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Green nano-semiconductors and nanometals to avert complex phenomena of antimicrobial resistance (AMR)

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Antimicrobial resistance (AMR) is a silent pandemic in the lens of One Health, which is impacting current global healthcare facilities/therapeutics and the environment. AMR is a complex system in which clinical misuse/overuse of antibiotics, environmental contamination, and microbial evolution form a dynamic/adaptive network of resistance propagation for conventional antibiotics, requiring urgent alternatives. This opinion highlights the potential of green-synthesised nano-semiconductors/nanometals (GNSS/GNMS) fabricated using biochemicals procured from plants, microbes, waste/green solvents, to combat AMR. They exhibit multifaceted antimicrobial mechanisms, including oxidative stress induction, membrane disruption, metal ion release, biofilm inhibition, quorum sensing interference, and antibiotic synergism. Moreover, they demonstrated transformative potential in diagnostics, wound healing, agriculture, and wastewater remediation owing to their exceptional physicochemical properties, including band-gap tunability, biocompatibility and low toxicity. The challenges, like synthesis variability and standardisation, that restrict their commercial adaptability are discussed with alternatives to establish them as sustainable solutions to AMR, considering the UN's SDGs.

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Introduction

Antimicrobial resistance (AMR) has emerged as one of the most pressing global One Health threats of the 21st century, undermining decades of medical progress [1]. The overuse, wrong use and misuse of antipathogens, especially antibiotics, in clinical, veterinary, and agricultural sectors have accelerated the development of multidrug-resistant (MDR) pathogens and are challenging present-day healthcare facilities [2]. The World Health Organisation (WHO) classifies AMR as a principal global One Health priority, anticipating that by 2050, drug-resistant contagions can lead to 10 million global mortalities annually [1]. Addressing this health crisis necessitates designing unconventional and innovative solutions through decoding this complex AMR system with multiple intricacies involving microbes, antibiotics, human health systems, and environmental factors, all interacting in nonlinear and dynamic ways, giving rise to an emergent behavior [3]. These systems show properties including nonlinearity, feedback loops, and self-organisation, where slight changes in one constituent can result in substantial impacts on the entire arrangement, thus complicating the fight against AMR.

Within this AMR framework, green nanotechnology, characterised by eco-sustainability, high reactivity, targeted ability and biocompatibility, provides powerful tools to influence these complex systems and address AMR through different mechanisms [4]. By introducing green nanomaterials, including nano-semiconductors and nanometals, the interactions within the microbial ecosystem and between microbes and host organisms can be manipulated in a sustainable way that can restore balance, or at least slow the advancement of resistance [4]. The antimicrobial efficacy of these nanomaterials is not simply additive, but they interact with the biological systems in a multidimensional manner, often triggering emergent properties. For example, nano-semiconductors produce reactive oxygen species (ROS) on exposure to light, which, in turn, activate a process of oxidative damage in bacteria and disrupt their metabolic pathways [5]. This interaction can result in a more effective suppression of resistant strains, causing a paradigm shift from conventional antibiotics toward green nanomaterial-based solutions.

The rise of green nanometals/semiconductors in AMR mitigation: classification and mechanisms

Unlike conventionally fabricated nanometals/semiconductors, green nanometals (GNM)/semiconductors (GNS) are synthesized adopting green chemistry principles through biological pathways, possessing merits including reduced chemical toxicity and avoiding synthesis-caused secondary contamination through byproducts, renewable features, abundant precursors, enhanced biocompatibility, and larger environmental sustainability [5]. Their precursors include biomaterials (like parts of plants: phytochemicals, microbes, agricultural waste, animal cells, and green solvents) or are directly derived from biomes [5]. These bio-precursors play a multifaceted role during the synthesis of GNMS/GNSS, including reduction, oxidation, surfactant, stabilizer, capping and catalysis [6]. Besides, the use of green precursors results in intended/unintended doping, which improves their efficiencies towards AMR resolution with additive merits [4].

