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Nanomaterials of Microbial Origin – Their Pharmaceutical & Therapeutical Applications

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Abstract

The advent of biogenic nanotechnology has fundamentally altered the pharmaceutical landscape. Microbial nanomaterials (MNMs), synthesized intracellularly or extracellularly by bacteria, fungi, yeast, and algae, represent a sustainable, "green" alternative to conventional physical and chemical synthesis strategies. These bio-fabricated materials are characterized by high biocompatibility, structural uniformity, and significantly lower environmental toxicity. Crucially, their inherent colloidal stability is provided by natural biological capping agents – such as proteins, lipids, and exopolysaccharides – which spontaneously coat the metallic core during bioreduction. This review examines critical advancements documented between 2015 and 2026, focusing specifically on the translation of MNMs into pharmaceutical utilities. We detail their multifaceted mechanisms in overcoming bacterial multidrug resistance (MDR) through membrane disruption and biofilm inhibition, facilitating targeted site-specific drug delivery, and enhancing oncological therapeutics via synergistic modalities like photodynamic therapy. Furthermore, we explore their capacity to accelerate tissue regeneration and angiogenesis in chronic wound management. While significant translational challenges regarding industrial scale-up, batch-to-batch reproducibility, and long-term systemic immunotoxicity remain to be fully resolved, MNMs unequivocally represent a cornerstone of next-generation precision medicine and targeted therapeutics.

Keywords: Antimicrobial resistance, biogenic nanoparticles, drug delivery, green nanomanufacturing, nanomedicine, oncology

INTRODUCTION

The rapid evolution of nanomedicine in recent times has fundamentally redefined the paradigms of modern pharmacotherapy and targeted diagnostics [1, 2]. Historically, the fabrication of nanoscale delivery systems and therapeutic agents relied heavily on physical methodologies such as mechanical milling, sputtering, laser ablation, and chemical reduction processes [3, 4]. While effective at producing materials in the 1 to 100 nanometer (nm) range, these conventional techniques frequently involve hazardous solvents, high energy consumption, and the generation of toxic biochemical byproducts that severely limit their *in vivo* biological applications. Consequently, pharmaceutical research has increasingly pivoted toward "green" nanomanufacturing, utilizing biological systems as living, ecologically sustainable foundries [5, 6]. Within this domain, microorganisms – such as bacteria, fungi, yeast, and microalgae – have emerged as highly efficient nano-factories [7, 8]. By leveraging their innate enzymatic machinery and metabolic pathways, these microbes can effectively reduce heavy metal ions into stable, elemental nanoclusters, yielding biogenic nanomaterials that

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exhibit unparalleled biocompatibility and inherent therapeutic properties suitable for diverse clinical applications [9–11].

The fundamental advantage of microbially synthesized nanoparticles over their chemically synthesized counterparts lies in their unique structural composition, particularly the spontaneous formation of a biological "corona" during biosynthesis [12, 13]. As microbes reduce metal precursors, they simultaneously secrete extracellular polymeric substances, stabilizing proteins, and various biomolecules that act as natural capping agents. This bio-organic coating not only imparts exceptional thermodynamic stability and prevents nanoparticle agglomeration but also significantly enhances the physiological compatibility of the nanomaterial (Table 1). The presence of this natural corona allows biogenic nanoparticles to evade rapid opsonization and clearance by the host's mononuclear phagocyte system, thereby extending their systemic circulation time [14]. Furthermore, the inherent biochemical functionality of these capping agents provides a versatile platform for the secondary attachment of specific targeting ligands, antibodies, or chemotherapeutic payloads, making microbially derived nanoparticles highly sophisticated vehicles for precision medicine [2, 15].

Table 1. Advantages of biogenic synthesis of nanoparticles.

S.N.	Chemical synthesis of nanoparticles	Biogenesis of nanoparticles
1	Involves complex procedures with expensive starting materials	Involves simple procedures with cheaper alternatives as starting materials.
2	Gives toxic or non-degradable byproducts	Does not release any toxic byproducts.
3	Requires elevated temperatures	Does not need high temperatures.
4	Involves the use of organic solvents and reagents	Involves natural or biological materials.
5	Accumulates large quantities of waste	Does not lead to waste accumulation.
6	Makes use of chemical derivatives	Makes the use of biocatalysts.
7	Does not have a good atom economy	Has a high atom economy.
8	May involve serious accident risk	Does not involve any accident risk.

One of the most critical therapeutic applications for biogenic nanomaterials is their deployment against the escalating global crisis of antimicrobial resistance (AMR). The proliferation of multidrug-resistant (MDR) bacterial and fungal strains has rendered many conventional antibiotics ineffective [16]. Microbially synthesized metal-based antimicrobial nanoparticles (AMNPs), particularly those formulated from silver (Ag), zinc (Zn), and copper (Cu), offer a robust, multi-modal mechanism of action that is exceptionally difficult for pathogens to circumvent [10, 17]. Upon contact with pathogenic cells, these biogenic nanoparticles induce severe oxidative stress through the localized generation of massive concentrations of reactive oxygen species (ROS). This oxidative burst compromises bacterial cell wall integrity interferes with cellular respiration and of inhibits DNA and RNA synthesis [18]. Furthermore, these biogenic nanomaterials have demonstrated remarkable efficacy against established microbial biofilms, complex, heterogeneous communities of microorganisms embedded in a self-produced matrix that are notoriously impervious to traditional pharmacological treatments [11, 19, 20]. Through advanced bioengineering, these nanomaterials can be functionalized with specific targeting ligands to achieve selective toxicity, effectively eradicating pathogenic strains while preserving the commensal host microbiome [21].

