RESEARCH PAPER

Engineering Antimicrobial Nanostructures to Combat Urban Drug-Resistant Biofilms: A Microbiology-Chemistry Approach with Public Health Implications

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ABSTRACT

Biofilms at the interface of healthcare systems, wastewater networks, densely populated built environments, and contaminated community surfaces are increasingly influencing urban antimicrobial resistance. These organized microbial communities shield pathogens against antibiotics, disinfectants, host defenses, and environmental stress, and are significant contributors to persistence, recurrence and further transmission. This review explores the ways in which antimicrobial nanostructures can be designed as drug-delivery and anti-biofilm systems to deal with resistant biofilms in urban environments. A microbiology-chemistry paradigm is highlighted: microbiology characterizes the target phenotype, ecological niche, and predominant resistance mechanisms, and chemistry and materials engineering characterize particle size, surface charge, ligand density, catalytic activity, payload release, and biocompatibility. We present the key types of nanostructures that are currently relevant to biofilm control, such as metal and metal oxide nanoparticles, polymeric and chitosan-based carriers, lipid-based systems, nitric oxide-releasing platforms, nanozymes, photodynamic systems, and metal-organic-framework hybrids. In these classes, successful designs are reduced to a few functional needs: matrix penetration, localized high drug concentration, membrane disruption, catalytic production of reactive species, and programmable or stimulus-responsive release. Translational opportunities in wound care, implant coating, catheter protection, hospital drainage systems, and urban wastewater-related surveillance are also assessed in the article, and the unresolved issues of toxicity, environmental release, manufacturing reproducibility, and regulatory standardization are mentioned. We suggest that the future generation of anti-biofilm nanostructures must be safe-by-design, context-specific, and tested in clinically and environmentally realistic systems and not just simplified mono-species assays. This combined viewpoint makes antimicrobial nanotechnology consistent with biomedical engineering and with the priorities of the public-health.

Keywords: Antimicrobial resistance; Biofilms; Nanostructures; Drug delivery; Urban wastewater; Public health; Polymeric nanoparticles; Metal-organic frameworks.

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1. INTRODUCTION

Antimicrobial resistance (AMR) has emerged as one of the most impactful health threats to the world, and bacterial AMR is estimated to have resulted in 1.27 million deaths directly in 2019 and to have caused a much greater burden of morbidity and mortality [1]. In this crisis, biofilms are particularly problematic since they enable microorganisms to survive as surface-attached communities within a self-produced extracellular polymeric substance (EPS) that makes them less susceptible to antimicrobials and protects the community against host and environmental insults [2-4]. Much more attention should be paid to the urban aspect of resistant biofilms. The modern cities create continuous interfaces of hospitals, household sewage, pharmaceutical residues, water treatment plants, chronic wound care, water distribution systems, and high-density human contact. Such environments are conducive to the development and propagation of biofilm-related pathogens and resistance genes, particularly in drains, sewer biofilms, wastewater channels, and device-laden healthcare settings [5-8]. The issue is not limited to environmental microbiology, urban wastewater and hospital plumbing are becoming more and more known as reservoirs that can be fed back into healthcare-associated infections, community exposure, and regional AMR surveillance programs [5],[8],[9].

The development of conventional antibiotics has not been sufficient to address the issue of biofilm recalcitrance, since most failures are at the delivery, retention, penetration, and local pharmacodynamics levels, and not merely due to the lack of antibacterial activity. It is because of this that nanostructure-based techniques have become of great interest as anti- biofilm and drug-delivery technologies. Well-designed nanoplatforms have the ability to target cargo to infected surfaces, destabilize the EPS matrix, produce reactive oxygen or nitrogen species, co-deliver adjuvants, and release agents in response to pH, enzymes, light, or redox gradients [10-13].

It is an overview of the discipline in a microbiology-chemistry perspective that has obvious public-health consequences. It does not enumerate nanomaterials per se, but rather examines how the microbiological understanding of urban drug-resistant biofilms can be applied to the material choice, nanoscale design, translational testing, and implementation in the real-world urban setting. The integrated microbiology–chemistry–public health framework guiding the design and deployment of antimicrobial nanostructures in urban biofilm settings is illustrated in Figure 1.