These nanomaterials possess diverse mechanisms to avert AMR, including oxidative stress induction by generating ROS, metal ion release, membrane disruption, biofilm disintegration, quorum sensing interference, gene expression modulation, targeted delivery and release, and antibiotic synergism [7]. While green nanomaterials possess overlapping merits, distinguishing between classes based on physicochemical properties and acting mechanism, like GNMS and GNSS, is crucial to realise their specific functions and potential [6]. For instance, GNSS, including ZnO, TiO_2, SnO_2 and g-C_3N_4, are known for their photocatalytic and ROS-generating efficacies, whereas GNSS, like silver, copper, and gold, exhibit antimicrobial properties by ion release and membrane disruption [5–7]. Both classes can be green-fabricated and further functionalized with biomolecules to improve selectivity and performance.

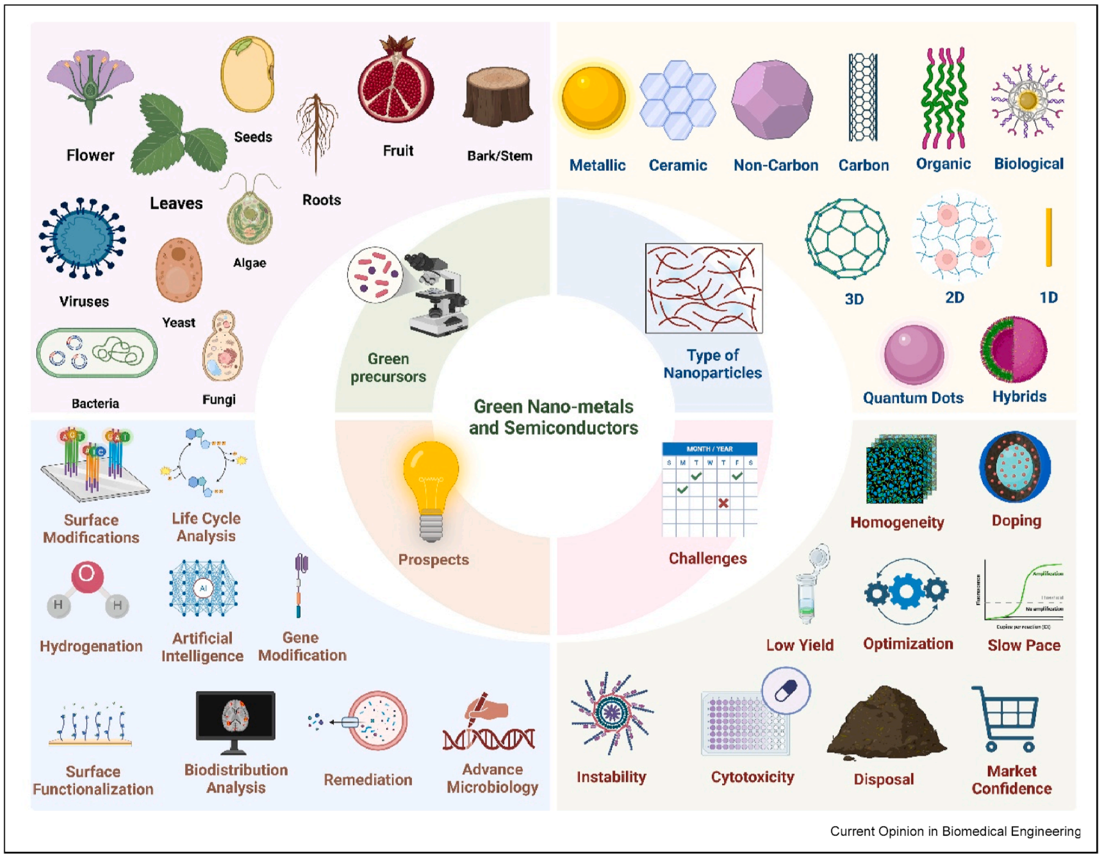
GNMS and GNSS are generally categorized based on the nature of the biogenic precursor and the type of green chemistry principle used for their fabrication [6]. One main category is plant-mediated GNMS and GNSS, fabricated using various parts of plants, including leaves, roots, fruits, and bark, which contain bioactive compounds such as polyphenols, alkaloids, and terpenoids that facilitate reduction, stabilization, and capping [8]. Phytochemicals from plants such as Azadirachta indica, Cymbopogon flexuosus, and Ocimum sanctum are often used for GNMS and GNSS fabrication [9]. The alternative method comprises microbial-assisted fabrication of GNMS and GNSS, wherein bacteria, fungi, algae, and viruses function as biofactories, producing amino acids, enzymes, vitamins, metabolites and polysaccharides that convert metal salts into nanoparticles [10]. Microorganisms such as *Bacillus subtilis*, *Fusarium oxysporum*, *Pseudomonas deptenis* and *Chlorella vulgaris* are frequently used [6]. A third, sustainable approach utilises waste-derived fabrication, where agricultural, human and food wastes, such as banana peels, tea waste, egg shells, tamarind waste or citrus rinds, are utilised as economical and eco-friendly precursors for GNMS and GNSS production [11,12]. Additionally, green solvent systems use benign solvents like water, ethanol, supercritical fluids, deep eutectic solvents and ionic liquids to confirm safe dispersion and stabilization of GNMS and GNSS [13]. These categorizations not only exhibit the resourcefulness and sustainability of biosynthesis of GNMS and GNSS but also endorse waste valorisation, waste-to-wealth modules and circular bioeconomy principles (Figure 1, Table 1).

