Green Synthesis of Silver Nanoparticles: A Review of Polymer and Antimicrobial Drug Combinations for Enhanced Antimicrobial

ADVANCED NANOBIOMED RESEARCH Open Access
www.advnanobiomedres.com

Green Synthesis of Silver Nanoparticles: A Review of Polymer and Antimicrobial Drug Combinations for Enhanced Antimicrobial Applications

Mukil Madhusudanan, Jian Zhang, Santosh Pandit, Priyanka Singh, Geum-Jae Jeong, Fazlurrahman Khan, and Ivan Mijakovic**

Silver nanoparticles (AgNPs) have emerged as a pivotal class of nanomaterials due to their potent medicinal properties, offering promising solutions for combating microbial resistance, which is a growing global health concern. Traditional methods of synthesizing AgNPs often involve toxic chemicals and energy-intensive processes, raising environmental and safety concerns. Green synthesis approaches have gained considerable attention utilizing plant and microbial extracts, natural polymers, and other eco-friendly reducing agents. These methods mitigate the environmental impact and enable the production of AgNPs with enhanced biocompatibility and tailored physicochemical properties. The synergistic effects of combining AgNPs with polymers result in improved stability, biocompatibility, and targeted delivery capabilities, while the incorporation of antimicrobial drugs generates composite materials with multifaceted modes of action against a wide range of microbial pathogens. This review delves into the green synthesis of AgNPs, focusing on the integration of natural and synthetic polymers, as well as antimicrobial drugs, to boost their antimicrobial efficacy. In addition, it is further explored that how these green-synthesized nanocomposites can be applied in areas such as wound healing and drug delivery, highlighting their potential in various biomedical fields. Moreover, the review critically examines the challenges and prospects of green synthesis, including scalability, cytotoxicity, biocompatibility, and stability hurdles.

1. Introduction

Silver nanoparticles (AgNPs) have gained significant attention in various fields due to their unique and distinctive properties. These tiny particles of silver exhibit optical, electrical, and thermal properties that make them useful in a wide range of applications, including medicine, electronics, catalysis, and antimicrobial applications[1] (**Figure 1**). Nanoparticles possess a high surface area-to-volume ratio, making them highly reactive with many active sites for chemical reactions. This also increases their potential for interactions with biological systems, making it one of their most significant characteristics.[2] The size and shape of AgNPs can be precisely controlled, which allows for tuning of their physical and chemical properties for specific applications. For instance, spherical-shaped nanoparticles are more stable than other shapes, while rod-shaped nanoparticles display unique optical properties.[3,4] The high electrical conductivity of AgNPs makes them valuable in electronic applications, including conductive inks, sensors, and flexible transparent conductive films.[5] Moreover, AgNPs exhibit a phenomenon known as surface plasmon resonance, caused by the collective oscillation of free electrons in the metal when excited by electromagnetic radiation. Building upon these unique physicochemical characteristics, AgNPs have demonstrated exceptional biological activity, particularly in antimicrobial, anticancer, and tissue regeneration applications.[6]

M. Madhusudanan, P. Singh, I. Mijakovic
The Novo Nordisk Foundation Center for Biosustainability
Technical University of Denmark
DK-2800 Kogens Lyngby, Denmark
E-mail: prisin@biosustain.dtu.dk; ivan.mijakovic@chalmers.se

The ORCID identification number(s) for the author(s) of this article can be found under https://doi.org/10.1002/anbr.202400194.

DOI: 10.1002/anbr.202400194

J. Zhang, S. Pandit, I. Mijakovic
Systems and Synthetic Biology Division
Department of Life Sciences
Chalmers University of Technology
SE-412 96 Gothenburg, Sweden

G.-J. Jeong
Department of Food Science and Technology
Pukyong National University
Busan 48513, Republic of Korea

F. Khan
Ocean and Fisheries Development International Cooperation Institute
Pukyong National University
Busan 48513, Republic of Korea

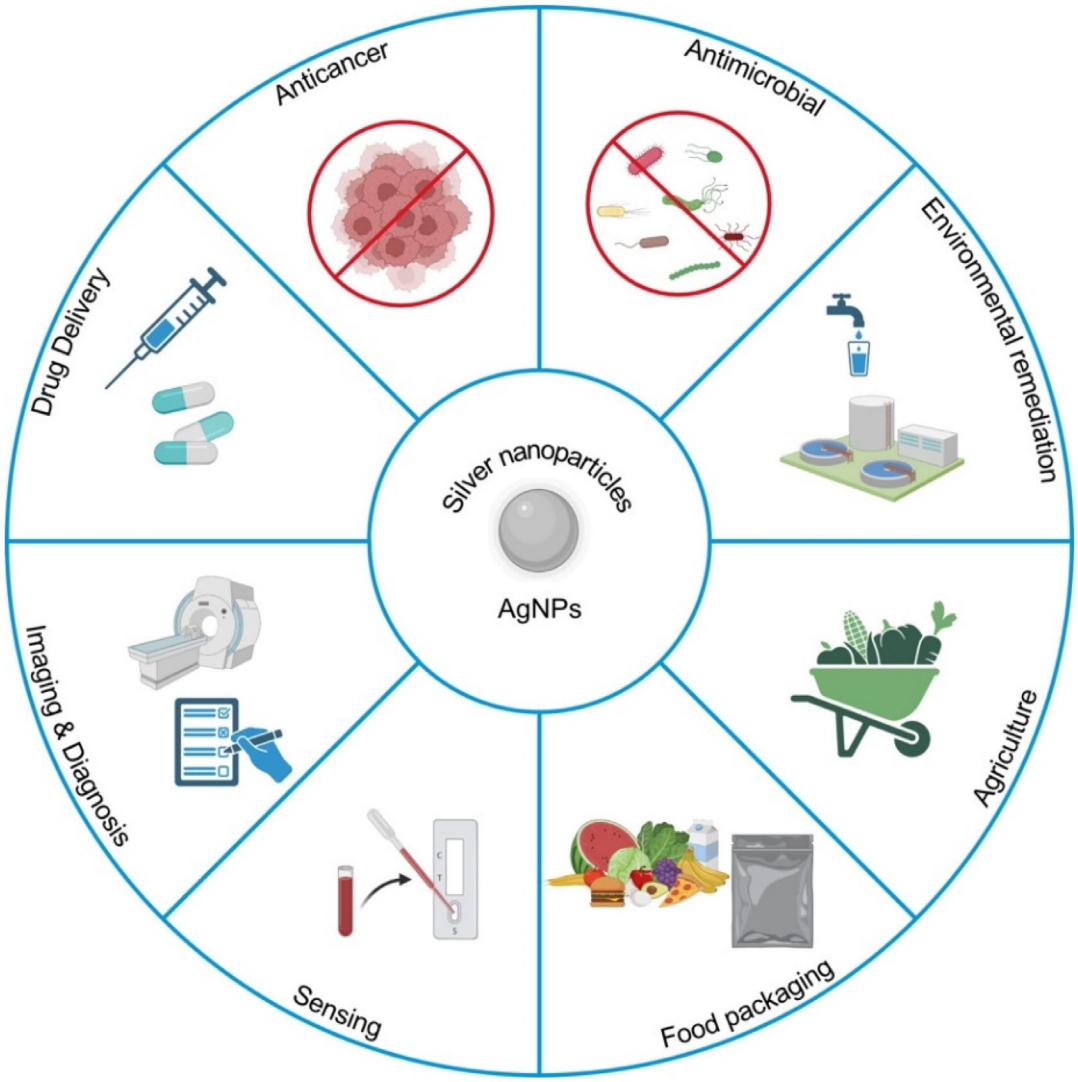

Figure 1. Multifunctional applications of AgNPs including anticancer therapy, antimicrobial activity, environmental remediation, agriculture, food packaging, sensing, imaging and diagnosis, and drug delivery, showcasing their broad biomedical, environmental, and industrial potential.

AgNPs exhibit strong antimicrobial properties and are effective against a wide range of pathogens, including multidrug-resistant (MDR) ones.[7] Their small size and ability to interact with biological systems make them promising candidates in nanomedicine.[8] In addition to their remarkable antimicrobial properties, AgNPs have been extensively studied for their potential as an anti-cancer agent.[9] Several studies have demonstrated the efficacy of AgNPs in inhibiting the growth of various cancer cell lines, including breast cancer, lung cancer, prostate cancer, and liver cancer. A study by Eltahawy et al. found that AgNPs induced apoptosis in prostate and colon cancer cells by activating caspases and downregulating anti-apoptotic Bcl-2 proteins.[10] In addition, AgNPs have shown potential in enhancing the efficacy of conventional cancer therapies, such as chemotherapy and radiotherapy.[11,12] AgNPs can be conjugated with various chemotherapeutic drugs or radiation sources and targeted to specific cancer cells or tissues, allowing for more efficient delivery of the therapy with reduced side effects.[13,14] AgNPs have also shown promise in wound healing and tissue regeneration. AgNPs can promote wound healing by reducing inflammation and enhancing angiogenesis.[15,16] Moreover, AgNPs can stimulate the growth of bone cells and promote bone regeneration. In a recent study by Du et al. AgNPs enhanced the osteogenic differentiation of mouse embryonic fibroblasts.[17] Similarly, Mira et al. found that AgNPs enhanced osteogenesis in human Wharton's jelly mesenchymal stem cells (hWJ-MSCs).[18] These studies underline the potential of AgNPs against MDR and cancer, as well as for wound healing and regenerative medicine.

AgNPs have also been shown to exhibit anti-inflammatory and immunomodulatory properties. AgNPs can inhibit the production of pro-inflammatory cytokines, such as IL-1β, IL-6, and TNF-α, and upregulate the production of anti-inflammatory cytokines, such as IL-10. This makes them an attractive candidate for the treatment of inflammatory disorders. Several studies

have investigated the anti-inflammatory activity of AgNPs and demonstrated that AgNPs reduced the production of pro-inflammatory cytokines in lipopolysaccharide (LPS)-stimulated macrophages.[19–21] For example, Khashan et al. demonstrated that AgNPs reduced inflammation in a Wistar rat arthritis model.[22] Similarly, David et al. and Moldovan et al. reported that AgNPs reduced inflammation in the acute inflammation model in Wistar rats.[23,24]

AgNPs also exhibit unique optical properties that make them useful in imaging applications, such as fluorescence and surface-enhanced Raman scattering. In a recent study by Cheng et al., a AgNPs/porous silicon Bragg mirror (AgNPs/PSB) composite was found to aid rapid and noninvasive diagnosis of breast cancer, enabling the discovery of new biomarkers for breast cancer.[25] Another study by Maiti et al. documented the enhancement of the fluorescent signal of fluorescein by AgNPs in human lung fibroblast cells, thereby increasing the resolution and contrast of the images.[26] These results show that AgNPs can have significant implications for cellular imaging applications. Among their various applications, the antimicrobial potential of AgNPs has been particularly notable, making them promising candidates for addressing the growing challenge of antimicrobial resistance (AMR). This review focuses on recent advancements in the green synthesis of AgNPs and their integration with polymers and antimicrobial agents to enhance their efficacy against drug-resistant pathogens.

The biosynthesis of nanoparticles involves the interaction of biogenic compounds from bacteria, plants, and microbial extracts with metal precursors, resulting in the formation of nanoparticle–protein complexes. This biological approach sets these nanoparticles apart from those synthesized via physicochemical methods, imparting them with distinct structural and functional properties. Biosynthesized AgNPs, often referred to as "green AgNPs" offer several advantages over conventionally synthesized nanoparticles. They exhibit enhanced biocompatibility, reduced toxicity, and environmentally friendly production processes. Additionally, the presence of biomolecules in biosynthesized AgNPs enhances their stability by acting as natural capping agents, improving their dispersion in aqueous media, and extending their functional applications. By understanding their synthesis and unique properties, researchers can further explore their role in antimicrobial applications and develop innovative strategies for combating microbial infections in an environmentally sustainable manner.

However, despite their promising antimicrobial and biomedical applications, the use of AgNPs raises concerns regarding cytotoxicity and potential adverse biological effects. While AgNPs exhibit strong antibacterial and anticancer properties, their interaction with human cells can lead to unintended toxicity, particularly at high concentrations or prolonged exposure.[27] Studies have shown that AgNPs can induce oxidative stress, DNA damage, and apoptosis in mammalian cells, highlighting the need for careful dose optimization and surface modifications to enhance biocompatibility. Moreover, their potential to accumulate in organs, trigger inflammatory responses, or interfere with normal cellular functions remains a challenge for clinical applications.[28] These concerns necessitate comprehensive safety evaluations, particularly for biomedical applications such as drug delivery, wound healing, and antimicrobial coatings. A detailed discussion on these cytotoxicity aspects and mitigation strategies is provided in Part 6 of this review.

2. Synthesis of AgNPs

Multiple methods have been developed to produce AgNPs with controlled size, shape, and morphology. Generally, AgNPs synthesis can be categorized into two major approaches: top-down and bottom-up. 1) Top-down approach: the top-down approach involves the reduction of bulk silver into nanoparticles. These methods include milling and grinding, laser ablation, electron beam irradiation, sputtering, and chemical etching. 2) Bottom-up approach: the bottom-up approach involves the nucleation and growth of AgNPs from a solution containing silver precursors and reducing agents. This includes chemical and biological methods. Both approaches have their advantages and limitations, and the choice of the synthesis method depends on the desired size, shape, surface properties, and application of AgNPs. The generalized mechanism of nanoparticle synthesis involves the reduction of the metal ions followed by nucleation, which is the formation of small clusters of atoms, growth of these clusters into larger particles, aggregation of the particles formed in the growth phase, and their capping to increase the thermodynamic stability of the nanoparticles.[29]

2.1. Chemical Synthesis of AgNPs

Chemical methods offer precise control over size and shape, often employing reducing agents such as sodium borohydride or citrate. Common chemical methods include reduction, precipitation, electrochemical, and microemulsion methods. There are hundreds of products in the consumer market incorporating AgNPs in cosmetics, clothing, and medicine. Due to this increased demand, the focus is shifting toward synthesizing these nanoparticles in an environmentally friendly and sustainable fashion.

2.2. Biological Synthesis of AgNPs

The biological synthesis of AgNPs presents an eco-friendly and sustainable alternative to chemical synthesis. This method utilizes biological agents such as plant extracts, fungi, bacteria, and algae to act as reducing, capping, and stabilizing agents for silver ions, resulting in the formation of stable and monodisperse AgNPs.[30] Compared to chemical synthesis, biological approaches offer enhanced biocompatibility, making them particularly suitable for biomedical applications.[31] Researchers have developed highly productive techniques using various plant and microbial sources, expanding the potential applications of biosynthesized AgNPs. By adjusting reaction conditions, such as temperature, pH, and reactant concentration, the size, shape, and stability of the nanoparticles can be controlled. This approach aligns with the principles of green chemistry, bridging biotechnology and nanotechnology to develop sustainable solutions for the production of nanomaterials. **Figure 2**

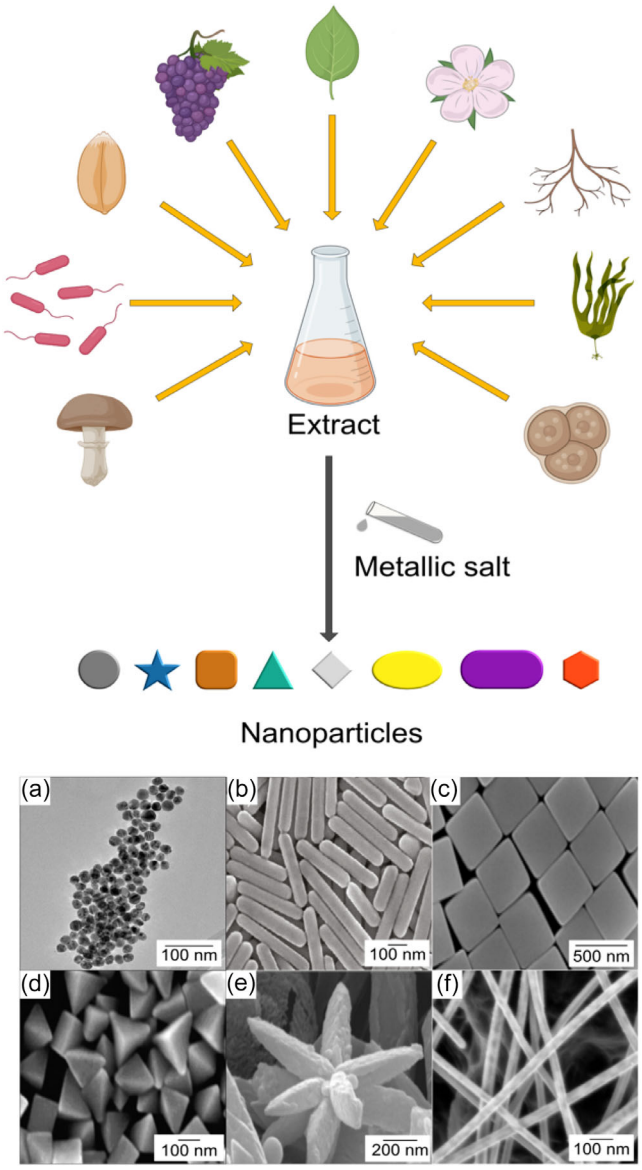

Figure 2. Biological synthesis of AgNPs from different sources and their morphologies: a) nanosphere, b) nanorods,[236] c) nanocubes,[237] d) nanopyramids,[238] e) nanoflower,[239] and f) nanowires.[240]

summarizes the biological synthesis process of AgNPs from various sources.

Several recent studies have reported the biological synthesis of AgNPs using various biological agents. For instance, a study by Rana and Parmar reported the biosynthesis of AgNPs using the leaf extract of *Azadirachta indica* and *Mangifera indica*.[32] The synthesized AgNPs exhibited excellent antimicrobial activity against various pathogenic bacteria and fungi. Another study by Viswanathan et al. reported the synthesis of AgNPs by algal extracts *of Champia parvula* possessing effective antimicrobial, antioxidant, and anticancer activity.[33] Additionally, a study by Singh et al. reported the synthesis of AgNPs by *Viridibacillus* sp. having excellent antimicrobial activity against pathogenic *E. coli* and *P. aeruginosa*.[34] Furthermore, Hayat et al. synthesized spherical AgNPs with fungal extract of *Penicillium chrysogenum*, showcasing strong antibacterial activity.[35]

An important aspect of biologically synthesized AgNPs is the formation of a nanoparticle–protein complex, commonly referred to as the "protein corona". This corona, formed from biogenic compounds in plant and microbial extracts, plays a crucial role in nanoparticle stability and bioactivity. It creates a protective layer of proteins around the nanoparticles, shielding them from interactions with other molecules in the body that could cause aggregation or dissolution. The protein corona can also affect the biocompatibility of nanoparticles. Furthermore, the protein corona can enhance the bioactivity of nanoparticles by providing a platform for the attachment and release of active agents such as drugs. Additionally, the proteins can regulate the release kinetics of the active agents, making them available at specific times and locations. Overall, the protein corona can modulate the biological fate of nanoparticles, impacting their stability, pharmacokinetics, biodistribution, and toxicity.[36] Recent studies have shed new light on the mechanisms underlying nanoparticle protein corona formation and its implications for nanomedicine. A study by Yeo et al. investigated the effect of the protein corona on the targeting and internalization of nanoparticles by cancer cells in vivo.[37] The authors demonstrated that the protein corona can enhance the cellular uptake of nanoparticles and improve tumor accumulation. Another study by Ju et al. focused on the role of the protein corona in the immune recognition and clearance of nanoparticles.[38] The authors demonstrated that the protein corona can shield nanoparticles from recognition by immune cells, reducing their clearance and prolonging their circulation time. However, they also found that certain proteins in the corona can trigger an immune response, leading to the activation of inflammatory pathways. Furthermore, a study by Oh et al. assessed the impact of protein corona on minimizing interactions with serum proteins and their effects on circulation, distribution, therapeutic activity, and toxicity of the nanoparticles.[39] Thus, the nanoparticle protein corona is a complex and dynamic phenomenon that can significantly impact the biological fate of nanoparticles in various ways.

2.2.1. Microbial Synthesis of AgNPs

Various microorganisms such as yeast, bacteria, fungi, and algae are preferred for this process due to their fast growth rate, easy growth conditions, and user-friendliness.[40] The process takes place under mild conditions, making it a sustainable alternative to traditional chemical methods for the fabrication of nanoparticles.[41] The synthesis of AgNPs by microorganisms is made possible by their inherent bioactivity and ability to reduce metal ions. Two approaches are used by microbes to synthesize AgNPs, namely extracellular and intracellular. Different mechanisms have been proposed to explain the process, including direct reduction by microbial enzymes, the formation of reducing compounds by microbial metabolism, and the stabilization of AgNPs by microbial extracellular polymeric substances.[42] Enzymes act as efficient biocatalysts to facilitate the transformation of silver ions into metallic nanoparticles. Organic molecules, such as proteins or polysaccharides, present on microbial surfaces, act as

capping agents, stabilizing AgNPs and influencing their size, morphology, and surface properties. Extracellular-mediated synthesis has garnered considerable research attention owing to its potential to reduce the downstream processing stages required for the recovery of AgNPs in intracellular synthesis. This method eliminates the need for sonication, centrifugation, and purification, which are typically necessary for AgNPs recovery in intracellular synthesis. Reducing these processing stages can lead to significant cost savings and increased efficiency in AgNPs production. The choice of microorganisms is critical in determining the size, shape, and surface properties of synthesized AgNPs, allowing for tunable properties for specific applications.

Various microbial species have been extensively explored for the formation of stable and biocompatible AgNPs. For instance, Faisal et al. synthesized spherical AgNPs with an average size of 25 nm using *Paraclostridium benzoelyticum*.[43] These nanoparticles exhibited antibacterial activity against *Haemophilus influenza, Streptococcus pyogenes, Moraxella catarrhalis, and Streptococcus pneumonia, as well as* anticancer activity toward the HeLa cell line. The nanoparticles were also found to possess anti-inflammatory, anti-aging, and antioxidant properties. Similarly, Bano et al. reported biogenic synthesis of AgNPs using the secondary metabolites of *Microbacterium proteolyticum and Streptomyces rochei*.[44] The spherical AgNPs, having an average size of 30 nm, successfully inhibited the growth of meningitis-causing bacteria, *S. pneumoniae, Haemophilus influenzae,* and *Neisseria meningitidis*. Vijaykumar et al. synthesized AgNPs using the probiotic bacteria *Lactiplantibacillus plantarum,* having spherical morphology with an average size of 14 nm.[45] The nanoparticles showed broad-spectrum antimicrobial activity against *E. coli*, *P. aeruginosa, S. aureus,* and *Bacillus subtilis*. In addition, the AgNPs possessed antioxidant activity, showed moderate to low cytotoxicity toward 3T3 normal fibroblast cell line, and were found to promote cell migration in wound healing assays. Mohammed et al. also reported the synthesis of spherical AgNPs using probiotic bacteria *Lactobacillus acidophilus*.[46] The nanoparticles exhibited antibacterial and antifungal efficacy against *E. coli, P. aeruginosa, Salmonella enterica, S. aureus, B. subtilis,* and *Candida albicans,* respectively. Moreover, the AgNPs showed cytotoxicity toward A549, Caco, and HepG2 cancer cell lines.

Similarly, multiple studies have reported AgNPs synthesis using fungal and algal sources. For example, Soliman et al. utilized the fungal strain *Trichoderma saturnisporum* to produce spherical AgNPs with a size range of 10–70 nm.[47] The nanoparticles were tested for their antimicrobial efficacy against multidrug-resistant bacteria (MRSA, methicillin-sensitive *S. aureus* (MSSA), *P. aeruginosa*, and *K. pneumoniae*). It was observed that the AgNPs inhibited their growth and prevented biofilm formation. Furthermore, the nanoparticles demonstrated antioxidant activity and showed anticancer effects against the MCF-7 breast cancer cell line with an IC50 value of 370.56 μg mL^{-1}. At the same concentration, they were minimally toxic to Vero cells. In addition, Veeragoni et al. synthesized biogenic AgNPs using marine algae *Padina tetrastromatica* and demonstrated their superior anticancer efficacy compared to chemically synthesized AgNPs.[48] These biogenic nanoparticles exhibited stronger cytotoxic effects against multiple cancer cell lines, including B16-F10 melanoma, MCF-7 breast, HepG2 liver, and HeLa cervical cells, while causing significantly lower toxicity in normal CHO-K1 cells. In a mouse melanoma model, treatment with green-synthesized AgNPs effectively suppressed tumor growth, which correlated with enhanced apoptosis. The improved therapeutic efficacy was attributed to increased silver-ion release in the tumor microenvironment, leading to elevated reactive oxygen species (ROS) generation, oxidative stress in cancer cells, and activation of p53-mediated cell death pathways. Furthermore, genotoxicity assays revealed that biosynthesized AgNPs were less genotoxic than their chemically synthesized counterparts, highlighting their potential for enhanced anticancer activity with reduced side effects. In another study, Rudrappa et al. synthesized spherical AgNPs using *Penicillium brasilianum* with an average size of 25.32 nm.[49] The AgNPs showed profound antimicrobial activity against bacterial (*E. coli*, *Shigella flexneri*, *S. aureus*, and *Bacillus cereus*) and fungal (*C. albicans*, *Candida glabrata*) strains. Additionally, the AgNPs exhibited anticancer activity against the MDA-MB-231 breast cancer cell line and photoprotective properties with a moderate sun protection factor value of 15. Algotiml et al. conducted a study where they synthesized AgNPs using various marine algae species like *Ulva rigida*, *Cystoseira myrica*, and *Gracilaria foliifera*.[50] The AgNPs were spherical in shape with average sizes of 12, 17, and 24 nm, respectively. The study found that AgNPs had inhibitory properties against multiple microbial strains and showed potential antineoplastic effects on the MCF-7 breast cancer cell line. Similarly, Hamida et al. reported the synthesis of spherical AgNPs using microalgae *Planophila laetevirens*.[51] The nanoparticles showed effective inhibition against the growth of *E. coli*, *B. cereus,* and *B. subtilis*. Furthermore, the study found that AgNPs showed potent anticancer activity against colon cancer (Sw620 and HT-29) and breast cancer (MDA-MB231 and MCF-7) cell lines while being biocompatible with human fibroblasts.

