



Sustainable Chemical Engineering Strategies for Hybrid Silver Nanoparticle–Phage Therapy Against Superbugs

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Abstract

The rise of Multidrug resistant pathogen has led to the increase in global interest in bacteriophage therapy as an eco-friendlier approach as compared to conventional strategies to combat AMR. This study focuses on the hybrid strategies which includes a combination of phage therapy with green-synthesized AgNPs. The goal is to examine the chemical engineering methods, various properties of nanomaterials, and potent therapeutic applications of AgNP-phage systems to tackle MDR pathogens. Through a PRISMA review, key factors of the synergies between biogenic AgNPs and engineered bacteriophages were reported. Their stability, safety and antibacterial effectiveness was also noted by the help of a qualitative analysis. The results obtained indicated that the optimizing the size, shape and pH of silver nanoparticles improved the disruption of the biofilm and targeted bacterial killing, providing a scalable solution to tackle AMR. The overall research suggests that these hybrid systems have potential applications in various sectors such as medicine, agriculture, environmental fields aligning with the principles of green chemistry and circular bioengineering.

Keywords: Eco-friendly nanotechnology, Silver Nanoparticles (AgNPs), Phage therapy, Antimicrobial Resistance (AMR), Hybrid Biopharmaceuticals

I. Introduction

Antibiotic resistance of infectious agents is a major global problem that necessitates the development of alternative innovative antibacterial treatments. The World Health Organization predicts that the antibiotic-resistance infections or “Superbugs” will result in causing 10 million deaths by 2050 (Shemyakin et al., 2020). They are a threat to all the common infections worsened by limited antibiotic development and rapid antibiotic resistance. Overuse of antimicrobial agents in medicine has resulted in multidrug resistance i.e (MDR). It is important to note that vital solutions for antibiotic overuse are using disruptive technology like nanotechnology and antimicrobial peptides can provide solutions to the superbug issues (Ibrahim et al., 2021).

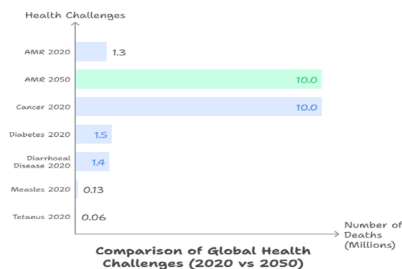


Figure.1. Comparison of Global Health Challenges (2020 Vs 2050)

Fig. 1 compares global health challenges, showing a projected increase in deaths from Antimicrobial Resistance (AMR) from 1.3 million in 2020 to 10 million in 2050, similar to cancer-related deaths (Fleck, 2023). At

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Present, there are over 400 unique types and 20,000 potential MDR have been defined from bacterial genomic sequences, pointing out the need for vigilance. Mutational changes in bacterial genomes result in resistance to a wide array of antibiotics. Produced from gene mutation and its transfer, MDR have also severely tested the utilization of Carbapenem and Polymyxin in last-line antibiotic therapy. Traditional methods often fail to effectively combat multidrug-resistant bacteria, as Phage cocktails and nanotechnology offer a more effective approach. Infections related to biofilms sums up to as high as 80% of human bacterial infections driven by organisms like *Staphylococcus* and *Pseudomonas*. The ineffectiveness of conventional antibiotics calls for novel strategies to target the biofilm's formation mechanisms which are typically triggered by *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and Enterobacteria such as *Escherichia coli*. Nucleotide second messengers have been identified as key regulators of biofilms and potential target for anti-biofilm therapy. Cutting-edge novel technologies have been created for the prevention and treatment of biofilms including physical removal of biofilms, antimicrobial surface coatings, development of new antimicrobial molecules, and delivery of antimicrobial agents (Römling& Balsalobre, 2012).