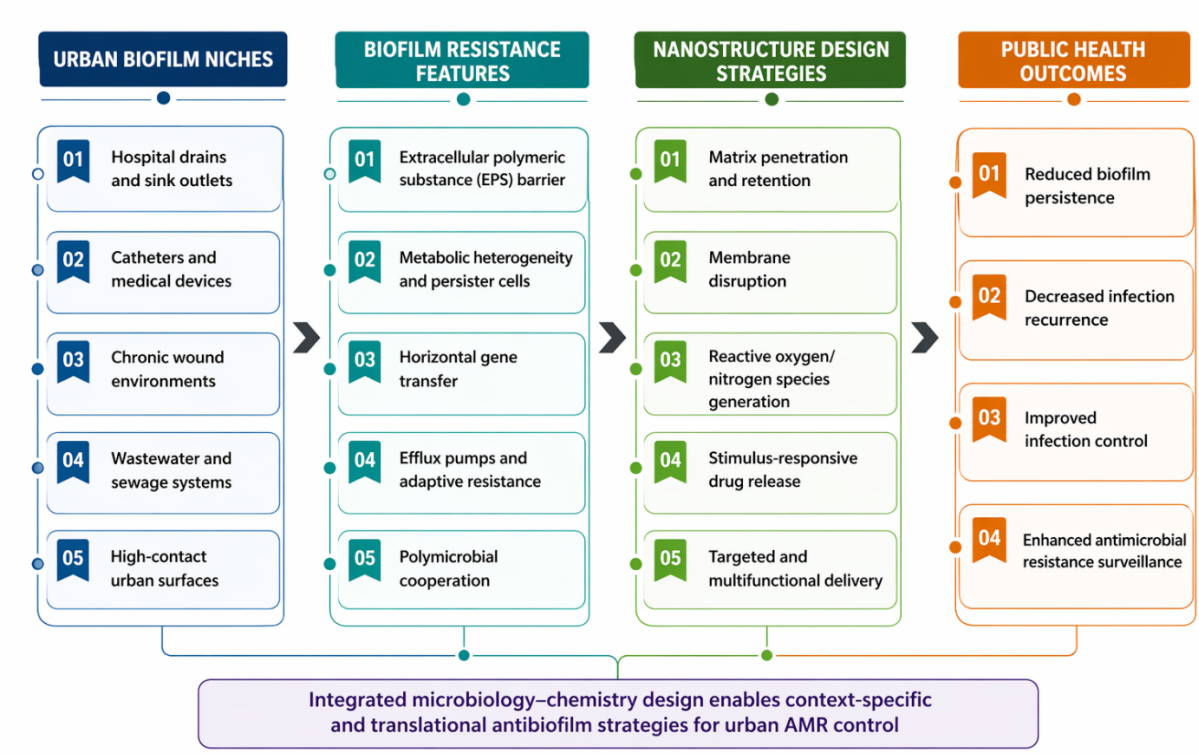

Figure 1. Microbiology–chemistry–public health framework for engineering antimicrobial nanostructures against urban drug-resistant biofilms.

2. REVIEW SCOPE AND LITERATURE APPROACH

The article is a narrative review. The discussion was constructed based on focused searches of records in publisher databases and biomedical databases, with a focus on the original biofilm articles and recent articles on antimicrobial nanostructures, urban wastewater-related AMR, implant biofilms, and translational anti-biofilm approaches. Mechanistic studies, high-quality reviews, clinically relevant models and recent reports that connect biofilm control to environmental and public-health

situations were prioritized.

3. URBAN DRUG-RESISTANT BIOFILMS AS A MICROBIOLOGICAL AND PUBLIC-HEALTH PROBLEM

The formation of biofilms is an adaptive survival mechanism and not a niche exception. Biofilms grow on hospital sink drains, endoscopes, catheters, prosthetic materials, dialysis devices, sewage pipes, sediment surfaces, and water-distribution interfaces in urban systems. The matrix maintains cells, nutrients, extracellular DNA, and signaling molecules, thus forming an efficient microenvironment to maintain and transfer resistance determinants [3],[14],[15]. Simultaneously, clinical pathogens including Staphylococcus aureus, Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae, Enterococcus faecium, and polymicrobial consortia are able to take advantage of these environments to create chronic reservoirs that are hard to eliminate [4],[9],[16]. The wastewater systems of cities are of particular interest since they combine human excreta, antibiotic residues, disinfectants, heavy metals, and a variety of microbial communities in an environment that may favor persistence and gene transfer. Recent studies indicate that hospital and urban wastewaters influence the composition of the matrix and active resistome of environmental biofilms, and Indian-based studies have shown contamination of river sediments and sewage microbiomes with last-resort antibiotic resistance genes [5-7]. The results reinforce the perception that AMR is a clinical, environmental, and infrastructural issue at the same time. Implications on the public-health are multilayered. To begin with, urban biofilms enhance the chances of chronic and recurrent infections due to shielding bacteria against treatment. Second, they are incubators of horizontal gene transfer and phenotypic tolerance. Third, they make it difficult to prevent infections in resource-constrained urban hospitals, in which drains, humid surfaces, and reusable medical equipment can be a continuing source of exposure. Lastly, they criticize surveillance, as culture-based methods might only inadequately capture the ecological scope of resistant communities [1],[8],[9],[16]. One conceptual change that can be useful is to consider urban resistant biofilms as ecological systems having clinical implications. This view clarifies that anti-biofilm technologies must not just be able to kill planktonic bacteria in vitro, but also operate in chemically complex, shear-dependent, polymicrobial, and frequently nutrient-variable environments that are similar to drains, wounds, mucosal surfaces, or implant-associated niches.

4. MICROBIOLOGICAL BASIS OF BIOFILM PERSISTENCE AND REDUCED ANTIMICROBIAL SUSCEPTIBILITY

The ability of any nanostructure to counter the biology of persistence determines its anti-biofilm performance. The overall process of biofilm development involves attachment, microcolony formation, maturation of the matrix and dispersal. At these phases, the EPS matrix stores polysaccharides, proteins, lipids, and extracellular DNA. This matrix is not just a passive barrier, it entraps and neutralises antimicrobials, retards diffusion, regulates local ionic strength and forms biochemical gradients, which influence cellular physiology [2],[3],[14]. Physiological heterogeneity is a significant cause of therapeutic failure. The cells on the periphery of the biofilm tend to be metabolically active, whereas the deeper layers may be oxygen-deprived, nutrient-deprived, acidic, or dormant. These subpopulations have different susceptibilities to antibiotics due to the fact that most traditional agents rely on active growth or membrane energetics to be most effective [4],[15],[17]. Slow growing subpopulations and persister cells thus endure exposures that easily kill planktonic counterparts, allowing post-treatment regrowth. Genetic and phenotypic mechanisms of resistance are also promoted in biofilms. Survival is facilitated by increased efflux activity, changes in outer-membrane permeability, stress-response pathways, expression of biofilm-specific genes, and close cell proximity. Extracellular DNA has the ability to stabilize the matrix structurally and also play a role in horizontal gene transfer. Moreover, polymicrobial biofilms can exhibit cooperative protection, such as shared enzymes, cross-feeding, matrix complementation, or redox buffering [4],[14],[15]. These processes justify why minimum inhibitory concentration data of planktonic assays tend to have poor correlation with biofilm eradication. They also support multifunctional anti-biofilm systems. An effective nanostructure is thus one that does multiple jobs simultaneously: get to the biofilm, stay there, disrupt the matrix or membrane, and ideally, inhibit regrowth or recolonization.