2.2.2. Plant-Mediated Synthesis

Plant-mediated synthesis is a simple, convenient, economical, and environmentally friendly approach that mitigates the involvement of toxic chemicals. Plants are readily available; their various parts contain numerous metabolites with pharmacological properties that can reduce the Ag ions and bind to the produced nanoparticles, thus improving their efficacy. Recently, several eco-friendly processes for the rapid synthesis of AgNPs have been reported using aqueous extracts of plant parts such as the leaf, stem, fruits, bark, roots, etc. Plants contain a variety of secondary metabolites, such as flavonoids, alkaloids, terpenoids, and phenols, which can reduce and stabilize silver ions to form AgNPs.[52] The generalized mechanism of plant-mediated synthesis of AgNPs is illustrated in **Figure 3**. This approach offers several advantages, including the ability to produce nanoparticles with controlled size and shape, and the potential for large-scale production. Plant-synthesized AgNPs exhibit superior antimicrobial and anticancer activity as compared to their chemical counterpart. For instance, Chavira et al. did a comparative study between AgNPs synthesized with *Jacaranda mimosifolia* flower extract and the chemical method.[53] The study

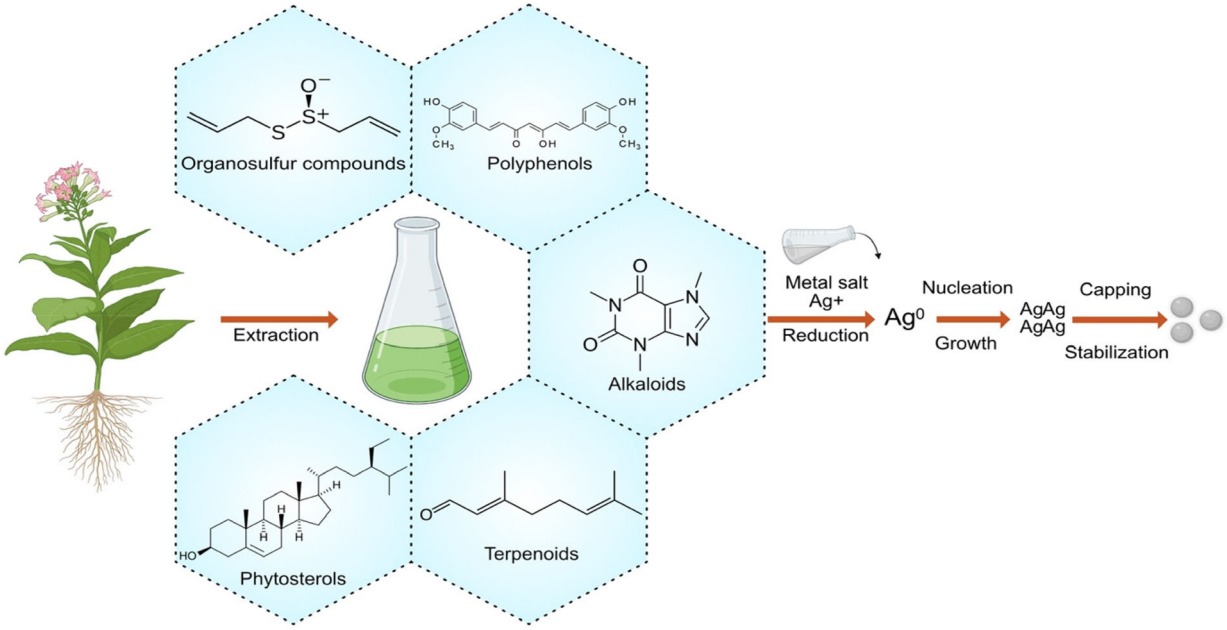

Figure 3. Schematic representation of green synthesis of AgNPs using plant extracts. The bioactive phytochemicals (organosulfur compounds, polyphenols, alkaloids, phytosterols, and terpenoids) present in the extract reduce Ag^{+} to Ag^{0}, leading to nanoparticle nucleation, growth, and stabilization.

concluded that the biologically produced nanoparticles exhibited more profound antibacterial and biofilm inhibition activity compared to chemically synthesized nanoparticles. Similarly, Ghetas et al. studied the antimicrobial potential of AgNPs produced by *Origanum vulgare* leaf extract to chemically produced AgNPs.[54] The results demonstrated that biologically produced nanoparticles exhibited more potent antibacterial and antifungal activity against fish pathogens than chemically produced nanoparticles. Moreover, Balaji et al. demonstrated that *Sida acuta* leaf extract-synthesized AgNPs showed enhanced antimicrobial, anticancer, antioxidant, anti-inflammatory, and antidiabetic activity in comparison to chemically produced NPs.[55] Plant-mediated AgNPs have demonstrated superior anticancer efficacy and lower toxicity compared to those synthesized through physical or chemical methods.[56] The presence of phytochemical capping molecules in biogenic AgNPs enhances their biological activity and allows for controlled release in the acidic tumor microenvironment, thereby synergistically increasing cytotoxicity. These nanoparticles have demonstrated potent anticancer effects across various cancer models, while minimizing damage to healthy cells, thereby improving therapeutic outcomes and reducing systemic toxicity.[57] For instance, Wang et al. synthesized AgNPs using *Mentha pulegium*, which displayed strong anticancer activity in vitro, with low IC50 values against human colon (HCT116), liver (HepG2), and cervical (HeLa) cancer cell lines.[58] The authors observed that the phytochemical-rich extract, under alkaline conditions, facilitated the formation of smaller, surface-charged AgNPs that significantly enhanced cancer cell inhibition compared to nonbiogenic nanoparticles.

Additionally, green-synthesized AgNPs provide a safer and more effective alternative for antidiabetic therapy compared to AgNPs produced via conventional physicochemical methods, which often involve hazardous chemicals. Plant-derived AgNPs have demonstrated potent antiglycation and antihyperglycemic properties in the management of type 2 diabetes mellitus, effectively lowering blood glucose levels while avoiding the toxicity concerns associated with chemically synthesized nanoparticles.[59] These biogenic AgNPs exert their antidiabetic effects through multiple mechanisms, including the inhibition of key carbohydrate-digesting enzymes (α-amylase and α-glucosidase) and the enhancement of insulin signaling. Additionally, their strong antioxidant properties help mitigate diabetes-related oxidative stress, further supporting their therapeutic potential and biocompatibility. For instance, Nagaraja et al. synthesized AgNPs using *Psidium guajava* leaf extract and demonstrated significant antidiabetic effects in vivo.[60] In streptozotocin (STZ)-induced diabetic rats, treatment with these guava leaf-derived AgNPs led to a marked reduction in blood glucose levels, comparable to the standard antidiabetic drug metformin. Notably, diabetic animals treated with biogenic AgNPs exhibited better glycemic control than those receiving only the plant extract, as the nanoparticles achieved greater blood sugar reduction even at lower doses. Over a 21-day-period, both 200 and 400 mg kg^{-1} doses of these green AgNPs significantly lowered fasting glucose levels and prevented diabetes-induced weight loss, indicating an overall restoration of metabolic balance and improved health outcomes. Similarly, biosynthesized AgNPs derived from *Azadirachta indica* (neem) extracts exhibited superior inhibition of α-amylase and α-glucosidase activity, reinforcing their enhanced antidiabetic potential.[61] The presence of embedded phytochemicals is believed to enhance the nanoparticles' biological activity, as evidenced by improved glucose uptake and increased enzyme inhibition in in vitro assays. These findings

suggest that plant-derived AgNPs improve glycemic control and leverage natural bioactive compounds to enhance antidiabetic efficacy while maintaining biocompatibility.

In another study, AgNPs synthesized using *Thymus serpyllum* (thyme) extract demonstrated significant antidiabetic effects in STZ-induced diabetic BALB/c mice.[62] Treatment with these biogenic AgNPs led to a substantial reduction in blood glucose levels, which was associated with the upregulation of insulin receptor substrate-1 (IRS1) and glucose transporter-2 (GLUT2) expression in pancreatic tissue. Additionally, the nanoparticles enhanced insulin secretion, correlating with improved glycemic control. Compared to untreated diabetic controls, AgNPs-treated groups exhibited better weight profiles and reduced markers of oxidative stress in key organs, suggesting lower diabetes-associated toxicity. The study further noted that biogenic AgNPs outperformed conventional antidiabetic agents in certain parameters, likely due to the presence of antioxidant and anti-inflammatory phytochemicals stabilizing the nanoparticles. Overall, these findings underscore the advantages of phytochemical-mediated AgNPs synthesis, which yields nanomaterials with enhanced antidiabetic efficacy and reduced toxicity compared to conventional diabetes drugs and chemically synthesized nanoparticles. By integrating bioactive plant compounds into AgNPs, green synthesis not only improves therapeutic outcomes at both molecular and systemic levels but also addresses safety concerns associated with traditional nanoformulations. As a result, biologically synthesized AgNPs represent a promising strategy for diabetes management, offering a more sustainable and biocompatible alternative for future therapeutic applications.

The choice of plant part depends on the availability of the plant, its medicinal properties, and the composition of the phytochemicals present in the extract (**Table 1**). However, the possible influence of phytochemicals and their concentrations in the plant extracts, extraction method, choice of solvent, and extraction and reaction temperature, pH, reaction time, and precursor concentration, on the size, morphology, and stability of the produced AgNPs is yet to be fully understood. A recent study by Ajaykumar et al. used the leaf extract of *Uvaria narum* to synthesize AgNPs with an average size of 16.5 nm and demonstrated that the nanoparticles exhibited excellent antibacterial activity against Gram-positive and Gram-negative bacteria along with strong anticancer properties.[63] Similarly, another study by Zubair et al. reported the biosynthesis of AgNPs using the extract of Acacia nilotica bark.[64] The synthesized AgNPs showed antioxidant and anticancer activities, making them potential candidates for biomedical applications. In another study by Tesfaye et al. Vernonia amygdalina leaf extract was used for the synthesis of AgNPs.[65] The extract was found to contain various phytochemicals such as tannins, flavonoids, saponins, and phenolic compounds that acted as reducing and capping agents for the synthesis of AgNPs. The nanoparticles exhibited profound antibacterial activity. Kumar et al. used the leaf extract of *Cleome rutidosperma* for AgNPs synthesis.[66] The extract was found to contain flavonoids, terpenoids, tannins, and glycosides, which were responsible for the reduction of silver ions and stabilization of AgNPs. The synthesized AgNPs were found to be spherical, with an average size of 15 nm. Singh et al. reported the synthesis of AgNPs using the root extract of *Premna integrifolia*.[67] The extract was found to contain quercetin, a flavonoid that acted as a reducing agent for the synthesis of AgNPs. The synthesized AgNPs were characterized, which confirmed the formation of spherical AgNPs with an average size of 35 nm. Khane et al. synthesized spherical AgNPs with an average size of 16 nm using Citrus limon zest extract.[68] The NPs exhibited strong antioxidant, antibacterial, and antifungal activity. Furthermore, the bark of cinnamon (*Cinnamomum zeylanicum*) has also been investigated for its potential in AgNPs synthesis. A study by El-Baz et al. reported the successful synthesis of AgNPs using cinnamon bark extract.[69] The phytochemicals present in the extract facilitated the reduction of silver ions, leading to the formation of stable nanoparticles with notable antioxidant and anticancer properties. In addition to leaves, roots, fruits, and bark, flower extracts have been explored for AgNPs synthesis. A study by Sabapathi et al. focused on the use of *Cassia auriculate* flower extracts for the green synthesis of AgNPs.[70] The resulting AgNPs exhibited significant antioxidant, antibacterial, and anticancer activities, demonstrating the potential of flower extracts as a source for synthesizing nanoparticles with diverse biological properties.

In addition to their biomedical applications, AgNPs have been used in food-related products. A study by Mouzahim et al. used the extract of *Ficus carica* leaves to synthesize AgNPs.[71] The nanoparticles were incorporated into chitosan (CS) food packaging film and showed strong antioxidant activity by effectively preserving fresh apple slices. Such composite films containing green synthesized AgNPs could potentially be used in food packaging to prevent the oxidation of lipids and other food components. AgNPs also show promise in the field of environmental remediation. A recent study by Irshad et al. reported the use of the extract of *Azadirachta indica* to synthesize AgNPs with an average size of 7 nm.[72] The nanoparticles were found to be highly effective in removing chromium (Cr) from contaminated water, making them a potential solution to the problem of water pollution. Moond et al. synthesized AgNPs using leaf extract of *Trigonella foenum-graecum L.*[73] The nanoparticles demonstrated effective catalytic degradation of methylene blue, methyl orange, and Rhodamine B dyes. In addition, the nanoparticles showed excellent colorimetric sensing capabilities against Hg^{2+} and Fe^{3+} ions. In another study by Dua et al., *Eupatorium adenophorum* leaf extracts were used for the synthesis of AgNPs.[74] The extract acted as both reducing and stabilizing agents, resulting in the formation of stable AgNPs. The synthesized nanoparticles, in addition to significant antibacterial and antioxidant activity, exhibited strong photocatalytic activity against Rhodamine B. Collectively, these studies underscore the versatility of plant extracts in the green synthesis of AgNPs, opening avenues for sustainable and environmentally friendly nanomaterial production.

2.3. Advantages and Limitations of Biosynthesized AgNPs

Biosynthetic approaches for AgNPs production offer significant advantages over traditional chemical synthesis methods, particularly in terms of environmental sustainability, cost-effectiveness, and biocompatibility. Unlike chemical synthesis, which often requires toxic reducing and stabilizing agents, biosynthetic methods utilize biological resources such as plant extracts, fungi, algae, and bacteria as natural reducing and capping agents. These

Table 1. Various plant parts used for AgNPs synthesis and their applications.

S No	Source of synthesis	Shape of NP	Size of NPs [nm]	Application	References
1	*Sambucus ebulus* leaf extract	Spherical	18.6	Antioxidant and antibacterial	[241]
2	*Anemopsis californica* leaf extract	Spherical	23	Photocatalytic degradation of dye	[242]
3	*Ageratum conyzoides* leaf extract	Spherical and triangular	27.85	Antioxidant, anti-inflammatory, and antidiabetic	[243]
4	*Solena amplexicaulis* leaf extract	Spherical	20–40	Photocatalytic degradation of dye	[244]
5	*Curcuma longa* rhizomes	Round, irregular	65–75	Antifungal, enhancing innate immunity of rice	[245]
6	*Sida acuta* leaf extract	Spherical	5–25	Antibacterial and anticancer	[55]
7	*Punica granatum* peel extract	Semi spherical	624.4	Antibacterial and antifungal	[246]
8	*Cuphea carthagenensis* leaf extract	Spherical	10.45	Antimicrobial and anti-infective	[247]
9	*Syzygium aromaticum* extract	Spherical	12.34	Antibacterial and photocatalytic degradation of dye	[248]
10	*Argyreia nervosa* leaf extract	Spherical	1–10	Antimicrobial, antioxidant, anti-inflammatory, and antidiabetic	[249]
11	*Olea europaea* fruit extract	Spherical	20.5–33.2	Anticancer	[250]
12	*Aloe vera* leaf extract	Spherical	50	Bioaerosol filtration (antibacterial)	[251]
13	*Rumex alpinus* leaf extract	Spherical	12–55	Antioxidant and cardioprotective agent	[252]
14	*Eucalyptus globulus* leaf extract	Spherical	25.42	Antibacterial and photocatalytic degradation of dye	[253]
15	*Heliotropium eichwaldi* extract	Irregular	30	Anti-Alzheimer (antiacetyl cholinesterase)	[254]
16	*Oplopanax elatus* root extract	Spherical	10–40	Antibacterial and antibiofilm	[255]
17	*Moringa oleifera* leaf extract	quasi-spherical	32	Plant disease protection (antibacterial)	[256]
18	*Azadirachta indica* leaf extract	Spherical to oval	22–30	Agriculture (plant growth)	[257]
19	*Calotropis procera* extract	Prism	28.8	Plant disease protection (antifungal)	[258]
20	*Echinophora platyloba* extract	Spherical	15	Antibacterial and catalytic degradation of dye	[259]
21	*Citrus limon* leaf and *Punica granatum* peel extract	Spherical	32 and 28	Antibacterial	[260]
22	*Diospyros montana* leaf extract	Quasi-spherical	16.75	Mosquitocidal	[261]
23	Grape pomace extract	Spherical	10–20	Antibacterial	[262]
24	*Serenoa repens* seed extract	Spherical	11.17–38.32	Antibacterial and antioxidant	[263]
25	*Syzygium aromaticum* extract	Spherical	10.99	Antibacterial and antibiofilm	[264]
26	*Parthenium hysterophorus* root extract	Spherical	11–20	Agriculture (seed germination and seedling growth)	[265]
27	*Nepeta sessilifolia* Bunge and *Salvia hydrangea* DC. ex Benth. Extracts	Cubic	10–50 and 10–80	Antibacterial	[266]
28	Gallic acid	Spherical	30–50	Anticancer	[267]
29	*Mikania cordata* leaf extract	Spherical	26.8–46	Antioxidant, antibacterial, and anticancer	[268]
30	Camptothecin	Spherical	10	Anticancer	[269]
31	*Coffea arabica* leaf extract	Spherical	28.65	Biosensor (cysteine)	[270]
32	*Viscum orientale* leaf extract	Spherical	119–222	Antibacterial, antioxidant, and anthelmintic	[271]
33	*Syzygium aromaticum* extract	Spherical	28	Antioxidant and mosquito larvicidal	[81]
34	*Mentha spicata* essential oil	Spherical	24	Antioxidant, antibacterial, and anticancer	[272]
35	*Clerodendrum infortunatum* flower extract	Spherical	27.75	Anthelmintic	[273]
36	*Perilla frutescens* leaf extract	Spherical	<61	Antioxidant, antibacterial, antifungal, and anticancer	[274]
37	*Allium sativum* leaf extract	Spherical	50–350	Increased sperm motility	[275]
38	*Cuphea procumbens* leaf extract	Quasi-spherical	23.45	Antibacterial, anticancer, and photocatalytic degradation of dye	[276]
39	*Fagonia cretica* extract	Spherical	143	Antioxidant and anticancer	[277]
40	*Teucrium polium* flower and leaf extract	Spherical	16	Antioxidant, antibacterial, and anticancer	[278]
41	Wheat crop leaf residue extract	Spherical	2–10	Antifungal, agriculture (increased chlorophyll, seed priming agent)	[279]
42	*Allium cepa* peel extract	Spherical	8.44–19.93	Antibacterial, antioxidant, and Alzheimer's disease management	[280]
43	*Eucalyptus* leaf extract	Spherical	5–20	Post-harvest management (banana)	[281]

Table 1. Continued.

S No	Source of synthesis	Shape of NP	Size of NPs [nm]	Application	References
44	*Bambusa arundinacea* leaf extract	Spherical	30–40	Antibacterial, antioxidant, anticancer, and photocatalytic degradation of dye	[282]
45	*Haloxylon salicornicum* leaf extract	Spherical	19.1	Antioxidant, antibacterial, and anticancer	[283]

biological entities not only facilitate nanoparticle formation but also contribute to functionalization, enhancing stability and biocompatibility.[75]

Compared to their chemically synthesized counterparts, biosynthesized AgNPs exhibit superior dispersibility in biological environments due to the presence of biogenic capping molecules such as flavonoids, proteins, and polysaccharides.[76] These biomolecules play a critical role in improving nanoparticle stability, reducing aggregation, and regulating the controlled release of silver ions—an attribute particularly beneficial for biomedical applications such as antimicrobial therapy, wound healing, and drug delivery.[77] Additionally, biosynthetic approaches allow better control over nanoparticle morphology, including size, shape, and crystallinity, which are essential factors in optimizing their physicochemical properties for specific applications.[78,79]

A key distinguishing feature of biosynthesized AgNPs is their enhanced biocompatibility. Several studies indicate that these nanoparticles exhibit reduced cytotoxicity due to the presence of naturally derived antioxidant and anti-inflammatory molecules from biological extracts, which help mitigate oxidative stress in mammalian cells.[80] In contrast, chemically synthesized AgNPs often induce high levels of ROS, leading to oxidative stress, apoptosis, and genotoxicity in human cells.[81] The enhanced interaction of biosynthesized AgNPs with biological systems makes them highly suitable for applications such as targeted drug delivery, anti-inflammatory treatments, and regenerative medicine. For instance, biogenic AgNPs have shown enhanced compatibility with fibroblast and epithelial cells, promoting cell proliferation and migration, which underscores their potential for wound healing and tissue engineering applications.[82] However, biocompatibility is not universally consistent across all biosynthetic approaches. Variations in plant or microbial extracts influence nanoparticle surface properties, and certain biosynthetic AgNPs, particularly those synthesized using fungal and bacterial methods, may elicit immunogenic responses. This necessitates further systematic comparative studies to assess their long-term in vivo safety and therapeutic applicability.[83]

The synthesis of AgNPs is governed by several critical factors, including reaction time, pH, temperature, the nature and concentration of reactants, and the type of biological source or extract used. These parameters, in turn, determine the physicochemical properties of the resulting nanoparticles, such as their size, morphology, stability, and biological activity. While biosynthetic approaches offer a green and sustainable alternative to conventional chemical synthesis, they also present unique challenges in process control and scalability. Few comparative challenges between chemical and biological NPs are listed as: 1) nanoparticle size and size distribution: Nanoparticle size is a critical determinant of biological interactions, surface reactivity, and functional properties. Smaller AgNPs (1–10 nm) exhibit higher antimicrobial and anticancer activity due to increased surface-area-to-volume ratio, whereas larger AgNPs (>50 nm) tend to have lower bioactivity but enhanced stability. Size distribution also affects AgNPs performance, with narrow distributions leading to uniform physicochemical properties, while broad distributions can cause variability in biological responses. Biosynthetic methods generally result in larger AgNPs (10–100 nm) due to the presence of biomolecular capping agents, whereas chemical reduction methods can yield more precise size control by adjusting reaction conditions such as temperature, pH, and reducing agent concentration. 2) Synthesis controllability and reproducibility: chemical methods allow for precise control over reaction kinetics, leading to consistent nanoparticle sizes and morphologies. In contrast, biosynthetic methods often exhibit batch-to-batch variability due to differences in the composition of plant extracts or microbial metabolites. Standardization of biosynthetic processes remains a major challenge, as variations in temperature, precursor concentration, and reaction time can significantly affect particle size and stability. Despite these challenges, optimization strategies such as the metabolic engineering of microbial strains and controlled bioreactor conditions are being explored to improve reproducibility in biosynthetic AgNPs production. 3) Scalability and industrial throughput: scalability remains one of the greatest challenges in biosynthetic AgNPs production. While chemical synthesis allows for high-throughput nanoparticle generation through continuous-flow and batch synthesis systems, biosynthetic methods often suffer from slow reaction kinetics and low production yields. Some of the key challenges affecting biosynthetic AgNPs scalability include: i) longer synthesis times compared to chemical methods. ii) Variability in biological extracts, affecting nanoparticle formation. iii) Complex purification steps are required to remove unwanted biomolecules.

However, recent advances in bioreactor-based biosynthesis have improved production throughput by optimizing microbial growth conditions, enzyme-mediated silver ion reduction, and automated monitoring of synthesis parameters. Studies suggest that engineered microbial systems can achieve AgNPs yields comparable to chemical reduction methods while maintaining eco-friendly and cost-effective production.