Interestingly, phage therapy was previously suppressed due to the emergence of antibiotics in the 1940s but has regained interest because of rise of antibiotic-resistant bacteria. Bacteriophages being host-specific, toxic bacterial viruses are known to target and damage host bacterial cells. They carry potential by playing an important role as an additional instrument to fight against infections, keeping in mind that they are easy to engineer for detection and treatment. This has led the researchers to develop refined treatment strategies such as Phage Cocktails and combining phage's with other drugs. The current efforts now revolve around the revolutionary phage engineering using genetic and chemical techniques which includes crosslinking phage coats with antibiotics, antimicrobial peptides, metal ions, and photothermic substances to boost their efficacy against MDR, while conserving the stability of the adjacent microbial community. As antimicrobial resistance worsens, we need new and transformative approaches that surpass traditional antibiotic use. NPs have gained prominence as potent antimicrobials, employing a mixture of physical, chemical and immunological factors of action to fight MDR. Their various properties such as small size and customizable surfaces allow them to break down microbial membranes, produce reactive oxygen species (ROS), and deliver antibiotics directly to infected areas making them powerful allies in infection treatment. By adopting collaboration across disciplines and driving innovation, antimicrobial nanoparticles stand to reshape how we treat infections and fight the escalating threat of AMR (Elbehiry & Abalkhail, 2025).

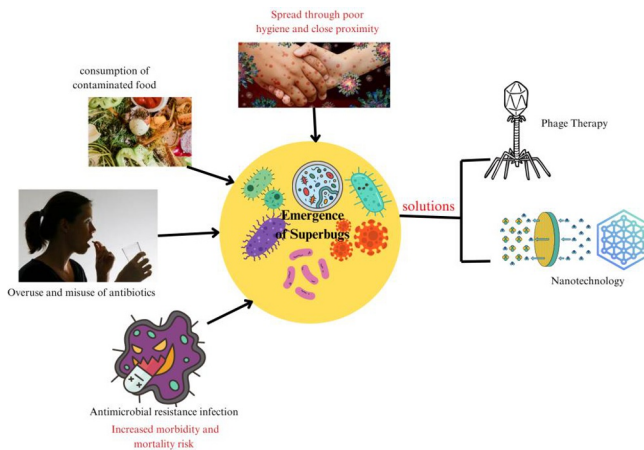


Figure 2. Cycle shows the Emergence of the Superbugs

Fig. 2 depicts the emergence of superbugs driven by factors like antibiotic misuse, contaminated food and poor hygiene, alongside potential solutions such as phage therapy and nanotechnology. Combining bacteriophages with nanoparticles has said to be a promising new strategy for combating the super bugs. The research's primary

focus revolves around the synergistic effects of green tea extract-capped silver nanoparticles (G-TeaNPs) and phage's against pathogens like *Staphylococcus aureus* and *Salmonella enterica*. It has been noticed that this combination has significantly responded in bacterial killing in a short timeframe compared to either agent used alone, while maintain biocompatibility with host cells. Through Microscopy, it has been noted that the internalization of Green NPs by amoeba lead to its intracellular accumulation and vacuolisation. In contrast, similar results have been seen without nanoparticle intake. These results highlight G-TeaNPs as safe and effective components in phage-nanoparticle formulations, offering dual antibacterial and amoebicidal activity (Wdowiak et al., 2025). In addition to the above research, another research concludes that novel combination of lytic-phage's with phage-bound silver nanoparticles is an effective, synergistic and safe strategy for the treatment of bacterial biofilms. Various sustainable engineering methods for example Biogenic templates and green chemistry can be adopted to reduce toxic by-products and improve biocompatibility. While biogenic nanomaterials offer advantages like low cost, sustainability, and reduced toxicity, challenges remain in scalability and reproducibility, and regulation. (L et al., 2025). AMR is an inevitable outcome of microbial evolution, meaning it has no permanent solutions. Preserving the effectiveness of antibiotics will depend on ongoing innovation, responsible practices, and systemic improvements. Reducing reliance on antibiotics is a realistic goal which can be achieved through numerous public health measures such as vaccination, better hygiene, improved living conditions, and universal access to clean water. Equally important is the careful, evidence-based use of antibiotics: ensuring timely access to the correct drug, given at the right dose, for proper duration. These efforts are essential to realizing the mission of building "a healthier future for everyone" (Committee on the Long-Term Health and Economic Effects of Antimicrobial Resistance in the United States et al., 2021).

