

Biogenic Nanocomposites in Biomedicine – A Review

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Abstract

The increasing demand for sustainable biomedical technologies has stimulated growing interest in green-synthesized nanocomposites as alternatives to conventionally fabricated nanomaterials. Plant-mediated synthesis offers an environmentally friendly approach in which naturally occurring phytochemicals act as reducing, stabilizing and capping agents during nanoparticle formation. The current review systematically examines plant-mediated green synthesis of metal and metal oxide nanoparticles incorporated with biopolymeric, polymeric and ceramic matrices with a focus on their synthesis, physicochemical characteristics, biological properties and biomedical applications. Also, it highlights the synergistic properties of green-synthesized nanocomposites and evaluates their reported antimicrobial, anticancer, antioxidant and antidiabetic activities. Their applications in controlled drug delivery, photothermal therapy, bioimaging, tissue engineering, wound healing and regenerative medicine particular emphasis on chitosan-based nanocomposite systems rather than individual nanoparticles hybrid nanocomposites. Moreover, the review investigates how interactions between nanoparticles and matrix components affect particle size, morphology, surface chemistry, stability, biocompatibility and therapeutic performance. Chitosan is especially regarded for its role as a versatile biodegradable matrix, owing to its inherent antimicrobial properties, mucoadhesion, biodegradability and potential for functional modification. Recent progress in multifunctional nanocomposites that integrate targeted delivery, imaging and therapeutic functions is also discussed. Moreover, key current challenges including reproducibility, scale-up toxicity, long-term stability, standardized characterization and regulatory approval are given critical attention. Overall, plant-based nanocomposite systems offer promising multifunctional platforms for creating safer, sustainable and clinically applicable biomedical technologies.

Keywords: Biogenic Nanocomposites, Bioimaging, Biomedical, Drug Delivery, Microbes, Photothermal.

Introduction

The achievements that science has made in the 21st century in the field of nanotechnology, especially in the fields of environment, agriculture, food, medicine, biomedicine and biotechnology. Its small size (1–100 nm) makes it an interdisciplinary tool in various fields (1). Nanotechnology is a sophisticated research technique that involves the synthesis, application and engineering of nanomaterials. The scientific community has developed a greener technological approach toward a more sustainable environment and improving human life has become an urgently needed task for better community development (2). The goal of sustainable biomedical nanocomposites is to ensure their nontoxicity, cytocompatibility and hemocompatibility throughout their life cycle. The use of renewable and

biodegradable materials, eco-friendly synthesis and energy-efficient fabrication methods in a sustainable manner, as well as the replacement of petroleum-derived polymers or hazardous chemical routes with plant-based polymers and green nanotechnology, minimizes environmental pollution and ensures long-term resource availability (3). Carbon nanomaterials, quantum dots, chitosan and metal/metal oxide nanocomposites play an emerging role in nano-technology for improved drug delivery, bioimaging, anticancer, biosensing and dental applications (4). Compared with those from other biological sources, the metabolites and phytochemicals isolated from plant extracts are better reducers of chemical compounds for synthesizing nanomaterials (5). At standard room temperature,

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active plant metabolites can reduce metal salts within minutes to hours. Ceramix Matrix Nanocomposites (CMNCs) enhance the properties of different nanoparticles; one or more ceramic phases are mixed to form a nanocomposite (6). The nanocomposite formed from CMNCs has high stability to thermal and chemical factors and is resistant to various factors, such as SiO_2/Fe , SiO_2/Ni and $\text{PbZrO}_3/\text{PbTiO}_2$. They are mainly used for catalysis, chemical sensors, data storage and electronics (7). These materials are mainly used for biomedical applications, such as bone and dental implants (CMNCs reinforced with graphene oxide, carbon nanotubes and zirconium oxide nanoparticles), tissue engineering scaffolds (fabricated via freeze-casting or 3D printing by releasing therapeutic ions Si^{4+} , Ca^{2+} and Zn^{2+} by stimulating regeneration of bones), drug delivery and antibacterial systems, bioimaging, biosensing and molecular diagnosis (8). Polymer Matrix Nanocomposites (PMNCs) reinforced with nanofillers, such as metal nanoparticles (Ag, Au and ZnO), carbon nanomaterials (graphene and CNTs), hydroxyapatite and silica, enhance bioactivity, mechanical strength and functional responsiveness. PMNCs have different characteristics, such as enhanced mechanical properties, lower gas permeability and high thermal stability. Nanofillers are typically linear, layered and powdery. These materials are mainly used for different applications, such as tissue engineering, diagnostic devices, wound healing, biosensors, energy storage and power tool housing (9). Metal Matrix Nanocomposites (MMNCs) are primarily composed of metal or alloy matrices embedded in nanosized supplemental materials (10). Compared with other nanocomposites, these materials are highly ductile, have greater strength and have a high modulus (6). These materials are mainly used in orthopedic treatment (magnesium-based biodegradable implants), dental implants, cardiovascular devices and biosensing (11). Over the past few decades, nanomaterials have been widely utilized across various fields, demonstrating their significant potential in a variety of applications.