2.4. Mechanistic Insights into the Green Synthesis of AgNPs Using Pure Bioactive Compounds

The green synthesis of AgNPs using pure bioactive compounds allows researchers to isolate the specific functional groups and molecular mechanisms responsible for nanoparticle formation. Unlike crude plant or microbial extracts, which contain a

complex mixture of biomolecules, the use of purified bioactive compounds enables a precise understanding of their roles in metal ion reduction, stabilization, and surface functionalization. Recent studies have explored a diverse range of bioactive compounds—including flavonoids, terpenoids, polysaccharides, and proteins—to elucidate their contributions to AgNPs biosynthesis. 1) Flavonoids as reducing and stabilizing agents: flavonoids are a class of polyphenolic compounds widely studied for their ability to act as both reducing and capping agents in the green synthesis of AgNPs. Jain and Mehata investigated the role of quercetin, a flavonoid from *Ocimum sanctum*, in AgNPs synthesis.[84] They found that the hydroxyl (—OH) groups facilitated Ag^+ reduction while simultaneously binding to the nanoparticle surface, ensuring stability and preventing aggregation. Similarly, Zhao et al. demonstrated that hesperidin, a citrus-derived flavonoid glycoside, effectively reduced Ag^+ to Ag^0, while its glycosylated structure contributed to nanoparticle stabilization, leading to well-dispersed, stable AgNPs.[85] These findings suggest that flavonoids with multiple hydroxyl groups can act as electron donors, undergoing oxidation to quinones while stabilizing AgNPs via their remaining functional groups. Furthermore, Katta et al. extended this concept by using naringenin, a flavanone, as a single-component reducing and capping agent.[86] The study found that naringenin's catechol-like dihydroxy structures played a critical role in Ag^+ reduction, while its phenolic rings adhered to AgNPs surfaces, imparting stability. This work highlights that even within flavonoids, variations in structure (e.g., presence or absence of glycosylation) influence the efficiency of AgNPs formation and stability. 2) Terpenoids and polysaccharides in AgNPs biosynthesis: terpenoids, particularly glycosylated triterpenoids, have also been shown to mediate AgNPs formation effectively. Feng et al. explored the role of glycyrrhizin, a triterpenoid saponin from liquorice root, in nanoparticle synthesis.[87] Their findings indicated that glycyrrhizin's glucuronic acid moiety played a crucial role in Ag^+ reduction, while its hydrophobic backbone contributed to nanoparticle capping, resulting in stable AgNPs with enhanced antimicrobial properties. The study provided mechanistic insights into how sugar-linked terpenoids function as bifunctional agents, simultaneously facilitating electron transfer for reduction and providing steric stabilization through their hydrophobic framework. Similarly, Zhao et al. demonstrated that pectin, a polysaccharide, enhanced the stability of AgNPs when combined with hesperidin.[85] The carboxyl and hydroxyl groups of pectin chelated silver ions and facilitated uniform nanoparticles formation, while also preventing aggregation. This underscores the importance of biopolymer–flavonoid synergy in fine-tuning AgNPs synthesis parameters such as particle size and stability. 3) Proteins as multifunctional templates in AgNPs synthesis: Proteins serve as excellent green synthesis agents due to their rich diversity of functional groups, which can both reduce and stabilize AgNPs. Masud et al. used silk sericin (SS), a fibrous silk protein, to synthesize AgNPs.[88] They found that the amino ($—NH_2$) and carboxyl (—COOH) groups of SS played distinct roles: the carboxyl groups donated electrons for Ag^+ reduction, while the amine and peptide backbones facilitated nanoparticle stabilization via electrostatic and hydrogen bonding interactions. This study highlighted how specific amino acid residues within proteins mediate nanoparticle formation, providing a molecular-level understanding of protein-based biosynthesis. 4) Polyphenols and their role in controlled nanoparticle formation: Gangwar et al. examined the role of tannic acid, a gallotannin polyphenol, in AgNPs synthesis.[89] The study found that tannic acid's catechol (—OH) and galloyl groups acted as powerful electron donors, driving rapid Ag^+ reduction while simultaneously coordinating with AgNPs surfaces to form stable colloids. Kinetic analyses revealed that tannic acid not only accelerated AgNPs formation but also controlled the size and morphology of the resulting nanoparticles, demonstrating hat polyphenolic compounds can modulate nucleation and growth rates.

Collectively, these studies reinforce that different bioactive compounds contribute to AgNPs biosynthesis through distinct yet complementary mechanisms. Flavonoids and polyphenols primarily act as redox-active agents, donating electrons while simultaneously stabilizing AgNPs through chelation or π-electron interactions. Terpenoids and polysaccharides introduce additional steric and electrostatic stabilization, reducing particle aggregation, and enhancing bioactivity. Proteins offer multifunctional roles, participating in both Ag^+ reduction and nanoparticle stabilization through diverse amino acid side chains. By isolating and studying the roles of individual bioactive compounds, researchers have significantly advanced the mechanistic understanding of green nanoparticle synthesis. These insights pave the way for the rational design of bio-inspired nanoparticle fabrication strategies, allowing for precise control over particle properties and improved biomedical applications.

3. Antimicrobial Properties of AgNPs

The widespread use of antibiotics has led to the emergence of antibiotic-resistant bacteria, making it difficult to treat infections.[90] In recent years, alternative methods to combat AMR have been explored, including the use of AgNPs.[91] One of the most significant advantages of AgNPs in medicine is their potent broad-spectrum antimicrobial activity against drug-resistant bacteria, viruses, and fungi. Several studies have demonstrated the efficacy of AgNPs against a range of bacterial pathogens, including methicillin-resistant *S. aureus* (MRSA), *P. aeruginosa*, *Enterococcus faecium*, *K. pneumoniae*, *Acinetobacter baumannii*, and *E. coli*, due to their unique mechanism of action. For instance, a recent study by Mohammed et al. found that AgNPs could effectively inhibit the growth of MRSA, a common drug-resistant bacterium that causes severe infections.[92] Similarly, Kumar et al. demonstrated that AgNPs could effectively inhibit the growth of MRSA by disrupting the bacterial cell membrane.[93] Another study by Singh et al. found that AgNPs were effective against pathogenic *E. coli* and *P. aeruginosa* at very low concentrations due to their ability to rupture the cell membrane and interfere with cellular functions.[34] These studies showed the effect of bare AgNPs. However, using AgNPs as an antimicrobial agent in combination with other compounds also has many potential applications, including wound dressings, medical devices, and water treatment. For example, a study by Awad et al. showed that AgNPs, when combined with vancomycin, showed synergistic effects and were effective against MRSA at concentrations as low as $0.39\ \mu g\ mL^{-1}$.[94]

3.1. Mechanism of Antimicrobial Action of AgNPs

The mechanism of action of AgNPs is multifaceted, involving interactions with microbial cells at multiple levels. AgNPs exhibit broad-spectrum antimicrobial activity, making them effective against both Gram-positive and Gram-negative bacteria, including MDR strains. Their antibacterial effects stem from multiple mechanisms, allowing them to disrupt bacterial survival through different pathways simultaneously (**Figure 4**). These mechanisms can be categorized into the following key processes:

3.1.1. Disruption of Microbial Cell Membranes

AgNPs interact with bacterial cell walls and membranes primarily through electrostatic interactions. This interaction leads to: 1) membrane penetration and permeability alteration: AgNPs physically interact with the cell membrane, causing structural damage, increased permeability, and leakage of intracellular components such as ions and proteins. 2) Loss of membrane integrity: The compromised membrane results in cellular content leakage, ion imbalance, and ultimately, cell death.[95,96]

3.1.2. Generation of ROS and Oxidative Stress

AgNPs induce oxidative stress within microbial cells by generating ROS, including superoxide radicals and hydrogen peroxide. These ROS contribute to microbial cell damage via the following mechanisms: 1) membrane depolarization and damage: ROS disrupt cellular membranes by interfering with the electron transport chain, leading to mitochondrial dysfunction. 2) Protein, lipid, and DNA oxidation: ROS interact with vital cellular components, causing oxidative stress that leads to protein denaturation, lipid peroxidation, and DNA damage, thereby impairing cellular function.[97,98]

3.1.3. Interaction with DNA and Inhibition of Genetic Functions

AgNPs directly bind to microbial DNA through electrostatic interactions with the negatively charged phosphate backbone, leading to: 1) structural modification of DNA: nanoparticles interact with the grooves of the DNA double helix via noncovalent interactions, affecting DNA conformation and stability. 2) Induction of DNA damage: ROS generated by AgNPs cause oxidative damage to DNA bases, resulting in mutations, strand breaks, and interference with DNA repair mechanisms. 3) Inhibition of replication and transcription: AgNPs hinder DNA replication and transcription processes, preventing microbial cells from replicating and synthesizing essential proteins, ultimately leading to cell death.[98,99]

3.1.4. Inhibition of Protein Synthesis and Enzymatic Activity

AgNPs interfere with microbial protein synthesis and enzymatic function by: 1) binding to ribosomes: disrupting translation machinery, thereby inhibiting the synthesis of essential proteins. 2) Denaturing proteins: interfering with the secondary and tertiary structures of proteins, leading to loss of function. 3) Enzyme inhibition: binding to active sites of microbial enzymes prevents catalytic activity and disrupts metabolic pathways. 4) Disrupting cellular signaling pathways: interfering with protein–protein

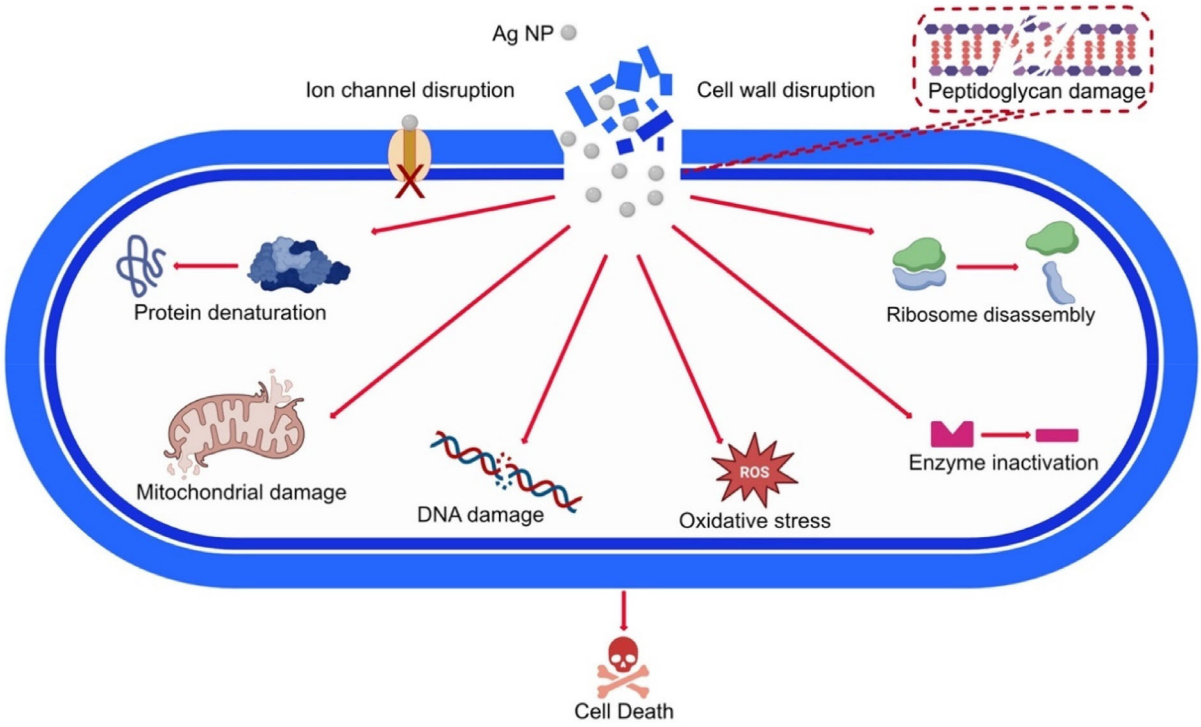

Figure 4. Illustrates how AgNPs exert antimicrobial effects by disrupting cell membranes, generating ROS that cause oxidative damage, and binding to proteins to inhibit essential cellular functions.

interactions, posttranslational modifications, and essential cellular processes, such as ATP production, ultimately affecting microbial viability.[100–102]

These mechanisms collectively contribute to the potent antimicrobial efficacy of AgNPs, making them valuable candidates for biomedical applications.

3.2. Factors Affecting Antimicrobial Activity

Various factors influence the antimicrobial activity of nanoparticles, and understanding these factors is crucial for optimizing their effectiveness. These factors include size, shape, concentrations, surface charge, coating, and corona layer. The size of nanoparticles influences their antimicrobial activity. Small nanoparticles have a higher surface area to volume ratio, which makes them more effective in interacting with bacterial cells and results in greater antimicrobial activity. Furthermore, their small size allows them to easily penetrate bacterial cell membrane, disrupting their structure and function. Additionally, smaller nanoparticles are more readily internalized by bacterial cells, which can induce higher cellular toxicity. Moreover, smaller nanoparticles are more readily internalized by bacterial cells, which can induce higher cellular toxicity. However, the stability and tendency of nanoparticles to aggregate can be affected by their size; smaller size results in higher surface energy, which can lead to nanoparticle aggregation. This aggregation increases the size, which may reduce the surface area of nanoparticles, thereby decreasing antimicrobial activity.[103,104]

The shape of nanoparticles can also significantly impact their antimicrobial activity. Differently shaped nanoparticles interact with bacterial cells in distinct ways, leading to variations in their ability to disrupt bacterial processes and cause cell death. For instance, spherical nanoparticles exhibit a high surface area-to-volume ratio, allowing efficient interaction with bacterial cells. Their smooth surface can promote adhesion to bacterial membranes, facilitating the transfer of active components into the cell. Meanwhile, due to their elongated structure, rod-shaped nanoparticles can exert mechanical stress on microbial structures to penetrate bacterial membranes more effectively than spherical nanoparticles. They can also generate localized stress on the membrane, enhancing its disruption and leading to cell death. Various studies have reported that nanoparticles with high surface curvature, such as spherical and rod-shaped, exhibit increased antimicrobial activity. It is important to note that the specific effects of nanoparticle shape can depend on various factors, including the type of nanoparticle, the microbial species involved, and the intended application.[105,106]

In general, the higher the concentration of nanoparticles, the more effective they tend to be at killing microbes. However, the relationship between the antibacterial activity of nanoparticles and their concentration is not always linear. While some studies have found that the antibacterial activity increases with concentration, others have found that there is a point where increasing the concentration beyond a certain threshold may not be effective or may even have negative effects. This can be attributed to high concentrations of nanoparticles, which can cause saturation and aggregation. When nanoparticles aggregate, they may have reduced surface area available for interactions with microbial cells, which can potentially reduce their antimicrobial effectiveness. Therefore, it is essential to find the optimal concentration of nanoparticles based on the specific type of nanoparticles, target bacteria, and desired therapeutic outcome to achieve maximum antimicrobial activity while minimizing the potential adverse side effects.[107,108]

The surface charge of nanoparticles plays a crucial role in their antimicrobial activity. Positively charged (cationic) nanoparticles tend to exhibit more potent antibacterial activity than negatively charged (anionic) or neutral nanoparticles. This is because the negatively charged outer membranes of bacteria tend to electrostatically attract cationic nanoparticles, leading to a more efficient interaction between the two. As a result, the structure and integrity of bacterial membranes get disrupted, causing leakage of essential cellular contents, ultimately leading to cell death. Also, cationic nanoparticles may be more readily taken up by cells through electrostatic interactions, allowing for intracellular antimicrobial effects. Nanoparticles are often designed with specific surface charges based on the intended application and the type of microorganisms they aim to target. The optimization of surface charge, in conjunction with other nanoparticle properties, is a critical aspect of developing effective and safe antimicrobial nanomaterials.[109] Surface coating or functionalization of nanoparticles can have a significant impact on their antimicrobial activity.[110,111] By modifying the nanoparticle's surface with functional groups such as amino, carboxyl, or hydroxyl groups, the particle can interact more effectively with bacterial cells, disrupting their membrane and causing cell death. Surface functionalization can improve the stability of nanoparticles in biological fluids and enhance their dispersion. This is crucial for maintaining the efficacy of nanoparticles and preventing aggregation, which may reduce their antimicrobial activity. Moreover, functionalization can improve the biocompatibility of nanoparticles, making them less likely to cause potential toxicity to host cells. It can also impart specificity by incorporating ligands or targeting moieties, allowing them to target specific bacterial species or strains. Polyethylene glycol (PEG) is a commonly used polymer that can improve biocompatibility and prolong the release of active components. CS is another polymer that can enhance cellular uptake and membrane permeability. AgNPs coated with CS are more effective against bacteria than uncoated nanoparticles.[112,113] Understanding these mechanisms is crucial for optimizing the design and application of AgNPs in various antimicrobial contexts, ranging from medical applications to water treatment and consumer products. Various ongoing research continues to explore the safety and environmental implications associated with the use of AgNPs.

The antimicrobial activity of nanoparticles is also influenced by the "protein corona" layer, which often forms around the nanoparticle either during synthesis, called the "primary corona layer", or when the nanoparticles interact with any biological moieties called the "secondary corona" layer. The nanoparticle protein corona is a dynamic layer of proteins, lipids, metabolites, and other biomolecules that coat the surface of the nanoparticle.[114] Protein corona is often divided into two categories: hard and soft corona. Hard corona contains higher affinity proteins bound irreversibly to the nanoparticle surface. Meanwhile, soft corona is formed by lower affinity proteins reversibly bound to nanoparticles, which showcase high exchange rates with

the media components.[115] This process is regulated by the intermolecular interactions between nanoparticle-protein and protein-protein in the media. Over time, proteins having weak interactions with the nanoparticle are replaced by those possessing higher affinity, thereby hardening the corona.[116] The formation of protein corona on nanoparticle is influenced by the physicochemical properties of the nanoparticle, such as the type, composition, size, shape, and surface charge.[117] In addition, ambient factors such as pH, temperature, ionic strength, protein concentration, and exposure time greatly influence the formation and composition of the protein corona.[118]

4. Polymer-AgNPs Nanoparticle Composites

Having established the advantages of green-synthesized AgNPs—including their eco-friendly fabrication, enhanced biocompatibility, and potent antimicrobial activity against a wide spectrum of drug-resistant pathogens—it becomes evident that their integration into composite systems offers further opportunities for optimization. While bare AgNPs exhibit impressive antimicrobial efficacy, their application can be limited by challenges such as aggregation, rapid ion release, and reduced stability under physiological conditions. To address these limitations and expand their functional scope, significant attention has been directed toward the development of polymer–AgNPs composites. These hybrid systems combine the antimicrobial potency of silver nanoparticles with the tunable physicochemical properties of polymers, resulting in materials that exhibit improved stability, sustained release profiles, enhanced mechanical strength, and, in some cases, targeted delivery capabilities. Polymer-AgNPs composites involve integrating AgNPs into polymer matrices through two synthesis methods: 1) direct synthesis of AgNPs within the polymer matrix using in situ reduction methods; 2) addition of presynthesized AgNPs to the polymer matrix through physical mixing or chemical bonding.[119] Polymer-AgNPs composites have shown promise in applications such as drug delivery systems, wound dressings, and tissue engineering due to their biocompatibility and ability to control the release of therapeutic agents.[120,121] Polymers play a crucial role in enhancing the effectiveness of AgNPs in medical applications due to several key factors: 1) stability enhancement: the polymer matrix provides a stable environment, preventing the aggregation or precipitation of AgNPs. This is essential for maintaining the desired properties and ensuring consistent composite performance. 2) Controlled release: engineered polymers enable the controlled release of silver ions, which is advantageous for sustaining antimicrobial or therapeutic effects in applications such as wound dressings or drug delivery systems. 3) Biocompatibility: biocompatible polymers, such as CS, ensure that the resulting material is suitable for contact with biological systems without causing adverse reactions. 4) Targeted delivery: incorporating AgNPs into polymer-based drug delivery systems allows for targeted delivery, enhancing therapeutic effects while minimizing impact on healthy cells. 5) Versatility: polymers, which can be modified to exhibit specific properties, allow for the tailoring of polymer-AgNPs composites into various forms, including films, hydrogels, or nanoparticles. This versatility meets diverse medical application requirements, ranging from wound healing to drug delivery. **Figure 5** illustrates the application of polymer-AgNPs in antibacterial and wound healing applications.

Polymer-AgNPs composites leverage synthetic (e.g., polyvinyl alcohol (PVA), PEG, polyvinylpyrrolidone (PVP)) and natural (e.g., cellulose, CS, sodium alginate) polymers as supporting biomaterials to enhance AgNPs' performance in medical applications.[122] AgNPs exhibit a propensity to undergo aggregation facilitated by van der Waals forces. The introduction of stabilizers proves effective in impeding the agglomeration of colloidal AgNPs.[123,124] Commonly employed end-capping agents such as PVA, PVP, and PEG play a pivotal role in preventing nanoparticle aggregation. AgNPs coated with these polymers can function as drug-delivery systems for medical treatments.[125,126] Elbaz et al. employed PVA, PEG, and PVP to synthesize three distinct types of core-shell Ag/polymer nanoparticles for encapsulating the chemotherapeutic agent doxorubicin (DOX). Remarkably, the synergistic anticancer activity of low doses of DOX-Ag/polymer nanocarriers was evident, with DOX-Ag/PVP demonstrating the highest cytotoxicity. The developed nanoparticle-based combination therapy exhibited significantly enhanced anticancer activity against breast cancer cells, underscoring its potent toxic effect.[127] Karuppaiah et al. employed PVP to stabilize colloidal AgNPs and prevent aggregation. For the first time, the AgNPs stabilized by PVP were loaded with gemcitabine (GEM) through electrostatic interactions. The investigation revealed that the GEM-PVP-AgNPs exhibited enhanced cytotoxic activity in MDA-MB-453 cells compared to GEM or AgNPs alone, demonstrating that GEM and PVP-AgNPs displayed synergistic effects on the breast cancer cells.[128]

4.1. PVA

PVA exhibits commendable attributes, including biocompatibility, biodegradability, fiber-forming capabilities, mechanical properties, and swelling properties. PVA nanofibers, crafted through electrospinning technology, possess the ability to absorb wound exudate and foster tissue regeneration.[129] Jatoi et al. synthesized AgNPs on the surface of carbon nanotubes and subsequently embedded them in PVA nanofibers. Within 72 h, the PVA/carbon nanotube-AgNPs nanofibers demonstrated outstanding bactericidal properties and growth inhibition against *E. coli* and *S. aureus* strains, indicating the suitability of this nanocomposite as a biocompatible, safe, sustainable, and effective material for wound dressing applications.[130] Hydrogels represent polymer network systems that exhibit substantial swelling in the presence of water or biological fluids. Notably, hydrogels emulate biological tissue characteristics owing to their significant water absorption capacity and flexibility. However, despite their advantages, hydrogels are susceptible to microbial infection in moist wound environments.[131] While antibiotics can maintain wound sterility, their misuse may lead to the proliferation of multiresistant microorganisms, posing significant challenges to health safety and sustainable development. An effective strategy to construct antibacterial biomaterials involves the incorporation of AgNPs into hydrogel matrices.[132] PVA-AgNPs hydrogels have been subject to extensive research due to their potential to address these challenges.[133–135] Bhowmick et al. employed a freeze-thaw method to synthesize a novel elastic, anti-adhesive, and

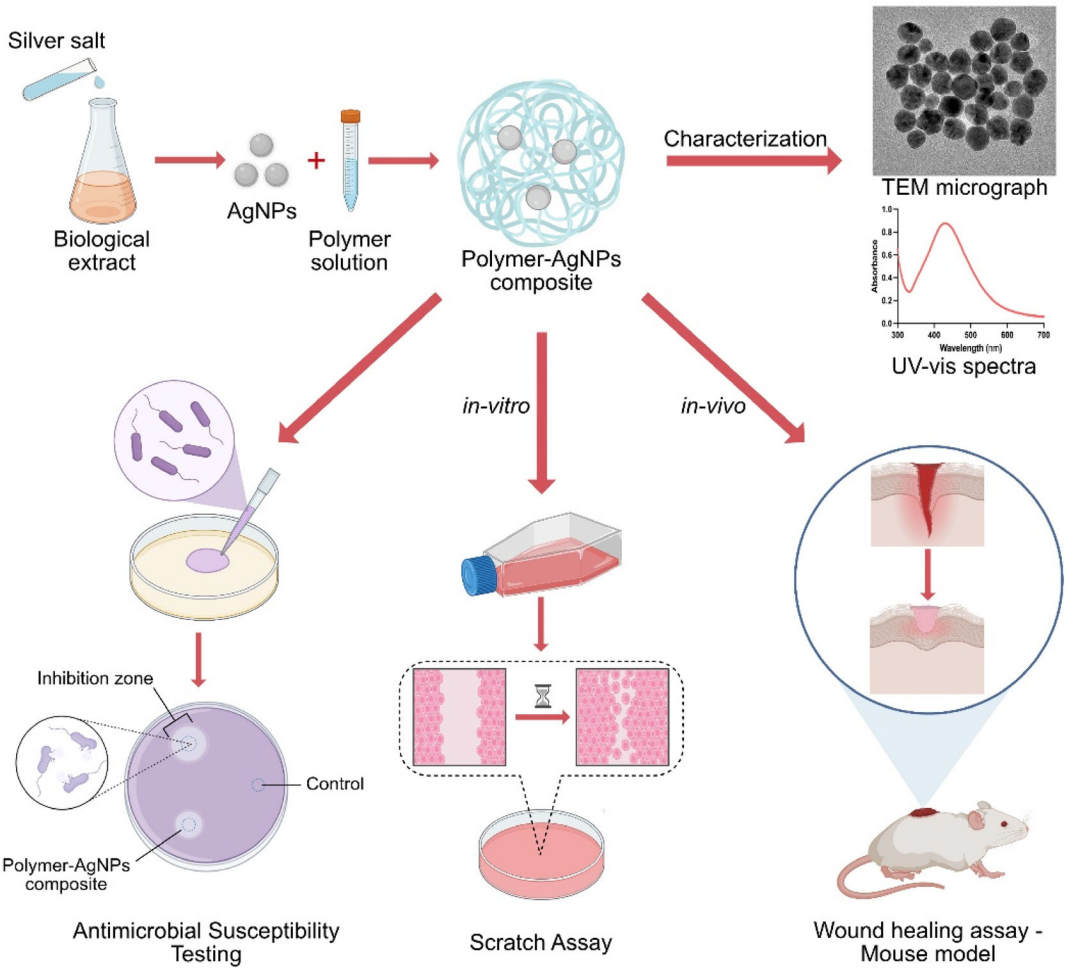

Figure 5. Synthesis, characterization, and application of polymer-AgNPs composite for wound healing.