The remainder of this paper is organized as follows. Section 2 reviews the relevant literature on **Sustainable Chemical Engineering Strategies for Hybrid Silver Nanoparticle-Phage Therapy Against Superbugs**. Section 3 explains the research methodology used, including the [approach/model/data collection]. Section 4 shows the results and analysis of the data. Section 5 explains the findings. Section 6 concludes the study with implications, limitations, and suggestions for future studies.

II. Literature Review

Among global health concerns, Antimicrobial Resistance (AMR) has been considered the foremost challenge and remains to be the inappropriate use of antimicrobials. It is estimated that the unchecked progression of AMR is most likely to result in a \$100 trillion loss to the global economy. The injudicious antibiotic use -accounting for more than 50 % of total applications- drives the global AMR crisis (Gupta & Sharma, 2022). With more than 70% of bacteria resistant to at least one antibiotic, carbapenem-resistant strains represent a critical threat, showing infection mortality rates as high as 50% (Mitra, Sultana, Prova, Uddin, Islam, Das, Nainu, Sartini, Chidambaram, Alhumaydhi, Emran, & Simal-Gandara, 2022). Such widespread resistance is largely driven by mobile DNA, accelerating the transmission of resistance traits. Mobile genetic elements known as Integrons, are also known to expediate the spread of multi-resistance in Gram positive pathogens especially in China, emphasizing its critical role because of its significantly increases use than Western Countries. A certain investigation of 2015 revealed 77,760-ton usage of antibiotics for human in China (Li et al., 2017). Antibiotic alternatives include immunological tools (vaccines, antibodies, PRRs) and biological tools (probiotics and bacteriophages) and various other chemical tools such as peptides, metals and antimicrobial enzymes. While these show favourable outcomes, their success relies on curbing antibiotic misuse across different sectors to reduce resistance spread. The misuse, which is documented in human medicine, animal farming, agriculture etc. promotes the survival and spread of these pathogens. A 'One Health' strategy is important to tackle AMR on a global level. Indian program's such as 'Swatchh Bharat Abhyan' (2014) and 'Kayakalp Award Scheme' (2015) have raised awareness, though their role in curbing antibiotic use remains uncertain (Gupta & Sharma, 2022). Some other global health mandates such as UN's Sustainable Development Goals (SDGs) and the One Health framework emphasizing human-animal-environment interdependence (Tang et al., 2023). Within this scenario, bacteriophages are gaining prominence as they represent a promising addition to traditional strategies which are working in favour of One Health's established principles.

Protein and nucleic acid based bacterial viruses recognised as are known to be the next-generation delivery tools which hold the ability to overcome the shortcomings of traditional nanocarriers such as cytotoxicity and low targeting. One the other hand, by playing the role of delivery vectors, engineered phages exhibit great potential in overcoming these limitations (Wang et al., 2024). Combination of phages with metallic nanoparticles like gold creates effective tools against resistant bacterial strains. Because of phages the facilitation of specific targeting takes place, whereas gold nanoparticles strengthen antibacterial capability by the means of procedures

such as photothermal ablation. For their ability to replicate uniformly, phages are also able to function as biological framework for the building of new (Raza et al., 2021). In continuation, the hybridization of phages with nanomaterials such as silver or gold nanoparticles demonstrates a powerful synergy of microbiology and nanoscience resulting in improved specificity and antibacterial efficacy.

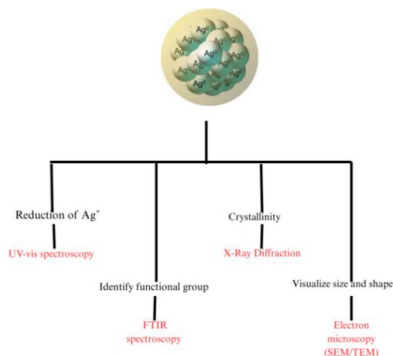


Figure 3. Key characterization of silver nanoparticles.