Mechanistic versatility of green nano-semiconductors and nano-metals

GNMS are distinctive owing to their band-gap tunability, enabling them to generate ROS comprising hydroxyl radicals, superoxide anions, and hydrogen peroxide under visible or UV light, which are destructive to pathogens by damaging lipids, DNA, and proteins [5]. For instance, green ZnO nanostructures exhibit improved photocatalytic efficacy due to a high surface-to-volume ratio and defect-induced oxygen vacancies [14]. Likewise, GNMS nanocomposites such as TiO_2 doped with different metals (Ag, Cu)/biochar/carbon quantum dots show dual mechanisms, including ROS generation and metal chelation toxicity, and achieve synergistic antimicrobial properties (Table 2) [15,16]. Their topology and morphology play a vital role in achieving antipathogenic features. For instance, innovative GNMS morphologies, including core—shell [17], flower-like [18], and hierarchical low-dimensional nanostructures [19], have exhibited excellent pathogen adhesion and membrane penetration. Furthermore, topological diversity through surface modifications by using phytochemicals not only improves dispersion in biological media but also regulates zeta potential, which influences pathogenic affinity [4].

GNMS, including silver (Ag), copper (Cu), and gold (Au), have exhibited enormous potential against AMR [6,20]. For instance, green Ag nanoparticles are proficient in generating Ag^+ ions that bind to thiol groups of proteins/enzymes, disrupt respiratory chains, and produce membrane permeability [21]. They can also penetrate cells and intercalate with DNA, resulting in the inhibition of replication. Likewise, Cu nanostructures exhibit Fenton-like interactions, producing

Figure 1



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State-of-the-art green synthesis of metallic and semiconductor nanoparticles using eco-friendly precursors. The schematic highlights the merits of this approach, including sustainability, biocompatibility, and reduced toxicity, along with diversified applications spanning antimicrobial resistance (AMR) mitigation, environmental remediation, biosensing, and theragnostic.

Table 1

Comparative analysis of GNSS and GNMS related to green synthesis and antimicrobial applications.