antibacterial PVA hydrogel, designed to encapsulate green AgNPs. The minimum inhibitory concentration (MIC) of these AgNPs against *S. aureus* and *E. coli* was determined to be 7.81 μg mL^{-1}, while the MIC against *P. aeruginosa* was ≈3.90 μg mL^{-1}. The PVA hydrogel loaded with AgNPs demonstrated a slow and continuous release of AgNPs. The antimicrobial efficacy of the scaffold persisted even 96 h after AgNPs release, indicating the potential of the scaffold to serve as a reservoir for AgNPs, maintaining a moist and sterile environment for an extended period.[134] Batool et al. utilized a casting method for the fabrication of nanocomposite films comprising PVA, starch, and AgNPs. The AgNPs were synthesized through green chemistry methods employing *Diospyros lotus* fruit extract. The AgNPs were incorporated into PVA and starch blends using an ex-situ method. Antimicrobial assessments of AgNPs and hydrogel films demonstrated results comparable to ciprofloxacin, underscoring the potential of such films for wound dressing applications.[133] While PVA-AgNPs composites have been extensively studied and utilized in the antibacterial field, the high preparation costs and limited biocompatibility pose challenges associated with synthetic polymers. In contrast, natural polymers, such as cellulose, CS, and alginate, which are abundant in nature, exhibit favorable biocompatibility and biodegradability. The utilization of green AgNPs in conjunction with natural polymers in antibacterial and medical applications has also been the subject of widespread research.[136]

4.2. Alginate

Alginate is a highly biocompatible and biodegradable polymer derived from seaweed, which finds application in various biomedical scenarios. The composite of alginate and AgNPs emerges as a promising material for wound dressing.[137,138] Sodium alginate (SA) serves as an effective stabilizer for the synthesis of AgNPs.[139] Pankongadisak et al. incorporated alginate beads loaded with AgNPs into gelatin scaffolds for potential application as wound dressings. The preparation of calcium alginate microspheres loaded with AgNPs involved the electrospray method, ultraviolet irradiation technology, and the emulsification/external gelation method. The gelatin scaffolds, laden with AgNPs-alginate beads demonstrated nontoxicity to normal human dermal fibroblasts[140] and exhibited robust antibacterial activity.[141,142] Correia et al. employed 3D printing for the fabrication of tricalcium phosphate (TCP)/SA scaffolds. Following this, PVP-AgNPs were introduced into the scaffold using two distinct

methods: direct incorporation and physical adsorption. The composite scaffolds produced by the direct incorporation of AgNPs are particularly well-suited for bone tissue regeneration, owing to their favorable mechanical properties, biocompatibility, and bactericidal activity.[143] Kumar and Jaiswal employed a green synthesis method utilizing *Ficus bengalensis* extract to synthesize AgNPs. The AgNPs were incorporated into a blend of PVA and SA, followed by cross-linking with boric acid and calcium chloride to fabricate spray hydrogel dressings. The dressing exhibited uniformly distributed AgNPs, high water retention, and biodegradable characteristics. Furthermore, it demonstrated sustained release of AgNPs with antibacterial activity over 24 h.[144] Hu et al. developed a hydrogel dressing utilizing calcium ions to cross-link SA molecular chains and incorporate gallic acid-functionalized AgNPs (GA@AgNPs) to form a three-dimensional network (GA@AgNPs-SA). The hydrogel dressing demonstrated outstanding biocompatibility and facilitated the sustained release of silver ions, ensuring prolonged antibacterial activity and hindering biofilm formation. Furthermore, in vivo studies revealed that the GA@AgNPs-SA hydrogel effectively reduced the expression of IL-6 and TNF-α, thereby mitigating the inflammatory response. Additionally, it promoted angiogenesis by upregulating the expression of CD31, α-SMA, and VEGF, significantly reducing the inflammatory response and accelerating the repair of infected wounds.[145]

4.3. Cellulose

Cellulose is an abundant polysaccharide that serves as a natural polymer that can be extracted from plants or bacteria. Its extensive utilization in the medical field is attributed to numerous appealing advantages, including biodegradability, excellent biocompatibility, nontoxicity, cost-effectiveness, and robust thermal and chemical stability.[146] Cellulose stands out as an exceptional carrier for AgNPs, with cellulose-AgNPs composites playing a distinctive role in the fabrication of wound healing dressing materials, showcasing notable antibacterial activity. The synthesis of AgNPs can be achieved in situ on the cellulose surface.[147,148] Shanmugam et al. employed a green synthesis method for in situ generation of AgNPs on the surface of a cellulose matrix using *Cissampelos pareira* leaf extract. The resulting cellulose-silver nanocomposite displayed potent antibacterial activity against *S. aureus*, *P. aeruginosa*, *Trichophyton rubrum*, and *C. albicans*, as assessed by the disk diffusion method.[149] Du et al. fabricated antibacterial materials by loading AgNPs onto periodate-oxidized dialdehyde cellulose (DAC) through an in situ method. The reduction of AgNPs occurred in situ on the DAC surface using $AgNO_3$ as the silver precursor and DAC as both the reducing agent and stabilizer, eliminating the need for additional reducing agents. The resulting spherical AgNPs were uniformly distributed on the DAC surface, and AgNPs-loaded DAC exhibited remarkable antibacterial efficacy against *E. coli* and *S. aureus*, with inhibition zones measuring 4.90 and 7.35 mm, respectively.[150] One approach for cellulose modification involves TEMPO-mediated oxidation of cellulose surface hydroxyl groups. This method facilitates the reduction of silver ions on the cellulose surface through an ion exchange reaction. The resulting AgNPs and cellulose composite demonstrate the controlled release of silver ions[151] and exhibit high biocompatibility.[152] Notably, the composite displays efficient antibacterial activity against *E. coli*, *Proteus mirabilis*, *P. aeruginosa*, *B. subtilis*, *S. aureus*, and *C. albicans*.[153]

Beyond the in situ synthesis of AgNPs on cellulose surfaces, biologically synthesized AgNPs can be embedded onto the cellulose surface to create antibacterial complexes.[154,155] Shaaban et al. assessed the effectiveness of bacterial cellulose impregnated with green-synthesized AgNPs as an antimicrobial film for wound healing treatment. The AgNPs were synthesized using *Moringa oleifera* leaf extract. Incorporating these green AgNPs into bacterial cellulose and filter paper disks demonstrated outstanding antimicrobial activity against *S. aureus* and *P. aeruginosa*.[155] Mariadoss et al. employed the β-catechin (CA)-mediated synthesis of AgNPs embedded in cellulose (CE) and graphene oxide (GO) nanocomposites to enhance antibacterial activity. The combination of CA-AgNPs and CE-GO demonstrated substantial antibacterial efficacy against Gram-positive and Gram-negative pathogens.[156]

Due to the abundant hydrophilic functional groups present in cellulose and its derivatives, they can be easily modified and cross-linked, rendering them ideal materials for hydrogel synthesis. Cellulose-based hydrogels find extensive applications in medical fields, including tissue engineering, controlled delivery systems, and wound dressings.[157] While cellulose hydrogels do not exhibit intrinsic antimicrobial activity, their excellent modification capabilities and compatibility with antibacterial materials, such as AgNPs, bestow upon them a significant potential for development into antibacterial hydrogels.[158,159] AgNPs can be synthesized in a green manner directly on the surface of a carboxymethylcellulose (CMC) polymer to fabricate a hybrid hydrogel.[160,161] For instance, Capanema et al. engineered a hybrid hydrogel incorporating AgNPs within a cross-linked network of CMC polymer. Additionally, this cross-linked network was coupled with the anticancer drug DOX. The results highlight the effective nucleation and stabilization effects of spherical AgNPs, exhibiting a uniform size distribution. The hybrid nanocomposite demonstrated antibacterial activity against Gram-positive and Gram-negative bacteria. The hybrid nanocomplexes exhibited finely tuned intracellular kinetics of DOX in vitro, showcasing synergy with AgNPs in combating melanoma cancer cells.[160]

4.4. CS

CS is another abundant polysaccharide that holds remarkable promise in biomedical advancement and tissue engineering applications owing to its exceptional biocompatibility, rapid biodegradation, potent antimicrobial capabilities, and tissue adhesive properties. Research has highlighted the collaborative potential of AgNPs with CS, particularly in wound healing and antibacterial activity.[162,163] The one-pot green synthesis of AgNPs, utilizing the stabilizing and reducing capabilities of CS, showcased their antibacterial efficacy and biocompatibility.[164–166] Wongpreecha et al. conducted the synthesis of CS-stabilized AgNPs (AgNPs-CS) in an autoclave, where CS served as both a reducing agent and stabilizer. The resultant AgNPs-CS demonstrated effective antibacterial activity against *E. coli* and *S. aureus*, with minimum bactericidal concentrations of 39.1 and 312.5 $\mu g\,mL^{-1}$, respectively. Importantly, no cytotoxicity to L-929 fibroblasts was observed.[167] Hajji et al. employed a green method to prepare CS-PVA-AgNPs

Table 2. Provides an overview of various AgNPs-polymer composites, including their synthesis methods and effectiveness against specific bacterial strains in antibacterial applications.

Materials	Synthesis methods	Comments	References
AgNPs/sodium alginate/ tannic acid	Tannic acid and sodium alginate were used as reducing agents and stabilizers to synthesize AgNPs.	MIC of the AgNPs against *S. aureus* ATCC 6538 was 31.25 μg mL^{-1}. AgNPs cause irreversible damage to the cell membrane of *S. aureus*.	[139]
AgNPs/CS/collagen/dextran (COC@AgNP)	AgNPs were synthesized in situ during the formation of COC hydrogel.	COC@AgNPs have good biocompatibility and excellent antibacterial properties. COC@AgNPs promote the formation of epithelium and blood vessels and accelerate the healing process of infected full-thickness skin defects.	[176]
AgNPs/cellulose (Cel/LCP/ Ag-NCs)	AgNPs were in situ generated on the surface of the cellulose matrix using *Cissampelos pareira* leaf extract.	Green Cel/LCP/Ag-NCs showed good DPPH radical and ABTS scavenging activities. Cel/LCP/Ag-NCs showed antibacterial activity against *S. aureus*, *P. aeruginosa, T. rubrum, and C. albicans*.	[149]
AgNPs/cellulose	AgNPs were greenly synthesized by *Moringa oleifera* leaf extract. AgNPs were incorporated into bacterial cellulose.	AgNPs incorporated into bacterial cellulose showed high antibacterial activity against *S. aureus* and *P. aeruginosa*. AgNPs have a distorting effect on bacterial cell morphology.	[155]
AgNPs/soybean polysaccharide/carrageenan (SSPS/CG/AgNPs)	AgNPs were obtained by SSPS as stabilizing and reducer. Nanocomposite films based on AgNPs were developed using the solution casting technique.	The addition of CG significantly improved the mechanical properties, thermal stability, and water resistance of the film. SSPS/CG/AgNPs nanocomposite film showed antibacterial activity against *E. coli* and *S. aureus*.	[284]
AgNPs/cellulose	AgNPs were synthesized using cellulosic polymer as reducing agents, coating agents, and stabilizers.	AgNPs-EC and AgNPs-HPMC exhibited significant antimicrobial activity. -AgNPs-EC and AgNPs-HPMC were internalized by *E. coli* cells compared to other formulations.	[285]
AgNPs/CS	AgNPs were synthesized using fungal biomass and coated with CS.	The capping of CS on AgNPs prevents agglomeration and promotes stability. Nanocomposites showed antimicrobial potential against pathogenic bacteria. The nanocomposite confirmed no cytotoxic effect on NIH/3T3 cell lines.	[286]
AgNPs/Gum Arabic (AgNPs-GA)	AgNPs were synthesized using gum Arabic as a stabilizer and reducing agent.	The MIC of AgNPs-GA against *A. hydrophila* and *P. aeruginosa* was 1.625 and 3.25 μg mL^{-1}, respectively. The AgNPs-GA significantly inhibit the formation of *A. hydrophila* and *P. aeruginosa* biofilm at concentrations of 1.625 μg mL^{-1}.	[287]
AgNPs/soluble soybean polysaccharide (SSPS)	AgNPs were synthesized using SSPS.	MIC of SA120 against *E. coli*, and *S. aureus* was 2 and 4 μg mL^{-1}. AgNPs colloidal dispersion coated kraft paper showed excellent antibacterial activity against *E. coli*, *S. aureus,* and *P. aeruginosa*.	[288]
AgNPs/soluble soybean polysaccharide (SSPS)	AgNPs were synthesized using SSPS and immobilized in SSPS film by film casting and drying methods.	The presence of AgNPs improves the thermal stability and UV-blocking properties of SSPS films. The SSPS/AgNPs film had excellent inhibitory activity against *E. coli* and *S. aureus*.	[289]
AgNPs/CS	AgNPs-CS nanocomposites (Ag/CS NC) were synthesized using Solanum nigrum seed as a reducing agent.	AgNPs showed effective antibacterial activity against *B. subtilis* and *E. coli*. AgNPs exhibited cytotoxicity against human cancer cell MDA-MB-231, PANC-1, SKOV-3, PC-3, Hela. Ag/CS NC-coated cotton fabric showed significant antibacterial activity against *B. subtilis* and *E. coli*.	[290]
AgNPs/CS	AgNPs were in situ synthesized on CS hydrogel coating on stainless steel electrodes via electrochemistry.	AgNPs-CS coating showed low cytotoxicity to NIH3T3 cells, good antibacterial properties against *E. coli* and *S. aureus* and unique pH-dependent controlled Ag^{+} release capability.	[291]
AgNPs/starch/agar	Starch/agar-based functional film was fabricated and integrated with the AgNPs prepared using Enoki mushroom extract.	AgNPs significantly enhanced the water vapor barrier and hydrophobicity of starch/agar-based film. Adding AgNPs did not affect the mechanical strength and thermal stability of the film. AgNPs-starch/agar films exhibited antibacterial activity against *E. coli* and *L. monocytogenes*.	[292]

Table 2. Continued.

Materials	Synthesis methods	Comments	References
AgNPs/polyacrylamide/ N-methylenebisacrylamide (PAA-MBA)	AgNPs were synthesized using varying amounts of $NaBH_4$. AgNPs of different shapes were encapsulated in the PAA-MBA hydrogel matrix.	AgNPs-doped hydrogels have higher storage modulus and Young's modulus. Although both spherical and triangular AgNPs-doped hydrogels exhibited strong antibacterial activity, the antibacterial activity of hydrogels containing rod-shaped AgNPs was relatively low.	[293]
AgNPs/locust bean gum/ PVA (LBG/PVA/AgNPs)	AgNPs were in situ synthesized in LBG/PVA/AgNPs hydrogels by fig leaf extract.	LBG/PVA/AgNPs hydrogels exhibited antibacterial activity against *E. coli*, *P. aeruginosa*, *S. aureus,* and *E. faecalis*.	[294]
AgNPs/CS/gelatin	Composite films were prepared using a solution casting method with CS, gelatin, and AgNPs prepared by *M. frondosa* leaf extract.	Due to the cross-linking movement of AgNPs, the swelling degree, moisturizing ability, and water vapor transmission rate decreased slightly. Compared with polyethylene films, composite films containing AgNPs can effectively reduce bacterial contamination.	[295]
AgNPs/PCL	AgNPs were synthesized using Cilembu sweet potato extract. PCL/AgNPs were fabricated using a screw-assisted extrusion system.	PCL/AgNPs scaffolds exhibit higher compressive strength and more hydrophilic and conductive functions compared to PCL scaffolds. PCL/AgNPs scaffolds show antibacterial properties against S. aureus (99.5%).	[296]
AgNPs/PVA	PVA electrospun nanofiber doped with AgNPs was in situ modified. The hydroxyl groups on the PVA chain can serve as reaction sites and stabilizers for AgNPs.	PVA nanofibers with different cross-linking degrees can control the release of Ag. PVA doped with AgNPs has good antibacterial efficacy against *S. aureus*. Ag@PVA nanofibers showed good compatibility with 293 T, NIH3T3, and U937 cells.	[297]
AgNPs/starch/gelatin	AgNPs-embedded starch-gelatin hydrogels were in situ synthesized without the use of any reducing agents and surfactants.	AgNPs-embedded hybrid hydrogel showed good antibacterial activity against *E. coli* and *S. aureus*. AgNPs-embedded starch-gelatin hydrogel has high mechanical strength, good hydrophilicity, biocompatibility, biodegradability, noncytotoxicity, and hemocompatibility.	[298]
AgNPs/Alginate	Alginate-AgNPs-LGO films were obtained by casting method.	The films showed strong antibacterial activity against *B. cereus, S. aureus, E. coli,* and *S. typhi*. The color of the film changes with temperature and the presence of light.	[299]
AgNPs/guar gum/gelatin (GG/Gl/Ag-N composites)	GG/Gl/Ag-N composites were synthesized via in situ method by maltose sugar reduction.	Guar gum and gelatin matrix act as capping agent for AgNPs. GG/G1/Ag-N-composite was determined to exhibit excellent antibacterial properties against *S. aureus*, *E. coli,* and *P. aeruginosa*.	[300]
AgNPs/starch (Cs)/ nanocellulose (NFC)	AgNPs were synthesized by microwave irradiation using NFC as a reducing agent and stabilizer. AgNPs were added to the mixture of Cs and NFC to obtain porous cryogel.	Porosity and specific surface area were reduced after incorporating AgNPs. The incorporation of AgNPs improved antibacterial properties significantly.	[301]
AgNPs/PLA	AgNPs were prepared with mango peel extract (MPE) as a reducing agent and stabilizer. PLA/MPE/AgNPs film was prepared using the solution casting method.	The addition of AgNPs improves the mechanical properties of the film and its barrier ability against water vapor and oxygen. The film shows excellent antibacterial properties, with an inhibition rate of more than 95% against *E. coli* and *S. aureus*.	[302]
AgNPs/PVA/sodium alginate	AgNPs were prepared by reduced metabolites obtained from green tea leaves. PVA/sodium alginate hydrogel was prepared by incorporating the AgNPs.	The hydrogels exhibited superior water absorption properties with a high swelling ratio (500–900%). The hydrogels exhibited good antimicrobial activity in assays with *E. coli* and *S. aureus*.	[303]
AgNPs/gelatin	AgNPs-gelatin fiber was prepared via UV-vis and wet-spinning methods.	The increase in AgNPs concentration increases the viscosity of the gelatin/AgNPs solution and greatly affects the morphology of wet-spun gelatin fibers. Sugar-mediated Maillard cross-linking improves water stability and provides sustained Ag^+ release. AgNPs-incorporated gelatin fibers show significant antibacterial activity against Gram-negative and Gram-positive bacteria.	[304]

Table 2. Continued.

Materials	Synthesis methods	Comments	References
AgNPs/polyethyleneimine/ Polyethersulfone (HPEI/PES)	Ag-HPEI/PES fibrous membrane was prepared via electrospinning on a commercial PES membrane.	The Ag-HPEI/PES nanofibrous membranes showed excellent antibacterial properties against *E. coli*, *S. aureus* and *P. aeruginosa* The Ag-HPEI/PES nanofibrous membranes showed antifouling characteristics toward BSA.	[305]
AgNPs/PLA/CS	AgNPs were introduced into the oligomeric lactic acid plasticized PLA using CS as a reducing agent and stabilizer.	AgNPs improved the mechanical and thermal properties of PLA. PLA/OLA/AgNPs composites showed antibacterial activity against *S. aureus* compared with the pristine matrix.	[306]
AgNPs/carrageenan (CAR)/ cellulose nanocrystals	AgNPs prepared by cellulose nanocrystals were added to CAR solution during the formation of cryogel.	Sustainable Ag^+ release profiles were detected for cross-linked carrageenan cryogels. AgNPs-loaded CAR showed 100% reduction against *S. aureus* and *E. coli*.	[307]
AgNPs/PVA	AgNPs were synthesized using black grape peel extract. AgNPs were incorporated into PVA matrix by electrospinning to develop a hybrid AgPVA nanofiber.	AgNPs and AgPVA nanofibers showed good antibacterial activity against tested food pathogenic strains. AgPVA nanofibers coated on citrus lemons and strawberries could prevent spoilage caused by food pathogens, thereby extending shelf life.	[308]
AgNPs/PVA	AgNPs were synthesized from cabbage extract. PVA hydrogel patches loaded with AgNPs and AgNPs/clay/activated carbon biocomposites were developed via a freeze-thaw method.	The MIC of AgNPs-HP and AgNPs-Bc-HP for *S. aureus* was 25 and 12.5 $\mu g\,mL^{-1}$, respectively, whereas for *E. coli*, it was 3.13 and 6.3 $\mu g\,mL^{-1}$, respectively. The controlled release of AgNPs from the hydrogel polymer maintains a sterile environment at the wound site, thus accelerating the healing process. Hydrogel patches have moisturizing properties and avoid scaling and dryness.	[309]
AgNPs/PVA/starch	Starch-AgNPs (S-AgNPs) were incorporated into PVA nanofibers prepared through electrospinning.	Nanofiber cross-linked with glutaraldehyde exhibits excellent Ag^+ release and stability in simulated body fluids (SBF). Glutaraldehyde cross-linked S-AgNPs-loaded PVA nanofibers exhibited antibacterial properties against *E. coli* and *S. aureus*.	[310]

(CS-AgNPs), utilizing CS and PVA as stabilizers. The CS-AgNPs exhibited heightened antioxidant activity compared to CS powder. Additionally, the prepared CS-AgNPs significantly promoted wound healing, attributing the observed effects to the synergistic antibacterial and antioxidant properties of AgNPs and CS.[168] In addition, CS-coated or modified green AgNPs can enhance the antibacterial ability, biocompatibility, and drug loading of the nanoparticles.[169,170] Farhadi et al. employed Spirulina extract for the green synthesis of AgNPs and CS polymers for surface modification. The study aimed to investigate the antibacterial effects and toxic impacts on cancer cells (AGS) and normal cells (H9c2). The findings revealed that AgNPs exhibited higher cytotoxicity against AGS cells compared to chemical AgNPs, while remaining safe for H9c2 cells. Surface modification with CS increased the safety profile against H9c2 cells but decreased cytotoxicity against AGS cells.[171] Elzoheiry et al. utilized the metabolites of *Streptomyces porphyris* to synthesize green AgNPs under sunlight. These nanoparticles were then coated with a curcumin-CS mixture for drug delivery in targeting CCl4-induced liver fibrosis in a mouse model. The simultaneous treatment with curcumin/CS-coated AgNPs exhibited a reversal of liver fibrosis induction.[172]

CS-green AgNPs nanocomposite, coatings, films, membranes, and hydrogels have also been widely studied as antibacterial modifications and wound dressings.[173–175] Zhao et al. engineered a multifunctional hydrogel (COC hydrogel) with double-crosslinking, incorporating quaternized CS, methacrylic anhydride-modified collagen, and oxidized dextran. In the COC hydrogel formation process, silver ions underwent rapid in situ bioreduction, transforming into AgNPs, effectively mitigating issues related to dispersion and agglomeration. The COC@AgNPs hydrogel demonstrated super biocompatibility and exhibited excellent antibacterial properties compared with hydrogel loaded with the same amount of commercial AgNPs.[176] Mohammed et al. investigated CS hydrogel and microspheres incorporating green-synthesized AgNPs. The stability of AgNPs was achieved using *R. officinalis* leaf extract. These AgNPs were embedded into CS to produce aerogel beads with a diameter ranging from 2 to 3 mm. The resulting hydrogel and microspheres demonstrated outstanding antibacterial efficacy against Gram-positive and Gram-negative bacteria.[177] Rafiq et al. employed CS-based hydrogels as carriers for biosynthesized, highly antibacterial AgNPs obtained from the plant extract of *Bischofia javanoca*. *In vitro* assessments of the AgNPs revealed potent antibacterial activity against various microorganisms, encompassing bacteria (*E. coli*, *S. aureus*, *P. aeruginosa*, *K. pneumoniae*) and fungi (*C. albicans*). Furthermore, the infection control and angiogenic potential of the AgNPs-loaded

hydrogel were assessed in a rat model with full-thickness infectious wounds, demonstrating efficacy against bacterial infection and promoting rapid wound healing without scar formation.[178] Aldakheel et al. employed green tea leaf extract as a natural reducing agent and utilized microwave irradiation technology for the synthesis of AgNPs incorporated into a CS-grafted PVA hydrogel. The wound healing capacity of the hydrogel samples was evaluated through both in vitro (fibroblast) and in vivo assessments using a rat model. The CS-grafted PVA, including AgNPs, demonstrated exceptional antibacterial activity against *E. coli* and *S. aureus*.[179] **Table 2** provides an overview of the AgNPs and polymer composites for antibacterial applications.