Although numerous studies have reported individual green-synthesized nanoparticles and their biomedical applications, an integrated assessment connecting plant-mediated synthesis, nanocomposite architecture, synergistic physico-

chemical properties, biological functions, sustainability and translational challenges remains comparatively limited. This review addresses this gap by systematically examining green-synthesized metal/metal oxides and hybrid nanocomposites across diverse biomedical applications, including drug delivery, antimicrobial and antidiabetic activities, photothermal therapy, bioimaging, tissue engineering and regenerative medicine. Particular emphasis is placed on the function of plant-derived phytochemicals as reducing, stabilizing and capping agents and their influence on nanocomposite stability, biocompatibility and biological performance (12). The current review critically identifies the major barriers to clinical translation, including reproducibility, standardization, scalability, toxicity, long-term biosafety, environmental persistence and regulatory requirements. Thus, the contribution of this review is not merely to summarize reported applications but to establish a sustainability, structure, function and application framework that can guide the rational development of safer multifunctional, scalable and clinically translatable green nanocomposites. Emerging opportunities involving bioinspired synthesis, surface engineering, machine-learning-assisted design, stimuli-responsive systems and theranostic platforms are also highlighted as future directions of research.

Green Synthesis of Plant-based Nanocomposites

The use of plant-based extracts for nanocomposite synthesis has numerous advantages over other physical and chemical synthesis methods. Compared with other methods, the green synthesis of hybrid nanocomposites is environmentally reliable, simple and economical. The parts of the plant used for the synthesis of nanoparticles are mainly the roots, seeds, fruits, stems and leaves of the plant. Phytochemicals act as stabilizing reducing agents for the synthesis of nanocomposites under mild and nontoxic conditions (13). Biomolecules present in plant extracts act as stabilizing capping agents for the synthesis of nanoparticles by attaching themselves to the nanocomposite surface and assisting in the characterization of its surface, shape and size. The concentration of the metal salt, temperature, pH and time directly affect the quality, size and purity of nanocomposites. There are two approaches for

synthesizing nanoparticles: top-down and bottom-up approaches. The use of biological, physical and chemical methods, such as ball milling, laser ablation and lithography, to disintegrate larger molecules into smaller ones is a top-down approach, whereas the method that starts at the microscopic scale and synthesizes nanoparticles through physical, chemical and biological processes is a bottom-up approach (14).

Green nanocomposites are increasingly used in controlled and targeted drug delivery, where biopolymeric matrices ensure biocompatibility and degradation and nanoscale fillers provide responsiveness to stimuli such as pH, temperature and magnetic fields (15). Future studies should focus on process standardization, mechanistic knowledge of biological synthesis and adaptable green production techniques to overcome the obstacles to increasing the sustainability of the synthesis of green nanoparticles. The environmentally friendly and large-scale manufacture of biomedical nanocomposites may be made possible by combining bioprocess engineering with machine learning to provide precise control and repeatability (16). Owing to its organic sealing ability, regulated particle scattering ability and strong adhesive bonding, green synthesis results in increased stability, which enhances the functional lifetime and biocompatibility of nanocomposite systems.