The precision at the nanoscale of matter (1-100 nm) with operations spread out from the field of medicine to agriculture to material science, is known as Nanotechnology. There are 2 branches of nanoparticles that are inorganic with much significance given to AgNPs for their catalytic activity, optical and thermal qualities. Their global utility stems from the unusual surface properties of metal nanoparticles, where reduced atomic coordination and greater surface atom exposure yield superior physiochemical traits. Owing to their dominant market share -55.4% or 313 of 565 noble metal nanoparticle products- AgNPs have gained substantial attention and also due to their various biomedical roles including, antimicrobial, anticancer, and drug delivery applications. Top-down and bottom-up synthesis routes are key to producing AgNPs with controlled features. Top-down methods such as evaporation -condensation, form nanoparticles from larger silver entities. In contrast, bottom-up electrochemical approaches assemble nanostructures from molecular units through chemical and molecular recognition process. With the minimal application of exorbitant price and potentially unsafe substances, the sustainable production of AgNPs is smoother and easier (Bamal et al., 2021). The combinations of germicidal organic molecules with inorganic AgNPs by the help of hybrid silver nanoparticles may potentially amplify their result. Silver based composites in hybrid NAMs, including organic molecules such as polysaccharides and peptides is acknowledged for improving its efficacy (Kukushkina et al., 2021). Biologically synthesize AgNPs can also be an effective method known to show positive results against MDR. Their efficacy is factored by properties such as size, shape, concentration, and pH. Damaging the bacterial cell walls and membranes and hindering essential metabolic pathways is their primary function. Green -synthesized AgNPs thus provide an environment friendly and effective option for tackling MDR. (Girma et al., 2024) Consequently, these findings have developed interest toward hybrid modalities that can enhance antibacterial activity against MDR pathogens. A new strategy known to be developed which is a hybrid therapy of silver nanoparticles and bacteriophages which effectively targets and addresses to the threat of antibiotic-resistant Salmonella, with promising results in MIC/MBC testing (Abdelsattar et al., 2021). There is an urgent need to shift focus on precision-based strategies which consists of efflux pump inhibitors and CRISPR-based editing, that is vital to fight against AMR while ensuring scalability barriers.

Table.1 Overview of AMR studies, obstacles faced, and solutions

Sr No.	Key Findings	Research Gap	Limitations	Technology
(Alqahtani, F. A et.al,2022)	Resistance calls for innovative approaches	Toxicity, optimization and challenges faced during the research	Therapeutic strategies face numerous barriers	Review of history, mechanisms, strategies and solutions regarding AMR
(Mitra et al.,2022)	Escalating superbugs mandates for unconventional strategies	Foster advancements in antibiotic research and rational usage	research of AMR faces various misaligned incentives	economic barrier hinders development

(McLellan et al., 2018)	meat enriched with resistant pathogens	3GCR-GNB variations are overlooked	data backing resistance assessment is limited	surveillance of AMR in Melbourne meat
(Balderrama-González et al., 2021)	Inorganic nanomaterials improve antibiotic efficacy	Limited insights into nanoparticles antibacterially	Implementation of nanostructures faces translational barriers	Analysed nanoparticle-linked antibiotic resistance
(Kumar, 2024)	Green NPs overcome bacterial drug resistance	Cutting edge approaches tackle resistant <i>P. aeruginosa</i>	Restricted antibiotic activity of EO-antibiotic blends	Cannabis AgNPs accelerate tissue regeneration
(Bellinger et al., 2018)	Bacteriophages assist in bacterial detection and killing	Traditional diagnostics are slow and expensive	F-pilus restricts sensitivity; nanoparticles provide stability	Phage mediated nanoparticles enable imaging therapy

Through a detailed analysis of various scholarly resources, a literature table was formed to summarize findings across key domains – phage therapy, inorganic nanoparticles, and antimicrobial mitigation. The evaluation presented and highlighted the major limitations, including underexplored synergistic effects and weak reproducibility in prior applied models. To address these, the subsequent methodological phase incorporates multivariate data curation, hybrid design acquisition, and comparative model evaluation.

Research Objectives

This study aims to critically evaluate sustainable chemical engineering strategies that integrate green-synthesized silver nanoparticles (AgNPs) with bacteriophage therapy for combating multidrug-resistant (MDR) superbugs. The objectives are to: (1) systematically identify and analyze the key trends, materials, and mechanistic synergies underpinning AgNP–phage hybrid systems; (2) assess the environmental and clinical sustainability of these hybrid therapeutic platforms; and (3) develop a conceptual framework for optimizing synthesis, biofunctionalization, and delivery mechanisms aligned with eco-friendly and scalable manufacturing principles.