5. Antimicrobials-Laced AgNPs

5.1. Introduction to Antibiotic Resistance and the Role of AgNPs

Antibiotics, also known as antibacterial or antimicrobial medications, constitute a group of medicines that have played a critical role in saving countless lives since their discovery. These drugs are produced by various microorganisms as secondary metabolites and are employed for treating infections caused by germs like bacteria and specific parasites.[180] Antibiotics are typically divided into two categories: bactericidal, which could deacivate bacteria, and bacteriostatic, which can inhibit bacterial growth.[181] Antibiotics with similar chemical structures usually exhibit similar characteristics in terms of effectiveness, toxicity, and associated adverse effects. Examples of common antibiotic classes based on chemical or molecular structures include β-lactams (penicillin, cephalosporins, monobactams, carbapenems), macrolides, tetracyclines, quinolones, aminoglycosides, sulphonamides, glycopeptides, and oxazolidinones. Nevertheless, bacteria exhibit a natural propensity for a resistance process driven by genetic mutations.[180] Once microbial cells acquire resistance, the drug loses its efficacy in inhibiting bacterial growth or deactivating the cells. Consequently, microbial cells continue to proliferate even in the presence of therapeutic levels of antibiotics. World Health Organization (WHO) has initiated an action plan aimed at promoting the exploration of antimicrobial agents that are both effective and safe, possessing multiple mechanisms of action.

One strategy to combat bacterial drug resistance involves the use of AgNPs, to treat bacterial infections. Despite the promising findings from existing studies, concerns have been raised about the potential toxicity of AgNPs at higher concentrations.[182] Therefore, a beneficial approach could involve combining AgNPs with other compounds possessing antibacterial effects, thereby enhancing the antibacterial properties while reducing the dosage and concurrently mitigating their potential toxicity.

5.2. Synergistic Potential of AgNPs with Antibiotics

It is noteworthy that the combination of AgNPs with commercial antibiotics has consistently demonstrated favorable antimicrobial properties, even against MDR strains.[183,184] Combining two or more substances in synergistic approaches results in enhanced efficacy compared to individual components. These nanoparticle conjugates offer several advantages, including multiple targets and mechanisms of action, suppression of antibiotic-resistance formation in pathogens, improved self-assembly for delivery systems, facilitation of intracellular targeting, prolonged circulation, and stabilization of drugs in the body, reduced individual dosages to minimize host toxicity, and an expanded spectrum of antimicrobial coverage during therapies.[185,186] Such drug combinations with nanoparticles are a prevalent strategy in clinical practice, demonstrating therapeutic success in conditions like acquired immunodeficiency syndrome (AIDS), cancer, cardiovascular disease, and microbial infections.[187]

Furthermore, the utilization of nanoparticle–antibiotic conjugates allows for a reduction in the dosage of both agents, thereby minimizing toxicity while amplifying antimicrobial properties. Moreover, these conjugates have demonstrated efficacy against resistant bacteria. The conjugation has been observed to facilitate an increased concentration of antibiotics at the site of contact between antibiotics and microbes, thereby expediting the binding process between microbes and antibiotics. Wan et al. documented a synergistic outcome when AgNPs were employed in conjunction with the antibiotics polymyxin B and rifampicin, while an additive effect was observed with AgNPs-tigecycline.[188] In vivo experiments demonstrated that the AgNPs–antibiotic combinations resulted in superior survival rates in mouse peritonitis induced by *A. baumannii* infection compared to the antibiotics alone. Additionally, Smekalova et al. conducted 40 distinct combination tests involving AgNPs and antibiotics, revealing seven instances of synergy, seventeen additive effects, and sixteen cases of indifference.[183] Interestingly, none of the tested combinations was found to exhibit an antagonistic effect. Most synergistic effects were noted in combinations involving AgNPs and gentamicin. Notably, the most substantial enhancement of antibacterial activity occurred with combined therapy using penicillin G against *A. pleuropneumoniae*. Furthermore, *A. pleuropneumoniae* and *P. multocida*, which display resistance to amoxicillin, gentamicin, and colistin, exhibited sensitivity to these antibiotics when combined with AgNPs. In another study, Lopez-Carrizales et al. investigated the efficacy of two categories of conventional antimicrobial agents (ampicillin and amikacin) both individually and in conjunction with AgNPs against a collection of ten MDR clinical isolates and two reference strains.[184] The researchers suggest that infections caused by MDR microorganisms could be effectively addressed through a synergistic combination of antimicrobial drugs and AgNPs. In this context, the amalgamation of AgNPs with antibiotics resulted in a reduction in nanoparticle size, demonstrated by transmission electron microscopy (TEM), decreasing from 8.57 ± 1.17 to 4.01 ± 0.80 nm with ampicillin and 6.03 ± 0.87 nm with amikacin. Dynamic light scattering and zeta potential results indicated increased nanoparticle stability when combined with ampicillin but decreased stability when amikacin was employed.

5.3. Clinical and Experimental Evidence Supporting AgNPs-Antibiotic Synergy

The effectiveness of antibiotics like vancomycin, gentamycin, streptomycin, ampicillin, and kanamycin was found to increase when they were used alongside AgNPs against *P. aeruginosa*, *S. aureus*, and *E. coli*.[189] These results were later supported by another study where the susceptibility of bacteria was

demonstrated to increase by 20–35% through a synergistic effect of antibiotics, including imipenem, gentamycin, vancomycin, and ciprofloxacin in combination with biologically synthesized AgNPs.[190] The combined impact of AgNPs and antibiotics, such as imipenem, gentamycin, and ciprofloxacin, demonstrated significant efficacy against various bacteria, including *E. coli*, *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, *Bacillus* sp., and *M. luteus*.

In addition, the antimicrobial activities of biologically synthesized AgNPs were evaluated in conjunction with antibiotics against Gram-negative and Gram-positive bacteria,[191] where ampicillin, chloramphenicol, erythromycin, and kanamycin were found to exhibit enhanced antibacterial activities in the presence of AgNPs. Among the tested antibiotics, ampicillin was found to be the most effective, with the highest synergistic effect. Higher dosages of both AgNPs (0–40 $\mu g\,mL^{-1}$) and amoxicillin (0–0.5 $mg\,mL^{-1}$) demonstrated increased antibacterial effects against *E. coli*. The application of amoxicillin impregnated with AgNPs resulted in superior antibacterial efficiency against *E. coli* cells compared to their separate application. Additionally, dynamic experiments revealed that this combination led to reduced and delayed exponential and stationary phases in bacterial growth.[192] An obvious increase in bactericidal activity with a higher concentration of nanoparticles was also observed. In another study, enoxacin, kanamycin, neomycin, and tetracycline exhibited synergistic antibacterial effects against *Salmonella typhimurium* when combined with AgNPs.[193] These antibiotic molecules also form complexes with AgNPs in a solution, resulting in the formation of antibiotic−AgNPs complexes. The authors propose a four-step pathway (**Figure 6**) to elucidate the observed synergistic activity: 1) antibiotic molecules, such as tetracycline, form complexes with AgNPs (tetracycline-AgNPs). 2) The tetracycline-AgNPs complexes bind to a bacterium. 3) Bacterium-attached tetracycline-AgNPs complexes release Ag^+ in higher amounts than AgNPs alone would under the same conditions, creating a temporary and localized high Ag^+ concentration near the bacterium's surface. 4) Ag^+ acts as an agent causing bacterium toxicity by binding to proteins and DNA molecules in the cell walls and within the cells, disrupting bacterial functions and leading to bacterial death. Although AgNPs alone can follow a similar pathway as shown in Pathway II, the presence of such antibiotics suggests that the primary pathway is through the antibiotic−AgNPs complex. However, pathway III was considered ineffective due to the resistance developed by the bacterium against the antibiotics. In a separate investigation, AgNPs were combined with Amikacin.[194] The researcher discovered that the MIC values of Amikacin-conjugated AgNPs against *A. baumannii*, *E. coli*, *K. pneumoniae*, and *P. aeruginosa* were over 10 times lower than those of Amikacin alone across.[194] Additionally, strains that exhibited resistance to Amikacin became susceptible to it when treated with Amikacin-conjugated AgNPs. In a different investigation, the combination of AgNPs with kanamycin exhibited a synergistic impact on bacterial growth in *E. coli*, *S. typhimurium*, and *S. aureus*.[96] Conversely, the combination of AgNPs with chloramphenicol showed an additive effect on the same bacterial strains. The *E. coli* strain tested in this study displayed resistance to ampicillin, and this resistance was successfully overcome by combining AgNPs with ampicillin. A similar effect was observed in a clinically isolated *S. aureus* strain, which demonstrated resistance to kanamycin. However, a synergistic effect was also observed when treated with AgNPs combined with kanamycin.

The combination of ciprofloxacin with AgNPs demonstrated the highest synergistic effect against 91.43% of ESBL *E. coli* isolates, with an additive effect observed in 8.57% of cases.[195] Concerning ESBL *K. pneumoniae* isolates, AgNPs combined with cefotaxime exhibited a synergistic effect in 75% of cases, followed

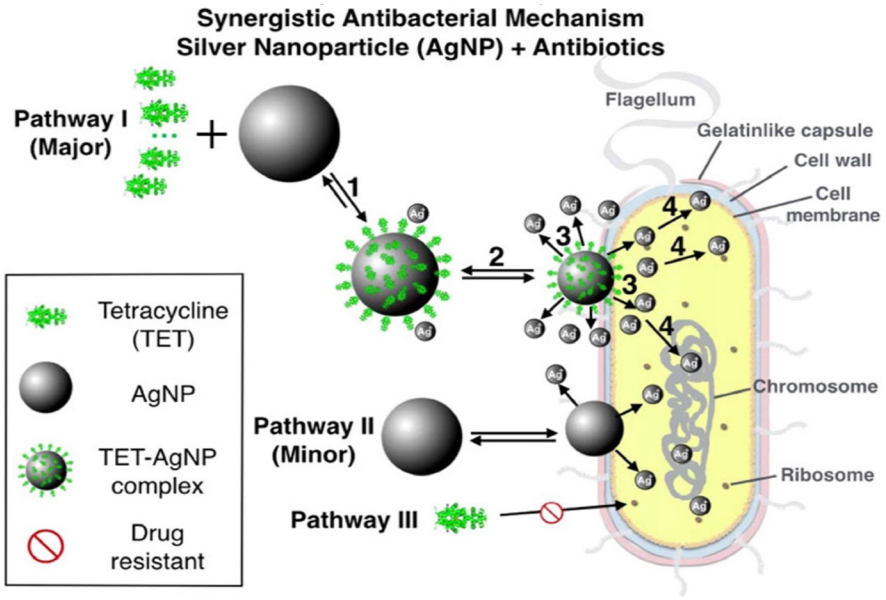

Figure 6. Schematic drawing of the synergistic antibacterial pathway of AgNPs with tetracycline against multidrug-resistant Salmonella. A four-step procedure is proposed as the major pathway leading to cell death. Pathway II is a minor pathway, and Pathway III is not effective due to antibacterial resistance by *Salmonella*. Adapted with permission.[193] Copyright 2016, ACS Publications.

by combinations with ceftazidime and ciprofloxacin (62.50%). The least effective combination identified in this study was ampicillin with AgNPs. In general, an enhancement in the activity of antibiotics was noted at the MIC of AgNPs. However, at lower concentrations of AgNPs, the enhanced effects were less pronounced. AgNPs were found to inhibit the production of beta-lactamase enzymes in 91.43% of *E. coli* isolates and 75% of *K. pneumoniae* isolates.[195] The combinations of Ag-PVP NPs with gentamicin demonstrated a noteworthy synergistic effect against both *E. coli* and *S. aureus*.[196] Gentamicin was observed to enhance the antibacterial activity of Ag-PVP NPs against the tested strains, including the gentamicin-resistant *E. coli* strain. However, the combined effect of Ag-PVP NPs and ampicillin was found to be antagonistic, while the combination of Ag-PVP NPs and penicillin G exhibited an additive effect, indicating a weak interaction between Ag-PVP NPs and these two antibiotics in the environment. When used alone at a concentration of 12.5 μg/mL, Ag-PVP NPs were unable to deactivate bacteria. However, when gentamicin was added, even at a concentration as low as 1 $\mu g\,mL^{-1}$, Ag-PVP NPs significantly inhibited the growth of *E. coli* and *S. aureus* by 97% and 80%, respectively. However, gentamicin appears to play a dual role within the complex system. The AgNPs-gentamicin complex exhibits lower toxicity than both free silver ions and free gentamicin. Consequently, the formation of a silver-gentamicin complex diminishes their individual antibacterial activities. Conversely, the silver-gentamicin complex can act as a reservoir of soluble silver ions, providing a source of silver ions for biomolecules (such as proteins) in biological media. If the quantity of AgNPs surpasses the binding capacity of gentamicin, an equilibrium shift leads to the dissolution of more AgNPs, gradually increasing the total amount of soluble silver ions. This includes free silver ions, silver–gentamicin complexes, and silver complexes with other biomolecules in biosystems, thereby enhancing their antibacterial activities. Additionally, gentamicin was found to facilitate the attachment of Ag-PVP NPs to the surface of bacteria by mitigating the negative charge of the NPs. This, in turn, increases antibacterial activity by elevating the local concentration.

Similarly, AgNPs form complexes with ampicillin, disrupting the peptidoglycan in the cell wall.[191] Due to their positive charge, they target the negative charges of transmembrane proteins, leading to the destruction of the cell membrane and blocking transport channels.[197] AgNPs also have the potential to penetrate bacterial cells, disrupting various cellular activities such as transportation, protein synthesis, and nucleic acid functioning.[198] Similarly, imipenem, in combination with positively charged AgNPs, inhibits and disrupts cell wall synthesis.[199] It has been suggested that silver ions can penetrate the cell, intercalate between pyrimidine and purine, and denature the DNA molecule.[200] The antibiotics ciprofloxacin and imipenem, when combined with these AgNPs, demonstrated the highest effectiveness in inhibiting bacteria.[190] In cases of resistance development to one of them, the other bactericidal agent would still eliminate the bacteria.

In synergism, the bactericidal effect is amplified by the interaction between active groups, such as hydroxyl and amino groups present in these antibiotics, with AgNPs through chelation.[192] This results in the formation of an antibiotic-AgNPs conjugate where an AgNPs core is surrounded by antibiotic molecules. Consequently, the antimicrobial concentration is increased at the focal site, leading to increased eradication of bacteria. However, more studies are required to uncover the exact mechanism of action for developing novel antimicrobial drug combinations against MDR bacteria.

Based on the current research and growing body of evidence, it is evident that there is a clear shift toward leveraging the combined properties of AgNPs and different antibiotics to achieve a synergistic outcome in neutralizing MDR bacteria. In a recent study, green AgNPs were functionalized with Amikacin modified by carbodiimide-based chemistry.[201] The bacteriostatic and bactericidal potential of prepared nanodrug was examined against amikacin-resistant *A. baumannii* strains. The MIC and MBC were found to be lower than 0.5 $\mu g\,mL^{-1}$ and biofilm metabolic activity of *A. baumannii* was reduced at rates of $\geq$50%. Another study constructed nanostructured antimicrobials by conjugating colistin and meropenem antibiotics with biosynthesized AgNPs using *Rosa damascena* extract.[202] The bacteriostatic and bactericidal activity of the developed nanostructure was evaluated against both standard and MDR clinical strains of *E. coli* and *K. pneumoniae*. Antibiotic-conjugated nanoparticles exhibited stronger antimicrobial efficiency by lowering the MIC up to 1024-fold compared to free antibiotics, suggesting the strong potential of antibiotic-conjugated nanoparticles against the MDR *E. coli* and *K. pneumoniae strains*. Similarly, the antimicrobial effect of capped AgNPs combined with imipenem was also tested against the *K. pneumoniae* strain.[203] In the biofilm analysis, the viability of bacterial cells was found to decrease by more than 80%. In another study, AgNPs were synthesized in the presence of ceftazidime, cefotaxime, ceftriaxone, and cefepime, along with the extract of *Mentha longifolia,* and their antimicrobial activity was tested against cephalosporin-resistant *P. aeruginosa*, *K. pneumoniae*, *S. aureus,* and *E. faecalis*.[204] The obtained results showed a significant increase in the antimicrobial activity of antibiotic-conjugated AgNPs against all tested strains compared to plant-based AgNPs alone. Pernas-Pleite et al. synthesized AgNPs using microalgae broth and tested the antibacterial efficiency of NPs in combination with various antibiotics against *E. coli* and *S. aureus*.[205] Most of the AgNPs were shown to render synergistic antibacterial effects against both bacteria with kanamycin and streptomycin. Furthermore, most AgNPs were observed to render a synergistic effect against *S. aureus* with ampicillin and against *E. coli* with tetracycline. This difference in synergistic effect could be due to the antibacterial potential of the antibiotics used against specific bacterial strains. However, this study also elucidates the enhanced generation of intracellular ROS by the combined treatment of AgNPs and antibiotics, suggesting that the degree of intracellular ROS generation could have been different with the combination of different antibiotics with AgNPs. In a recent study, iron-coated AgNPs were produced using *Cupressus sempervirens*, and their antibacterial activity was examined against methicillin-resistant *S. aureus* with and without cefoxitin.[206] The results obtained in this study showed a synergistic effect of iron-coated AgNPs and cefoxitin against 90% of MRSA infections, while an additive effect against 10% of infections.

Not all studies in the field seem to follow the standard method for synergistic activity calculation, such as fractional inhibitory

concentration index and statistical analysis. Future studies must follow the standard method to properly define synergistic, additive, and antagonistic effects to be more conclusive. Most studies' synergistic effects are demonstrated based on in vitro analysis. In vitro, results may not always complement those in vivo due to the complex environment within the host. Thus, in vivo studies are required to demonstrate a similar synergistic effect of AgNPs with antibiotics. Furthermore, studies are needed to fully understand the mechanisms involved and ensure these combinations' safety and efficacy in clinical applications.

6. Challenges for the Development/ Implementation of Green-Synthesized AgNPs-Based Antimicrobial Agents

Several obstacles restrict the applicability of AgNPs in the pharmaceutical, and medical industries. The mechanism by which AgNPs display antimicrobial properties is not fully known, nor are the deep insights into how extracts utilized as biological reducing agents facilitate the production of AgNPs. It is necessary to research the biomolecules found in extracts from a wide variety of organisms, including plants, animals, and microbes, to determine whether or not these biomolecules are involved in producing AgNPs. According to Anthony et al., to clearly define the mechanism of AgNPs synthesis utilizing extracts, it is necessary to conduct future research focusing on particular biomolecules involved in producing AgNPs.[207] Kokila et al. studied the biomolecules in the *Carica papaya* peel extract involved in manufacturing AgNPs.[208] Further investigation of the biomolecules found in the extracts and their specific chemical reactions will enable the development of stable and homogenous AgNPs with customized properties. Furthermore, it is critical to optimize several reaction parameters such as $AgNO_3$ concentration, extract concentration, reaction time, and reaction temperature in AgNPs synthesis, as well as solvent, temperature, and pH conditions in organism extraction. Saxena et al. improved the synthesis method for the quick synthesis of AgNPs utilizing the fungus *Sclerotinia sclerotiorum* by manipulating many reaction parameters (medium, fungal biomass, $AgNO_3$ concentration, pH, and temperature).[209] Liaqat et al. optimized parameters such as $AgNO_3$ concentration, time, pH, and temperature to ensure that AgNPs using *Eucalyptus camaldulensis* and *Terminalia arjuna* extracts had maximum yield, tuned size, and stability.[210] Optimization of various reaction parameters can control the size and shape of AgNPs, enabling large-scale production of AgNPs for commercial purposes. The practicality, economics, and cost-effectiveness of raw materials used as extraction materials should be verified to enable industrial production and large-scale application of green synthesized AgNPs. Overcoming seasonal and regional raw material availability enables large-scale economic production of AgNPs. In addition, due to the inherent properties of nanomaterials, their physicochemical properties may change as the production scale increases, so careful consideration should be given to expanding the production scale of AgNPs. Avanti et al. performed process optimization for large-scale production of AgNPs using medicinal plant extracts, resulting in a 10-fold increase in synthesis volume compared to previously reported processes.[211] Besides, biocompatibility and safety issues need to be addressed regarding the use of green synthesized AgNPs in animal models and clinical studies for higher applications as antibacterial agents. Lethongkam et al. used a human urine-supplemented medium, a host mimicking media, to mimic the microenvironment during infection instead of in vivo testing to confirm the antibiofilm effect of AgNPs using *E. camaldulensis* leaf extract.[212]

6.1. Interaction of AgNPs in the Biological Environment

The rapid surge in the usage of AgNPs has generated concerns about their effect on persons and the environment. During the manufacture, distribution, use, and disposal of AgNPs-containing items, AgNPs may be released or deposited in the environment. After AgNPs are released into the environment, their interaction with other ecosystem components may result in ecotoxicity. Furthermore, AgNPs' toxicity to organisms may be physiologically extended across the trophic chain. As a result, research on the ecotoxicity of AgNPs in soil, water, and associated organisms has been done. Dobias and Latmani evaluated the impact of AgNPs on natural waters by releasing AgNPs of different sizes into rivers and lakes for up to 4 months.[213] AgNPs smaller than 10 nm showed a loss of more than 80% but did not completely dissolve, and AgNPs with a size of 50 nm did not lose 50% of their initial silver content. These results suggested that AgNPs have the potential to persist in natural water for a long period and can act as a source of Ag^+. Kwak et al. exposed AgNPs to the soil to confirm the effects of AgNPs on soil and plants in the ground ecosystem.[214] 20 mg AgNPs/kg soil treatment significantly impacted soil and organisms by inducing developmental delay, inhibiting growth, reducing photosynthetic activity, producing small amounts of fruit, and decreasing soil enzyme activity. Ribeiro et al. evaluated the toxicological effects of AgNPs obtained using fungi *Aspergillus tubingensis* on shrimp (*Palaemon pandaliformis*), which showed lower toxicity to shrimps compared to $AgNO_3$ even at concentrations 100 times higher than $AgNO_3$.[215] These findings contributed to understanding the toxicity of AgNPs produced using fungi on aquatic organisms. However, most toxicological studies have focused on AgNPs exposure to cultures grown in laboratory media. Laboratory research is necessary to reveal the ecotoxicity mechanism, but applying the results to the ecosystem is difficult. Moreover, laboratory studies are limited in predicting the impacts of AgNPs due to the numerous direct and indirect interactions that occur in the complex terrestrial environment. These interactions can be challenging to replicate accurately in a laboratory setting, which hinders the ability to fully understand the environmental exposure to AgNPs. The transport mechanism of AgNPs once they are released into the environment is yet to be determined. There is a tremendous need to collect sufficient data on the transport mechanisms of AgNPs since AgNPs may cause damage to the environment after being discharged into the ecosystem. Furthermore, data acquired from laboratory trials lack validation for predictive modeling, needing further studies in standardized settings. These efforts are needed to fill the information gap on the toxicity of AgNPs to comprehend their risks for individuals and the environment.