During biogenic reduction, active natural biomolecules act as stabilizing and reducing agents for metal nanoparticles. Green-synthesized nanomaterials are a sustainable alternative to chemical and physical methods. It has wide applications in antimicrobial therapy, cancer treatment, environmental remediation and agriculture. The advantages of biogenic reduction are that it is scalable, cost-effective, eco-friendly, stable and biomedically compatible (17). The presence of secondary metabolites in plant extracts, such as flavonoids, phenolics, terpenoids, alkaloids and tannins, acts as reducing agents to reduce various metal ions to produce

nanoparticles. Additionally, it acts as a capping agent by preventing aggregation and stabilizing nanoparticles (18).

Metal/Metal Oxide and Hybrid Nanocomposites

Metal and metal oxide nanocomposites (MMONs) are hybrid materials composed of metal nanoparticles, such as Ag, Au and Cu and metal oxide nanoparticles, such as TiO₂, ZnO and Fe₃O₄, integrated into various matrices, such as polymers, carbon-based supports and ceramic-based nanocomposites (19). These nanocomposites exhibit enhanced physicochemical properties owing to the synergistic effects between their components (20). The antimicrobial films synthesized using Ag/CuO and Ag/ZnO nanocomposites disrupted cell walls and generated ROS. TiO₂, ZnO and Fe₂O₃ + C/N materials were used as photocatalysts for removing pollutants by absorbing UV/visible light. Au, Pt, Au/ZnO, Au/NiO and Pt/ZnO nanocomposites were used as electrochemical sensors to enhance the signal transduction. SiO₂, Al₂O₃ and Fe₃O₄ nanocomposites are used in polymer composites to improve their thermal and tensile properties. The SnO₂/Ag, WO₃ and ZnO/SnO₂ nanocomposites used as gas sensors are highly sensitive and selective (21). Chitosan, a natural biocompatible polymer derived from chitin, is increasingly used to form hybrid nanostructures with enhanced properties (22). Chitosan-based nanocomposites in different biomedical applications. Hybrid nanocomposites typically involve chitosan combined with inorganic nanoparticles such as silver, ZnO, TiO₂, Fe₃O₄, graphene, or other biopolymers to create multifunctional materials. Biosynthesized nanocomposites have a wide range of biomedical applications, including antimicrobial, anticancer and antioxidant activities; enhanced mechanical strength, biodegradability and targeted delivery; water purification; pollutant removal; and biosensing in Figure 1 and Table 1 (23).

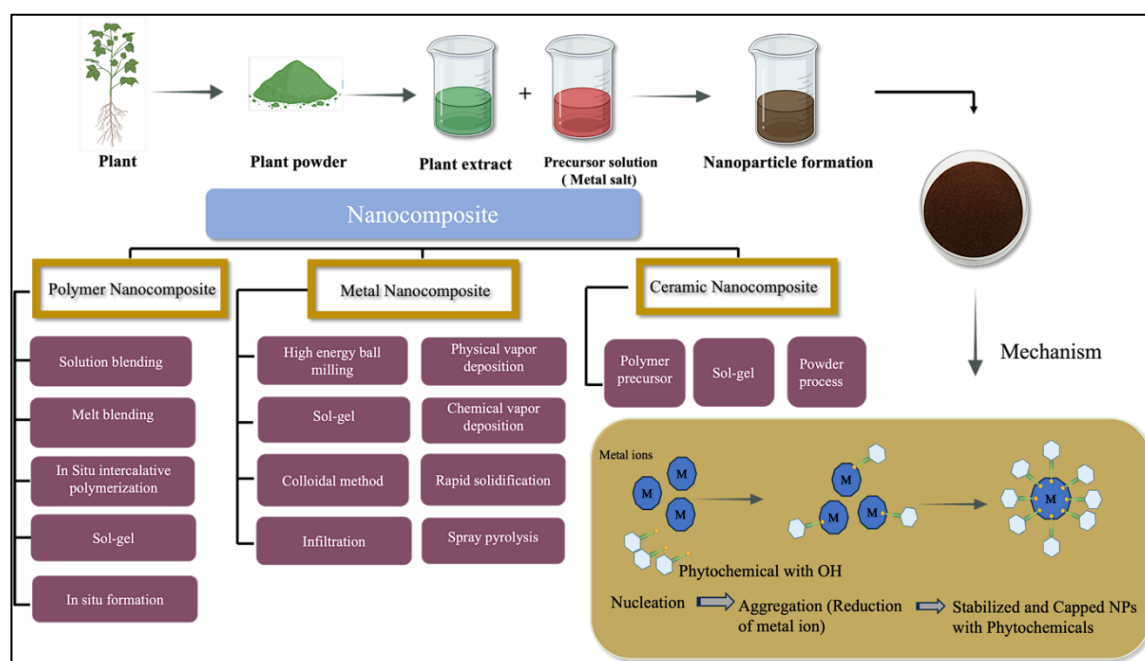


Figure 1: Green Synthesis Strategy for Nanocomposites with Schematic Mechanistic Representation