5. CHEMISTRY-GUIDED DESIGN RULES FOR ANTIMICROBIAL NANOSTRUCTURES

In terms of materials, antimicrobial nanostructures are successful when physicochemical properties are carefully aligned to the microbial target and delivery environment. The diameter of particles affects diffusion via EPS pores, host cell uptake, renal clearance, and ligand presentation surface area. The shape influences margination, membrane contact, and penetration, whereas the surface charge has a strong influence on association with negatively charged bacterial envelopes and matrix components. Additional factors affecting adsorption, protein corona formation, and local retention are hydrophobicity, roughness, and ligand architecture [10],[13],[18],[19]. To design anti-biofilm, it is not enough to reduce the size. Particles of very small size can penetrate effectively but can be cleared quickly or cause toxicity, in contrast to strongly cationic systems which adsorb to EPS but can bind too tightly at the biofilm edge, or damage mammalian membranes. The most promising designs are thus those that strike a balance between penetration and controlled retention and prefer context-sensitive activation. They can be pH-responsive carriers, releasing antibiotics in acidic sites of infection, enzyme-responsive shells, which are broken down by bacterial enzymes, or redox-sensitive systems, which take advantage of the oxidative microenvironment of inflamed tissues

[12],[20],[21]. Combination therapy at the nanoscale is also possible with the help of chemical engineering. To overcome several resistance mechanisms simultaneously, antibiotics may be co-loaded with membrane-active agents, quorum-sensing inhibitors, chelators, photosensitizers or nitric oxide donors. Biofilm localization may be enhanced by surface functionalization with peptides, antibodies, or polysaccharide-binding motifs. Immobilized nanostructures could be used in coating applications to transform a passive medical surface into an active antibiofilm interface, without compromising biocompatibility and device functionality [10],[11],[22],[23]. An urban-use-case of chemistry-guided framework is particularly useful. Hospital drain biofilms, such as, are not similar to chronic wound biofilms in terms of ionic composition, shear stress, nutrient inputs and tolerable toxicity levels. Urban wastewater applications can be compatible with other carrier chemistries not compatible with implant coating or topical wound formulations. It is not possible to presuppose that the same nanomaterial will work best in all of these environments.

6. MAJOR CLASSES OF ANTIMICROBIAL NANOSTRUCTURES FOR RESISTANT BIOFILMS

Given the structural and functional diversity of currently available antibiofilm nanosystems, it is useful to classify these platforms according to their material architecture and dominant mechanisms of action. The major classes of antimicrobial nanostructures relevant to resistant biofilm control, together with their principal antibiofilm functions, are presented in Figure 2.

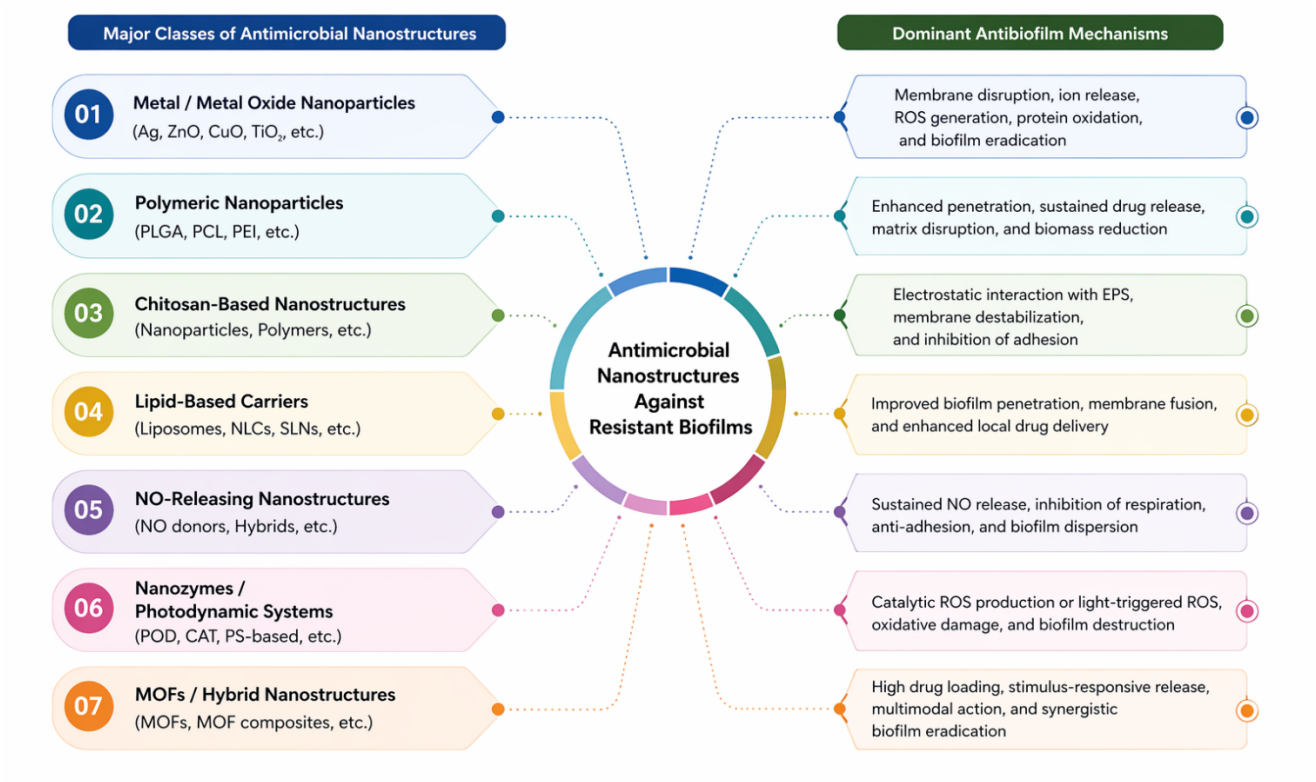

Figure 2. Major classes of antimicrobial nanostructures used against resistant biofilms and their dominant antibiofilm mechanisms