Beyond infection control, microbial nanomaterials are revolutionizing the landscape of targeted drug delivery and advanced oncology [5, 22]. Conventional systemic chemotherapy is frequently plagued by poor drug bioavailability, rapid degradation, and severe off-target cytotoxicity. Biogenic nanocarriers address these limitations by encapsulating both hydrophilic and lipophilic therapeutic agents, protecting them from premature enzymatic breakdown and facilitating their transport across formidable physiological barriers. In the context of cancer therapeutics, microbially synthesized nanoparticles, especially silver nanoparticles (AgNPs), exhibit potent, standalone tumoricidal activity. These nanoscale structures passively accumulate within the disorganized vasculature of tumor

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microenvironments via the enhanced permeability and retention (EPR) effect. Once localized, biogenic nanoparticles actively disrupt mitochondrial function, induce DNA damage, and activate intrinsic apoptotic pathways within neoplastic cells [1, 15, 23]. Recent advancements also highlight their synergistic potential; biogenic nanomaterials are increasingly utilized as advanced photosensitizers in photodynamic therapy and as immunomodulatory agents capable of reprogramming tumor-associated macrophages to stimulate a robust anti-tumor immune response [6, 24].

This comprehensive review synthesizes empirical evidence spanning the last fifteen years to critically evaluate the pharmaceutical applications of microbially synthesized nanomaterials. By systematically analyzing their mechanisms of biosynthesis, structural advantages, and expansive therapeutic utility across drug delivery, infectious disease management, and oncology, this report aims to delineate the current capabilities and future translational hurdles of biogenic nanotechnology. As research progresses toward commercial biopharmaceutical implementation, understanding the profound therapeutic potential of these microbial nanofactories may prove paramount for the continued evolution of precision medicine and allied fields, as discussed in the coming text.

METHODOLOGY

The present review work has been carried out by citing the recent scientific literature and data. The literature was retrieved from PubMed, Medline, Google Scholar, Academia Edu, Live-DNA, Wiley-Online, Cochrane database, and manual search from Elsevier, Springer, Taylor & Francis, and Bentham Publishers databases. A total of 150 research articles were pooled, and 44 were selected for the present study using PRISMA guidelines. The studies done by authors related to green synthesis of NPs by plant sources, without any medical/diagnostic/therapeutic/ pharmacological applications, were excluded. The research papers published before 2015 were excluded from the present study. The image generation was facilitated by Gemini Pro, licensed to the author.

ADVANCED ANTIMICROBIAL AND ANTIBIOFILM APPLICATIONS

One of the most urgent applications for MNMs is the mitigation of the global antimicrobial resistance (AMR) crisis [7, 17, 19, 25]. Biogenic nanoparticles offer a multi-targeted approach that makes the development of resistance by pathogens significantly more difficult compared to traditional monotherapy antibiotics.

Mechanism of Action Against MDR Pathogens

Biogenic AgNPs, gold (AuNPs), and zinc oxide (ZnO) nanoparticles exert their effect through several simultaneous pathways:

- *Relieving Oxidative Stress:* The generation of reactive oxygen species (ROS) leads to the peroxidation of lipid membranes and damage to proteins and DNA.
- *Physical Disruption:* Nanoparticles adhere to and penetrate the bacterial cell wall, causing physical leakage of cytoplasmic contents.
- *Enzymatic Inhibition:* Metal ions released from the nanoparticles interfere with essential metabolic enzymes, exerting bioactivity.

Antibiofilm Efficacy of Biogenic-Nanoparticles

Pathogenic biofilms, such as those formed by *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA), represent one of the most formidable challenges in modern pharmacotherapy. These complex bacterial communities are encased in a self-produced extracellular polymeric substance (EPS) matrix, making them up to 1,000 times more resistant to traditional antibiotics than their planktonic counterparts [8, 22, 26]. Microbial nanomaterials are uniquely suited for biofilm penetration due to their nanoscale dimensions and the presence of natural biological capping agents [24, 27]. These bio-organic coronas, composed of microbial proteins, peptides, and exopolysaccharides, facilitate superior electrostatic interactions with the EPS matrix. Unlike purely synthetic nanoparticles that often aggregate or are repelled by the biofilm's surface charge, microbially

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synthesized nanoparticles can seamlessly navigate the aqueous channels of the biofilm architecture, effectively delivering their microbicidal payloads deep into the core of the colony. Once optimal penetration is achieved, the therapeutic efficacy of these biogenic nanomaterials is driven by potent, multi-modal bactericidal mechanisms [28]. Upon localization within the matrix, they actively begin to degrade the structural integrity of the biofilm by inducing severe, localized oxidative stress through the continuous generation of reactive oxygen species (ROS). Thus, leading to the catastrophic peroxidation of bacterial lipid membranes and the irreversible degradation of intracellular DNA and transport proteins [23]. Furthermore, the sustained release of heavy metal cations directly inhibits the vital enzymatic pathways necessary for bacterial respiration and metabolism within the biofilm's deepest, anoxic layers.