Feature	GNSS (e.g., ZnO, TiO_2, SnO_2, g-C_3N_4)	GNMS (e.g., Ag, Cu, Au)
Green synthesis routes	Plant-mediated using phytochemicals, microbial-assisted via enzymes and metabolites, green solvents (water, ethanol, ionic liquids), waste-derived (e.g., citrus peels, tea waste)	Similar biosynthetic routes (plant, microbial, waste, solvents), often involving stronger reductants for metal salt conversion
Physicochemical features	Wide bandgap semiconductors, high surface area, doping-dependent optoelectronic properties, tunable photocatalytic activity	Metallic nanoparticles with plasmonic activity, high conductivity, strong surface reactivity, tunable ion release profiles
Primary antimicrobial mechanisms	Photocatalytic ROS generation under light irradiation, antibiotic synergism, oxidative stress, biofilm inhibition, DNA and protein damage	Metal ion release (Ag^+, Cu^{2+}, Au^{3+}), direct enzyme inactivation, disruption of membranes and proteins, quorum sensing inhibition, oxidative stress
Distinct advantages	Visible/UV light-driven antimicrobial action, potential for reusable coatings and photocatalytic sterilization	Broad-spectrum bactericidal activity at low concentrations, strong biofilm penetration, effective in dark environments
Translational barriers	Limited activity in absence of light, photo corrosion, stability issues, scale-up challenges for uniform doping	Cytotoxicity at higher doses, aggregation affecting stability, regulatory hurdles, ion leaching into ecosystems

hydroxyl radicals and resulting in oxidative disruption [22]. Besides, AuNPs, though less intrinsically toxic, are exceptional carriers for antipathogens and can damage pathogenic membrane potential through surface plasmon resonance effects [23]. Biogenic fabrication of nanometals, particularly using Cymbopogon flexuosus,

Table 2

Synergistic interactions of GNMs/GNSs with major antibiotic classes.

Antibiotic Class	Mechanism of Action	Synergy with GNMs/ GNSs	Primary Synergistic Mechanism	Evidence and Key Findings	References
β-Lactams (e.g., ampicillin, cefotaxime)	Inhibits cell wall synthesis	Strong Synergy	Membrane Disruption: GNMs/GNSs damage the bacterial outer membrane, allowing the antibiotic to reach its target.	Widespread reports of enhanced efficacy against Gram-negative bacteria, including multi-drug-resistant strains.	[30,31]
Aminoglycosides (e.g., gentamicin, amikacin)	Inhibits protein synthesis (ribosome)	Strong Synergy	Enhanced Uptake: Nanomaterials increase membrane permeability, facilitating the entry of the antibiotic into the cell.	Significant reduction in the minimum inhibitory concentration (MIC) of aminoglycosides, particularly with silver nanoparticles.	[32,33]
Fluoroquinolones (e.g., ciprofloxacin, levofloxacin)	Inhibits DNA replication	Moderate to Strong Synergy	Oxidative Stress: Nanomaterial-induced ROS amplifies the DNA damage caused by the antibiotic, leading to increased bacterial cell death.	Documented enhancement of ciprofloxacin activity against various bacterial species.	[34,35]
Glycopeptides (e.g., vancomycin, teicoplanin)	Inhibits cell wall synthesis	Moderate to Strong Synergy	Improved Delivery/Bioavailability: Nanomaterials can act as carriers, enhancing the stability and delivery of the antibiotic.	Synergy observed, especially in methicillin-resistant *S. aureus* (MRSA) with reduced vancomycin susceptibility.	[36,37]
Tetracyclines (e.g., doxycycline, minocycline)	Inhibits protein synthesis (ribosome)	Limited/ Less Studied	N/A	Less direct synergistic evidence. Their internal accumulation may not be significantly improved by membrane-disrupting NPs.	[38–40]
Macrolides (e.g., erythromycin, azithromycin)	Inhibits protein synthesis (ribosome)	Limited/ Less Studied	N/A	Synergy is not a primary research focus; their action is often independent of the nanomaterial's common synergistic mechanisms.	[41,42]

Azadirachta indica, or bacterial filtrates, not only diminishes cytotoxicity but also provides further bioactivity through phytochemical capping [24]. A distinctive merit of GNMS is their biofilm-damaging efficacy [25]. Biofilms, which are communities of bacteria rooted in self-produced matrices, present intense resistance to antibiotics [22]. GNMS can penetrate these biofilms by generating local oxidative stress and preventing quorum sensing, resulting in excellent antibiotic performance (Figure 2).