6.1 Metal and metal oxide nanoparticles

Nanostructures made of metal are still one of the most actively researched antibiofilm systems. Silver, zinc oxide, copper oxide, iron oxide, and composite metallic platforms have overlapping actions that encompass destabilization of membranes, dysfunction of proteins, release of ions, oxidative stress, and disruption of DNA replication. Their key benefit is mechanistic breadth: in contrast to most single-target antibiotics, metallic nanoparticles can damage many bacterial structures simultaneously and thus are appealing to tolerant biofilm populations [18],[19],[24],[25]. Nevertheless, the reactivity which contributes to antibacterial performance may also result in host toxicity, environmental retention, and size, coating chemistry, and medium composition variability [10],[26].

6.2 Polymeric and chitosan-based nanostructures

A more controllable path to local delivery of antibiofilms is offered by polymeric nanocarriers. They have strengths such as controlled drug release, structural versatility, cargo protection, and more readily incorporation of targeting ligands or adjuvants. Chitosan is of special interest as its cationic amino groups facilitate adhesion to bacterial surfaces and can also destabilize membranes and modify matrix integrity. The structure-activity relationships are based on the molecular weight, the extent of deacetylation,

and chemical substitution, and chitosan is a good model of how minor chemical alterations can significantly modify antimicrobial behavior [20],[27],[28]. Wound dressings, topical films, and injectable depots are also good applications of polymeric platforms, where sustained local exposure is desirable, rather than systemic dosing [12],[21].

6.3 Lipid-based carriers and hybrid lipid-polymer systems

Conventional liposomes, solid lipid nanoparticles, nanostructured lipid carriers, and lipid-polymer hybrids are lipidic systems that have proven beneficial in delivering hydrophobic drugs, membrane-active compounds, and synergistic adjuvants. Since lipid vesicles are able to fuse with bacterial membranes or incorporate into matrix lipophilic domains, they have the potential to increase intracellular or intra-biofilm access to the drug payload. Their usefulness in minimizing systemic exposure and targeting treatment to infected tissues is also highlighted in several reviews [29-32]. In the case of biofilms, lipidic nanocarriers are particularly appealing when the pharmacokinetics of the antibiotics are otherwise unfavourable or when the payload of interest is unstable in solution [12].

6.4 Nitric oxide-releasing nanostructures

Nitric oxide (NO) is in a unique position since it may serve as a direct antimicrobial mediator and as a biofilm-dispersing signal. Sustained NO-releasing nanoparticles have demonstrated activity in S. aureus infection models, and have disrupted methicillin-resistant S. aureus adhesion and catheter-associated biofilm formation in vivo [33],[34]. These platforms demonstrate a significant rule that successful anti-biofilm nanostructures do not necessarily have to be based solely on classical antibiotics. The spatial and temporal control of gasotransmitter delivery can disrupt biofilm architecture and re-expose the biofilm to companion agents.

6.5 Nanozymes, photodynamic systems, and catalytic oxidative platforms

A fast-growing frontier is catalytic nanostructures. Nanozymes can be used to replicate peroxidase, oxidase, or catalase-like functions to produce bactericidal reactive species in infection-relevant conditions and photodynamic systems can be used to produce cytotoxic oxidants within biofilms by using light-activated photosensitizers [35-37]. These methods are appealing as they may overcome certain traditional resistance mechanisms and provide on-demand activity. Their disadvantages are also significant: it can be challenging to induce external triggering in deep tissues, oxygen constraints can decrease photodynamic efficacy, and the trade-off between bacterial destruction and host compatibility is highly context-dependent [13].

6.6 Metal-organic frameworks and multifunctional hybrid nanosystems

Metal-organic frameworks (MOFs) and hybrid nanostructures (based on them) combine high surface area, adjustable porosity, catalytic activity, and large cargo-loading capacity. They can function as carriers, stimuli-responsive depots, catalytic antibacterials, or multimodal platforms integrating antibiotic release with photodynamic, photothermal, or ion-mediated effects [38],[39]. The combination of MOFs or catalytic nanocomponents with polymeric shells, metallic cores, or lipidic envelopes is especially promising as it allows controlling penetration, payload release, and microenvironmental activation simultaneously [13],[18].

Representative quantitative performance metrics of antimicrobial nanostructures against drug-resistant biofilms reported in the literature are summarized in Table 1.

Table 1. Quantitative performance of representative antimicrobial nanostructures against resistant biofilms.

Nanostructure platform	Target biofilm / organism	Particle size (nm)	Surface charge / zeta potential (mV)	Active component / functional feature	Effective concentration	Quantitative antibiofilm outcome	Exposure time / test condition
Silver nanoparticles	*S. aureus*, *P. aeruginosa* biofilms	10–100	+10 to +35 / variable	Silver ion release, membrane disruption	5–100 µg/mL	50–99% biomass reduction; 2–5 log CFU reduction	6–24 h, in vitro
Zinc oxide nanoparticles	Gram-positive and Gram-negative biofilms	20–150	+5 to +30 / variable	ROS generation, membrane damage	10–200 µg/mL	40–90% biofilm inhibition	12–24 h, in vitro
Polymeric nanoparticles	Drug-resistant bacterial biofilms	80–250	−10 to +25	Sustained antibiotic/adjuvant release	0.5–10× MIC	60–95% biomass reduction	24–72 h, in vitro / ex vivo