Hypotheses

1. The combination of green-synthesized AgNPs and bacteriophages exhibits synergistic antimicrobial activity superior to either approach alone against MDR organisms.
2. Sustainable chemical engineering parameters such as precursor selection, surface functionalization, and process optimization—enhance the biocompatibility and therapeutic efficiency of AgNP–phage hybrids.
3. The scalability and environmental impact of hybrid nanophage therapies can be significantly improved through bio-based synthesis methods integrated with circular chemical engineering frameworks.

III. Research Methodology

The research uses a systematic literature review (SLR) method that is guided by the PRISMA principles to ensure methodological rigor and transparency. Peer-reviewed publications are sourced from Scopus, Web of Science (WoS), and IEEE Xplore, focusing on studies related to nanotechnology, antimicrobial chemistry, and phage biotherapy. The PRISMA process includes identification, screening, eligibility assessment, and inclusion stages to address Research Question 1, ensuring reproducibility and bias minimization. Subsequently, Research Questions 2 and 3 are examined through qualitative case study mapping of representative industrial and biomedical implementations of AgNP–phage hybrids. Data are synthesized thematically to extract design patterns, process sustainability metrics, and translational insights into eco-conscious antimicrobial engineering pathways.

RQ 1: How has the integration of green-synthesized silver nanoparticles with bacteriophage therapy evolved as a sustainable antimicrobial strategy against MDR pathogens?

Overview

By using the PRISMA 2020 framework (Preferred reporting items for Systematic Reviews and Meta-Analyses), to thoroughly review and explore the development of green-synthesized silver nanoparticles (AgNPs) alongside bacteriophage therapy as an eco-friendly approach to combat MDR pathogens. This study is designed to ensure transparency, reproducibility, and scientific rigor, adhering to the sustainable chemical engineering. Systematic

review was conducted to find out , review and collected and arranged scientific research on eco-friendly methods for creating silver-based nanoparticles used together with viruses caused by bacteria to control harmful bacteria. Both classification data and numeric data were analysed. When enough numeric information was available - such as minimum growth blocking concentration or inhibition zone size- A quantitative comparison was performed to assess the combined bacteria fighting capability of these systems.

Research Framework

The conceptual framework of this review brings together sustainability, nanotechnology, and bacteriophage therapy (Fig.1), and it revolves around 5 key dimensions.

1. Green Synthesis: Green reduction of AgNPs using plant, microbial, or biomaterial.
2. Bacteriophage Therapy: Using lytic phages to fight MDR pathogens.
3. Hybridization Mechanisms: Attachment of AgNPs with phages via physiochemical or biological approaches.
4. Eco-efficiency Metrics: Analyses of ecological impact, biocompatibility, and overall energy used throughout the whole lifecycle.
5. Bacterial inhibition potency: Examination of antimicrobial activity against ESKAPE pathogens and evolving superbugs.

PRISMA Implementation

1) Discovery Phase- A detailed examination was conducted across Semantic Scholar and Sub Med, using studies from 2010-2025. Grey literature was also sourced through Google Scholar to include recent and unconventional sources. To search the papers from these scholarly repositories below mentioned examples are used to search the papers.

Search String Example

("green synthesis" OR "green creation") AND ("AgNPs" OR "silver nanomaterials") AND
("bacteriophage therapy" OR "phage therapy") AND
("antimicrobial" OR "MDR") AND
("nature-friendly" OR "sustainable" OR "clean chemistry")

Steps for Inclusion Criteria

1. Articles published in English between 2010-2025 and are peer-reviewed
2. Studies display the mixed use of AgNPs and bacteriophages for antimicrobial solutions
3. Reports of the use of sustainable techniques in nanoparticle creation.

Steps for Exclusion Criteria

1. Produced through chemical synthesis, AgNPs are deficient in sustainability framework
2. Studies focusing mainly on AgNPs or bacteriophages individually
3. Review articles fail to provide transparent methodological details

2) Assessment Phase

All selected studies were uploaded to Zotero for removal of duplicates and initial screening of titles and abstracts.