6.2. Challenges with Morphology Control and Surface Corona

The shape and size of the AgNPs are the two most important factors that determine how they might be used in various biological applications. The synthesis of AgNPs has been carried out using several different approaches to realize the desired shape and size of the particles. To this point, several physical, chemical, electrochemical, ultrasonic, microwave, irradiation, hydrothermal, and biological processes have been used to produce the various morphologies of AgNPs.[216] Because of the way this process is carried out, AgNPs of many distinct morphologies are produced, including dendrites, flower-like structures, nanocubes, nanoprisms, nanoplates, nanowires, nanorods, and nanospheres.[217]

Because there is a significant probability of contact between AgNPs and biomolecules, especially proteins, these various morphologies of AgNPs will affect their activity in the biological system. The tight and specific or nonspecific interaction of proteins with NPs creates a surface coating layer known as the protein corona, which underpins the biological identity of AgNPs and, as a result, affects their functionality and reactivity.[218] The adsorptive and composition of the corona that surrounds AgNPs are both affected by the size, surface characteristics, morphology, composition, surface hydrophobicity, surface charge, and incubation conditions (pH and time) of the AgNPs (**Figure 7**).[219] The protein corona formed within the host affects the activity of various biological systems, including cytotoxicity, cellular uptake, physiological stability, and aggregation (**Figure 8**).[220,221] Accordingly, several studies have adjusted some of the properties of AgNPs to control the protein corona surrounding them. Bhargava et al. modulated the surface properties of AgNPs through protein precoating. Protein-precoated AgNPs disrupted protein corona formation, resulting in improved stability in biological media and altered cytotoxicity profile.[220] Barbalinardo et al. modulated the surface properties of AgNPs by replacing the native ligands that favor protein adsorption with oligo (ethylene glycol)-based ligands that could increase protein adsorption resistance to control their effects on cellular uptake and cytotoxicity.[221] In fact, cellular silver uptake and toxicity decreased dramatically as oligo (ethylene glycol) density increased, suggesting that tuning the surface properties of AgNPs could modulate their biological properties. Additionally, the presence of the protein corona on the surface of the AgNPs would provide stability and protect against toxicity effects.[222] The interaction of the AgNPs with the various kinds of corona proteins has been shown in a number of in vitro experiments. Recently, Zhang et al. revealed that the incubation of AgNPs of varied morphology, such as nanospheres, nanorods, and nanotriangles, with the bovine serum albumin (BSA) resulted in distinct morphological modifications.[223] When compared to the control group, the size of the nanospheres and nanorods that have been encapsulated by the BSA corona is much larger. However, the size of the nanotriangles was not altered

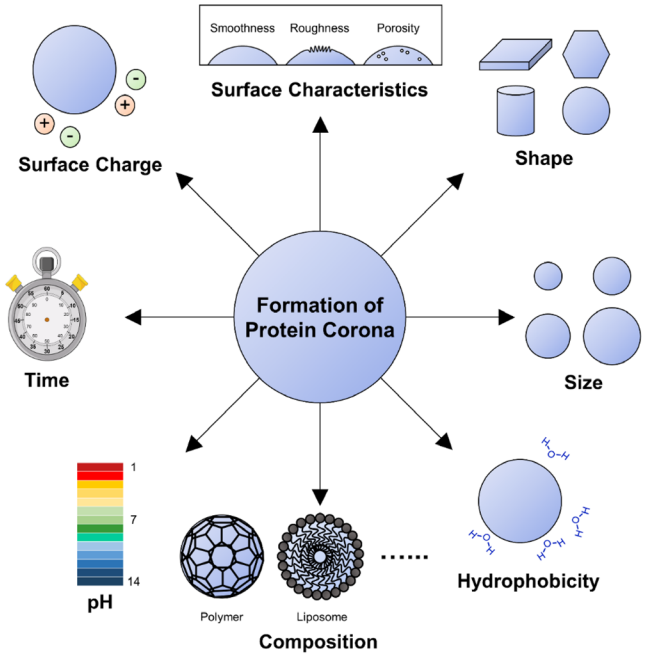

Figure 7. Nanoparticles and protein corona formation. Specific or nonspecific interactions of proteins with nanoparticles form a surface coating layer called the protein corona. Protein corona formation is affected by size, surface characteristics, morphology, composition, surface hydrophobicity, surface charge, and incubation conditions (pH and time) of nanoparticles.[219]

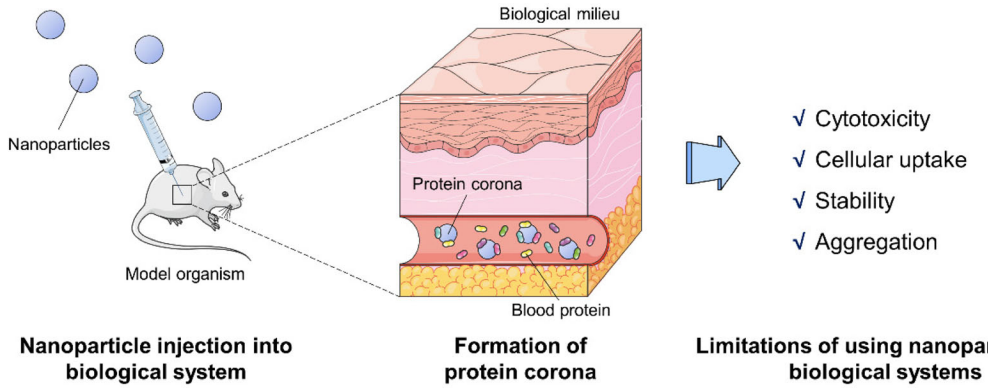

Figure 8. Protein coronas affect a variety of biological milieu, including cytotoxicity, cellular uptake, physiological stability, and aggregation.[220,221]

in any way by the BSA corona; instead, the shape of the nanotriangles was transformed into a nanodisc.

6.3. Challenges with Biocompatibility and Toxicity in the Human Body

In general, AgNPs can trigger apoptosis in human cells. AgNPs first reach the cell interior via endocytosis or diffusion. Cytoplasmic enzymes oxidize some AgNPs that enter the cell, releasing Ag^+. The liberated Ag^+ binds to the thiol groups of mitochondrial membrane proteins, causing mitochondrial malfunction and ROS production. ROS at low levels controls a variety of cellular processes.[224] In contrast, high quantities of ROS may induce protein, lipid, and DNA damage, eventually leading to cell death.[225] Excessive ROS generation has been shown to impact the viability of several human cancer cells, including lung, colon, breast, prostate, and pancreatic tumors.[226] Depending on the shape, size, reducing agent, and cell line being investigated, the cytotoxicity of AgNPs might vary.

Some in vitro studies have demonstrated the toxicity of AgNPs in different human cancerous and noncancerous cell lines. Recent studies discussing the cytotoxicity of green synthesized AgNPs in human cell lines are summarized as follows. AgNPs synthesized from the marine algae *Chaetomorpha linum* were found to be an agent capable of inducing apoptosis (IC_{50} $48.84 \pm 0.78\ \mu g\ mL^{-1}$) in colon cancer cell HCT-116 due to their small size and spherical shape.[227] AgNPs synthesized using *Carica papaya* leaf extract were shown to have better effectiveness against various human cancer cells (DU145, A549, MCF-7, and A431) and lower toxicity to normal cells.[228] Upon exposure to AgNPs containing *Zingiber officinale* leaf extract, HUVEC standard cell lines exhibited high viability and demonstrated substantial anti-human pancreatic cancer properties against human pancreatic cancer cell lines (PANC-1, AsPC-1, MIA PaCa-2), resulting in low cell viability. This was consistent with the high antioxidant activity investigated in the same study.[229] AgNPs prepared from *Juniperus chinensis* leaf extract showed no toxicity to normal cells (HEK293) and cytotoxic effects to cancer cell lines (A549), which was attributed to the synergistic properties of a group of biomolecules derived from *J. polycarpos*.[230] Meanwhile, AgNPs synthesized from *Rhizophora apiculata* aqueous leaf extract showed higher toxicity to normal cells (HEK293) compared to cancer cells (HeLa), suggesting the need for additional research to develop anticancer drugs.[231] AgNPs biosynthesized using aqueous *Eucalyptus camaldulensis* leaf extract not only exhibited potent antifungal and antibiofilm activities but also exhibited noncytotoxicity toward HeLa and HaCaT cells, suggesting that they can be used as therapeutic agents for fungal and biofilm control.[232] AgNPs using aqueous leaf extract of *Ocimum americanum* showed cytotoxic activity (IC_{50} $25\ \mu g\ mL^{-1}$) against A549 lung cancer cells through ROS generation and cell cycle arrest.[233] AgNPs using *Ruellia tuberosa* leaf extract were tested on the A549 lung cancer cell line, and as the concentration of AgNPs increased, the proliferation of cancer cells decreased rapidly (IC_{50} $68\ \mu g\ mL^{-1}$).[234] AgNPs synthesized using *Streptomyces hirsutus* strain SNPGA-8 not only significantly inhibited the growth of A549 (IC_{50} $31.41\ \mu g\ mL^{-1}$) but also induced an increase in ROS production at IC_{50} concentration.[235] In addition, cytotoxicity analysis (MTT assay, Hoechst and AO/EtBr staining, ROS measurement, mitochondrial membrane potential, clonogenic, and wound healing assays) on AgNPs synthesized using root extract of *Premna integrifolia* showed that AgNPs exhibit strong cytotoxicity against HepG2.[67]

For the widespread application of AgNPs, it is imperative to establish conditions for their safe use. When evaluating the toxicity of AgNPs, it is important to emphasize that at low doses, they exhibit minimal to no toxicity toward normal cells. The low toxicity of green synthesized AgNPs in normal cells may be a result of the natural compounds capped on the surface. However, despite data from numerous studies, the unpredictable release of silver ions makes it challenging to determine whether the toxicity of AgNPs is due to the ions or the nanoparticles themselves. Nonetheless, high concentrations of AgNPs can have negative effects on human cells. In most studies, the toxicity of AgNPs synthesized by various methods was evaluated after an arbitrary exposure period. Additionally, because various studies used different human cell lines and assays in assessing AgNPs toxicity, it is difficult to link the collected information. Furthermore, the toxicity of AgNPs may be due to their physical properties, chemical composition, surface coating, or Ag^+ release, so the effect of the physicochemical properties of AgNPs should be clearly characterized. Accordingly, the application of green synthesized AgNPs in food, medicine, and pharmaceutical fields requires in-depth research to accumulate consistent basic data.

7. Conclusion and Future Perspectives

Biosynthetic approaches for AgNPs production offer multiple advantages over conventional chemical methods, including sustainability, biocompatibility, and tunable physicochemical properties. The ability to utilize naturally derived reducing and stabilizing agents provides an opportunity for large-scale, cost-effective production while reducing environmental hazards. Future advancements in biosynthetic strategies, such as optimization of biological precursors and improving synthesis conditions, will further enhance the applicability of green-synthesized AgNPs in medicine, environmental remediation, and industrial applications.

The integration of biosynthesized AgNPs with polymers, antimicrobial drugs, and protein corona presents significant potential for advanced antimicrobial applications. Especially, advancements in the functionalization of AgNPs have highlighted their potential. However, to fully harness the capabilities of these nanomaterials, several challenges and knowledge gaps must be addressed. One critical area that requires further research is the evaluation of the antibacterial effectiveness of AgNPs in host-relevant systems. Most studies to date have focused on in vitro experiments, which may not accurately reflect the behavior of AgNPs in complex biological environments, especially against polymicrobial species. To better assess their clinical potential, conducting extensive studies under conditions that mimic the host environment is essential.

Understanding the interactions between AgNPs and biological components such as blood, bodily fluids, and proteins is another

critical area for future research. These interactions, particularly the formation of a protein corona on AgNPs, play a significant role in determining their behavior and efficacy in biological systems. Future studies should focus on elucidating the molecular mechanisms underlying these interactions, particularly how protein-AgNPs interactions influence protein unfolding and subsequent cellular responses. Additionally, exploring strategies to guide or minimize protein corona formation to achieve desired effects in vivo should be a key research focus. Furthermore, it is essential to conduct thorough assessments of the toxicity, biotransformation, and long-term effects of AgNPs within biological systems. Advanced analytical techniques must be employed to enhance the accuracy of predicting the harmful effects of AgNPs. Methodologies for quantifying the release of Ag+ ions from AgNPs in vivo and determining the surface ionization fraction to select AgNPs with optimal size and surface chemistry for clinical use are important. Addressing these challenges will be vital for translating the promising potential of AgNPs into safe and effective clinical therapies.

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement no. 955626 to I.M. Lundbeckfonden to P.S. (R303-2018-3499), Novo Nordisk Fonden grant number: NNF20CC0035580, Danmarks Frie Forskningsfond, Thematic research-Independent green research (2023): 3164-00026A, and the NordForsk (project number 105121) to I.M. This research was supported by the Basic Science Research Program through the National Research Foundation (NRF) of Korea, grant funded by the Ministry of Education (RS-2023-00241461 to F. Khan).

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Mukil Madhusudanan: conceptualization (lead); data curation (lead); investigation (lead); methodology (lead); validation (lead); visualization (lead); writing—original draft (lead); writing—review & editing (equal). **Jian Zhang**: investigation (equal); methodology (equal); writing—original draft (equal). **Santosh Pandit**: investigation (equal); methodology (equal); validation (equal); writing—original draft (equal). **Priyanka Singh**: conceptualization (lead); funding acquisition (lead); methodology (equal); validation (equal); visualization (equal); writing—original draft (equal); writing—review & editing (lead). **Geum-Jae Jeong**: methodology (equal); writing—original draft (equal). **Fazlurrahman Khan**: methodology (equal); supervision (equal); writing—original draft (equal). **Ivan Mijakovic**: funding acquisition (lead); supervision (lead); writing—review & editing (lead).

Keywords

antimicrobials, drugs, green synthesis, polymers, silver nanoparticles

Received: December 3, 2024
Revised: April 4, 2025
Published online: September 4, 2025

[1] K. A. Altammar, *Front. Microbiol.* **2023**, *14*, 1155622.
[2] Y. Liu, C.-H. Liu, T. Debnath, Y. Wang, D. Pohl, L. V. Besteiro, D. M. Meira, S. Huang, F. Yang, B. Rellinghaus, M. Chaker, D. F. Perepichka, D. Ma, *Nat. Commun.* **2023**, *14*, 541.
[3] X. Huang, M. A. El-Sayed, *J. Adv. Res.* **2010**, *1*, 13.
[4] A. Carone, S. Emilsson, P. Mariani, A. Désert, S. Parola, *Nanoscale Adv.* **2023**, *5*, 2017.
[5] A. Bouafia, S. E. Laouini, A. S. A. Ahmed, A. V. Soldatov, H. Algarni, K. Feng Chong, G. A. M. Ali, *Nanomaterials* **2021**, *11*, 2318.
[6] Y. Li, Q. Liao, W. Hou, L. Qin, *Int. J. Mol. Sci.* **2023**, *24*, 4142.
[7] M. Amr, S. H. Abu-Hussien, R. Ismail, A. Aboubakr, R. Wael, M. Yasser, B. Hemdan, S. M. El-Sayed, A. Bakry, N. M. Ebeed, H. Elhariry, A. Galal, B. T. Abd-Elhalim, *Sci. Rep.* **2023**, *13*, 15048.
[8] S. H. Lee, B.-H. Jun, *Int. J. Mol. Sci.* **2019**, *20*, 865.
[9] Z. A. Ratan, M. F. Haidere, M. Nurunnabi, S. M. Shahriar, A. J. S. Ahammad, Y. Y. Shim, M. J. T. Reaney, J. Y. Cho, *Cancers* **2020**, *12*, 855.
[10] N. A. Eltahawy, S. A. Swidan, M. S. Nafie, A. S. Saeedan, A. M. Nasr, J. M. Badr, R. F. A. Abdelhameed, *J. Biomol. Struct. Dyn.* **2024**, *42*, 12077.
[11] T. Tunç, *Cancer Nanotechnol.* **2024**, *15*, 2.
[12] M. Morais, V. Machado, P. Figueiredo, F. Dias, R. Craveiro, J. Lencart, C. Palmeira, K. S. Mikkonen, A. L. Teixeira, R. Medeiros, *Antioxidants* **2023**, *12*, 2051.
[13] H. I. O. Gomes, C. S. M. Martins, J. A. V. Prior, *Nanomaterials* **2021**, *11*, 964.
[14] D. H. Hanna, M. H. El-Mazaly, R. R. Mohamed, *Int. J. Biol. Macromol.* **2023**, *231*, 123364.
[15] M. Rybka, Ł. Mazurek, M. Konop, *Life* **2023**, *13*, 69.
[16] M. Mohseni, A. Shamloo, Z. Aghababaie, H. Afjoul, S. Abdi, H. Moravvej, M. Vossoughi, *Int. J. Pharm.* **2019**, *564*, 350.
[17] J. Du, X. Liu, C. W. Y. Wong, C.-N. Lok, Z. Yang, Z. Yuan, K. K. Y. Wong, *Am. J. Stem Cells* **2023**, *12*, 51.
[18] M. Mira, A. Wibowo, G. U. N. Tajalla, G. Cooper, P. J. D. S. Bartolo, A. Barlian, *Mater. Adv.* **2023**, *4*, 6407.
[19] B.-E. Bold, E. Urnukhsaikhan, T. Mishig-Ochir, *Front. Chem.* **2022**, *10*, 972534.
[20] C. Tyavambiza, A. M. Elbagory, A. M. Madiehe, M. Meyer, S. Meyer, *Nanomaterials* **2021**, *11*, 1343.
[21] Z. Xu, X. Zha, R. Ji, H. Zhao, S. Zhou, *ACS Appl. Mater. Interfaces* **2023**, *15*, 13983.
[22] A. A. Khashan, Y. Dawood, Y. H. Khalaf, *Results Chem.* **2023**, *5*, 100913.
[23] L. David, B. Moldovan, A. Vulcu, L. Olenic, M. Perde-Schrepler, E. Fischer-Fodor, A. Florea, M. Crisan, I. Chiorean, S. Clichici, G. A. Filip, *Colloids Surf., B* **2014**, *122*, 767.
[24] B. Moldovan, L. David, A. Vulcu, L. Olenic, M. Perde-Schrepler, E. Fischer-Fodor, I. Baldea, S. Clichici, G. A. Filip, *Mater. Sci. Eng., C* **2017**, *79*, 720.
[25] Z. Cheng, H. Li, C. Chen, X. Lv, E. G. Zuo, X. Xie, Z. Li, P. Liu, H. Li, C. Chen, *Photodiagn. Photodyn. Ther.* **2023**, *41*, 103284.
[26] P. Maiti, S. Sarkar, T. Singha, S. Dutta Roy, M. Mahato, P. Karmakar, S. Paul, P. K. Paul, *Langmuir* **2023**, *39*, 6713.
[27] H. T. T. Do, N. P. U. Nguyen, S. I. Saeed, N. T. Dang, L. Doan, T. T. H. Nguyen, *Appl. Nanosci.* **2025**, *15*, 1.
[28] M. Dias, R. Zhang, T. Lammers, R. M. Pallares, *Drug Delivery Transl. Res.* **2025**, *15*, 789.
[29] V. V. Makarov, A. J. Love, O. V. Sinitsyna, S. S. Makarova, I. V. Yaminsky, M. E. Taliansky, N. O. Kalinina, *Acta Nat.* **2014**, *6*, 35.
[30] N. P. U. Nguyen, N. T. Dang, L. Doan, T. T. H. Nguyen, *Processes* **2023**, *11*, 2617.
[31] A. Naganthran, G. Verasoundarapandian, F. E. Khalid, M. J. Masarudin, A. Zulkharnain, N. M. Nawawi, M. Karim, C. A. Che Abdullah, S. A. Ahmad, *Materials* **2022**, *15*, 427.

[32] A. Rana, A. S. Parmar, *Nanotechnol. Environ. Eng.* **2023**, *8*, 789.
[33] S. Viswanathan, T. Palaniyandi, R. Shanmugam, S. Karunakaran, M. Pandi, M. R. A. Wahab, G. Baskar, B. K. Rajendran, A. Sivaji, M. Moovendhan, *Biomass Convers. Biorefin.* **2024**, *14*, 7387.
[34] P. Singh, I. Mijakovic, *Front. Microbiol.* **2022**, *13*, 820048.
[35] P. Hayat, I. Khan, A. Rehman, T. Jamil, A. Hayat, M. U. Rehman, N. Ullah, A. Sarwar, A. A. Alharbi, A. S. Dablool, Z. Daudzai, A. S. Alamri, M. Alhomrani, T. Aziz, *Molecules* **2023**, *28*, 637.
[36] A. Tomak, S. Cesmeli, B. D. Hanoglu, D. Winkler, C. Oksel Karakus, *Nanotoxicology* **2021**, *15*, 1331.
[37] E. L. L. Yeo, P. S. P. Thong, K. C. Soo, J. C. Y. Kah, *Nanoscale* **2018**, *10*, 2461.
[38] Y. Ju, H. G. Kelly, L. F. Dagley, A. Reynaldi, T. E. Schlub, S. K. Spall, C. A. Bell, J. Cui, A. J. Mitchell, Z. Lin, A. K. Wheatley, K. J. Thurecht, M. P. Davenport, A. I. Webb, F. Caruso, S. J. Kent, *ACS Nano* **2020**, *14*, 15723.
[39] J. Y. Oh, H. S. Kim, L. Palanikumar, E. M. Go, B. Jana, S. A. Park, H. Y. Kim, K. Kim, J. K. Seo, S. K. Kwak, C. Kim, S. Kang, J.-H. Ryu, *Nat. Commun.* **2018**, *9*, 4548.
[40] K. Vadakkan, N. P. Rumjit, A. K. Ngangbam, S. Vijayanand, N. K. Nedumpillil, *Coord. Chem. Rev.* **2024**, *499*, 215528.
[41] M. Bokolia, D. Baliyan, A. Kumar, R. Das, R. Kumar, B. Singh, *Int. J. Environ. Anal. Chem.* **2024**, 1, https://doi.org/10.1080/03067319.2024.2305238.
[42] P. R. More, S. Pandit, A. D. Filippis, G. Franci, I. Mijakovic, M. Galdiero, *Microorganisms* **2023**, *11*, 369.
[43] S. Faisal, R. Ullah, A. Alotaibi, S. Zafar, M. Rizwan, M. H. Tariq, *Microsc. Res. Tech.* **2023**, *86*, 846.
[44] N. Bano, D. Iqbal, A. Al Othaim, M. Kamal, H. M. Albadrani, N. A. Algehainy, H. Alyenbaawi, F. Alghofaili, M. Amir, M. Roohi, *Sci. Rep.* **2023**, *13*, 4150.
[45] G. Vijayakumar, H. J. Kim, S. K. Rangarajulu, *Antibiotics* **2023**, *12*, 141.
[46] A. B. A. Mohammed, A. E. Hegazy, A. Salah, *Appl. Nanosci.* **2023**, *13*, 633.
[47] M. K. Y. Soliman, S. S. Salem, M. Abu-Elghait, M. S. Azab, *Appl. Biochem. Biotechnol.* **2023**, *195*, 1158.
[48] D. Veeragoni, S. Deshpande, H. K. Rachamalla, A. Ande, S. Misra, S. R. Mutheneni, *ACS Appl. Bio Mater.* **2022**, *5*, 2324.
[49] M. Rudrappa, R. S. Kumar, S. K. Nagaraja, H. Hiremath, P. V. Gunagambhire, A. I. Almansour, K. Perumal, S. Nayaka, *Antibiotics* **2023**, *12*, 567.
[50] R. Algotiml, A. Gab-Alla, R. Seoudi, H. H. Abulreesh, M. Z. El-Readi, K. Elbanna, *Sci. Rep.* **2022**, *12*, 2421.
[51] R. S. Hamida, M. A. Ali, N. Mugren, M. I. Al-Zaban, M. M. Bin-Meferij, A. Redhwan, *ACS Omega* **2023**, *8*, 29169.
[52] F. Khan, G.-J. Jeong, P. Singh, N. Tabassum, I. Mijakovic, Y.-M. Kim, *Nanoscale* **2022**, *14*, 14824.
[53] K. Verduzco-Chavira, A. A. Vallejo-Cardona, A. S. González-Garibay, O. R. Torres-González, I. M. Sánchez-Hernández, J. M. Flores-Fernández, E. Padilla-Camberos, *Antibiotics* **2023**, *12*, 1084.
[54] H. A. Ghetas, N. Abdel-Razek, M. S. Shakweer, M. M. Abotaleb, B. Ahamad Paray, S. Ali, E. A. Eldessouki, M. A. O. Dawood, R. H. Khalil, *Saudi J. Biol. Sci.* **2022**, *29*, 1298.
[55] V. Balaji, S. Perumal, S. Palanisamy, M. Karuppaiah, S. Asaithambi, D. Velauthapillai, P. Kumar, R. Yuvakkumar, G. Ravi, *J. Alloys Compd.* **2023**, *966*, 171503.
[56] G. Kah, R. Chandran, H. Abrahamse, *Cells* **2023**, *12*, 2012.
[57] R. Dhir, S. Chauhan, P. Subham, S. Kumar, P. Sharma, A. Shidiki, G. Kumar, *Front. Bioeng. Biotechnol.* **2024**, *11*, 1324805.
[58] Y. Wang, S. Wei, *ACS Omega* **2022**, *7*, 1494.
[59] M. Wahab, S. Janaswamy, *Funct. Food Sci.* **2023**, *3*, 93.
[60] S. Nagaraja, S. S. Ahmed, B. D. R., P. Goudanavar, R. K. M., S. Fattepur, G. Meravanige, A. Shariff, P. N. Shiroorkar, M. Habeebuddin, M. Telsang, *Molecules* **2022**, *27*, 4336.
[61] G. Rehman, M. Umar, N. Shah, M. Hamayun, A. Ali, W. Khan, A. Khan, S. Ahmad, A. F. Alrefaei, M. H. Almutairi, Y.-S. Moon, S. Ali, *Pharmaceuticals* **2023**, *16*, 1677.
[62] M. Wahab, A. Bhatti, P. John, *Polymers* **2022**, *14*, 3138.
[63] A. P. Ajaykumar, A. Mathew, A. P. Chandni, S. R. Varma, K. N. Jayaraj, O. Sabira, V. A. Rasheed, V. S. Binitha, T. R. Swaminathan, V. S. Basheer, S. Giri, S. Chatterjee, *Antibiotics* **2023**, *12*, 564.
[64] M. Zubair, M. Azeem, R. Mumtaz, M. Younas, M. Adrees, E. Zubair, A. Khalid, F. Hafeez, M. Rizwan, S. Ali, *Environ. Pollut.* **2022**, *304*, 119249.
[65] M. Tesfaye, Y. Gonfa, G. Tadesse, T. Temesgen, S. Periyasamy, *Heliyon* **2023**, *9*, e17356.
[66] A. Ganesh Kumar, E. Pugazhenthi, P. Sankarganesh, C. Muthusamy, M. Rajasekaran, E. Lokesh, A. Khusro, G. Kavya, *Biomass Convers. Biorefin.* **2024**, *14*, 28971.
[67] C. Singh, S. K. Anand, R. Upadhyay, N. Pandey, P. Kumar, D. Singh, P. Tiwari, R. Saini, K. N. Tiwari, S. K. Mishra, R. Tilak, *Mater. Chem. Phys.* **2023**, *297*, 127413.
[68] Y. Khane, K. Benouis, S. Albukhaty, G. M. Sulaiman, M. M. Abomughaid, A. Al Ali, D. Aouf, F. Fenniche, S. Khane, W. Chaibi, A. Henni, H. D. Bouras, N. Dizge, *Nanomaterials* **2022**, *12*, 2013.
[69] Y. G. El-Baz, A. Moustafa, M. A. Ali, G. E. El-Desoky, S. M. Wabaidur, M. M. Faisal, *Nanomaterials* **2023**, *13*, 945.
[70] N. Sabapathi, S. Ramalingam, K. N. Aruljothi, J. Lee, S. Barathi, *Plants* **2023**, *12*, 707.
[71] M. E. Mouzahim, E. M. Eddarai, S. Eladaoui, A. Guenbour, A. Bellaouchou, A. Zarrouk, R. Boussen, *Food Chem.* **2023**, *410*, 135470.
[72] M. A. Irshad, S. Sattar, A. A. Al-Huqail, S. M. S. Alghanem, R. Nawaz, N. Ain, K. M. Hussaini, A. H. A. Abeed, *Environ. Sci. Pollut. Res.* **2023**, *30*, 112575.
[73] M. Moond, S. Singh, S. Sangwan, P. Devi, A. Beniwal, J. Rani, A. Kumari, S. Rani, *Molecules* **2023**, *28*, 951.
[74] T. K. Dua, S. Giri, G. Nandi, R. Sahu, T. K. Shaw, P. Paul, *Chem. Pap.* **2023**, *77*, 2947.
[75] M. A. Dheyab, A. A. Aziz, S. H. Nowfal, F. S. Braim, W. Abdullah, W. H. Kasasbeh, M. S. Jameel, S. T. Alanezi, M. Alrosan, N. Oladzadabbasabadi, *J. Environ. Chem. Eng.* **2025**, *13*, 115998.
[76] H. R. El-Seedi, R. M. El-Shabasy, S. A. M. Khalifa, A. Saeed, A. Shah, R. Shah, F. J. Iftikhar, M. M. Abdel-Daim, A. Omri, N. H. Hajrahand, J. S. M. Sabir, X. Zou, M. F. Halabi, W. Sarhan, W. Guo, *RSC Adv.* **2019**, *9*, 24539.
[77] H. Singh, M. F. Desimone, S. Pandya, S. Jasani, N. George, M. Adnan, A. Aldarhami, A. S. Bazaid, S. A. Alderhami, *Int. J. Nanomed.* **2023**, *18*, 4727.
[78] L. Colleselli, M. Mutschlechner, M. Spruck, F. Albrecht, O. I. Strube, P. Vrabl, S. Zeilinger, H. Schöbel, *Bioprocess. Biosyst. Eng.* **2024**, *47*, 1669.
[79] H. R. El-Seedi, M. S. Omara, A. H. Omar, M. M. Elakshar, Y. M. Shoukhba, H. Duman, S. Karav, A. K. Rashwan, A. H. El-Seedi, H. A. Altaleb, H. Gao, A. Saeed, O. A. Jefri, Z. Guo, S. A. M. Khalifa, *Bioengineering* **2024**, *11*, 1095.
[80] N. Al Moudani, I. Ouahidi, S. Laaraj, L. Aarab, *ChemistrySelect* **2025**, *10*, e202404860.
[81] R. Yadav, S. Preet, *Sci. Rep.* **2023**, *13*, 8152.
[82] C. Tyavambiza, M. Meyer, A. D. Wusu, A. M. Madiehe, S. Meyer, *Int. J. Mol. Sci.* **2022**, *23*, 16094.
[83] T. Santana Da Costa, M. Rodrigues Da Silva, J. C. Jerônimo Barbosa, U. Da Silva Das Neves, M. B. De Jesus, L. Tasic, *RSC Adv.* **2024**, *14*, 2192.