From a pharmaceutical perspective, this profound antibiofilm activity is being heavily leveraged to develop next-generation medical interventions and delivery systems. Biogenic nanomaterials are currently being integrated into advanced hydrogel wound dressings for chronic, non-healing diabetic ulcers, where they continuously suppress biofilm colonization while simultaneously promoting localized tissue re-epithelialization. Additionally, formulating nanocoatings for indwelling medical devices, such as urinary catheters and orthopedic implants, utilizing microbially synthesized nanoparticles has shown immense promise in curtailing device-related hospital-acquired infections [29]. Crucially, recent pharmacological research highlights a strong synergistic effect when these biogenic nanoparticles are co-administered with conventional antibiotics. This combination therapy not only restores the efficacy of previously obsolete antimicrobial drugs against multidrug-resistant strains but also allows for significantly lower therapeutic dosages, thereby minimizing systemic toxicity and slowing the overall pace of microbial resistance evolution.

TARGETED DRUG DELIVERY SYSTEMS (DDS)

Microbial nanomaterials (MNMs) have revolutionized precision pharmacotherapy by ensuring that therapeutic payloads reach their exact physiological targets while drastically minimizing systemic exposure and off-target cytotoxicity [30–34].

Biogenic Nanocarriers

Bacteria-derived nanoscale structures, particularly outer membrane vesicles (OMVs) and chromosomeless "minicells," are being increasingly utilized as sophisticated vehicles to transport high doses of potent chemotherapeutic agents directly to neoplastic tissues. Due to their unique biochemical composition, MNMs can efficiently encapsulate highly hydrophobic drugs, substantially improving their aqueous solubility, stability, and systemic bioavailability. Beyond small-molecule chemotherapeutics, these biogenic carriers are highly effective at protecting labile biological macromolecules, such as small interfering RNA (siRNA) and targeted therapeutic proteins, from premature enzymatic degradation in the bloodstream. Furthermore, by functionalizing MNMs with stimuli-responsive polymers or leveraging their innate structural sensitivities, drug release kinetics can be precisely calibrated [35]. For instance, the nanocarriers can be engineered to degrade and release their payload strictly in response to the localized acidic pH characteristic of a tumor microenvironment or upon encountering specific overexpressed intratumoral enzymes [36, 37]. This ensures a concentrated therapeutic burst precisely at the site of pathology while sparing healthy surrounding tissues.

Crossing Physiological Barriers

The spontaneous biological "corona" formed around microbially synthesized particles provides a profound advantage in overcoming some of the most formidable physiological hurdles in medicine [29]. This natural capping layer often includes specific microbial proteins, exopolysaccharides, and peptides that facilitate active transport mechanisms, allowing MNMs to successfully bypass the highly restrictive Blood-Brain Barrier more effectively than bare, chemically synthesized counterparts [31, 25]. By engaging in receptor-mediated transcytosis, these particles open unprecedented avenues for delivering neurotherapeutics to treat complex central nervous system disorders such as Alzheimer's and

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Parkinson's diseases [2]. Additionally, these resilient bio-organic coronas protect active pharmaceutical ingredients from the harsh, acidic environment of the gastrointestinal tract and the degradative action of digestive enzymes [32, 35]. This inherent shielding effect, combined with enhanced mucosal adhesion, significantly improves the absorption profiles of oral drug delivery systems, offering a viable and highly efficient alternative to invasive intravenous administration protocols.

ONCOLOGY AND CANCER THERAPEUTICS

In modern oncology, MNMs have transitioned from being viewed merely as passive delivery vehicles to being recognized as active therapeutic participants capable of directly modulating tumor cell survival (Figure 1).

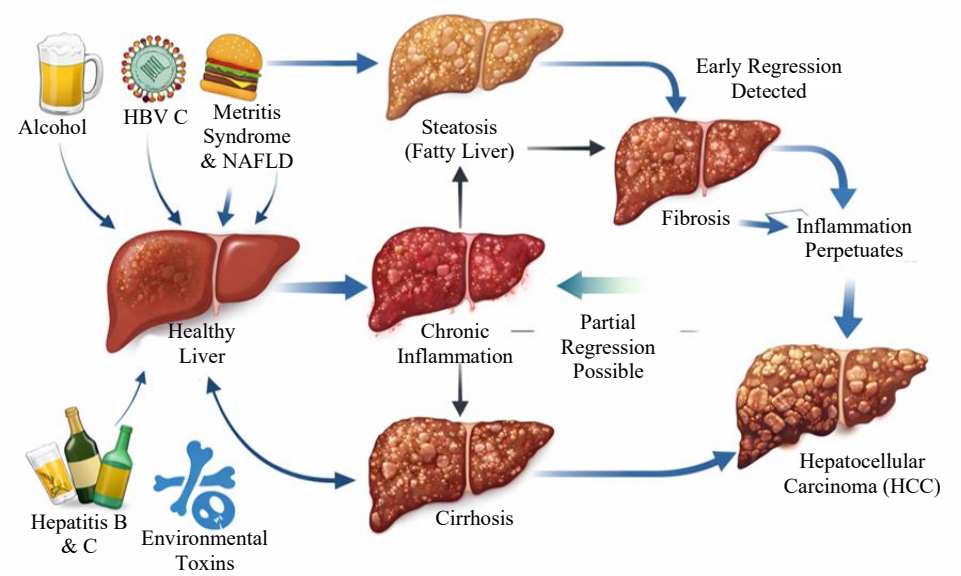


Figure 1. The progression of hepatic ailments under influence of various physico-chemical affectors.