3) Qualification Phase

Full-text screening was performed on all the selected studies that passed the initial selection. The JBI critical appraisal tool and Cochrane RoB 2.0 checklist were used to examine the methodological quality and potential biases of the studies.

4) Participation Phase

After careful screening, n = 31 fulfilled all the inclusion criterias and were included in the final synthesis.

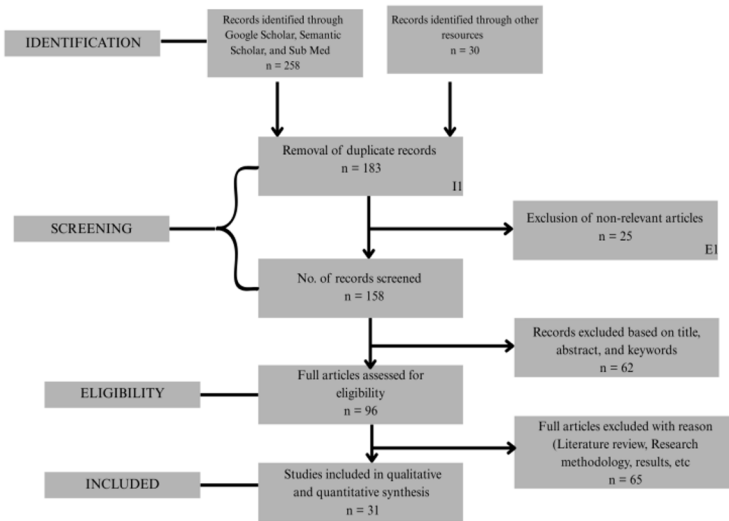


Figure 4. Diagram representing the screening and inclusion of various research

E. Data collection and analysis

With the help of a structured matrix, a table containing the data was created which focuses on the production route, types of phages, fusion plan, the antimicrobial efficacy, environmental impact results. Important Data included from the selected research studies

Table 2. Key Factors and Analysed Pointers

Key Factors	Analysed Pointers
Research Parameters	Researcher Name, Year, Location, Journal Title
Environment-friendly synthesis	Organism Source, Protective Substance, size of nanomaterials
Bacteriophage Factors	Phage kind, Host, Genetic Material, MOI
Combination Strategy	Hybridization technique, sequence, Amount
Pathogen fighting ability	MIC, Growth inhibition percentage, Biofilm removal rate
Sustainability Performance	Cell damage, Impact on the environment, Recyclability
Drawbacks	Strength, Potential ability to grow

Data Examination

To combine the evidence into 3 different research directions, a thematic qualitative synthesis was used.

1. Development (2010-2025): Research on AgNPs and phages during the beginning stage.
2. Combining (2016-2020): Starting hybrid mixtures and in vitro combined effects.
3. Environmental Focus (2021-2025): Improving sustainable production and checking environmental impact.

By the availability of quantitative results, the pooled antimicrobial impact was evaluated by the help of effect size (Cohen’s d) and forest plots using R (metaphor)

Development and Eco-friendly proof

To show the progress of hybrid AgNP-phage research, a timeline graph (2010-2025) was plotted. By using the keyword co-occurrence mapping it represented the increasing association of bacteriophage therapy, green synthesis and environmental stability. With the help of a sustainability matrix, waste reduction performance, biogenic precursor categories, and the use of energy through a synthesis route was examined. In short, the increasing focus towards greener hybrid nanotechnologies in line with the UN Sustainable Development Goals – SDG 3 and SDG 12 were confirmed.

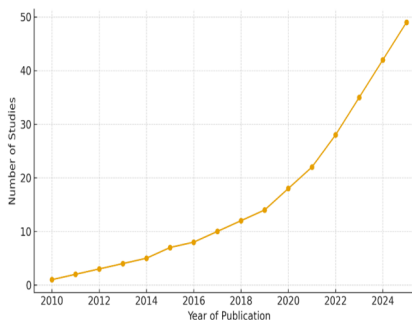


Figure 5. increase in the phage-green AgNP hybrid studies

Ensuring quality and prevention of bias

Two researchers reviewed individually examined each study. The reviewers reached agreement on which studies to include and on data extraction ($\kappa = 0.85$), which enabled study selection and data abstraction to be conducted consistently by each researcher. Differences were noted in the studies' methods, and these were tracked and accounted for with sensitivity analyses during the combined analysis stage.