Table 1: Role of Metal/Metal Oxide and Hybrid Nanocomposites

Feature	Role in Hybrid Nanocomposites	Device Class Use	References
Biodegradability	Enables the material to degrade <i>in situ</i> after serving its function, avoiding need for removal or long-term persistence	Bioresorbable stents, degradable scaffolds, temporary implants	(23)
Biocompatibility	Ensures that the composite does not provoke toxicity, immunogenicity, or adverse biological response, allowing safe contact with tissues or bodily fluids	Implantable devices, sensors, drug-delivery coatings, wound dressings	(24)
Antimicrobial Activity	Provides intrinsic ability to kill or inhibit microbes, prevent biofilm formation	Catheter coatings, urinary devices, wound dressings, implant surfaces	(25)
Film Forming Ability	Allows the composite to form continuous, conformal coatings (films/membranes) that adhere to surfaces, cover gaps and maintain structural integrity	Catheter coating, membrane in microfluidics, barrier coating, sensor encapsulation	(26)
Functional Groups	Enable chemical binding, crosslinking, immobilization of biomolecules (drugs, ligands), surface modification and functionalization	Drug eluting coatings, ligand-functionalized sensors, targeted delivery, crosslinked membranes	(27)

Biomedical Applications

Biogenic nanocomposites have emerged as promising materials for a wide range of biomedical applications because of their unique physico-chemical properties, biocompatibility and diverse biological activities. They have shown promising potential in anticancer therapy, antimicrobial treatment, wound healing, antioxidant protection, cardiovascular and hepatoprotective applications, antidiabetic therapy, biosensing, dental applications and targeted therapeutic delivery.

Their biological effects are associated with several mechanisms as shown in Figure 2, including the generation of reactive oxygen species, disruption of cellular membranes, mitochondrial dysfunction, inhibition of enzyme activity and cellular signalling, interference with the electron transport chain (ETC), inhibition of ATP synthesis, DNA fragmentation and induction of programmed cell death (28-32). These multifunctional characteristics make biogenic nanocomposites attractive candidates for developing innovative therapeutic and diagnostic strategies in modern biomedicine.



Figure 2: A Schematic Diagram Illustrating the Biosynthesized Nanocomposites Applications in Biomedicine

Drug Delivery System

Drugs are targeted to tumors or infected sites via controlled release to reduce the dosing frequency. The solubility and absorption of combined therapies for imaging and diagnosis can be improved. Three types of interactions are common: physical, chemical and biological. In physical interactions, drug absorption at the surface of a nanocomposite occurs via weak forces, such as van der Waals interactions, hydrogen bonding and electrostatic interactions, where positively charged drugs bind to negatively charged chitosan graphene oxide nanocomposites via electrostatic interactions (33). The encapsulation/entrapment of drugs involves physical trapping inside the nanocomposite matrix or pores without chemical bonding to the drug. Hydroxyapatite nanoparticles embedded in chitosan scaffolds can encapsulate small-molecule drugs and release them gradually through diffusion. In contrast, in chemical interactions, drugs form covalent bonds with functional groups on the nanocomposite surface through reactions such as amide or ester formation. Doxorubicin is conjugated to PEG - PLA nanocomposites via hydrazone linkages, which are acid-labile and release the drug in acidic tumor microenvironments in Table 2. Ionic interactions, such as electrostatic attractions, occur between

charged drugs and oppositely charged nanocomposite surfaces. Negatively charged DNA binds to cationic chitosan nanoparticles for efficient gene delivery.