Chitosan-based nanoparticles	Mixed-species or wound-associated biofilms	100–300	+20 to +50	Electrostatic matrix interaction, membrane destabilization	50–500 µg/mL	50–90% reduction in viability / biomass	12–48 h, pH-dependent
Lipid-based nanocarriers	Resistant biofilms with poor drug penetration	80–250	−15 to +10	Fusion-assisted delivery of hydrophobic drugs	1–10× MIC	40–85% higher local antibiofilm effect than free drug	24–48 h
NO-releasing nanoparticles	*S. aureus* / MRSA biofilms	50–200	Variable	Sustained nitric oxide release	0.5–5 µmol NO flux	Significant inhibition of adhesion and biofilm formation; reduced bacterial burden	Hours to days; in vivo / device model
Nanozymes	Mature bacterial biofilms	20–200	Variable	Catalytic ROS generation	10–200 µg/mL	60–95% bacterial killing under catalytic conditions	Trigger-dependent
Photodynamic nanosystems	Accessible surface biofilms	50–300	Variable	Light-activated ROS production	1–100 µg/mL photosensitizer equivalent	70–99% biomass / viability reduction after irradiation	Minutes to hours; light-triggered
MOF-based systems	Drug-resistant mono- or polymicrobial biofilms	50–200	Variable	High loading, responsive release, multimodal action	5–50 µg/mL	60–95% antibiofilm reduction depending on trigger and cargo	12–48 h

Note: *Values are presented as representative numerical ranges reported across the antibiofilm nanomaterial literature and may vary according to formulation chemistry, microbial species, biofilm maturity, and assay conditions. MIC = minimum inhibitory concentration; NO = nitric oxide; ROS = reactive oxygen species; MOF = metal-organic framework.*

7. TRANSLATION TO CLINICAL AND URBAN USE-CASES

Clinical translation is best developed in situations where local delivery is evidently superior to systemic exposure. These are chronic wounds, catheter-associated infections, orthopedic implants, dental biofilms and device coatings. The logic of drug delivery in these environments is strong: keep the local concentration high, minimize off-target toxicity, avoid early colonization and inhibit matrix formation before the formation of mature biofilms [9],[12],[23]. Indwelling device coating strategies can be particularly beneficial since they change the treatment of mature biofilms to prevention of initial attachment and formation of microcolonies [22],[23].

The conceptually newer yet highly relevant applications of urban environment are the applications of urban environment. Recurrent biofilm reservoirs include hospital drainage systems, trap seals, sink outlets, and wastewater conduits, which can be targeted using surface-active coating, local catalytic treatment, or environmentally contained formulations that can suppress biofilm biomass and minimize the release of resistant organisms. Meanwhile, the AMR surveillance related to wastewater can provide information on where such interventions are most reasonable and how their performance should be measured [5],[7],[8].

One of the most important translational lessons is that efficacy should be equalized to place. The wound beds, sewer biofilms, and stainless-steel drains present various limitations to the release kinetics, biodegradability, shear stability, light accessibility, and containment. A site-first design logic can be used to ensure that advanced nanomaterials do not only pass simple in vitro tests.

Table 2. Representative Nanostructure Platforms for Drug-Resistant Biofilms

Platform class	Representative design logic	Primary antibiofilm mechanism(s)	Likely urban/clinical use-case	Major caution
Metal / metal oxide nanoparticles	Ag, ZnO, CuO, Fe-based, or core-shell catalytic particles	Membrane disruption, ion release, ROS generation, multisite damage	Topical formulations, coatings, surface decontamination, drain-facing materials	Host toxicity, environmental persistence, medium-dependent activity
Polymeric nanoparticles	Biodegradable carriers with controlled release and ligand functionalization	Improved retention, sustained local antibiotic exposure, co-delivery of adjuvants	Wounds, implant-adjacent depots, catheter lock formulations	Scale-up reproducibility and polymer-drug compatibility
Chitosan-based systems	Cationic polysaccharide nanoparticles, films, hydrogels	Electrostatic interaction with bacterial envelopes, matrix destabilization, payload delivery	Wound dressings, oral formulations, mucosal biofilms	Charge-driven cytotoxicity and variable performance across pH
Lipid / liposome / NLC systems	Membrane-interacting vesicles and lipid-polymer hybrids	Fusion-assisted delivery, improved transport of hydrophobic cargo, local concentration	Skin and soft tissue infection, implant coatings, localized antibiofilm delivery	Stability during storage and sterilization
NO-releasing nanoparticles	Sustained gasotransmitter release from nanoscale depot	Biofilm dispersal, oxidative/nitrosative stress, synergy with antibiotics	Catheters, wound infection, surface protection	Dose control, off-target tissue effects, shelf-life constraints
Nanozymes / photodynamic platforms	Catalytic or light-activated ROS-generating systems	On-demand oxidative killing and matrix injury	Accessible wound beds, dental plaques, exposed device surfaces	Need for trigger conditions; limited deep-tissue utility
MOFs and hybrid multifunctional systems	Porous high-loading frameworks with responsive release or multimodal action	Carrier function plus catalytic, photodynamic, or ion-mediated effects	Advanced local delivery and smart coatings	Complex manufacturing and regulatory classification

Note: The most promising platforms integrate local delivery with matrix disruption or catalytic killing; platform selection should be guided by the intended biofilm niche

8. SAFETY, ECOLOGICAL, AND REGULATORY CHALLENGES

Anti-biofilm nanostructures have a number of translational challenges, despite the impressive preclinical promise. The most apparent one is toxicity. Cationic or extremely oxidative nanomaterials can cause harm to host membrane, slow healing of wounds, disrupt beneficial microbiota, or be deposited in organs following repeated exposure. Persistent metallic or catalytic particle release in the environment brings up further concerns regarding sedimentation, non-target toxicity, and resistance co-selection [10],[18],[19].