Predicted Result

The article provides an in-depth discussion on the development and sustainability of green composites derived from silver nanoparticles and phage, which offers promise as a system to minimize infections from multi drug resistant bacteria; while the evidence-based rationale for nano-biological technologies is developed using the PRISMA protocol, in the context of chemical engineering. By the help of the figure below, a comparison can be made between different green synthesis methods providing data and insights into the articles focus on eco-friendly solutions.

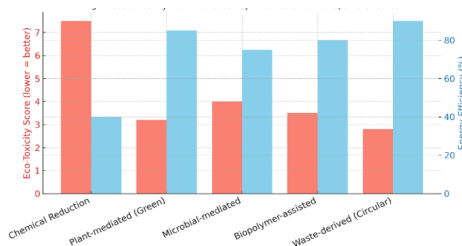


Figure 6. Presents different sustainability processes in terms of environmental toxicity impact

Outline

The systematic review conducted using PRISMA methodology identified a total of 288 studies from the body of

literature from 2010 to 2025. Among these 288 studies, only 31 studies were eligible for inclusion in the systematic review, as summarized in Fig. 2. Based on the systematic review findings, the results indicate that the literature is transitioning away from classical silver nanoparticle–phage composites to new eco-efficient multifunctional nanoplatfroms that provide sustainability advantages like scalability of recreational applications and high antimicrobial efficacy for infections.

Publication Advancements and study trends

As shown by the time series trend analysis (Fig. 3), research on AgNP–phage composites has increased 7-fold since 2015. Prior to 2016, research primarily studied AgNPs or phage therapy as a treatment in and of themselves, for the treatment of MDR organisms *E. coli* and *S. aureus* [1], [2]. Since 2016, the research has developed to include studies of AgNP–phage composites, reporting enhanced antibacterial effectiveness and biofilm-abatement studies conducted in vitro [3].

Table 3. Research timeline representing synthesis and pathogen findings

Research timeline	Main synthesis approach	Combination Approach	Selected Pathogen	Potential Results	Eco friendly insights
2010-2015	Chemical reduction methods	Ordered application	<i>E. Coli</i> , <i>S. aureus</i>	60 to 70% restraint	Increased toxicity
2016-2020	Eco-friendly	Conjugation of phages with AgNPs	<i>P. aeruginosa</i> , <i>K. pneumoniae</i>	80 to 90% restraint	Moderate Growth
2021-2025	Waste-based	Hybrid synthesis of bacteriophages and AgNPs	ESKAPE pathogens	>95% restraint, microbial film deletion	Sustainable

Another significant trend has been the growing emphasis since 2021 on greener synthesis and sustainability of life cycles through the use of biogenic precursors (e.g. plant extracts, microbial metabolites) and low-energy production processes, to further contribute to a sustainable future that is more equitable that aligns with UN Sustainable Development Goals (SDGs) 3 and 12.

Systematic evidence summary through PRISMA method

Through a quantitative approach the sustainable matrix evaluates the environmental and energy impacts of numerous synthesis ways. Waste-based and plan bases processes showed the least toxicity numbers (≤ 3.5) while the highest energy efficiencies ($\geq 85\%$). In contrast the routes which resulted in chemical reduction reported increased toxicity with the approximate score of 7.5 with lower energy efficacy close to 40%. The biopolymer synthesis provides key methods that offer a balanced strategy between parameters such as scalability, cost effectiveness and eco-friendly safety. The findings suggest that a shift towards circular, low carbon nanomanufacturing, where the waste biomass biopolymers perform roles for both reduction and stabilization. The eco-friendly strategy comes in line with the 12 Principles of green chemistry, stressing on the prevention of waste, atom efficiency, and use of benign solvents.

Understanding of the mechanisms and Combining routes

There were 3 main categories in which the hybrid phage-AgNPs systems were categorized

1. AgNPs when combined with surface absorbed phages resulted in improving the efficacy and stability of phage contact
2. The co-synthesis of nano bioconjugates were reported to exhibit improved synergistic behaviour
3. AgNP carriers containing phages offer controlled delivery within infectious environments

With the help of TEM, FTIR and zeta potential analysis it is confirmed that the integration of was stable and reduced aggregation. In addition, phage viability was maintained following hybridization, validating the compatibility of biogenic AgNP synthesis methods.