Green nanomaterials exhibit potent antimicrobial effects through multiple mechanisms. For example, Ag-based GNMS have demonstrated ≥5 log reduction in *E. coli* and *S. aureus* at MICs of 8–16 μg/mL, while ZnO GNSS achieved 70–85 % biofilm inhibition in *Pseudomonas aeruginosa*. Photocatalytic GNSS such as TiO_2 and g-C_3N_4 show reactive oxygen species (ROS) generation efficiencies of 60–90 % under UV/visible light, enhancing bacterial killing and degradation of antibiotic residues. These quantitative metrics provide measurable evidence of the mechanistic efficacy of green nanomaterials in combating AMR [26–29].

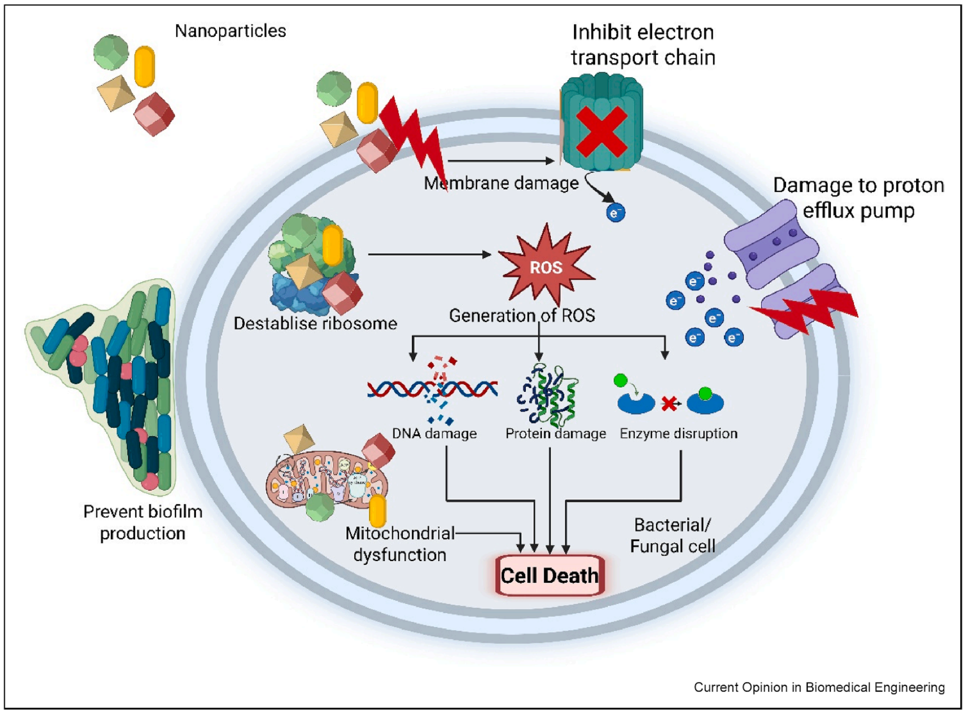
Multifaceted applications of green nano-semiconductors and nano-metals to avert AMR

A crucial approach to avert AMR is restoring the effectiveness of prevailing antibiotics [4]. GNMS/GNSS can aid as allies, improving drug penetration or affecting efflux mechanisms [4]. For instance, Ag nanostructures combined with vancomycin/ciprofloxacin exhibit enhanced bactericidal properties against MDR strains such as *Pseudomonas aeruginosa* [43]. ZnO and CuO nanosystems address distinct MDR strains by injuring membranes, thereby enabling antibiotic entry into the biological system [44]. Besides, functionalization of GNMS/GNSS with antibiotics/enzymes (like lysozyme) allows site-selective delivery and diminishes systemic side effects [45]. For example, chitosan-coated Ag nanosystems synergize with colistin to avert carbapenem-resistant Enterobacteriaceae [46]. These hybrid nanosystems hold potential in decreasing dosage, toxicity, and resistance growth.

The adaptability of GNMS/GNSS extends to diagnostics by employing them in electrochemical and optical nanosensors functionalized with antibodies or aptamers [4,47]. These nanosensors can detect AMR genes/resistance proteins at femtomolar concentrations, which is quite essential for designing point-of-care diagnostics [4,48,49]. For instance, biogenic ZnO nanowires and Au nanorods have been used in advanced biosensors for real-time, label-free and on-site detection of resistant pathogens[47–49].

