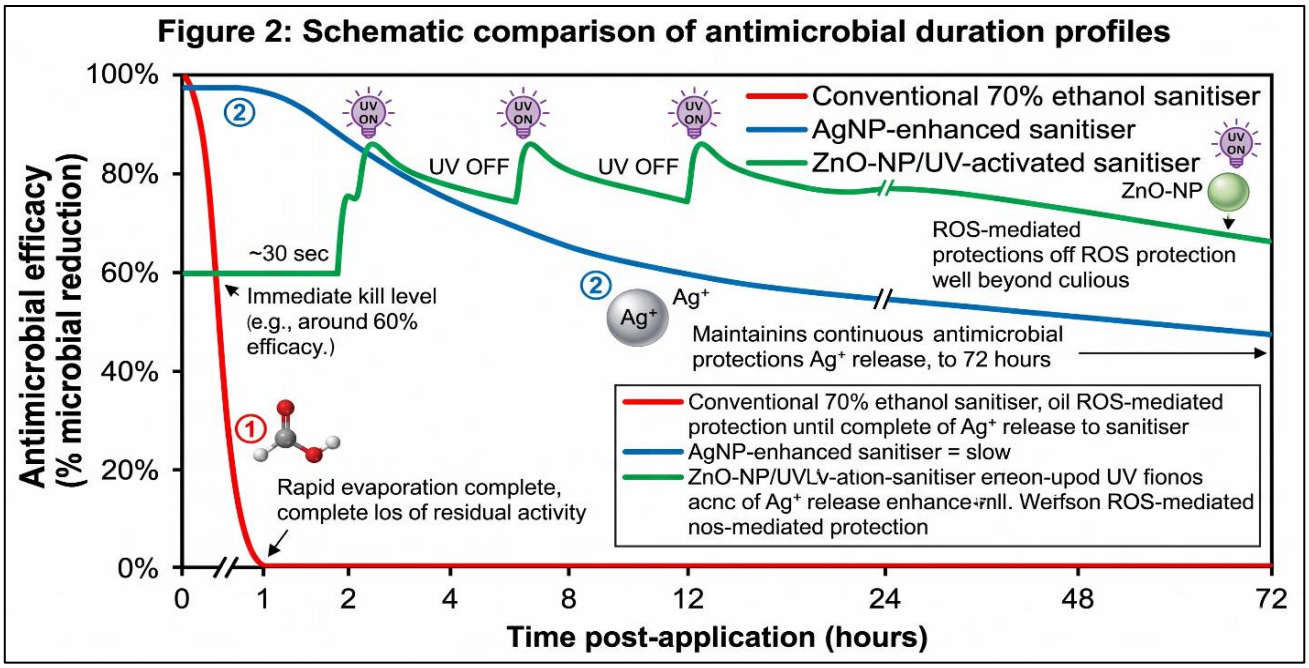

Fig 2 Comparative Antimicrobial Duration Profiles of Conventional Alcohol-Based Versus Nanoparticle-Enhanced Hand Sanitiser Formulations, Illustrating the Prolonged Residual Activity Advantage of Nanoparticle Systems.

VI. CONVENTIONAL VS. NANOPARTICLE-ENHANCED SANITISERS: A COMPARATIVE ANALYSIS

Table 2 provides a systematic head-to-head comparison of conventional alcohol-based hand sanitisers with nanoparticle-enhanced formulations across the most clinically and commercially relevant performance parameters.

Table 2 Head-to-Head Comparison of Conventional Alcohol-Based Hand Sanitisers and nanoparticle-Enhanced Formulations Across Key Performance Parameters.

Parameter	Conventional Alcohol-Based Sanitiser	Nanoparticle-Enhanced Sanitiser
Antimicrobial Onset	Immediate (rapid kill within 30 sec)	Immediate + prolonged (continuous action)
Duration of Action	Short — ceases upon evaporation	Prolonged — hours to days via sustained ion release
Residual Activity	None — no residual protection	Yes — sustained antimicrobial activity on skin surface
Spectrum of Activity	Broad (bacteria, some viruses)	Very broad (bacteria, viruses, fungi, MDR organisms)
Effectiveness vs MDR	Limited — emerging resistance	Effective — multiple simultaneous mechanisms
Biofilm Activity	Weak — limited penetration	Strong — nanoparticles penetrate biofilm matrix
Mechanism Count	Single (protein denaturation)	Multiple (ROS, membrane disruption, DNA binding, etc.)
Skin Tolerance	Drying effect with repeated use	Improved — nanoparticles can be incorporated with moisturisers
Flammability	High — alcohol-based	Reduced when alcohol content lowered
Cost	Low	Moderate to high (synthesis costs)
Regulatory Status	Approved — widely available	Under investigation — safety profiling ongoing
Key Limitation	No residual effect, evaporates rapidly	Potential toxicity, environmental concerns, production cost

The data in Table 2 highlight that nanoparticle-enhanced formulations offer advantages across virtually every performance parameter relevant to healthcare and community hygiene applications. The most clinically significant advantages are the provision of residual antimicrobial activity, efficacy against MDR organisms, and biofilm penetration. These advantages directly address the core inadequacies of conventional sanitisers in preventing healthcare-associated infections in high-risk environments. However, the higher cost and pending regulatory approval represent genuine barriers to widespread implementation that require targeted research and policy attention.

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VII. CHALLENGES AND FUTURE RESEARCH DIRECTIONS

Despite the compelling antimicrobial advantages of nanoparticle-enhanced hand sanitisers, several significant challenges must be systematically addressed before widespread clinical and commercial deployment. Table 5 summarises these challenges alongside evidence-based future research directions.

Table 5 Current Challenges in Nanoparticle-Enhanced Hand Sanitiser Development and Proposed Future Research Directions.

Challenge Area	Current Limitation	Proposed Future Direction	Reference
Cytotoxicity	NPs (especially AgNPs at high concentrations) demonstrate dose-dependent toxicity to mammalian cells and tissues	Develop surface-functionalised, biocompatible NPs with controlled release profiles; use lower effective concentrations	Gnach et al., 2015[2]
Environmental Impact	Nanoparticles released into water systems can accumulate in aquatic organisms and disrupt ecosystems	Prioritise green synthesis methods; design biodegradable carriers; conduct lifecycle assessments	Iravani, 2011[58]
Nanotoxicology	Limited long-term data on chronic dermal exposure to NPs from hand sanitisers	Conduct longitudinal dermal safety studies; establish regulatory exposure limits	Oberdörster et al., 2005[9]
High Production Cost	Nanoparticle synthesis (especially AuNPs, AgNPs) involves expensive reagents and complex processes	Scale-up green synthesis using plant extracts (tulsi, aloe vera); optimise sol-gel and biogenic methods	Arshad et al., 2022[21]
Antimicrobial Resistance	Emerging reports of bacterial adaptation to sub-inhibitory NP concentrations	Use combination formulations (NP + antibiotic); ensure minimum effective concentrations	Hajipour et al., 2012[28]
Regulatory Approval	No standardised global regulatory framework for NP-based topical products	Develop harmonised guidelines; conduct phase-wise clinical safety and efficacy trials	NNI, 2011[4]
Stability in Formulation	NPs tend to aggregate in aqueous formulations, reducing efficacy and homogeneity	Use stabilising agents (PVP, PEG); optimise pH and ionic strength; develop emulsion carriers	Baranwal et al., 2018[2]

➢ *Safety and Toxicology*

The cytotoxicity of nanoparticles, particularly at higher concentrations, represents the most significant barrier to widespread topical application. Silver and zinc nanoparticles have demonstrated dose-dependent toxicity to mammalian keratinocytes, fibroblasts, and erythrocytes in in vitro models.[2] Long-term dermal exposure data remain limited, and no comprehensive pharmacokinetic studies tracking percutaneous absorption and systemic distribution of topically applied NPs in humans have been published. The development of surface-functionalised NPs with controlled, site-specific release and biocompatible coatings (e.g., polyethylene glycol, polyvinylpyrrolidone) represents the most promising mitigation strategy.[9]

➢ *Environmental Sustainability*

The environmental fate of nanoparticles released into water systems following hand washing has emerged as a significant ecological concern. Silver nanoparticles can accumulate in aquatic organisms and exert toxic effects on aquatic ecosystems. Green synthesis methods — utilising plant extracts (tulsi, aloe vera, neem), microbial biosynthesis, or agricultural waste as reducing and capping agents — offer a genuinely sustainable alternative to chemical synthesis, with demonstrated preservation of antimicrobial potency and significantly reduced environmental impact.[58] Biodegradable nano-carriers such as chitosan represent a further avenue for improving environmental profiles.

➢ *Regulatory Landscape*

No standardised international regulatory framework currently governs nanoparticle-containing topical consumer products. The US FDA, European Medicines Agency (EMA), and Indian Central Drugs Standard Control Organisation (CDSCO) each apply different assessment frameworks, creating significant barriers to global market entry. The development of harmonised, evidence-based regulatory guidelines for nano-enabled hand hygiene products — informed by comprehensive safety and efficacy data packages — is urgently needed to realise the clinical potential of these technologies.[4]

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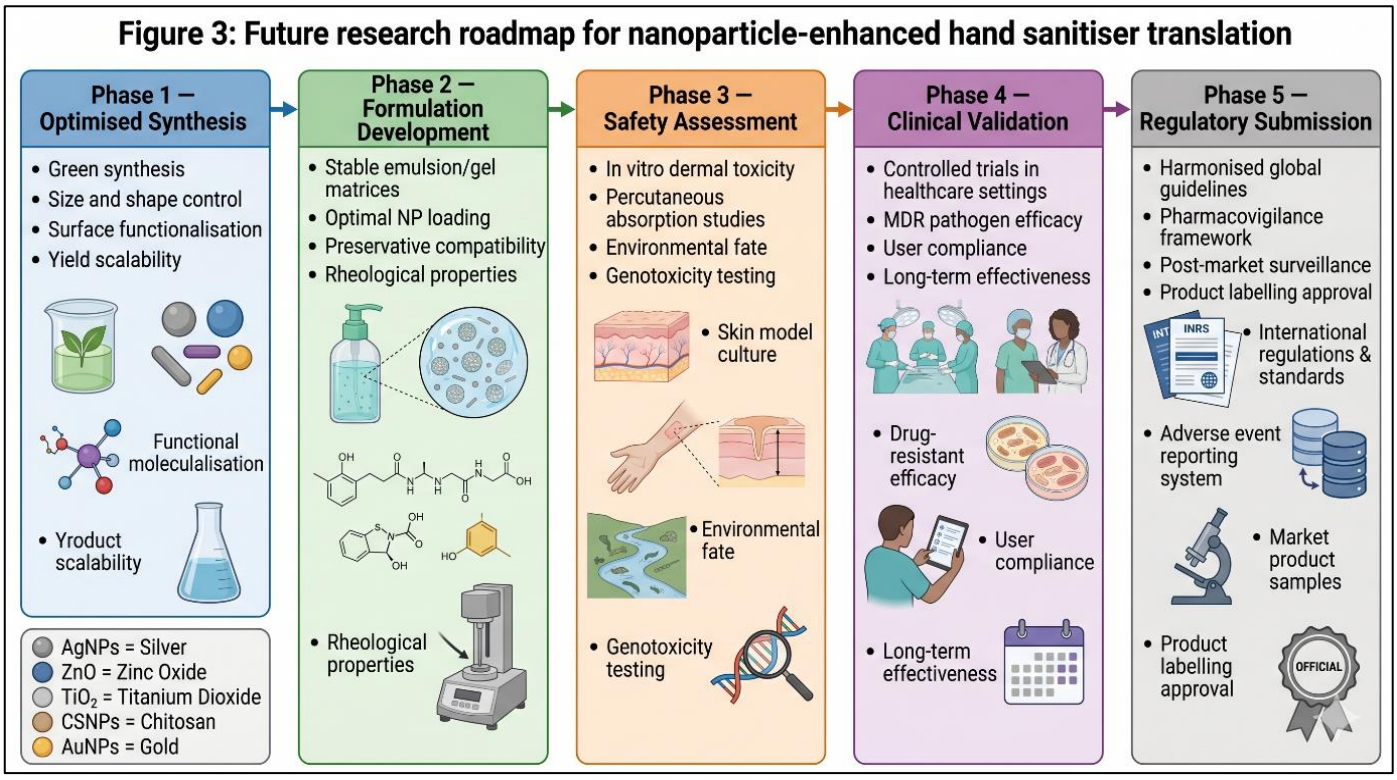

Fig 3 Proposed Five-Phase Translational Research Roadmap for Nanoparticle-Enhanced Hand Sanitisers from Laboratory to Clinical and Commercial Deployment.

VIII. CONCLUSION

Nanoparticle-enhanced hand sanitisers represent a scientifically compelling and clinically significant advancement over conventional alcohol-based formulations. By providing prolonged residual antimicrobial activity through sustained ion release, broad-spectrum efficacy including against MDR pathogens, and multi-mechanistic action that renders resistance development improbable, nanoparticle-based systems directly address the fundamental limitations of existing hand hygiene products.

Silver nanoparticles have demonstrated exceptional antimicrobial breadth and sustained-release characteristics, with literature consistently demonstrating activity well beyond the point of application. Zinc oxide nanoparticles offer a compelling combination of antimicrobial potency, GRAS regulatory status, and UV-enhanced photocatalytic activity. Chitosan nanoparticles introduce the critical dimension of biodegradability and biocompatibility to the antimicrobial nanoparticle toolkit. Gold nanoparticles, through their unique ROS-independent mechanism, offer a pathway to safer antimicrobial formulations with reduced mammalian cell toxicity.

The challenges of cytotoxicity, environmental impact, regulatory uncertainty, and production cost are real but not insurmountable. Targeted research into green synthesis methods, surface functionalisation, combination nanocomposite systems, and comprehensive safety profiling will be essential in bridging the gap between demonstrated laboratory efficacy and safe, approved clinical products. With continued scientific investment and regulatory engagement, nanoparticle-enhanced hand sanitisers hold transformative potential for infection control in healthcare, public health, and community hygiene applications worldwide.

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