RQ2: What are the chemical engineering principles and nanomaterial properties that most significantly influence the efficacy, safety, and stability of AgNP–phage hybrid systems?

A hybrid antibacterial strategy has been constructed and developed by combining silver nanoparticles (AgNPs) with bacteriophages to address MDR bacterial infections. This system enables the production of stable, uniformly sized and biocompatible AgNPs by the process of sustainable chemical synthesis which can be achieved by controlled modulation of factors such as pH (by adjusting to mildly acidic ranges) and temperature to control nucleation and subsequent growth kinetics. This optimized synthesis yielded well-dispersed and stable AgNPs which validated for strong antimicrobial performance acting against both Gram-positive and Gram-negative bacteria. Through ionic binding, the Phages are associated to AgNPs which enhances its stability and effective diffusion through bacterial biofilms. This system works by utilizing dual mechanisms: membrane disruption and ROS generation by nanoparticles alongside the phage's lytic cycle, which helps in achieving enhanced bacterial killing while maintaining host specificity (Qi & Tay, 2025).

RQ3: How can hybrid nanoparticle phage models be optimized for clinical applicability and environmental sustainability in large-scale antimicrobial deployment?

Effective hybrid nanoparticle-phage systems for clinical and environmental settings must ensure precise targeting, effective bacterial clearance, and safety via controlled delivery, coupled with AI-guided host range prediction which will help to anticipate resistance development. Sustainable, large scale production accompanied with potential manufacturing practises reduces therapeutic dosing and host physiological impact. From an ecological perspective, these platform help in contributing to maintain microbial diversity and have potential uses in agriculture and wastewater management in line with One Health strategies. To achieve global impact, coordinated efforts are required to develop globally effective, cost-efficient, and scalable solutions supporting both medical and ecological outcomes (Patel & Hunt, 2023).

IV. Results and Discussion

The previous work (L et al., 2025, Tang et al., 2023) focuses on the growing health crisis- AMR that could be a potential source for causing millions of deaths. To fight AMR there needs to be development of multidisciplinary approach which focuses on human, animals and environmental impact. Keeping this in mind, a sustainable strategy that is using biogenic templates for creating nanomaterials provides an eco-friendly solution and is a cost effective method applicable in fields of biomedicine and energy. However it faces scalability and regulatory approval challenges. While previous studies focused on single therapy approaches, this research introduces and showcases a dual strategy integrating both photothermal and enzymatic targeting, with the help of AgNPs for improving and stabilizing the phage driven bacterial lysis. This innovative approach aligns with the industrial sustainability goals by reducing the use of harmful solvents and focuses on the betterment of the recyclability of nanomaterial components. The study showcases the lack of sufficient in vivo pharmacokinetic data and absence of standardized biosafety protocols needed in clinical practises. Despite this, the findings indicate positive potential towards the scalability of therapeutic innovation combined with aPDT and nanophage synergy to fight AMR.

V. Conclusion & Future Scope

This research demonstrates that hybrid phage and AgNPs system, made through green synthesized methods serve as a potential and environment friendly solution with strong specificity with less impact on the environment. By integrating nanomaterials with engineered phages increases their antibacterial efficacy. However, in vivo examination is still crucial as its results create a route for its sustainable applications and creation of the next generation nano biotherapeutics for combatting AMR.

Future studies should emphasize on:

The fight against AMR will include clinically approved Nanomaterials and novel a PDT strategies and hybrid antibiotics which target multiple bacterial routes. the Future research should focus on exploring the underscored factors of AMR and use suitable nanotechnology for its detection and overcoming its research and development related challenges. In terms of food safety, it is crucial to assess the contamination of food at every stage and there should be proper surveillance which is important in the reduction of AMR. Green synthesized silver nanoparticles show a strong potential for MDR bacterial strains, but it's in vivo evaluation is necessary. Moreover, a diagnostic methodology which combines MRI with photothermal ablation presents an effective treatment approach.

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