Besides, in wound healing, green GNMS/GNSS-embedded hydrogels/films function as antimicrobial barriers while stimulating tissue regeneration and angiogenesis [50]. For instance, the addition of biogenic nano-ZnO/green Ag nanofibers/graphene oxide in

Figure 2



Schematic illustrating the anti-AMR mechanisms of nanoparticles (NPs) against resistant bacteria and fungi. NPs combat AMR by disrupting microbial cell walls and membranes, inhibiting biofilm formation, and enhancing host immune responses. Additional mechanisms include the generation of reactive oxygen species (ROS) and induction of intracellular damage, such as enzyme inactivation, DNA fragmentation, and protein degradation—collectively overcoming conventional resistance pathways.

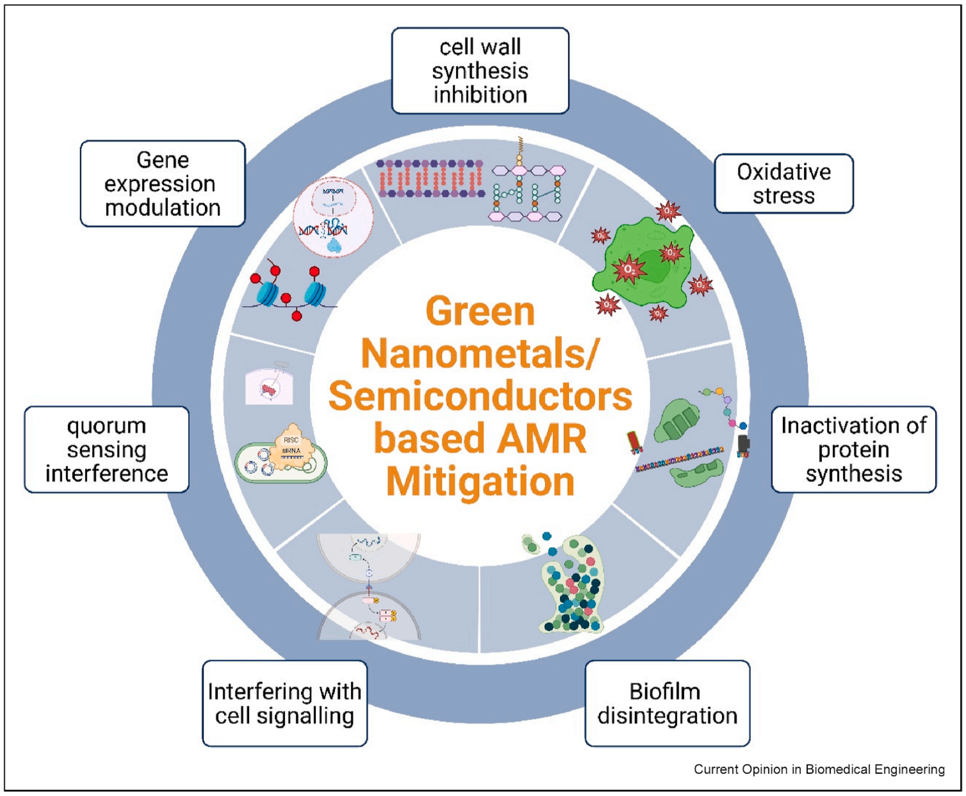
dressing resources improves mechanical properties, breathability and ROS-assisted bacterial annihilation [51,52]. Smart bandages/dressings with the ability to automatically respond to infection-triggered pH or exudate levels are under development using GNMS/GNSS for precision, intelligent and sustainable wound care[50—52].

Furthermore, wastewater remediation is another crucial avenue from the lens of One Health management [53]. Green nanocomposites including Fe_3O_4—Ag efficiently exhibited remediation efficacy against bacterial contaminants and antibiotic residues, which is essential from a community health perspective [54]. For instance, solar-assisted photocatalytic disinfection strategies employing biogenic g-C_3N_4 hybrids provide decentralized sustainable and energy-efficient solutions, particularly in low-resource settings [55]. Functionalized magnetic GNMS/GNSS also allow facile recovery and reuse, aligning with sustainability goals [56].