[84] S. Jain, M. S. Mehata, *Sci. Rep.* **2017**, *7*, 15867.
[85] Z. Zhao, P. Li, R. Xie, X. Cao, D. Su, Y. Shan, *Int. J. Biol. Macromol.* **2022**, *214*, 220.
[86] C. Katta, A. S. Shaikh, N. Bhale, V. G. S. S. Jyothi, V. R. Kaki, A. G. Dikundwar, P. K. Singh, R. Shukla, K. Mishra, J. Madan, *AAPS PharmSciTech* **2023**, *24*, 126.
[87] D. Feng, R. Zhang, M. Zhang, A. Fang, F. Shi, *Nanomaterials* **2022**, *12*, 2636.
[88] M. A. Al Masud, H. Shaikh, M. S. Alam, M. M. Karim, M. A. Momin, M. A. Islam, G. M. A. Khan, *J. Genet. Eng. Biotechnol.* **2021**, *19*, 74.
[89] C. Gangwar, B. Yaseen, I. Kumar, N. K. Singh, R. M. Naik, *ACS Omega* **2021**, *6*, 22344.
[90] A. H. Holmes, L. S. P. Moore, A. Sundsfjord, M. Steinbakk, S. Regmi, A. Karkey, P. J. Guerin, L. J. V. Piddock, *Lancet* **2016**, *387*, 176.
[91] K. S. Ikuta, L. R. Swetschinski, G. Robles Aguilar, F. Sharara, T. Mestrovic, A. P. Gray, N. Davis Weaver, E. E. Wool, C. Han, A. Gershberg Hayoon, A. Aali, S. M. Abate, M. Abbasi-Kangevari, Z. Abbasi-Kangevari, S. Abd-Elsalam, G. Abebe, A. Abedi, A. P. Abhari, H. Abidi, R. G. Aboagye, A. Absalan, H. Abubaker Ali, J. M. Acuna, T. D. Adane, I. Y. Addo, O. A. Adegboye, M. Adnan, Q. E. S. Adnani, M. S. Afzal, S. Afzal, et al., *Lancet* **2022**, *400*, 2221.
[92] H. A. Mohammed, M. A. Amin, G. Zayed, Y. Hassan, M. El-Mokhtar, M. S. Saddik, *J. Antibiot.* **2023**, *76*, 291.
[93] S. Kumar, H. M. Khan, F. M. Husain, R. Ahmad, F. A. Qais, M. A. Khan, M. Jalal, U. Tayyaba, S. G. Ali, A. Singh, M. Shahid, B.-I. Lee, *Front. Mol. Biosci.* **2023**, *10*, 1292509.
[94] M. Awad, M. Yosri, M. M. Abdel-Aziz, A. M. Younis, N. M. Sidkey, *Biol. Trace Elem. Res.* **2021**, *199*, 4225.
[95] O. M. Bondarenko, M. Sihtmäe, J. Kuzmičiova, L. Ragelienė, A. Kahru, R. Daugelavičius, *Int. J. Nanomed.* **2018**, *13*, 6779.
[96] R. Vazquez-Muñoz, A. Meza-Villezcas, P. G. J. Fournier, E. Soria-Castro, K. Juarez-Moreno, A. L. Gallego-Hernández, N. Bogdanchikova, R. Vazquez-Duhalt, A. Huerta-Saquero, Y. K. Mishra, *PLoS One* **2019**, *14*, 0224904.
[97] Y.-G. Yuan, Q.-L. Peng, S. Gurunathan, *Int. J. Mol. Sci.* **2017**, *18*, 569.
[98] J. A. Lemire, J. J. Harrison, R. J. Turner, *Nat. Rev. Microbiol.* **2013**, *11*, 371.
[99] S. Ashique, A. Upadhyay, A. Hussain, S. Bag, D. Chaterjee, M. Rihan, N. Mishra, S. Bhatt, V. Puri, A. Sharma, P. Prasher, S. K. Singh, D. K. Chellappan, G. Gupta, K. Dua, *J. Drug Delivery Sci. Technol.* **2022**, *77*, 103876.
[100] A. S. Joshi, P. Singh, I. Mijakovic, *Int. J. Mol. Sci.* **2020**, *21*, 7658.
[101] Y. Zhang, X. Pan, S. Liao, C. Jiang, L. Wang, Y. Tang, G. Wu, G. Dai, L. Chen, *J. Proteome Res.* **2020**, *19*, 3109.
[102] H. N. Abdelhamid, H.-F. Wu, *TrAC, Trends Anal. Chem.* **2015**, *65*, 30.
[103] E. M. Mateo, M. Jiménez, *Antibiotics* **2022**, *11*, 1205.
[104] S. Shrestha, B. Wang, P. Dutta, *Adv. Colloid Interface Sci.* **2020**, *279*, 102162.
[105] N. S. Alduraihem, R. S. Bhat, S. A. Al-Zahrani, D. M. Elnagar, H. M. Alobaid, M. H. Daghestani, *Processes* **2023**, *11*, 301.
[106] F. A.-Z. Sayed, N. G. Eissa, Y. Shen, D. A. Hunstad, K. L. Wooley, M. Elsabahy, *J. Nanobiotechnol.* **2022**, *20*, 536.
[107] Q. Zhang, Y. Hu, C. M. Masterson, W. Jang, Z. Xiao, A. Bohloul, D. Garcia-Rojas, H. L. Puppala, G. Bennett, V. L. Colvin, *iScience* **2022**, *25*, 104475.
[108] C. Vanlalveni, S. Lallianrawna, A. Biswas, M. Selvaraj, B. Changmai, S. L. Rokhum, *RSC Adv.* **2021**, *11*, 2804.
[109] A. Menichetti, A. Mavridi-Printezi, D. Mordini, M. Montalti, *J. Funct. Biomater.* **2023**, *14*, 244.
[110] T. Ameh, K. Zarzosa, W. E. Braswell, C. M. Sayes, *Front. Toxicol.* **2023**, *5*, 1119547.
[111] A. M. Ferreira, A. Vikulina, M. Loughlin, D. Volodkin, *RSC Adv.* **2023**, *13*, 10542.
[112] S. Mumtaz, S. Ali, S. Mumtaz, T. A. Mughal, H. M. Tahir, H. A. Shakir, *Polym. Bull.* **2023**, *80*, 4719.
[113] H. Haidari, R. Bright, Z. Kopecki, P. S. Zilm, S. Garg, A. J. Cowin, K. Vasilev, N. Goswami, *ACS Appl. Mater. Interfaces* **2022**, *14*, 390.
[114] J. G. Turner, C. J. Murphy, *Langmuir* **2021**, *37*, 9910.
[115] F. E. Galdino, A. S. Picco, L. B. Capeletti, J. Bettini, M. B. Cardoso, *Nano Lett.* **2021**, *21*, 8250.
[116] V. H. Nguyen, B.-J. Lee, *Int. J. Nanomed.* **2017**, *12*, 3137.
[117] K. Ranoszek-Soliwoda, E. Czechowska, E. Tomaszewska, A. Pudlarz, J. Szemraj, G. Celichowski, J. Grobelny, *Colloids Surf., A* **2020**, *600*, 125003.
[118] G. Bashiri, M. S. Padilla, K. L. Swingle, S. J. Shepherd, M. J. Mitchell, K. Wang, *Lab Chip* **2023**, *23*, 1432.
[119] T. Hanemann, D. V. Szabó, *Materials* **2010**, *3*, 3468.
[120] S. S. D. Kumar, N. K. Rajendran, N. N. Houreld, H. Abrahamse, *Int. J. Biol. Macromol.* **2018**, *115*, 165.
[121] P. Dallas, V. K. Sharma, R. Zboril, *Adv. Colloid Interface Sci.* **2011**, *166*, 119.
[122] M. Alavi, M. Rai, *Appl. Microbiol. Biotechnol.* **2019**, *103*, 8669.
[123] A. M. Garcia, M. A. Bizeto, V. B. Ferrari, D. N. Okamoto, S. P. De Vasconcellos, F. F. Camilo, *J. Nanopart. Res.* **2020**, *22*, https://doi.org/10.1007/s11051-020-04863-1.
[124] M. R. Mulenos, H. Lujan, L. R. Pitts, C. M. Sayes, *Nanomaterials* **2020**, *10*, 1953.
[125] B. Ajitha, Y. A. Kumar Reddy, P. S. Reddy, H.-J. Jeon, C. W. Ahn, *RSC Adv.* **2016**, *6*, 36171.
[126] M. Madkour, A. Bumajdad, F. Al-Sagheer, *Adv. Colloid Interface Sci.* **2019**, *270*, 38.
[127] N. M. Elbaz, L. Ziko, R. Siam, W. Mamdouh, *Sci. Rep.* **2016**, *6*, 30729.
[128] A. Karuppaiah, K. Siram, D. Selvaraj, M. Ramasamy, D. Babu, V. Sankar, *Mater. Today Commun.* **2020**, *23*, 100884.
[129] Y. Chen, X. Dong, M. Shafiq, G. Myles, N. Radacsi, X. Mo, *Adv. Fiber Mater.* **2022**, *4*, 959.
[130] A. W. Jatoi, H. Ogasawara, I. S. Kim, Q.-Q. Ni, *Mater. Lett.* **2019**, *241*, 168.
[131] S. Mantha, S. Pillai, P. Khayambashi, A. Upadhyay, Y. Zhang, O. Tao, H. M. Pham, S. D. Tran, *Materials* **2019**, *12*, 3323.
[132] K. Yang, Q. Han, B. Chen, Y. Zheng, K. Zhang, Q. Li, J. Wang, *Int. J. Nanomed.* **2018**, *13*, 2217.
[133] S. Batool, Z. Hussain, M. B. K. Niazi, U. Liaqat, M. Afzal, *J. Drug Delivery Sci. Technol.* **2019**, *52*, 403.
[134] S. Bhowmick, V. Koul, *Mater. Sci. Eng., C* **2016**, *59*, 109.
[135] F. Zhang, J. Wu, D. Kang, H. Zhang, *J. Biomater. Sci., Polym. Ed.* **2013**, *24*, 1410.
[136] W. H. Binder, *Macromol. Rapid Commun.* **2019**, *40*, https://doi.org/10.1002/marc.201800610.
[137] A. S. Montaser, A. M. Abdel-Mohsen, M. A. Ramadan, A. A. Sleem, N. M. Sahffie, J. Jancar, A. Hebeish, *Int. J. Biol. Macromol.* **2016**, *92*, 739.
[138] M. Zakia, J. M. Koo, D. Kim, K. Ji, P. H. Huh, J. Yoon, S. I. Yoo, *Green Chem. Lett. Rev.* **2020**, *13*, 34.
[139] S. Tian, Y. Hu, X. Chen, C. Liu, Y. Xue, B. Han, *Int. J. Biol. Macromol.* **2022**, *195*, 515.
[140] P. Pankongadisak, U. R. Ruktanonchai, P. Supaphol, O. Suwantong, *AAPS PharmSciTech* **2014**, *15*, 1105.
[141] P. Pankongadisak, U. R. Ruktanonchai, P. Supaphol, O. Suwantong, *Polym. Int.* **2015**, *64*, 275.
[142] P. Pankongadisak, U. R. Ruktanonchai, P. Supaphol, O. Suwantong, *Polym. Adv. Technol.* **2017**, *28*, 849.

[143] T. R. Correia, D. R. Figueira, K. D. De Sá, S. P. Miguel, R. G. Fradique, A. G. Mendonça, I. J. Correia, *Int. J. Biol. Macromol.* **2016**, *93*, 1432.
[144] A. Kumar, M. Jaiswal, *J. Appl. Polym. Sci.* **2016**, *133*, https://doi.org/10.1002/app.43260.
[145] Q. Hu, Y. Nie, J. Xiang, J. Xie, H. Si, D. Li, S. Zhang, M. Li, S. Huang, *Int. J. Biol. Macromol.* **2023**, *234*, 123691.
[146] H. Seddiqi, E. Oliaei, H. Honarkar, J. Jin, L. C. Geonzon, R. G. Bacabac, J. Klein-Nulend, *Cellulose* **2021**, *28*, 1893.
[147] S. S. Salem, A. H. Hashem, A.-A. M. Sallam, A. S. Doghish, A. A. Al-Askar, A. A. Arishi, A. M. Shehabeldine, *Polymers* **2022**, *14*, 3352.
[148] P. L. Bhutiya, N. Misra, M. A. Rasheed, S. Z. Hasan, *Bionanoscience* **2020**, *10*, 23.
[149] C. Shanmugam, G. Sivasubramanian, P. Govindhan, P. Bera, K. Baskaran, V. R. I. Parameswaran, *J. Cluster Sci.* **2022**, *33*, 1727.
[150] P. Du, Y. Xu, Y. Shi, Q. Xu, S. Li, M. Gao, *Cellulose* **2022**, *29*, 6831.
[151] J. Li, L. Kang, B. Wang, K. Chen, X. Tian, Z. Ge, J. Zeng, J. Xu, W. Gao, *ACS Sustainable Chem. Eng.* **2019**, *7*, 1146.
[152] C.-N. Wu, S.-C. Fuh, S.-P. Lin, Y.-Y. Lin, H.-Y. Chen, J.-M. Liu, K.-C. Cheng, *Biomacromolecules* **2018**, *19*, 544.
[153] E. S. Madivoli, P. G. Kareru, A. N. Gachanja, D. S. Makhanu, S. M. Mugo, *J. Inorg. Organomet. Polym. Mater.* **2022**, *32*, 854.
[154] S. Audtarat, P. Hongsachart, T. Dasri, S. Chio-Srichan, S. Soontaranon, W. Wongsinlatam, S. Sompech, *Nanocomposites* **2022**, *8*, 34.
[155] M. T. Shaaban, M. Zayed, H. S. Salama, *Curr. Microbiol.* **2023**, *80*, 75.
[156] A. V. A. Mariadoss, K. Saravanakumar, A. Sathiyaseelan, A. S. Sivakumar, X. Zhang, H. Bin Choi, M. S. Jeong, M. Choi, M.-H. Wang, *Mater. Today Commun.* **2023**, *35*, 105652.
[157] Y. Bao, J. He, K. Song, J. Guo, X. Zhou, S. Liu, *Polymers* **2022**, *14*, 769.
[158] R. Liu, L. Dai, C. Si, Z. Zeng, *Carbohydr. Polym.* **2018**, *195*, 63.
[159] A. Fadakar Sarkandi, M. Montazer, T. Harifi, M. Mahmoudi Rad, *J. Appl. Polym. Sci.* **2021**, *138*, 49824.
[160] N. S. V. Capanema, I. C. Carvalho, A. A. P. Mansur, S. M. Carvalho, A. P. Lage, H. S. Mansur, *ACS Appl. Nano Mater.* **2019**, *2*, 7393.
[161] J. Yang, X. Zhang, L. Chen, X. Zhou, X. Fan, Y. Hu, X. Niu, X. Xu, G. Zhou, N. Ullah, X. Feng, *Int. J. Biol. Macromol.* **2022**, *213*, 621.
[162] L. Ding, X. Shan, X. Zhao, H. Zha, X. Chen, J. Wang, C. Cai, X. Wang, G. Li, J. Hao, G. Yu, *Carbohydr. Polym.* **2017**, *157*, 1538.
[163] H. Ye, J. Cheng, K. Yu, *Int. J. Biol. Macromol.* **2019**, *121*, 633.
[164] M. A. M. Fathil, F. Y. Faris Taufeq, S. Suleman Ismail Abdalla, H. Katas, *RSC Adv.* **2022**, *12*, 19297.
[165] H. Katas, M. A. Mohd Akhmar, S. Suleman Ismail Abdalla, *J. Bioact. Compat. Polym.* **2021**, *36*, 111.
[166] T. Suteewong, J. Wongpreecha, D. Polpanich, K. Jangpatarapongsa, C. Kaewsaneha, P. Tangboriboonrat, *Colloids Surf., B* **2019**, *174*, 544.
[167] J. Wongpreecha, D. Polpanich, T. Suteewong, C. Kaewsaneha, P. Tangboriboonrat, *Carbohydr. Polym.* **2018**, *199*, 641.
[168] S. Hajji, S. B. Khedir, I. Hamza-Mnif, M. Hamdi, I. Jedidi, R. Kallel, S. Boufi, M. Nasri, *Biochim. Biophys. Acta,– Gen. Subj.* **2019**, *1863*, 241.
[169] M. A. Asghar, R. I. Yousuf, M. H. Shoaib, M. A. Asghar, *Int. J. Biol. Macromol.* **2020**, *160*, 934.
[170] T. R. Santiago, C. C. Bonatto, M. Rossato, C. A. P. Lopes, C. A. Lopes, E. S. G Mizubuti, L. P. Silva, *J. Sci. Food Agric.* **2019**, *99*, 4248.
[171] L. Farhadi, M. Mohtashami, J. Saeidi, M. Azimi-Nezhad, G. Taheri, R. Khojasteh-Taheri, A. Rezagholizade-Shirvan, E. Shamloo, A. Ghasemi, *J. Inorg. Organomet. Polym. Mater.* **2022**, *32*, 1637.
[172] A. Elzoheiry, E. Ayad, N. Omar, K. Elbakry, A. Hyder, *Sci. Rep.* **2022**, *12*, 18403.
[173] J. Shao, B. Wang, J. Li, J. A. Jansen, X. F. Walboomers, F. Yang, *Mater. Sci. Eng., C* **2019**, *98*, 1053.
[174] J. Yang, Y. Chen, L. Zhao, Z. Feng, K. Peng, A. Wei, Y. Wang, Z. Tong, B. Cheng, *Composites, Part B* **2020**, *197*, 108139.
[175] W. Zhang, W. Jiang, *Int. J. Biol. Macromol.* **2020**, *155*, 1252.
[176] F. Zhao, Y. Liu, T. Song, B. Zhang, D. Li, Y. Xiao, X. Zhang, *J. Mater. Chem. B* **2022**, *10*, 2135.
[177] A. M. Mohammed, K. T. Hassan, O. M. Hassan, *Int. J. Biol. Macromol.* **2023**, *233*, 123580.
[178] A. Rafiq, S. Tehseen, T. A. Khan, M. Awais, A. R. Sodhozai, C. H. Javed, M. F. Ullah, N. Ali, M. Y. Alshahrani, M. I. Khan, A. M. Galal, *Biomass Convers. Biorefin.* **2023**, *13*, 15531.
[179] F. Aldakheel, D. Mohsen, M. El Sayed, K. Alawam, A. K. Binshaya, S. Alduraywish, *Molecules* **2023**, *28*, 3241.
[180] R. M. Epand, C. Walker, R. F. Epand, N. A. Magarvey, *Biochim. Biophys. Acta, Biomembr.* **2016**, *1858*, 980.
[181] S. Bernatová, O. Samek, Z. Pilát, M. Šerý, J. Ježek, P. Jákl, M. Šiler, V. Krzyžánek, P. Zemánek, V. Holá, M. Dvořáčková, F. Růžička, *Molecules* **2013**, *18*, 13188.
[182] Y.-H. Shih, R. Pranata, Y.-C. Chen, M.-Y. Liao, Y.-H. Cheng, Y.-Y. Chen, Y.-H. Lai, P.-J. Tsai, R.-J. Chen, *Environ. Sci. Nano* **2023**, *10*, 2115.
[183] M. Smekalova, V. Aragon, A. Panacek, R. Prucek, R. Zboril, L. Kvitek, *Vet. J.* **2016**, *209*, 174.
[184] M. Lopez-Carrizales, K. I. Velasco, C. Castillo, A. Flores, M. Magaña, G. A. Martinez-Castanon, F. Martinez-Gutierrez, *Antibiotics* **2018**, *7*, 50.
[185] X. Xu, L. Xu, G. Yuan, Y. Wang, Y. Qu, M. Zhou, *Sci. Rep.* **2018**, *8*, 7237.
[186] M. Tyers, G. D. Wright, *Nat. Rev. Microbiol.* **2019**, *17*, 141.
[187] T. Pemovska, J. W. Bigenzahn, G. Superti-Furga, *Curr. Opin. Pharmacol.* **2018**, *42*, 102.
[188] G. Wan, L. Ruan, Y. Yin, T. Yang, M. Ge, X. Cheng, *Int. J. Nanomed.* **2016**, *11*, 3789.
[189] S. S. Birla, V. V. Tiwari, A. K. Gade, A. P. Ingle, A. P. Yadav, M. K. Rai, *Lett. Appl. Microbiol.* **2009**, *48*, 173.
[190] S. Z. Naqvi, U. Kiran, U. Ali, U. Jamal, U. Hameed, U. Ahmed, U. Ali, *Int. J. Nanomed.* **2013**, *8*, 3187.
[191] A. M. Fayaz, K. Balaji, M. Girilal, R. Yadav, P. T. Kalaichelvan, R. Venketesan, *Nanomedicine* **2010**, *6*, 103.
[192] P. Li, J. Li, C. Wu, Q. Wu, J. Li, *Nanotechnology* **2005**, *16*, 1912.
[193] H. Deng, D. Mcshan, Y. Zhang, S. S. Sinha, Z. Arslan, P. C. Ray, H. Yu, *Environ. Sci. Technol.* **2016**, *50*, 8840.
[194] M. Palau, E. Muñoz, M. F. Gusta, N. Larrosa, X. Gomis, J. Gilabert, B. Almirante, V. Puntes, R. Texidó, J. Gavaldà, K. M. Papp-Wallace, *Microbiol. Spectrum* **2023**, *11*, e0028023.
[195] A. S. A. Mohammed, M. I. Mourad, F. Z. Alsewy, N. F. A. E. M. Azzam, *Beni-Suef Univ. J. Basic Appl. Sci.* **2021**, *10*, 58.
[196] Y.-W. Wang, H. Tang, D. Wu, D. Liu, Y. Liu, A. Cao, H. Wang, *Environ. Sci. Nano* **2016**, *3*, 788.
[197] R. L. Davies, S. F. Etris, *Catal. Today* **1997**, *36*, 107.
[198] M. Yamanaka, K. Hara, J. Kudo, *Appl. Environ. Microbiol.* **2005**, *71*, 7589.
[199] B. S. Sekhon, Metalloantibiotics and Antibiotic Mimics - An Overview. https://api.semanticscholar.org/CorpusID:86148110 (accessed: 2010).
[200] M. K. Rai, S. D. Deshmukh, A. P. Ingle, A. K. Gade, *J. Appl. Microbiol.* **2012**, *112*, 841.
[201] L. O. Camargo, I. Fontoura, T. S. Veriato, L. Raniero, M. L. Castilho, *Am. J. Infect. Control.* **2023**, *51*, 871.
[202] M. C. Şirin, Y. Cezaroğlu, E. Sesli Çetin, B. Arıdoğan, D. Trak, Y. Arslan, *J. Basic Microbiol.* **2023**, *63*, 1397.
[203] I. Fontoura, T. S. Veriato, L. J. Raniero, M. L. Castilho, *Antibiotics* **2023**, *12*, 535.
[204] M. Adil, S. Alam, U. Amin, I. Ullah, M. Muhammad, M. Ullah, A. Rehman, T. Khan, *AMB Express* **2023**, *13*, 115.