Biological interactions, with an emphasis on receptor-ligand binding and enzyme-induced release. By binding to certain cell receptors, nanocomposites functionalized with targeting ligands like folic acid or antibiotics may deliver medications to sick cells. Anticancer medications are also delivered to folate receptor-positive tumor cells via folic acid-decorated chitosan-gold nanocomposites (26). Drug release is caused by the enzymatic breakage of the polymer bonds in the nanocomposite. Matrix metalloproteinase (MMP)-sensitive peptide binder hydrogel nanocomposites break down in tumor tissue, releasing the medication they contain (27). Both chemically synthesized and green nanocomposites may result in difficulties in growth, such as decreased hatching rates and increased mortality, according to studies on zebrafish embryos. To improve the safety profile of green-synthesized nanocomposites, the lowest effective toxicity-decreasing concentration is determined via dose optimization. Surface functionalization of nanoparticles increases their biocompatibility and decreases harmful reactions (34). Environmental monitoring and biodegradability assessments

guarantee that nanocomposites gradually break down into environmentally friendly byproducts. However, these assessments require long-term

research to evaluate their effects on ecosystems and animal health.

Table 2: Nanocomposites and Their Applications in Drug Delivery System

Nanocomposite	Drug	Key feature	Application	References
PCL-chitosan	Tamoxifen	Sustained release/slowly release	Breast cancer	(25)
Fe ₃ O ₄ -CS-MOF	Curcumin	Magnetic release	Tumour targeting	(35)
Zn-Al LDH	Antimicrobials	Protection and release	Infection control	(36)
ZnO/Ch-alginate	Quercetin	Dual therapy	Cancer and microbes	(37)
CNMCF	Pyropheophorbide	Immune activation	Cancer immunotherapy	(38)
CS-CQD-PVP	Doxorubicin	Targeted anti-cancer	Oncology	(27)
OPS-SA	DOX	pH-sensitive hydrogel	Colon cancer	(39)

Note: PCL = Polyε-caprolactone, CS = Chitosan, MOF = Metal-organic Framework, Fe₃O₄ = Magnetite/Iron Oxide, LDH = Layered Double Hydroxide, ZnO = Zinc Oxide, CQD = Carbon Quantum Dot, PVP = Polyvinylpyrrolidone, OPS: Oxidized Pullulan Polysaccharide, SA: Sodium Alginate, DOX: Doxorubicin.

Bioactivity Against Microbes

The emergence of resistance to known antibiotics in microorganisms is a serious threat to human health. Current antimicrobial medicines have various drawbacks, such as a lack of diversity, antagonistic interactions and germ resistance. The robust antimicrobial properties of novel phytomediated synthetic nanomaterials are significant in drug delivery. The results that are challenging to achieve independently when combined with nanocomposites have attracted increasing attention from the scientific community. These nanocomposites inactivate the biofilm activity of microorganisms owing to their enhanced surface reactivity, charge distribution and sustained release in Table 3. Nanocomposites formed by dispersing nanoparticles are more

convenient than conventional nanocomposites because of their various multi-operational properties (40). Nanocomposites formed from synergistic interactions between two distinct green synthesized nanoparticles exhibit more desirable antibiotic resistance than monometallic nanoparticles. When different nanocomposites interact, they often damage the protein and DNA of bacteria because of the presence of superoxide (O₂⁻) and hydroxyl (OH⁻) free radicals. The cytotoxicity to mammalian cells and antimicrobial potency of nanocomposites are closely linked to their composition, surface chemistry and ROS-generating potential (41). The possible mechanisms underlying the antimicrobial effects of plant-mediated nanocomposites of bacteria are illustrated in Figure 3.