Targeted Toxicity and the Enhanced Permeability and Retention Effect

Nanoparticles of microbial origin demonstrate a sophisticated ability to naturally accumulate within malignant tissues by exploiting the Enhanced Permeability and Retention (EPR) effect [30, 38]. This phenomenon is driven by the disorganized, "leaky" nature of neoplastic vasculature combined with impaired lymphatic drainage, which allows biogenic particles to preferentially extravasate and remain within the tumor interstitial space. Unlike many synthetic counterparts, biogenic AgNPs synthesized by bacteria or fungi exhibit potent, intrinsic tumoricidal activity [16, 21]. Empirical evidence has shown that these biogenic AgNPs trigger intrinsic apoptotic pathways specifically within various cancer cell lines, such as MCF-7 breast cancer cells, by inducing mitochondrial dysfunction and irreversible DNA damage [39]. Crucially, these MNMs demonstrate high therapeutic selectivity; they exhibit profound cytotoxicity toward malignant cells while remaining significantly less toxic to healthy human fibroblast cells (Table 2). This selectivity is largely governed by the microbial-derived capping agents, which enhance biocompatibility and modulate the particle's interaction with specific cellular receptors.

Table 2. Therapeutic potential of biogenic AgNPs on the hepatocellular carcinoma.

Drug/nanomaterial	Method used	Particle size (nm)	Zeta potential (mV)	Model used	Main limitations/notes	Conclusion
Cymodocea serrulata–AgNPs	Biogenic synthesis	30.5 ± 2.5	–	A549	Evaluated in non-HCC models no in vivo tumor validation; synthesis	Demonstrated anticancer potential via green synthesis.

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					reproducibility not addressed.	
Ananas comosus–AgNPs	Green synthesis	–	–	HepG2	Primarily exploratory multifunctional study; limited mechanistic depth; no *in vivo* validation.	Dose-dependent cytotoxicity and antioxidant activity.
Kaempferol–AgNPs	Green synthesis	200	−20.2	HepG2	Single HCC cell line; no normal hepatocyte comparison or *in vivo* validation.	Inhibited migration and induced ROS-mediated apoptosis.
Alnus nitida–AgNPs	Green synthesis	150.25 ± 5.30	−19.85 ± 2.35	Multiple cancer lines incl. HepG2	*In vitro* only, no tumor-bearing animal MO Ag^+ release kinetics did not standardize.	Selective cytotoxicity toward cancer cells.
Schinus molle–AgNPs	Green synthesis	35.8	−24.9	HepG2	*In vitro* evidence only; autophagy/apoptosis pathways not validated *in vivo*.	Induced oxidative stress and apoptosis.
Nigella sativa–AgNPs	Green synthesis	10–20	18.8 ± 0.372	HepG2	Limited mechanistic investigation; no animal validation.	Promising alternative anticancer approach.
Dragon fruit peel–AgNPs	Green synthesis	10–50	–	HepG2	Short-term (24 h) cytotoxicity only; no pharmacokinetic or *in vivo* assessment.	Dose-dependent apoptosis induction.
Zea mays–AgNPs	Green synthesis	100	–	HepG2	Focus on antioxidant + cytotoxic activity; tumor selectivity not fully evaluated.	Significant cytotoxic and antioxidant effects.
Reynoutria japonica–AgNPs	Green synthesis	35–100	−28.5	Multiple cancer lines incl. HepG2	No *in vivo* tumor MO systemic toxicity not evaluated.	Selective cytotoxicity toward cancer cells.
Fusarium oxysporum–AgNPs	Biogenic synthesis	56.43 ± 19.18	−26.8 ± 7.55	Huh7	Limited anticancer efficacy; no animal validation.	Moderate anticancer activity.
Limosilactobacillus fermentum–AgNPs	Probiotic biosynthesis	6–23	−7.11	Huh7	High IC_{50} values; moderate potency; no *in vivo* validation.	Dose-dependent cytotoxicity.
Anabaena variabilis–AgNPs	Green synthesis	17–35	−19.5	Cancer lines HepG2	*In vitro* only; no long-term safety assessment.	Selective anticancer activity.
Sargassum vulgare–AgNPs	Phyco-synthesis	6.9–16.97	−29.6	Multiple cancer lines incl. HepG2	Mixed hepatoprotective/ cytotoxic findings; mechanistic clarity limited.	Anticancer and antioxidant activity.
Senna sophera–AgNPs	Biogenic synthesis	30.6	−12	HepG2	Relatively high IC_{50}; no animal tumor model validation.	Cytotoxic and antioxidant effects.
Conocarpus lancifolius–AgNPs	Green synthesis	5–30	–	Breast cancer cells	Evaluated in non-HCC MO, limited hepatic relevance.	ROS-mediated cytotoxicity.
Morus alba–AgNPs	Biogenic synthesis	10–50	−11.3	HepG2 + rat model	Dual hepatoprotective and cytotoxic effects; mechanistic separation unclear.	Restored redox balance in liver model.

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Rumex hastatus–AgNPs	Green synthesis	20.34–54.67	–	HepG2 + mouse model	Concurrent hepatoprotective and cytotoxic roles require clarification; vell safety not addressed.	Cytotoxic and hepatoprotective potential.
Clerodendron phlomoides–AgNPs	Green synthesis	125	−6.02	Rat HCC model	Rodent model only; biodistribution, chronic toxicity not evaluated.	Demonstrated anticancer efficacy *in vivo*.
Achillea fragrantissima–AgNPs	Green synthesis	16–22	–	HepG2 + MCF-7	*In vitro*-only evidence; no pharmacokinetic evaluation.	Strong cytotoxicity and apoptosis induction.
Artemisia carvifolia–AgNPs	Biogenic synthesis	80 ± 6	–	HepG2	Mechanistic focus on Rap2A; requires validation in animal tumor models.	Downregulated Rap2A and induced apoptosis.
Catharanthus roseus–AgNPs	Green synthesis	–	–	HepG2 + THLE-3	Transcriptomics limited to *in vitro* model no *in vivo* safety profiling.	Selective cytotoxicity and pathway modulation.
Berberine–AgNPs	Green synthesis	171.5 ± 4.2	−12.4	HepG2 + normal cells	No tumor-bearing animal validation; biodistribution not studied.	Enhanced apoptosis and anticancer activity.
Taraxaci extract–AgNPs	Green synthesis	218.7	−39.54	HepG2 + HUVEC	*In vitro* co-treatment only; immune and hepatic cells not evaluated.	Strong cytotoxicity and improved drug tolerance.
Pyracantha crenulata–AgNPs	Biogenic synthesis	1340.8	−18.7	Hep-2	Reported size (>1 µm) raises NPs classification concerns	Suppressed liver cancer cell proliferation.
DFPAE–AgNPs	Green synthesis	10–50	–	HepG2	Short-term cytotoxicity only; no long-term safety.	Induced apoptosis with IC_{50} 37.98 µg/mL.

Synergistic Photodynamic Therapy (PDT)

The therapeutic efficacy of MNMs has been further amplified through their integration into Photodynamic Therapy (PDT). In this synergistic modality, biogenic AuNPs and silver nanoparticles act as advanced photosensitizers or resonance enhancers [12, 40]. When triggered by specific wavelengths of light, these particles facilitate the localized generation of lethal ROS, including singlet oxygen, which induces catastrophic oxidative damage to the tumor's structural and metabolic components (Table 3). Recent research highlights the "surgical precision" of this biogenic approach [3]; because ROS generation is strictly confined to the site of light irradiation and nanoparticle accumulation, systemic side effects are virtually eliminated (Figure 2). Furthermore, the phytochemicals present in the biogenic corona can act as auxiliary reducing agents, helping to overcome the hypoxia typical of solid tumors and ensuring promising control in advanced cancer management.

Table 3. Role of metal-specific nanomaterials in bioactivities.

Application type	Specific nanomaterial	Microbial source	Pharmaceutical benefit
Anticancer	Biogenic AgNPs	*Bacillus sp.*	Intrinsic apoptosis in tumor cells
Drug Delivery	Magnetic NPs	*Magnetospirillum*	Magnetic-guided targeted delivery
Wound Healing	ZnO Nanocomposites	*Aspergillus niger*	Reepithelialization/ infection control

WOUND HEALING AND TISSUE ENGINEERING

Chronic wounds, including diabetic foot ulcers, severe burn lesions, and venous leg ulcers, represent a profound clinical and pharmaceutical challenge (Table 4). These wounds are frequently stalled in a state of persistent inflammation, characterized by localized hypoxia, excessive exudate, and a high

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susceptibility to polymicrobial infections [13, 41]. Traditional topical formulations often fail to address these multifaceted biological barriers simultaneously [18, 27, 37]. In this context, MNMs have emerged as highly efficacious, multi-functional therapeutic agents that significantly accelerate the complex physiological phases of wound healing and tissue regeneration [14, 42].

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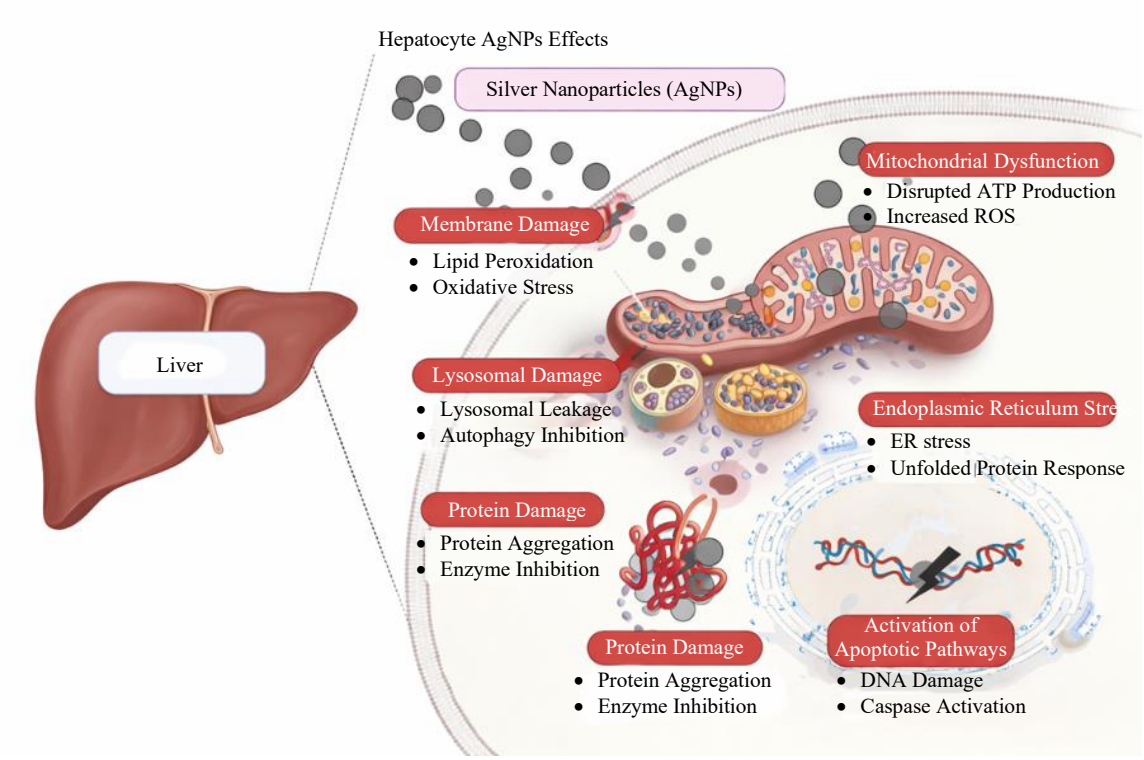


Figure 2. Effect of biogenic AgNPs on hepatocyte detoxification and reversal of hepatic cancer.

Hemostasis, Inflammation, and Proliferation

The normal wound healing cascade relies on a seamless transition from inflammation to tissue proliferation. Biogenic nanoparticles actively facilitate this transition by modulating the local immune microenvironment; they rapidly downregulate pro-inflammatory cytokines while simultaneously acting as potent ROS scavengers, protecting delicate newly formed tissues from oxidative degradation [18].

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As the wound enters the proliferative phase, MNMs act as profound biochemical stimuli. They promote the rapid migration and proliferation of essential cellular components, particularly keratinocytes and fibroblasts. Furthermore, MNMs have been shown to upregulate critical signaling molecules, such as vascular endothelial growth factor (VEGF), driving prompt angiogenesis, the formation of new capillary networks for delivering oxygen and essential nutrients to the ischemic wound bed (Figure 3). MNMs enhance the dense deposition and cross-linking of collagen, accelerating the reconstitution of the extracellular matrix for long-term tensile strength of the healed tissue (Table 4, Figures 3 & 4). These platforms leverage natural biomolecular capping layers (microbial proteins, peptides etc,) that naturally reduce cytotoxicity while providing powerful synergistic therapeutic activities along various steps of tissue repair [16].

Table 4. Mechanisms of nanomaterial-based tissue engineering in the normal healing process.

Wound healing phase	Specific cellular targets	Molecular signatures & biological stimuli	Key nanomaterial mechanism & function	Ultimate physiological outcome
Inflammatory Phase	Local immune cells, macrophages, and neutrophils	Pro-inflammatory cytokines Excess free radicals / Oxidative stress	Immune Microenvironment Modulation: Rapidly neutralize pro-inflammatory markers. ROS scavengers	Mitigates prolonged inflammation and protects newly forming delicate tissues from oxidative stress.
Proliferative Phase *(Cell Migration)*	Keratinocytes, dermal fibroblasts	Intrinsic growth-promoting genes Cellular migratory pathways	Structural Initiation: Promotes cellular migration, rapid mitogenic proliferation across the wound margins	Initiates structural tissue re-epithelialization and the dynamic formation of functional granulation tissue.
Proliferative Phase *(Angiogenesis)*	Endothelial cells, capillary endothelial networks	Vascular Endothelial Growth Factor (VEGF) Pro-angiogenic signaling cascades	Neovascularization Induction: Upregulates critical signaling proteins like VEGF. Drives robust capillary budding and vessel sprout formation	Reverses tissue ischemia by establishing fresh vascular networks that deliver vital oxygen and metabolic nutrients to the wound bed.
Remodeling Phase	Extracellular Matrix (ECM), myofibroblasts	Structural collagen fibril types Matrix cross-linking enzymes	ECM Matrix Reconstitution: Enhances dense deposition of structural collagen causing cross-linking of fibres	Reconstitutes a organized extracellular matrix architectural framework, securing optimal long-term tensile tissue strength.

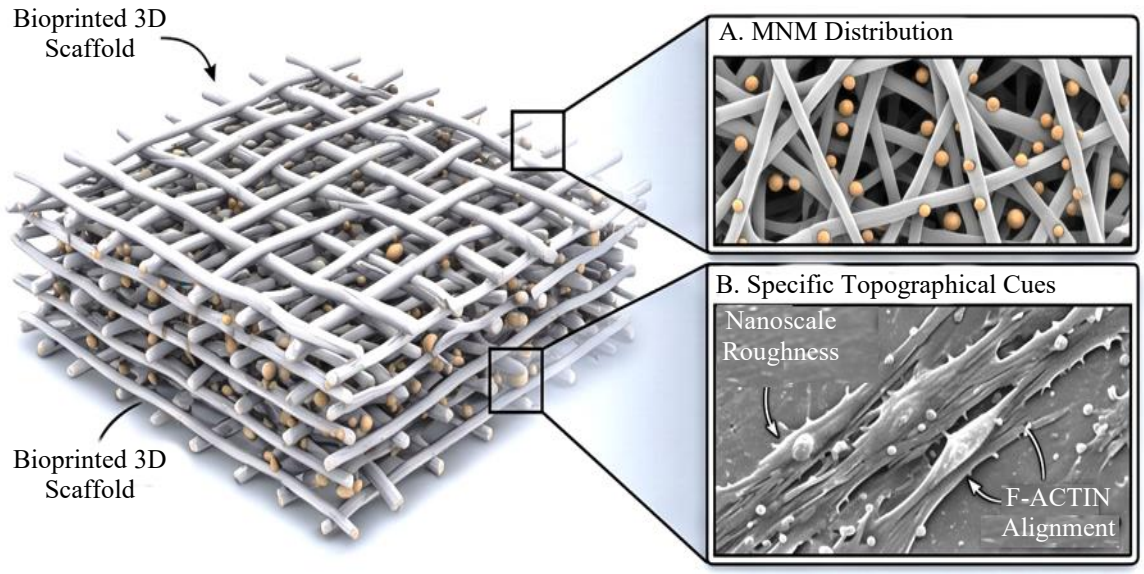


Figure 3. 3D scaffolding: (a) and Topographical cues and (b) of infected, torn or wounded tissue by biogenic nanomaterials.

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Infection Control and Advanced Bioscaffolds

Maintaining a sterile microenvironment is an absolute prerequisite for unimpeded tissue regeneration. Microbially synthesized nanomaterials, notably biogenic silver (AgNPs) and zinc oxide (ZnO) nanoparticles, are increasingly being formulated into advanced pharmaceutical architectures, including electrospun nanofibrous scaffolds, biocompatible hydrogels, and "smart" wound dressing [4, 20, 38, 43, 44]. These matrices allow for the sustained, localized release of antimicrobial metal ions directly into the wound exudate over extended periods.

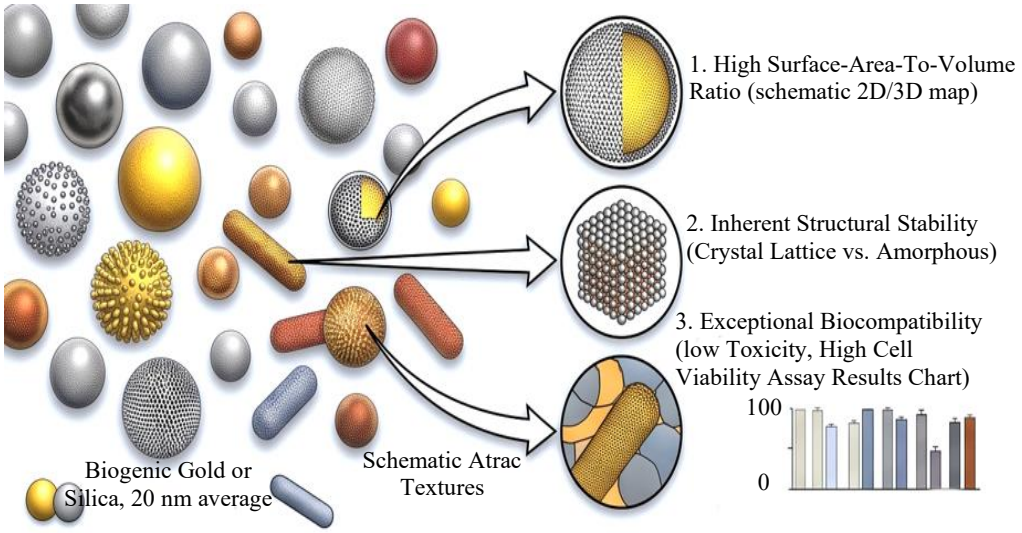


Figure 4. Physico-chemical properties of biogenic nanomaterials.

This continuous delivery mechanism successfully eradicates opportunistic pathogens and actively prevents the formation of impenetrable bacterial biofilms. Crucially, the natural biological capping agents (the "corona") present on MNMs significantly mitigate the localized cytotoxicity that is notoriously associated with chemically synthesized heavy metal nanoparticles. This ensures that the robust bactericidal activity does not inadvertently hinder mammalian cellular growth [6, 15].

Expansion into Regenerative Medicine

Beyond topical wound management, the pharmaceutical applications of MNMs extend deeply into complex tissue engineering. Because of their exceptional biocompatibility, inherent structural stability, and high surface-area-to-volume ratio, biogenic nanoparticles are ideal dopants for three-dimensional bioscaffolds used in regenerative medicine. Recent pharmacological research highlights their unique capacity to interact with and direct the lineage-specific differentiation of human mesenchymal stem cells (Figure 5). By providing specific topographical cues and biochemical signals, MNMs show immense promise in advanced reconstructive therapies, including accelerated osteogenesis (bone regeneration) and chondrogenesis (cartilage repair) (Figures 5, 6), firmly establishing their role at the forefront of next-generation regenerative pharmacology.

CONCLUSION

Nanomaterials of microbial origin have fundamentally transitioned from a mere laboratory curiosity to a foundational cornerstone of modern pharmaceutical research. This paradigm shift is largely driven by the urgent clinical need to move away from conventional physicochemical synthesis, which frequently leaves behind toxic chemical residues that severely limit *in vivo* translation. By utilizing microbial nanofactories, such as bacteria, fungi, and microalgae, researchers can harvest biogenic nanoparticles that are naturally cloaked in a biologically active "corona" of microbial proteins, peptides, and exopolysaccharides. This unique bio-organic coating grants them extraordinary structural stability, high physiological biocompatibility, and a significantly reduced immunogenic profile upon systemic administration, making them vastly superior to many chemically synthesized alternatives.

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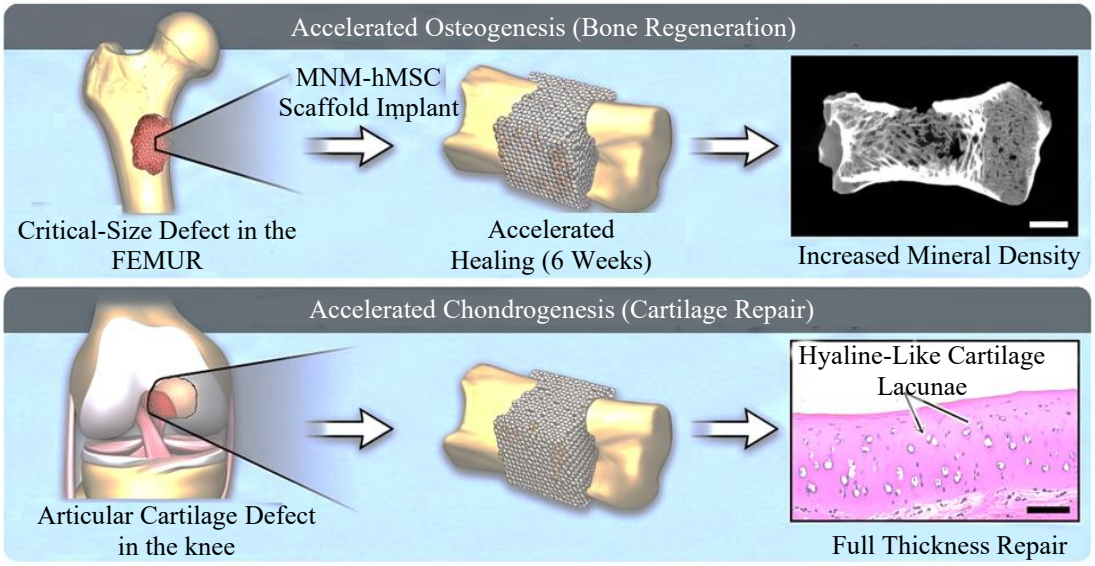


Figure 5. Impact of biogenic nanomaterials on advanced reconstructive therapies & repair of connective tissues.

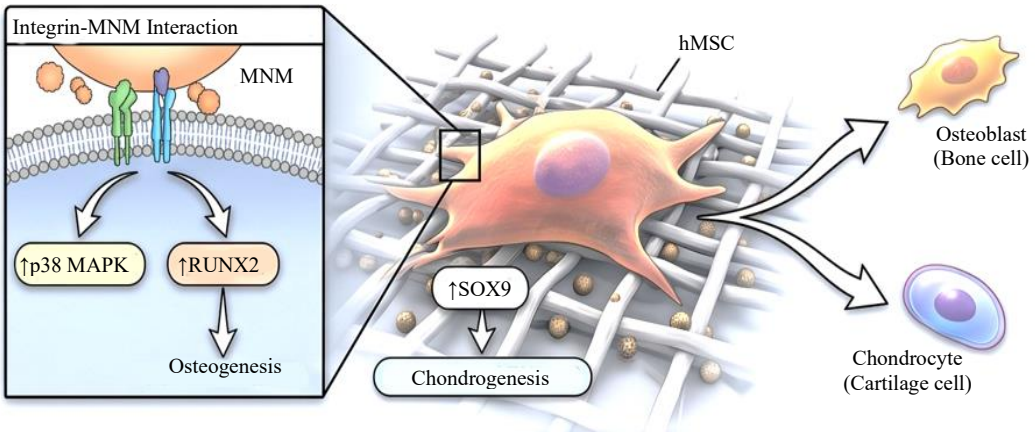


Figure 6. Advanced pharmacotherapy – the forefront of regenerative constructive medicine.

The true pharmacological value of these microbially derived nanomaterials lies in their inherently multi-functional nature (Chander & Lovejot, 2026). They seamlessly integrate advanced, targeted drug delivery capabilities with intrinsic therapeutic activities. For instance, biogenic AgNPs and AuNPs can efficiently encapsulate highly potent, hydrophobic chemotherapeutic agents, ensuring these drugs remain protected from premature enzymatic degradation in the bloodstream. Concurrently, these nanocarriers are not simply inert vessels; they actively participate in the clinical intervention. They exhibit intrinsic antimicrobial, anti-inflammatory, and tumor-suppressive properties, creating a potent synergistic therapeutic effect that traditional, single-target chemical drugs cannot replicate.

As we move toward the next decade and approach 2030, pharmaceutical research will increasingly shift toward the development of "smart," stimuli-responsive biogenic nanomaterials designed specifically for theranostics, the seamless integration of simultaneous biological diagnosis and targeted treatment. Microbially synthesized nanoparticles are exceptionally suited for this dual clinical role. For example, magnetosomes naturally produced by magnetotactic bacteria serve as highly effective, non-toxic contrast agents for magnetic resonance imaging (MRI), allowing oncologists to pinpoint deep-tissue tumor locations with high-resolution accuracy. Furthermore, the next generation of biogenic theranostics will be engineered to react dynamically to the specific pathophysiological conditions of the patient's internal microenvironment. By functionalizing these nanomaterials to release their therapeutic

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payloads strictly in response to localized biological triggers, such as the acidic pH of a tumor, specific overexpressed enzymes, or the elevated oxidative stress of chronically inflamed tissue, systemic side effects can be virtually eliminated. This precise, closed-loop approach will ultimately allow for a highly personalized pharmaceutical experience, where therapies are dynamically adjusted based on real-time diagnostic feedback provided by the biogenic nanomaterials themselves, firmly establishing a new era of precision nanomedicine.

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