[205] C. Pernas-Pleite, A. M. Conejo-Martínez, P. Fernández Freire, M. J. Hazen, I. Marín, J. P. Abad, *Int. J. Mol. Sci.* **2023**, *24*, 16183.
[206] N. Hadi, S. Nakhaeitazreji, F. Kakian, Z. Hashemizadeh, A. Ebrahiminezhad, J. W. R. Chong, A. Berenjian, P. L. Show, *Mol. Biotechnol.* **2024**, *66*, 3573.
[207] K. J. P. Anthony, M. Murugan, M. Jeyaraj, N. K. Rathinam, G. Sangiliyandi, *J. Ind. Eng. Chem.* **2014**, *20*, 2325.
[208] T. Kokila, P. S. Ramesh, D. Geetha, *Ecotoxicol. Environ. Saf.* **2016**, *134*, 467.
[209] J. Saxena, P. K. Sharma, M. M. Sharma, A. Singh, *Springerplus* **2016**, *5*, 861.
[210] N. Liaqat, N. Jahan, N. Khalil-Ur-Rahman, T. Anwar, H. Qureshi, *Front. Chem.* **2022**, *10*, 952006.
[211] C. Avanti, S. Qoyimah, I. H. Suliman, M. A. Flora, K. C. Rani, J. Sukweenadhi, K. Kartini, *J. Res. Pharm.* **2024**, *28*, 1369.
[212] S. Lethongkam, S. Paosen, S. Bilhman, K. Dumjun, S. Wunnoo, S. Choojit, R. Siri, C. Daengngam, S. P. Voravuthikunchai, T. Bejrananda, *Nanomaterials* **2022**, *12*, 4059.
[213] J. Dobias, R. Bernier-Latmani, *Environ. Sci. Technol.* **2013**, *47*, 4140.
[214] J. I. Kwak, S.-H. Nam, Y.-J. An, *Comp. Biochem. Physiol., Part C: Toxicol. Pharmacol.* **2023**, *269*, 109631.
[215] L. G. Ribeiro, K. F. O. Rezende, E. Barbieri, A. O. De Souza, *Environ. Sci. Nano* **2023**, *10*, 1715.
[216] B. Khodashenas, H. R. Ghorbani, *Arabian J. Chem.* **2019**, *12*, 1823.
[217] M. A. Shenashen, S. A. El-Safty, E. A. Elshehy, *Part. Part. Syst. Charact.* **2014**, *31*, 293.
[218] N. Liu, M. Tang, J. Ding, *Chemosphere* **2020**, *245*, 125624.
[219] G. Cui, W. Su, M. Tan, *Compr. Rev. Food Sci. Food Saf.* **2022**, *21*, 2002.
[220] A. Bhargava, A. Dev, S. J. Mohanbhai, V. Pareek, N. Jain, S. R. Choudhury, J. Panwar, S. Karmakar, *Sci. Total Environ.* **2021**, *772*, 144797.
[221] M. Barbalinardo, J. Bertacchini, L. Bergamini, M. S. Magarò, L. Ortolani, A. Sanson, C. Palumbo, M. Cavallini, D. Gentili, *Nanoscale* **2021**, *13*, 14119.
[222] F. N. Spagnoletti, F. Kronberg, C. Spedalieri, E. Munarriz, R. Giacometti, *J. Environ. Manage.* **2021**, *297*, 113434.
[223] J. Zhang, X. Fu, C. Yan, G. Wang, *Materials* **2023**, *16*, 5821.
[224] C. Lennicke, H. M. Cochemé, *Mol. Cell.* **2021**, *81*, 3691.
[225] T. Jaswal, J. Gupta, *Mater. Today Proc.* **2023**, *81*, 859.
[226] M. Bin-Jumah, M. Al-Abdan, G. Albasher, S. Alarifi, *Int. J. Nanomed.* **2020**, *15*, 1537.
[227] D. Acharya, S. Satapathy, P. Somu, U. K. Parida, G. Mishra, *Biol. Trace Elem. Res.* **2021**, *199*, 1812.
[228] S. P. Singh, A. Mishra, R. K. Shyanti, R. P. Singh, A. Acharya, *Biol. Trace Elem. Res.* **2021**, *199*, 1316.
[229] Y. Wang, A. Chinnathambi, O. Nasif, S. A. Alharbi, *Arabian J. Chem.* **2021**, *14*, 103081.
[230] H. Noorbazargan, S. Amintehrani, A. Dolatabadi, A. Mashayekhi, N. Khayam, P. Moulavi, M. Naghizadeh, A. Mirzaie, F. Mirzaei Rad, M. Kavousi, *AMB Express* **2021**, *11*, 61.
[231] X. Liu, K. Shan, X. Shao, X. Shi, Y. He, Z. Liu, J. A. Jacob, L. Deng, *Int. J. Nanomed.* **2021**, *16*, 753.
[232] S. Wunnoo, S. Paosen, S. Lethongkam, R. Sukkurd, T. Waen-Ngoen, T. Nuidate, M. Phengmak, S. P. Voravuthikunchai, *Biotechnol. Bioeng.* **2021**, *118*, 1578.
[233] D. B. Manikandan, A. Sridhar, R. Krishnasamy Sekar, B. Perumalsamy, S. Veeran, M. Arumugam, P. Karuppaiah, T. Ramasamy, *J. Environ. Chem. Eng.* **2021**, *9*, 104845.
[234] V. Seerangaraj, S. Sathiyavimal, S. N. Shankar, J. G. T. Nandagopal, P. Balashanmugam, F. A. Al-Misned, M. Shanmugavel, P. Senthilkumar, A. Pugazhendhi, *J. Environ. Chem. Eng.* **2021**, *9*, 105088.
[235] P. S.S., H. A. Rudayni, A. Bepari, S. K. Niazi, S. Nayaka, *Saudi J. Biol. Sci.* **2022**, *29*, 228.
[236] X. Li, X. Tian, S. Liu, C. Wu, Y. Han, L. Meng, L. Song, Y. Zhang, *J. Mater. Sci.* **2020**, *55*, 14019.
[237] M. Yu, Q. Tian, G. He, K. Cui, J. Zhang, *Adv. Fiber Mater.* **2021**, *3*, 349.
[238] B. J. Wiley, S. H. Im, Z.-Y. Li, J. Mclellan, A. Siekkinen, Y. Xia, *J. Phys. Chem. B* **2006**, *110*, 15666.
[239] A. Pourjavadi, R. Soleyman, *Mater. Res. Bull.* **2011**, *46*, 1860.
[240] A. Przewłoka, S. Smirnov, I. Nefedova, A. Krajewska, I. S. Nefedov, P. S. Demchenko, D. V. Zykov, V. S. Chebotarev, D. B. But, K. Stelmaszczyk, M. Dub, D. Zasada, A. Lisauskas, J. Oberhammer, M. K. Khodzitsky, W. Knap, D. Lioubtchenko, *Materials* **2021**, *14*, 7399.
[241] T. Karan, Z. Gonulalan, R. Erenler, U. Kolemen, O. Eminagaoglu, *J. Mol. Struct.* **2024**, *1296*, 136836.
[242] S. G. Hernandez-Castro, L. Z. Flores-López, H. Espinoza-Gomez, G. Alonso-Nuñez, *Int. J. Biol. Macromol.* **2024**, *254*, 127805.
[243] J. O. Igbalaye, A. G. Adeyemo, A. O. Adenubi, O. Ahmodu, B. O. Shodimu, F. O. Hazeez, S. A. Hassan, *Asian J. Green Chem.* **2024**, *8*, 25.
[244] A. A. Joicy, R. Selvamani, C. Janani, C. Balasubramanian, K. Prabhu, K. Marimuthu, G. Bupesh, T. S. Vijayakumar, K. M. Saravanan, *Lett. Appl. NanoBioSci.* **2022**, *12*, 102.
[245] S. Chintala, R. Laishram, P. Mondal, K. Pal, P. Kantamraju, S. Ghosh, K. Karmakar, H. Chakdar, R. Mukhopadhyay, R. Sen, A. Choudhury, S. Mandal, N. Sahana, *Ind. Crops Prod.* **2023**, *206*, 117616.
[246] S. M. Farouk, S. H. Abu-Hussien, B. T. Abd-Elhalim, R. M. Mohamed, N. M. Arabe, A. A. T. Hussain, M. E. Mostafa, B. Hemdan, S. M. El-Sayed, A. Bakry, N. M. Ebeed, M. Salah, H. Elhariry, A. Galal, *Sci. Rep.* **2023**, *13*, 19469.
[247] M. A. Rather, M. Mandal, *Microb. Pathogen.* **2023**, *185*, 106433.
[248] S. Sikdar, M. Sikdar, *Bioresour. Technol. Rep.* **2023**, *24*, 101669.
[249] K. Krishnamoorthy, S. Jayaraman, R. Krishnamoorthy, S. Manoharadas, M. A. Alshuniaber, B. Vikas, V. P. Veeraraghavan, *J. King Saud Univ. Sci.* **2023**, *35*, 102955.
[250] N. S. Alharbi, A. I. Felimban, *J. King Saud Univ. Sci.* **2023**, *35*, 102972.
[251] R. Roy, R. Jan, U. Joshi, R. B, P. G. Satsangi, *Mater. Today Sustainability* **2023**, *24*, 100546.
[252] N. Xu, T. Zhang, X. Wang, L. Wang, *Inorg. Chem. Commun.* **2023**, *158*, 111525.
[253] V. Rocha, P. Ferreira-Santos, Z. Genisheva, E. Coelho, I. C. Neves, T. Tavares, *J. Water Process Eng.* **2023**, *56*, 104431.
[254] N. Sher, M. Ahmed, N. Mushtaq, *Bionanoscience* **2023**, *13*, 1753.
[255] L.-L. Liu, M.-Z. Fan, Y.-J. Hao, K.-X. Zhang, X.-C. Piao, M.-Y. Jin, M.-L. Lian, J. Jiang, *J. Environ. Chem. Eng.* **2023**, *11*, 111309.
[256] D. Y. Mercado-Meza, R. G. Guevara-González, K. Esquivel, I. Carbajal-Valenzuela, G. D. Avila-Quezada, *Plant Stress* **2023**, *10*, 100256.
[257] M. Ansari, S. Ahmed, A. Abbasi, M. T. Khan, M. Subhan, N. A. Bukhari, A. A. Hatamleh, N. R. Abdelsalam, *Sci. Rep.* **2023**, *13*, 18048.
[258] S. Fahmid, R. Jabeen, S. Mehar, N. Sajjad, F. Behlil, M. Riaz, N. Jameel, H. Ishtiyaq, F. Mukhtar, N. Khan, J. Ali, *J. Mol. Liq.* **2023**, *391*, 123217.
[259] N. Rahmatian, S. Abbasi, M. Tavakkoli Yaraki, N. Abbasi, *J. Mol. Liq.* **2023**, *391*, 123327.
[260] M. Abdelrazik, H. H. Elkotaby, A. Yousef, A. F. El-Sayed, M. Khedr, *J. Genet. Eng. Biotechnol.* **2023**, *21*, 97.
[261] R. K. Malla, G. Chandra, *Sci. Rep.* **2023**, *13*, 17202.
[262] V. Vorobyova, M. Skiba, O. Horodniuk, L. Khrokalo, G. Vasyliev, *Bionanoscience* **2023**, *13*, 1726.
[263] A. M. Abdel-Aty, A. Z. Barakat, R. I. Bassuiny, S. A. Mohamed, *Sci. Rep.* **2023**, *13*, 15605.

[264] H. S. El-Bastawisy, G. S. El-Sayyad, F. A. Abu Safe, *BMC Microbiol.* **2023**, *23*, 262.
[265] R. Koley, A. Mondal, N. K. Mondal, *Energy Ecol. Environ.* **2023**, *8*, 537.
[266] M. Ghavam, *BMC Complementary Med. Ther.* **2023**, *23*, 299.
[267] A. M. Chelegahi, S. Reiisi, R. Heidari, B. Karimi, *Bionanoscience* **2023**, *13*, 1817.
[268] M. Khatun, Z. Khatun, M. R. Karim, M. R. Habib, M. H. Rahman, M. A. Aziz, *Food Chem. Adv.* **2023**, *3*, 100386.
[269] A. Raj, R. K. Thomas, L. Vidya, V. M. Aparna, S. Neelima, C. Sudarsanakumar, *Sci. Rep.* **2023**, *13*, 9045.
[270] E. S. Harsha Haridas, S. Bhattacharya, M. K. R. Varma, G. K. Chandra, *Sci. Rep.* **2023**, *13*, 8651.
[271] D. G. Kumar, R. R. Achar, J. R. Kumar, G. Amala, V. K. Gopalakrishnan, S. Pradeep, A. A. Shati, M. Y. Alfaifi, S. E. I. Elbehairi, E. Silina, V. Stupin, N. Manturova, C. Shivamallu, S. P. Kollur, *BMC Complementary Med. Ther.* **2023**, *23*, 167.
[272] M.-H. Moosavy, M. De La Guardia, A. Mokhtarzadeh, S. A. Khatibi, N. Hosseinzadeh, N. Hajipour, *Sci. Rep.* **2023**, *13*, 7230.
[273] R. Majumdar, P. K. Kar, *Sci. Rep.* **2023**, *13*, 7415.
[274] M. Tavan, P. Hanachi, M. H. Mirjalili, A. Dashtbani-Roozbehani, *Sci. Rep.* **2023**, *13*, 6391.
[275] I. A. M. Ali, A. B. Ahmed, H. I. Al-Ahmed, *Sci. Rep.* **2023**, *13*, 2256.
[276] M. G. González-Pedroza, A. R. T. Benítez, S. A. Navarro-Marchal, E. Martínez-Martínez, J. A. Marchal, H. Boulaiz, R. A. Morales-Luckie, *Sci. Rep.* **2023**, *13*, 790.
[277] W. Ahmed, Q. Mansoor, M. S. Ahmad, T. Zainab, M. A. Shah, *Sci. Rep.* **2023**, *13*, 671.
[278] G. Hashemitabar, F. Aflakian, A. H. Sabzevar, *J. Mol. Struct.* **2023**, *1291*, 136076.
[279] M. Mondéjar-López, A. J. López-Jimenez, O. Ahrazem, L. Gómez-Gómez, E. Niza, *Int. J. Biol. Macromol.* **2023**, *225*, 964.
[280] M. F. Baran, C. Keskin, A. Baran, A. Hatipoğlu, M. Yildiztekin, S. Küçükaydin, K. Kurt, H. Hoşgören, M. M. R. Sarker, A. Sufianov, O. Beylerli, R. Khalilov, A. Eftekhari, *Molecules* **2023**, *28*, 2310.
[281] D. Nayab, S. Akhtar, M. Irfan, *PLoS One* **2023**, *18*, e0281675.
[282] N. Jayarambabu, S. Velupla, A. Akshaykranth, N. Anitha, T. V. Rao, *Appl. Phys. A: Mater. Sci. Process.* **2023**, *129*, 13.
[283] R. S. Hamida, M. A. Ali, H. E. Alfassam, M. A. Momenah, M. A. Alkhateeb, M. M. Bin-Meferij, *Pharmaceutics* **2023**, *15*, 529.
[284] J. Liu, Y. Dong, Z. Ma, Z. Rao, X. Zheng, K. Tang, *ACS Appl. Polym. Mater.* **2022**, *4*, 5608.
[285] A. A. H. Abdellatif, H. N. H. Alturki, H. M. Tawfeek, *Sci. Rep.* **2021**, *11*, 84.
[286] S. Raza, A. Ansari, N. N. Siddiqui, F. Ibrahim, M. I. Abro, A. Aman, *Sci. Rep.* **2021**, *11*, 10500.
[287] M. M. El-Adawy, A. E. Eissa, M. Shaalan, A. A. Ahmed, N. A. Younis, M. M. Ismail, M. Abdelsalam, *Aquacult. Res.* **2021**, *52*, 1247.
[288] Z. Ma, J. Liu, Y. Liu, X. Zheng, K. Tang, *Int. J. Biol. Macromol.* **2021**, *166*, 567.
[289] J. Liu, Z. Ma, Y. Liu, X. Zheng, Y. Pei, K. Tang, *Food Packag. Shelf Life* **2022**, *31*, 100800.
[290] P. Kanniah, P. Chelliah, J. R. Thangapandi, G. Gnanadhas, V. Mahendran, M. Robert, *Int. J. Biol. Macromol.* **2021**, *189*, 18.
[291] K. Yan, F. Xu, W. Wei, C. Yang, D. Wang, X. Shi, *Colloids Surf., B* **2021**, *202*, 111711.
[292] S. Roy, J.-W. Rhim, *Food Biosci.* **2022**, *49*, 101867.
[293] C. Ferrag, S. Li, K. Jeon, N. M. Andoy, R. M. A. Sullan, S. Mikhaylichenko, K. Kerman, *Colloids Surf., B* **2021**, *197*, 111397.
[294] G. H. Matar, M. Andac, *Polym. Bull.* **2021**, *78*, 6095.
[295] S. Ediyilyam, B. George, S. S. Shankar, T. T. Dennis, S. Wacławek, M. Černík, V. V. T. Padil, *Polymers* **2021**, *13*, 1680.
[296] A. Wibowo, G. U. N. Tajalla, M. A. Marsudi, G. Cooper, L. A. T. W. Asri, F. Liu, H. Ardy, P. J. D. S. Bartolo, *Molecules* **2021**, *26*, 2042.
[297] X. Wei, J. Cai, S. Lin, F. Li, F. Tian, *Colloids Surf., B* **2021**, *197*, 111370.
[298] S. Sethi, S. Saruchi, S. Medha, S. Thakur, B. S. Kaith, N. Sharma, S. Ansar, S. Pandey, V. Kuma, *Biomass Convers. Biorefin.* **2022**, *12*, 5363.
[299] L. Motelica, D. Ficai, O.-C. Oprea, A. Ficai, V.-L. Ene, B.-S. Vasile, E. Andronescu, A.-M. Holban, *Nanomaterials* **2021**, *11*, 2377.
[300] N. Khan, D. Kumar, P. Kumar, *Colloid Interface Sci. Commun.* **2020**, *35*, 100242.
[301] E. K. Radwan, M. E. El-Naggar, A. Abdel-Karim, A. R. Wassel, *Int. J. Biol. Macromol.* **2021**, *189*, 420.
[302] J. Cheng, X. Lin, X. Wu, Q. Liu, S. Wan, Y. Zhang, *Int. J. Biol. Macromol.* **2021**, *188*, 678.
[303] T. Wang, F. Zhang, R. Zhao, C. Wang, K. Hu, Y. Sun, C. Politis, A. Shavandi, L. Nie, *Des. Monomers Polym.* **2020**, *23*, 118.
[304] H. W. Kwak, J. E. Kim, K. H. Lee, *React. Funct. Polym.* **2019**, *136*, 86.
[305] K. Maziya, B. C. Dlamini, S. P. Malinga, *React. Funct. Polym.* **2020**, *148*, 104494.
[306] A. Sonseca, S. Madani, A. Muñoz-Bonilla, M. Fernández-García, L. Peponi, A. Leonés, G. Rodríguez, C. Echeverría, D. López, *Nanomaterials* **2020**, *10*, 1065.
[307] A. M. Abdelgawad, M. E. El-Naggar, D. A. Elsherbiny, S. Ali, M. S. Abdel-Aziz, Y. K. Abdel-Monem, *J. Environ. Chem. Eng.* **2020**, *8*, 104276.
[308] E. Kowsalya, K. MosaChristas, P. Balashanmugam, A. Tamil Selvi, I. Jaquline Chinna Rani, *Food Packag. Shelf Life* **2019**, *21*, 100379.
[309] A. Ahsan, M. A. Farooq, *J. Drug Delivery Sci. Technol.* **2019**, *54*, 101308.
[310] A. Aktürk, M. Erol Taygun, F. Karbancıoğlu Güler, G. Goller, S. Küçükbayrak, *Colloids Surf., A* **2019**, *562*, 255.

Mukil Madhusudanan holds a master's degree in nanotechnology from Amity University Uttar Pradesh and earned his Ph.D. from the Technical University of Denmark in 2024. He previously led a three-year research project on enhancing zinc micronutrient uptake in cereal crops using engineered nanoparticles. His current research focuses on the green synthesis of nanomaterials and their integration into polymer-based composites for biomedical applications, including antimicrobial and anticancer therapies.

Jian Zhang is a postdoc researcher in the Department of Life Sciences at Chalmers University of Technology. He received his Ph.D. degree in materials from École Centrale de Lyon, University of Lyon in 2018. Now, his research interests mainly focus on biomaterials for medical engineering.

Priyanka Singh, Ph.D., is a senior researcher at DTU Biosustain, Technical University of Denmark, with expertise in developing green, biocompatible nanomaterials for cancer and infection therapy. Her research integrates bio-nanotechnology, cell biology, and microbiology to design multifunctional nanoparticles for targeted drug delivery, photothermal therapy, and real-time imaging. She employs advanced 2D/3D cell cultures and animal models to evaluate therapeutic efficacy. With over a decade of international research experience, Dr. Singh leads interdisciplinary projects aimed at advancing sustainable nanomedicine for oncology and infectious disease applications.

Ivan Mijakovic has been a chaired professor of Bacterial Systems Biology at Chalmers University of Technology since 2013, and professor at the Technical University of Denmark since 2017. His research group is working with several topics at the interface between molecular biology, microbiology, and nanomaterials science. The core competence of the Mijakovic laboratory is bacterial protein phosphorylation, its physiological role, and means to use it to engineer bacterial cell factories and fight bacterial infections. Other topics in the group include metabolic engineering of bacterial cell factories for biotechnology and environmental protection applications, as well as biomedical applications of various nanomaterials.