Biogenic GNMS/GNSS are used in sustainable agricultural practices for plant protection and crop enhancement [57]. Green nano-pesticides and nano-fungicides using biogenic Ag, Cu, or ZnO nanosystems are efficient against prominent plant pathogens while diminishing chemical utilization [58]. GNMS/GNSS are also used to improve nutrient uptake through seed priming and foliar sprays [59]. Biodegradable GNMS/GNSS carriers functionalized with microbial consortia or plant growth regulators enable optimised release and ecological replacements to conventional agrochemicals, which have high ecological footprints [57,59].

Quorum sensing (QS) is also responsible for bacterial coordination, virulence, and resistance. GNMS/GNSS can inhibit QS by damaging signalling molecules, including acyl-homoserine lactones, or blocking receptors [60]. For instance, Cu and Ag nanosystems have exhibited quorum-quenching efficacies against Gram-negative bacteria by decreasing biofilm formation and toxin production [60]. Also, several GNMS/GNSS can downregulate resistance gene expression, such as blandm-1 and meca, thereby reversing resistance [61]. Transcriptomic and proteomic examinations disclose that GNMS/GNSS interaction changes stress response and efflux pump regulation [62]. It opens possibilities for using GNMS/GNSS as gene-silencing components or allies in CRISPR-based AMR averting systems [63] (Figure 3).

Figure 3



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Application of GNMS/GNSS in the mitigation of antimicrobial resistance (AMR), illustrating their functional roles, associated challenges, and strategic solutions for clinical and environmental deployment.

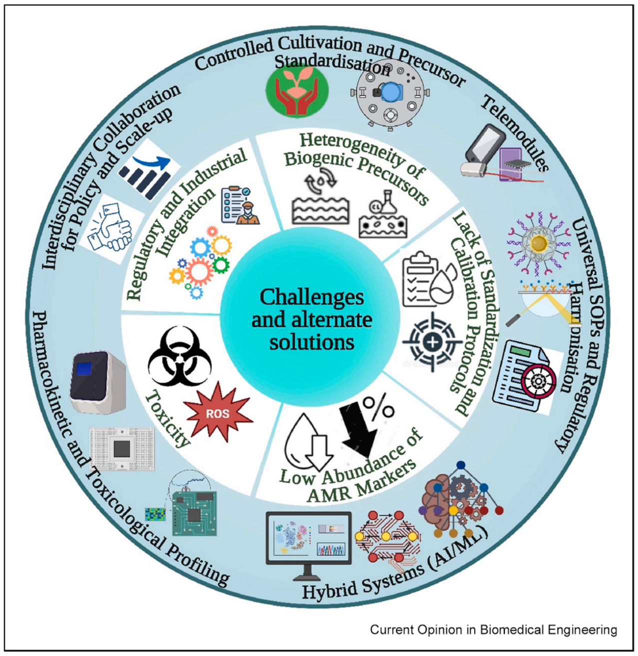
Green nanomaterials offer multifunctional interventions across One Health domains. In clinical settings, GNMS/GNSS-enhanced wound dressings, coatings, and antibiotic adjuncts are closest to translational readiness due to controlled dosing and established safety assessments. Veterinary applications, such as feed additives or topical treatments, are emerging but require more in vivo safety and pharmacokinetic data. Agricultural and wastewater domains face major gaps, including large-scale delivery, environmental persistence, and ecosystem-level impacts, necessitating comprehensive risk assessment and regulatory guidance before widespread implementation [64–67].