The other issue is that there is the likelihood of adaptive responses to the nanomaterials themselves. Even though broad-spectrum physical and catalytic mechanisms can help mitigate the risk of classic target-based resistance, bacteria can still modify membrane composition, control efflux, enhance EPS production, or increase antioxidant defenses in a manner that blunts nanoparticle activity. The discipline must not take the naive stance that nanomaterials are resistant-proof, however. Rather, they can be interpreted as mechanisms that can reduce selective pressure or expand killing mechanisms when used rationally in conjunction with stewardship principles [10],[25],[40].

It is also important to standardize. Most of the reported studies employ fixed mono-species biofilms, brief exposure times, undefined coronas of particles, and minimal toxicology. These models are handy yet do not tend to reflect clinical or urban environments. More informative pipelines ought to comprise flow-cell systems, polymicrobial consortia, mature biofilms, ex vivo tissues, device-relevant substrates, wastewater-mimicking media and direct comparison to standard-of-care antibiotics or disinfectants [13],[21],[23].

The production and control can become critical bottlenecks. Before it can be widely used, batch-to-batch reproducibility, sterilization stability, shelf life, ligand integrity, and scalable synthesis have to be resolved. Regulatory assessment will also require to take into account whether a product is acting more like a drug, a drug coating, a combination product or an environmental antimicrobial material. This applies especially to urban infrastructure applications that lie between clinical care, environmental engineering, and public-health governance.

Table 3. A Microbiology-Chemistry-Public Health Roadmap for Development

Development stage	Microbiology question	Chemistry / engineering action	Public-health relevance	Preferred readout
1. Niche selection	Which urban biofilm niche is being targeted (wound, drain, catheter, sediment, implant)?	Define acceptable size, coating, release, and containment window	Prevents technology drift away from real need	Context-specific target product profile
2. Pathogen profiling	Which organisms, matrix traits, and resistance mechanisms dominate?	Tune charge, ligand density, cargo combination, catalytic activity	Improves relevance to local AMR epidemiology	Biofilm biomass, viable count, resistance-gene profile
3. Model construction	Does the test system mimic mature, polymicrobial, shear-exposed biofilms?	Select substrate, flow, trigger mechanism, dosing schedule	Supports evidence useful for infection control or wastewater policy	Eradication under flow, recolonization delay, matrix disruption
4. Safety evaluation	What host or environmental compartments may be exposed?	Measure cytotoxicity, degradation, ion release, particle fate	Addresses stewardship and environmental health	Toxicology, biodegradation, non-target effects
5. Translational deployment	Is the platform best used as therapy, prevention, coating, or adjunct?	Optimize formulation stability, sterilization, and scale-up	Aligns intervention with hospital or infrastructure practice	Shelf life, manufacturability, cost, implementation feasibility
6. Surveillance feedback	Can intervention performance be tracked through culture, genomics, or wastewater signals?	Link formulation decisions to measurable surveillance outputs	Enables iterative and equitable public-health deployment	Reduced AMR markers, reduced recurrence, operational usability

Note: Translation is strongest when microbiological target definition, nanoscale design, and surveillance-relevant outcomes are specified together.

Key quantitative indicators related to safety, efficacy, and translational feasibility of antimicrobial nanostructures are summarized in Table 4.

Table 4. Quantitative safety and translational indicators for antimicrobial nanostructure-based antibiofilm systems.

Platform	Effective antibiofilm concentration	Cytotoxicity (cell viability)	Release duration / activity window	Trigger / activation condition	Translational limitation
Metal / metal oxide nanoparticles (Ag, ZnO, CuO)	5–100 µg/mL	60–90% viability (dose-dependent)	Immediate to short-term (hours–days)	Intrinsic catalytic / ion release	Host toxicity; environmental persistence
Polymeric nanoparticles	0.5–10× MIC (drug-dependent)	75–95% viability	Sustained (24–120 h)	pH-, enzyme-, or diffusion-controlled release	Scale-up reproducibility; polymer–drug compatibility
Chitosan-based systems	50–500 µg/mL	70–90% viability	Moderate (12–72 h)	Electrostatic interaction; pH-sensitive behavior	Charge-related cytotoxicity; pH variability
Lipid-based carriers (liposomes, NLCs)	1–10× MIC	80–98% viability	Sustained (24–96 h)	Membrane fusion / passive release	Storage stability; sterilization sensitivity

NO-releasing nanoparticles	0.5–5 µmol NO flux	65–90% viability (dose-dependent)	Controlled release (hours–days)	Chemical NO donor decomposition	Dose control; off-target tissue effects
Nanozymes / photodynamic systems	10–200 µg/mL (material-dependent)	60–85% viability	On-demand (minutes–hours)	Light activation / catalytic ROS generation	Limited penetration; requirement of trigger
MOFs / hybrid systems	5–50 µg/mL	70–90% viability	Tunable (hours–days)	pH-, redox-, or light-responsive release	Complex synthesis; regulatory classification

Note: Values represent typical ranges reported across recent studies and vary depending on nanostructure composition, biofilm model, and experimental conditions. MIC = minimum inhibitory concentration; NO = nitric oxide; ROS = reactive oxygen species.

9. FUTURE DIRECTIONS

Maximal material complexity as an end in itself is not the most fruitful avenue of the field, but intelligent adaptation of formulation logic to microbial ecology. Safe-by-design, biofilm-niche-targeted, and benchmarked against well-defined translational endpoints (e.g., biofilm elimination in flow, less recolonization of medical surfaces, less resistance gene release, or better wound healing) should be the characteristics of future anti-biofilm nanostructures. Multifunctional systems will probably continue to be significant, but must be supported by quantifiable benefits over simple carriers [13],[18],[21].