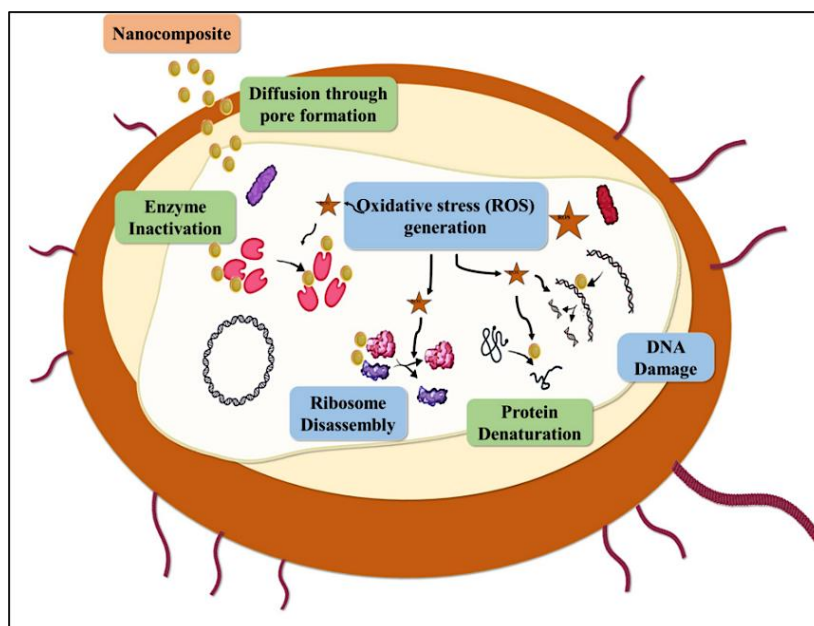


Figure 3: A Schematic Illustration of Nanocomposite Induced Oxidative Stress (ROS) in Bacteria

Table 3: Bioactivity of Green-synthesized Nanocomposite Against Microbial Agent

Plant Extract	Metal/Metal Oxide Nanocomposite	Antimicrobial Activity	References
Mulberry leaves; <i>Aloe vera</i>	Magnetic copper oxide-doped silver/zeolitic imidazolate framework/polyacrylonitrile/zeolitic nanocomposite	<i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Escherichia coli</i>	(42)
<i>Artocarpus heterophyllus</i>	Ag–Au bimetallic nanocomposite	Gram-negative and Gram-positive bacteria	(43)
<i>Artocarpus heterophyllus</i>	Copper–nickel hybrid nanocomposite	<i>Neisseria gonorrhoeae</i> , <i>Escherichia coli</i> , <i>Yersinia pestis</i> , <i>Chlamydia trachomatis</i> , <i>Pseudomonas aeruginosa</i> , <i>Vibrio cholerae</i>	(44)
<i>Gardenia jasminoides</i>	Silver–iron bimetallic nanocomposite	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i>	(45)
<i>Terminalia chebula</i>	Pd–Ag bimetallic nanocomposite	<i>Pseudomonas aeruginosa</i> and methicillin-resistant <i>Staphylococcus aureus</i>	(46)
<i>Ocimum basilicum</i>	Gold–silver bimetallic nanoparticles	<i>Pseudomonas aeruginosa</i> , <i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Escherichia coli</i>	(47)
Lemon extract	Chitosan–Au nanocomposite	<i>Candida albicans</i>	(48)
<i>Prosopis farcta</i>	ZnO–chitosan nanocomposite	<i>Candida albicans</i>	(49)
<i>Ficus religiosa</i>	Mg–ZnO nanoparticles	<i>Aspergillus niger</i>	(50)
Fenugreek leaf extract	Silver–zinc oxide nanocomposite	<i>Candida albicans</i>	(51)
Lemon peel extract	Chitosan-coated selenium nanocomposite	<i>Sclerotinia sclerotiorum</i>	(52)

Note: Ag = Silver, Au = Gold, Cu = Copper, Ni = Nickel, Fe = Iron, Pd = Palladium, Mg = Magnesium, ZnO = Zinc Oxide, CS = Chitosan, Se = Selenium, NPs: Nanoparticles, ZIF = Zeolitic Imidazolate Framework, MRSA: Methicillin-resistant *Staphylococcus aureus*.

Antidiabetic Activity

According to the latest report from the IDF Diabetes Atlas (2025), (53), approximately 11%, of the adult population ranging between 20 and 79 years are in the act of diabetes, whereas 4 in 10 are not aware that they have this condition. The IDF projects that by 2050, one out of eight adults will be prone to diabetes, with an increasing percentage of 46%. More than 90% of people are prone to type 2 diabetes due to various sociological factors, such as environmental, demographic, ecological and genetic factors. The use of nanomedicine for the treatment of patients with diabetes has created new possibilities for the scientific community (54). The use of nanostructures to identify glucose levels in diagnosis and the ability of nanocomposites to reach internal cellular regions has created a novel approach. ZnO/TiO₂ and CuO/TiO₂ nanocomposites better inhibit α -glucosidase activity and exhibit antioxidant activity with wider biomedical efficacy (55). AgO-loaded chitosan nanocomposites synthesized through green synthesis exhibit greater antidiabetic activity than standalone AgO NPs