Challenges and prospects

Despite exhibiting promising anti-AMR properties, several challenges persist in adopting GNMS/GNSS as a practical solution and their scalability, including batch-to-batch variability in biogenic fabrication, the absence of standardised protocols, and an inadequate understanding of in vivo pharmacokinetics, obstructing their clinical translation and practical adaptability. *In vivo* studies show that GNSS (e.g., ZnO, TiO_2) can induce oxidative stress and mild hepatic effects at high doses, while GNMS (e.g., Ag, Cu) may cause ion-release–mediated renal stress and inflammation. Green synthesis improves tolerance, but long-term toxicological evaluation remains essential [5,6,68]. The heterogeneity of phytochemical capping agents impacts properties such as reproducibility and long-term stability. It is because GNMS/GNSS are synthesised using biogenic precursors that their physicochemical properties may differ with the position and altitude of sites from which they were obtained [69]. Besides, the accessibility and choice of precursors also limit their scalable fabrication, including regional accessibility of plants/microbes, impurities related to the precursors and varied chemical configuration [5,68] (Figure 4).

Toxicity is not totally eliminated in GNMS/GNSS and remains a concern. Although green nanomaterials demonstrate enhanced biocompatibility and reduced toxicity relative to conventional nanomaterials. Residual risks may arise from ion release, surface reactivity, or bioaccumulation, highlighting the need for careful dose optimization and comprehensive toxicological assessment prior to clinical or environmental utilization. While green synthesis reduces the use of harsh chemicals, the

Figure 4



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Overview of key challenges and alternate solutions for the adoption of GNMS/GNSS in combating AMR, highlighting issues in fabrication, standardisation, biosafety, precursor variability, and regulatory integration.

in vivo fate of GNMS and GNSS requires careful evaluation. These nanomaterials can exhibit preferential accumulation in organs, potentially trigger immune responses, and alter host microbiota composition. Such effects underscore the necessity for methodical assessment of biodistribution, immunogenicity, and systemic impacts to ensure both safety and therapeutic efficacy before clinical or environmental application [5,68].

Scaling GNMS/GNSS and integration into regulatory frameworks require interdisciplinary efforts [68]. Automation of biofabrication of GNMS/GNSS using microfluidic or artificial intelligence (AI)-assisted tools has the potential to standardize and scale manufacturing. Lifecycle assessment and eco-toxicological examinations must be done, which can guide safe-by-design methodologies [5,68,70]. It requires dedicated collaborative efforts amongst academia, industry, clinicians, engineers, social scientists, artists and policymakers to expedite regulatory approvals and public acceptance [71].

Looking ahead, incorporating AI and physics-guided machine learning to predict antimicrobial interactions, GNMS/GNSS behaviour and lifetime, and fabrication results has the potential to revolutionise green nanotechnology[47— [49,71]. Besides, the interface of several biological, chemical, and physical processes in green nanotechnology can be mapped to the dynamics of complex systems and network theory, where trivial variations in one constituent can lead to excessively large impacts [3,4]. The expansion and implementation of GNMS/GNSS as a constituent of an integrated and complex systems-based model can offer pioneering solutions to overcoming the challenges posed by AMR [3]. Besides, Smart biogenic nanomaterials that respond to various factors like pH, enzymes, or bacterial metabolites are required to be developed for targeted delivery and real-time feedback [4,47,48]. Multifunctional platforms combining diagnostics, therapeutics, and monitoring, termed as theranostics, are within reach by incorporating modern-age technologies with green nanotechnology to avert AMR [4,47,48,71].

Conclusions

Green nanomaterials, including GNMS/GNSS, describe a paradigm shift in fighting AMR, providing eco-friendly, biocompatible, and multifunctional allies to conventional antimicrobials. Their diverse mechanisms, ranging from oxidative stress to gene modulation, allow them to avert AMR more efficiently than conventional approaches. With synergetic potential, wide-ranging applications, and sustainable fabrication, they play a transformative role in antimicrobial stewardship. Yet, addressing translational challenges through standardisation, scalability, safety validation, and public trust is essential. Addressing AMR necessitates a holistic, interdisciplinary and systematic approach, where both technological and societal aspects must be considered for the highest control. In a modern era, vulnerable to a post-antibiotic future, green nanotechnology offers hope for alternative strategies to mitigate AMR, enabling sustainable antimicrobial solutions and saving numerous human mortalities.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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The review highlights the necessity of an integrated approach and efforts from the whole community, including scientists, artists, doctors, engineers, academicians, etc, to work as teams to fight global health problems and educate the masses to adopt digital-age intelligent technologies.