The need to be more closely integrated with epidemiology and urban public health is also a strong one. Monitoring of wastewater, mapping of hospital drains, genomic resistance profiling, and clinical outbreak investigation can be used to determine the biofilm niches where nanostructure-based interventions would be most effective. On the other hand, the environmental fate, antimicrobial stewardship, and implementation constraints must be included in the initial design by material scientists. This is particularly pertinent to the fast urbanizing and resource-limited areas, where the biofilm-related AMR can be enhanced by overcrowding, poor water infrastructure, and high burden of infectious diseases [1],[6],[7],[16].

A significant translational opportunity is hybrid use, as opposed to replacement. Nanostructures can be of greatest use as adjuvant systems to resensitize biofilms to pre-existing antibiotics, increase local residence time, or prevent recolonization following debridement and disinfection. These approaches are more in line with the objectives of stewardship than an unregulated increase in the number of new antimicrobial products.

10. CONCLUSION

Urban drug-resistant biofilms is an interface of microbiology, chemistry, biomedical engineering, and public health. They are resilient due to the protection of the matrix, physiological heterogeneity, horizontal gene transfer, and the selection pressures that are produced by healthcare and wastewater systems. Antimicrobial nanostructures offer a viable route to improved control since they can be designed to access biofilms, deliver concentrated cargoes, cause catalytic damage, and convert passive surfaces into active antibiofilm interfaces [4],[10],[13].

However, development will not be founded on novelty as such but disciplined translation. The following generation of platforms ought to be considered in realistic models, optimized to a specific urban or clinical niche, and created with explicit consideration of toxicology, environmental release, reproducibility, and regulatory fit. The most reasonable way to go, in nanostructure-enabled control of resistant biofilms, is a microbiology-chemistry approach, associated with surveillance and public-health priorities.

Declarations

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REFERENCES

1. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022;399(10325):629-655. doi:10.1016/S0140-6736(21)02724-0.
2. Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. Science. 1999;284(5418):1318-1322. doi:10.1126/science.284.5418.1318.
3. Flemming HC, Wingender J, Szewzyk U, Steinberg P, Rice SA, Kjelleberg S. Biofilms: an emergent form of bacterial life. Nat Rev Microbiol. 2016;14(9):563-575. doi:10.1038/nrmicro.2016.94.
4. Ciofu O, Moser C, Jensen PØ, Høiby N. Tolerance and resistance of microbial biofilms. Nat Rev Microbiol. 2022;20(10):621-635. doi:10.1038/s41579-022-00682-4.

5. Buelow E, Dauga C, Carrion C, Mathé-Hubert H, Achaibou S, Gaschet M, et al. Hospital and urban wastewaters shape the matrix and active resistome of environmental biofilms. Water Res. 2023;244:120408. doi:10.1016/j.watres.2023.120408.
6. Marathe NP, Pal C, Gaikwad SS, Jonsson V, Kristiansson E, Larsson DGJ. Untreated urban waste contaminates Indian river sediments with resistance genes to last resort antibiotics. Water Res. 2017;124:388-397. doi:10.1016/j.watres.2017.07.060.
7. Paul D, Talukdar D, Kapuganti RS, Gupta V, Narendrakumar L, Jana P, et al. Antibiotic contamination and antimicrobial resistance dynamics in the urban sewage microbiome in India. Nat Commun. 2026;17:1274. doi:10.1038/s41467-025-68034-3.
8. Hassoun-Kheir N, de Kraker MEA, Bertrand X, Van Hoorde K, Graham DW, Hocquet D. How to establish a hospital wastewater surveillance program for antimicrobial resistance: current experience and future knowledge gaps. CMI Commun. 2025;2:105087. doi:10.1016/j.cmicom.2025.105087.
9. Biswas R, Jangra B, Ganapathy A, Ravichandiran V, Mohan U. Current strategies for combating biofilm-forming pathogens in clinical healthcare-associated infections. Indian J Microbiol. 2024;64(3):781-796. doi:10.1007/s12088-024-01221-w.
10. Makabenta JMV, Nabawy A, Li CH, Schmidt-Malan S, Patel R, Rotello VM. Nanomaterial-based therapeutics for antibiotic-resistant bacterial infections. Nat Rev Microbiol. 2021;19(1):23-36. doi:10.1038/s41579-020-0420-1.
11. Huh AJ, Kwon YJ. Nanoantibiotics: a new paradigm for treating infectious diseases using nanomaterials in the antibiotics-resistant era. J Control Release. 2011;156(2):128-145. doi:10.1016/j.jconrel.2011.07.002.
12. Gao W, Chen Y, Zhang Y, Zhang Q, Zhang L. Nanoparticle-based local antimicrobial drug delivery. Adv Drug Deliv Rev. 2018;127:46-57. doi:10.1016/j.addr.2017.09.015.
13. Xie Y, Liu H, Teng Z, Ma J, Liu G. Nanomaterial-enabled anti-biofilm strategies: new opportunities for treatment of bacterial infections. Nanoscale. 2025;17:5605-5628. doi:10.1039/D4NR04774E.
14. Hall CW, Mah TF. Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. FEMS Microbiol Rev. 2017;41(3):276-301. doi:10.1093/femsre/fux010.
15. Liu HY, Prentice EL, Webber MA. Mechanisms of antimicrobial resistance in biofilms. npj Antimicrob Resist. 2024;2(1):27. doi:10.1038/s44259-024-00046-3.
16. Datta S, Nag S, Roy DN, et al. Biofilm-producing antibiotic-resistant bacteria in Indian patients: a comprehensive review. Curr Med Res Opin. 2024;40(3):403-422. doi:10.1080/03007995.2024.2305241.
17. Stewart PS, Franklin MJ. Physiological heterogeneity in biofilms. Nat Rev Microbiol. 2008;6(3):199-210. doi:10.1038/nrmicro1838.
18. Parvin N, Joo SW, Mandal TK. Nanomaterial-based strategies to combat antibiotic resistance: mechanisms and applications. Antibiotics (Basel). 2025;14(2):207. doi:10.3390/antibiotics14020207.
19. Mondal SK, Chakraborty S, Manna S, Mandal SM. Antimicrobial nanoparticles: current landscape and future challenges. RSC Pharm. 2024;1(3):388-402. doi:10.1039/D4PM00032C.
20. Wang Y, Sun H. Polymeric nanomaterials for efficient delivery of antimicrobial agents. Pharmaceutics. 2021;13(12):2108. doi:10.3390/pharmaceutics13122108.
21. Obeid MA, Alyamani H, Alenaizat A, Tunç T, Aljabali AAA, Alsaadi MM. Nanomaterial-based drug delivery systems in overcoming bacterial resistance: current review. Microb Pathog. 2025;203:107455. doi:10.1016/j.micpath.2025.107455.
22. Ferreres G, Ivanova K, Ivanov I, Tzanov T. Nanomaterials and coatings for managing antibiotic-resistant biofilms. Antibiotics (Basel). 2023;12(2):310. doi:10.3390/antibiotics12020310.
23. Scalia AC, Najmi Z. Targeting bacterial biofilms on medical implants: current and emerging approaches. Antibiotics (Basel). 2025;14(8):802. doi:10.3390/antibiotics14080802.
24. Dakal TC, Kumar A, Majumdar RS, Yadav V. Mechanistic basis of antimicrobial actions of silver nanoparticles. Front Microbiol. 2016;7:1831. doi:10.3389/fmicb.2016.01831.
25. Baptista PV, McCusker MP, Carvalho A, Ferreira DA, Mohan NM, Martins M, Fernandes AR. Nano-strategies to fight multidrug resistant bacteria - 'A battle of the titans'. Front Microbiol. 2018;9:1441. doi:10.3389/fmicb.2018.01441.
26. Munir MU, Ahmad MM. Nanomaterials aiming to tackle antibiotic-resistant bacteria. Pharmaceutics. 2022;14(3):582. doi:10.3390/pharmaceutics14030582.
27. Ke CL, Deng FS, Chuang CY, Lin CH. Antimicrobial actions and applications of chitosan. Polymers (Basel). 2021;13(6):904. doi:10.3390/polym13060904.
28. Sahariah P, Másson M. Antimicrobial chitosan and chitosan derivatives: a review of the structure-activity relationship. Biomacromolecules. 2017;18(11):3846-3868. doi:10.1021/acs.biomac.7b01058.
29. Forier K, Raemdonck K, De Smedt SC, Demeester J, Coenye T, Braeckmans K. Lipid and polymer nanoparticles for drug delivery to bacterial biofilms. J Control Release. 2014;190:607-623. doi:10.1016/j.jconrel.2014.03.055.

30. Wang DY, van der Mei HC, Ren Y, Busscher HJ, Shi L. Lipid-based antimicrobial delivery-systems for the treatment of bacterial infections. Front Chem. 2020;7:872. doi:10.3389/fchem.2019.00872.
31. Ghosh R, De M. Liposome-based antibacterial delivery: an emergent approach to combat bacterial infections. ACS Omega. 2023;8(39):35442-35451. doi:10.1021/acsomega.3c04893.
32. Ahsan A, Thomas N, Barnes TJ, Subramaniam S, Loh TC, Joyce P, Prestidge CA. Lipid nanocarriers-enabled delivery of antibiotics and antimicrobial adjuvants to overcome bacterial biofilms. Pharmaceutics. 2024;16(3):396. doi:10.3390/pharmaceutics16030396.
33. Martinez LR, Han G, Chacko M, Mihu MR, Jacobson M, Gialanella P, et al. Antimicrobial and healing efficacy of sustained release nitric oxide nanoparticles against Staphylococcus aureus skin infection. J Invest Dermatol. 2009;129(10):2463-2469. doi:10.1038/jid.2009.95.
34. Mihu MR, Cabral V, Pattabhi R, Tar M, Davies KP, Friedman AJ, et al. Sustained nitric oxide-releasing nanoparticles interfere with methicillin-resistant Staphylococcus aureus adhesion and biofilm formation in a rat central venous catheter model. Antimicrob Agents Chemother. 2017;61(1):e02020-16. doi:10.1128/AAC.02020-16.
35. Zhao K, Zhao Y, Wang Y, Han B, Lian M. Progress in antibacterial applications of nanozymes. Front Chem. 2024;12:1478273. doi:10.3389/fchem.2024.1478273.
36. Hu X, Huang YY, Wang Y, Wang X, Hamblin MR. Antimicrobial photodynamic therapy to control clinically relevant biofilm infections. Front Microbiol. 2018;9:1299. doi:10.3389/fmicb.2018.01299.
37. Warrier A, Mazumder N, Prabhu S, Satyamoorthy K, Murali TS. Photodynamic therapy to control microbial biofilms. Photodiagnosis Photodyn Ther. 2021;33:102090. doi:10.1016/j.pdpdt.2020.102090.
38. Li R, Chen T, Pan X. Metal-organic-framework-based materials for antimicrobial applications. ACS Nano. 2021;15(3):3808-3848. doi:10.1021/acsnano.0c09617.
39. Chen Z, Xing F, Yu P, Zhou Y, Luo R, Liu M, et al. Metal-organic-framework-based advanced therapeutic tools for antimicrobial applications. Acta Biomater. 2024;175:27-54. doi:10.1016/j.actbio.2023.12.023.
40. Joshi AA, Patil RH. Nanoparticles targeting biofilms: a new era in combating antimicrobial resistance. Med Microecol. 2025;26:100156. doi:10.1016/j.medmic.2025.100156.