because of the synergistic interactions between the molecules (56). The plant-mediated green synthesis of ZnO/MgO composites inhibits diabetic enzymes and is effective under saline conditions for various pharmacological applications (57). The biosynthesis of Se/ZnO nanocomposites with antidiabetic applications enhances their photocatalytic and enzyme-inhibitory activities via green synthesis (58). Cerium-doped ZnO enhanced by g-C₃N₄ 2D structures shows excellent α -glucosidase inhibition. Flower-shaped curcumin-loaded ZnO/Ag₂O nanocomposites significantly inhibited α -glucosidase activity (59). In another study, cashew extract was used to synthesize nanocomposites with 67% α -glucosidase inhibition, which demonstrated antioxidant, antibacterial and anti-inflammatory properties and ZnO/MgO nanocomposites using lemon juice with high antidiabetic enzyme inhibition (60). Multifunctional lignin GA composites exhibit robust antidiabetic activity via laccase-catalyzed green synthesis. Silver nanoparticles synthesized from mint and thyme extracts, which exhibit strong enzyme inhibition and antioxidant effects,

constitute the basis for future herbal diabetes therapies (52).

Photothermal therapy

The conversion of light energy to heat energy using light-absorbing agents is known as photothermal therapy. Recent advancements have focused on the use of combined nanoparticles to form nanocomposites, which can be used to enhance engineered materials, such as enhancing effectiveness, targeting and multifunctional therapy (61). Photothermal therapy can be used as a powerful tool against cancer treatment by combining heat generation, drug delivery and imaging by optimizing their design and checking their clinical

potential (62). Near-infrared (NIR) light is used to absorb two-dimensional (2D) materials and carbon-based nanocomposites by efficiently converting them into heat, thereby increasing the local temperature to induce cancer cell death. Some nanocomposites trigger a therapeutic effect in response to specific stimuli, such as the tumor microenvironment, for controlled, targeted therapy (63). NIR radiation triggers the destruction of microbial biofilms, especially those used for antibacterial and antifungal activities in Table 4. Its use in regenerative medicine to enhance the survival of transplanted stem cells and stimulate blood vessel growth (angiogenesis) is quite beneficial.

Table 4: Green Synthesized Nanocomposites Used in Photothermal Therapy

Photothermal Agent	Nanocomposite Type	λ (nm)	ΔT (°C)	Model	Outcome	References
IR780, ICG	Graphene Oxide	808	29.1 °C	<i>In vitro</i> dispersion or GO-dye system	Achieved 29.1 °C in first NIR cycle	(64)
MoS ₂	MoS ₂ / PEG	808	40 -50 °C	<i>In vitro</i> tumor model	Good photothermal heating, tumor suppression	(65)
Copper sulfide (CuS)	CuS/ Hydrogel	1064	30 -90 °C	Aqueous solution / hydrogel	PEG-DA-CuS system and Irradiation raised	(66)
Gold nano shell	Gold/ chitosan	808	40 °C	Tumor or phantom models	Produced hyperthermia sufficient for tumor ablation	(67)

Note: IR780 = Indocyanine green derivative IR780, ICG = Indocyanine Green, GO = Graphene Oxide, MoS₂ = Molybdenum Disulfide, PEG = Polyethylene Glycol, CuS = Copper Sulfide, PEG-DA = Polyethylene Glycol Diacrylate, λ = Wavelength, ΔT = Change in Temperature, NIR = Near-infrared.

Bioimaging

Bioimaging techniques are used to visualize and analyze the biological structures and processes within living organisms or tissues. These methods include magnetic resonance imaging (MRI) and ultrasound (US) for studying biological functions and monitoring real-time changes (68). The use of nanocomposites in bioimaging has improved results because of their ability to perform targeted imaging by functionalizing their surfaces with targeting ligands, thereby improving the specificity and sensitivity of imaging (69). In bioimaging, contrast enhancement relies on the ability of nanocomposites to effectively absorb, scatter and emit light or magnetic signals. Green synthesis introduces biogenic capping agents, such as green-synthesis nanocomposites that combine radioisotopes, such as ