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SURFACE PERFORMANCE OF NANOPARTICLES IN INTERACTIONS WITH MICROBES

Khushi Athya[1], Dr. Pradeep Kumar[1]
[1]Department of Microbiology, Kalinga University, Raipur-492101, Chhattisgarh, India
Correspondence: khushiathya132003@gmail.com

ABSTRACT

Due to their unique size-dependent properties, Nanoparticles (NP) have emerged as potential tools in microbial control. There are numerous factors which affect their interactions with microbes, surface processes, and these play a critical role. This review explores how modifications affect the nanoparticle surface with functional groups, biomolecules, or how polymers can enhance antimicrobial efficacy, target the specificity and how it stabilises itself in biological environments. The working of the NPs shows various result which improves solubility, biofilm inhibition, and lastly the ability to isolate and then interact with microbial membranes, proteins, and DNA. Different mechanisms, not restricted to membrane disruption, reactive oxygen species (ROS) generation, and intracellular targeting, reinforce the antimicrobial actions. Although advancements are present, challenges such as toxicity, environmental restrictions and lack of standardization persist. In the future, further research will be directed towards eco-friendly coatings, response-stimuli nanoplatforms and multifunctional systems targeted for antimicrobial delivery. The task for the review is to shed light on the importance of surface functionalization in efficiently dealing with NP-microbe interactions and in some ways guiding the working of the newer generation of antimicrobial nanomaterials.

Keywords: Nanoparticle-Microbe Contact, Polymeric Nanoparticles, Metal-Built Nanoparticles, Lipid-Based Nanoparticles, Carbon-Based Nanoparticles

1. Introduction

Nanotechnology, as expected, is an expanding and significant field of science and technology which enables us to operate materials at an extraordinarily small scale, such as individual atoms and molecules. There are crucial aspects of nanotechnology which involve the application of nanoparticles, commonly referred to as NPs. These particles hold distinct physical and chemical features. Their surface area is extensive, which relates to their size; they behave inversely due to their compactness, and their surfaces are more sensitive. These exceptional features distinguish nanoparticles from larger-sized materials, giving them distinct and different capacities. This allows them to be in a beneficial area to be in biology and the environmental system [1,2].

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It is the most pressing issue globally, the effective management of microbial populations, especially those relating to pathogenic microorganisms such as bacteria, fungi and viruses. The organism can be rooted as a dire infection that can be caused by them in clinical settings, compromise food safety and disrupt agricultural productivity. The issue escalates the very problem of antimicrobial resistance (AMR) that involves the overuse and misuse of conventional antibiotics. The traditional way to treat microbial infection often comes with limitations like less solubility, low bioavailability and ineffectiveness against biofilms-structured communities of the microbial structure that are fundamentally resistant to antibiotics and immunity comeback [3,4].

Contextually, nanoparticles offer a potential substitute or an aide to conventional strategies. Discussing the small size of the nanoparticle, which enables them to infiltrate biological membranes and biofilms, while their surface properties can be very well engineered to enhance interaction with microbial targets. Based on the compositional qualities- whether metallic, carbon built, polymeric or lipid-based. NPs can exert antimicrobial effects through various ways, including membrane disruption, generation of reactive oxygen species (ROS), and interference with intracellular processes [5,6].

However, the biological behaviour of nanoparticles is not solely determined by their core material or size. Increasing evidence suggests that surface properties, including surface charge, hydrophobicity, and chemical functionality, critically influence how NPs interact with microbial cells and biological environments. To optimise these interactions, scientists employ surface functionalization—the deliberate modification of NP surfaces using chemical or biological moieties—to tailor their physicochemical and biological characteristics [7,8].

Surface functionalization augments the colloidal control of nanoparticles by avoiding aggregation in aqueous media and physiological environments. It is through this that the enhancement of improved biocompatibility has increased, warranting more controlled drug release and targeted antimicrobial activity through the attachments of ligands such as antibodies, peptides, aptamers, or polysaccharides. These alterations can increase the affinity of NPs for precise microbial species or assemblies, such as lipopolysaccharides on gram-negative bacteria or exopolysaccharides within these biofilms [9,10].

Moreover, functionalized NPs can be engineered to react to environmental cues, like ph, temperature, or enzymatic activity—thus facilitating an “intelligent” antimicrobial scheme that triggers solely in the presence of pathogens. This enhances the treatment efficiency, thereby reducing off-target effects and environmental harm.

Shedding light on the surface processing of nanoparticles signifies a vital area of research for enhancing their antimicrobial performance while minimising unintended effects. This functionality is what this review paper deals with. Exploring the categories which have been employed in microbial applications, we discuss the most common and ever-emerging functionalization schemes which have real-world applications. Lastly, addressing current

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limitations and upcoming opportunities in the expansion of next-generation functionalized nanomaterials.

2. Role and Functions of Surface Functionalization

Surface modifications are a vital approach, yet act as a catalyst for both physicochemical elements and biological interactions of nanoparticles (NPs). This procedure entails the intentional modification of NP Surfaces, which uses their functional groups, polymers, or biomolecules, so that it improves efficacy across varied applications. A key benefit would be its enhanced capacity to increase solubility and colloidal stability, which is dynamic for ensuring consistent dispersion in aqueous and biological settings. Moreover, it improves the bioavailability and attacks only the specificity of nanoparticles, especially in interwoven biological systems where accurate delivery is crucial. [1,2]. By reducing aggregation tendencies and preventing premature elimination from the body's circulatory or cellular systems, functionalized NPs can maintain prolonged activity at the site of action [2,3].

A crucial role is the promoting factor for ligand conjugation- like antibodies, peptides and aptamers- these allow for specific identification and attachment to microbial surface markers, including those found in biofilms [4,5]. This focused interaction greatly enhances the administration of antimicrobial agents, thereby reducing the adversative side effects on non-target cells, and boosting overall therapeutic effectiveness [6].

Moreover, tailored surface alterations can render stimuli-responsive characteristics on nanoparticles, enabling them to discharge their therapeutic payloads in response to environmental signals such as ph changes, enzyme action, or oxidative stress [7,8].

This degree of control provides for spatiotemporal management of antimicrobial effects, greatly increasing the treatment accuracy while reducing systemic toxicity. Together, surface functionalization alters normally inactive nanoparticles into intelligent, multifunctional systems capable of diagnostic and therapeutic applications in microbial regulators.

3. Types of NPs applicable in Microbial Applications

Nanoparticles used in microbial habitats differ greatly in their compositions, which in turn influences their physicochemical characteristics, antimicrobial effectiveness and alignment with surface functionalization techniques.

3.1 Nanoparticles which are Metal-Based

Metallic and metal oxide NPs are among the most extensively studied owing to their sturdy antimicrobial characteristics. Few examples include:

- Silver nanoparticles (AgNPs) exhibit broad-spectrum antimicrobial activity in contradiction of both gram-positive and gram-negative bacteria, fungi, and viruses. Their

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job is through multiple mechanisms, including membrane mutilation, reactive oxygen species (ROS) cohort, and DNA interface [11,12]. Functionalization with polymers like chitosan or PEG augments their firmness and diminishes collection in biological fluids [13].

- Zinc oxide (ZnO) and titanium dioxide (TiO_2) nanoparticles are photocatalytic and can produce ROS under UV or visible light, leading to oxidative strain in microbial cells. Superficial coatings with biomolecules or dopants can rally their microbial targeting and diminish cytotoxicity to mammalian cells [14,15].
- Gold nanoparticles (AuNPs), though less innately antimicrobial, serve as outstanding carriers for antimicrobial peptides or drugs owing to their biocompatibility and effortlessness of functionalization via thiol-gold chemistry [16].
- Copper oxide (CuO) and titanium dioxide (TiO_2) display potent oxidative impairment. Functional coverings like silica or dextran improve their biocompatibility [7].

3.2 Nano Particles, which are Carbon-Based

Carbon-based nanostructures like fullerenes, graphene oxide (GO), and carbon nanotubes (CNTs) also exhibit antimicrobial capacity.

- Graphene oxide (GO) can disrupt bacterial membranes through sharp edges and make oxidative tension. Functionalization with quaternary ammonium composites or silver ions boosts this movement [17,18].
- Carbon nanotubes (CNTs) have high mechanical strength and can pierce microbial membranes, causing physical disruption. When functionalized with hydrophilic polymers or antimicrobial agents, CNTs become more dispersible and biologically active [19].

3.3 Polymeric Nanoparticles

Polymeric nanoparticles are shaped from natural (e.g., chitosan, alginate) or synthetic (e.g., PLGA, PEG) polymers and are extremely appropriate for meticulous drug distribution.

- Chitosan nanoparticles inherently possess antimicrobial activity due to their polycationic nature, which enables electrostatic interactions with microbial membranes. Functionalization can enhance their solubility and allow conjugation with antibiotics or targeting ligands [20].
- PLGA nanoparticles are biodegradable and approved by regulatory agencies for drug delivery. Surface functionalization with ligands or mucoadhesive polymers can enhance their specificity and residence time at infection sites [21].

3.4 Nanoparticles in Lipid-Based Forms

Lipid-based nanoparticles such as liposomes and solid lipid nanoparticles (SLNs) are well-established drug carriers with applications in antimicrobial therapy.

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- Liposomes, which are vesicles composed of phospholipid bilayers, can encapsulate both hydrophilic and hydrophobic antimicrobial agents. Surface modification with PEG, antibodies, or aptamers improves circulation time and targeting capabilities [22].
- Solid lipid nanoparticles (SLNs) combine the advantages of liposomes and polymeric NPs, offering biocompatibility and controlled release. They are often functionalized with surfactants or ligands to improve microbial affinity and stability [23].

4. Surface Functionalization Techniques

Surface functionalization enhances NP-microbe interactions by improving stability, biocompatibility, and targeting efficiency.

- Physical Adsorption**:** Involves non-covalent attachment of biomolecules (e.g., peptides, polysaccharides) via van der Waals forces or electrostatic interactions. This method is simple but less stable under physiological conditions [15].
- Covalent Bonding**:** Covalent functionalization yields stable modifications. For example, EDC/NHS chemistry links amine-containing ligands to carboxylate NPs. Thiol-Au chemistry is widely used for gold NPs [16].
- Ligand Exchange: Used to replace weakly bound surfactants with functional ligands like citrate, mercaptoundecanoic acid, or polyethene glycol (PEG). This improves colloidal stability and biocompatibility [17].
- Polymer Coating: Polymers like PEG, PVP, or chitosan are applied to prevent aggregation and improve stealth in biological systems. Some coatings (e.g., zwitterionic polymers) reduce non-specific binding [18].
- Biofunctionalization**:** Linking of aiming moieties like antibodies, aptamers, and/or antimicrobial peptides allows species-specific binding and enhanced internalization. This technique is key for smart and responsive antimicrobial platforms [19,20].

5. Mechanisms of Interaction with Microbial Cells

Functionalized nanoparticles disrupt microbial processes through diverse pathways.

- Membrane Interruption: Cationic NPs network with negatively charged bacterial sheaths, causing structural damage and leakage. Functionalization with AMPs or quaternary ammonium salts enhances this effect [21].
- Reactive Oxygen Species (ROS) Generation**:** Metal oxides (ZnO, TiO_2) or functionalized carbon NPs induce ROS production, leading to oxidative stress and apoptosis. Functionalization can tune ROS levels to balance efficacy and safety [22].
- Biofilm Penetration and Inhibition**:** NPs penetrate biofilms more effectively than antibiotics. Functional groups like DNase or dispersion B degrade the EPS matrix, allowing deeper access and improved microbial eradication [23].

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- Intracellular Targeting: Functionalized NPs can bypass cell walls and deliver antimicrobial agents directly into the cytoplasm or nuclei, disrupting vital processes like DNA replication and protein synthesis [24].

6. Applications of Functionalized Nanoparticles

- Biomedical Applications: Used in wound coverings, scion veneers, and targeted drug distribution arrangements. Functionalized AgNPs and liposomes are applied for skin infections, osteomyelitis, and sepsis [25].
- Food Safety: Nanoparticles functionalized with bacteriophages or specific antibodies are integrated into packaging materials for pathogen detection and prevention [26].
- Environmental Applications: Magnetically recoverable functionalized NPs remove pathogenic microbes from wastewater and contaminated soils [27].
- Agricultural Uses**:** Functionalized silica or chitosan NPs deliver fungicides and bactericides in a controlled manner to crops, reducing chemical load and resistance buildup [28].

7. Futuristic Options

With enormous advancement, there exist varied challenges:

- Toxicity and Biocompatibility: Functionalization can mitigate but not fully eliminate off-target effects. More studies are needed on long-term safety and environmental impact [29].
- Regulatory Hurdles: Lack of standardization in NP synthesis and characterisation hinders clinical translation [30].
- Scalability: Many functionalization methods are costly or complex, limiting commercial applications.

8. Future Outlook

Emerging trends include:

- Stimuli-Responsive Nanoplatforms: One promising direction involves designing NPs that respond to infection-specific stimuli, such as low pH, elevated enzyme levels, or oxidative stress. These smart-systems can release antimicrobial agents selectively at the infection site, improving efficacy while reducing systemic toxicity. For example, pH-responsive or enzyme-triggered drug release mechanisms are increasingly being explored for targeted antimicrobial therapy [31].
- Biomimetic and Bioinspired Coatings: Bioinspired functionalization, such as coating NPs with natural antimicrobial peptides or cellular membranes, enhances targeting, biocompatibility, and immune evasion. These biomimetic strategies are gaining attention for their ability to mimic host-defence systems and evade immune clearance, enabling prolonged circulation and site-specific delivery [32].

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- Multifunctional and Theranostic Nanoparticles: There is a shift towards multifunctional NPs that integrate antimicrobial activity with diagnostics and real-time monitoring. These "theranostic" platforms combine drug transport with imagery (e.g., fluorescence, magnetic resonance), offering personalised treatment and early detection of infections [32].
- Eco-Friendly and Biodegradable Systems: As concerns about environmental impact grow, research is moving toward green synthesis methods and biodegradable materials. Functionalized NPs derived from natural polymers like chitosan or synthesised using plant extracts show reduced toxicity and greater environmental compatibility [6,8,29].
- Combating Antimicrobial Resistance (AMR): Surface functionalization enables the co-delivery of multiple agents, such as antibiotics combined with efflux pump inhibitors or quorum sensing blockers, enhancing effectiveness against resistant strains. Such multifunctional systems help overcome microbial defence mechanisms and reduce the chance of resistance development [4,19,24].
- Scalable and Cost-Effective Fabrication: Despite their efficacy, many current functionalization techniques face challenges in scalability. To ensure real-world application, cost-effective and reproducible methods for nanoparticle production, such as microfluidic synthesis, must be developed and standardised [30].
- Regulatory Harmonisation and Clinical Translation: A significant barrier remains in the lack of regulatory standardisation for nanoparticle-based therapeutics. Without harmonised guidelines for toxicity, stability, and efficacy testing, clinical translation remains slow. Addressing these gaps through collaborative efforts can streamline the approval of functionalized NP systems [30].
- Integration with Digital and Predictive Tools: Machine learning and artificial intelligence are being applied to predict nanoparticle–microbe interactions, optimise surface modifications, and model biological responses. This integration can accelerate the design of safe and efficient nanotherapeutics [31,32].

9. Conclusion

The article emphasises that surface functionalization is a pivotal strategy for enhancing the interactions between nanoparticles (NPs) and microbes. By altering the external of NPs with working groups, biomolecules, or polymers, researchers can significantly improve the stability, biocompatibility, specificity, and antimicrobial efficacy of these nanomaterials. Functionalized NPs can more effectively penetrate biofilms, disorder microbial films, create reactive oxygen species (ROS), and deliver antimicrobial agents intracellularly.Various types of nanoparticles—metallic, carbon-based, polymeric, and lipid-based—are employed, each benefiting uniquely from surface modifications. Techniques such as covalent bonding, polymer coating, and biofunctionalisation have enabled targeted and stimuli-responsive antimicrobial

actions, making these systems suitable for diverse applications in medicine, food safety, environmental sanitation, and agriculture. Despite the progress, challenges such as toxicity, scalability, and regulatory barriers remain. Future research is expected to focus on eco-friendly materials, smart stimuli-responsive systems, and multifunctional platforms, all of which will play an important role in advancing next-generation antimicrobial nanotechnologies.

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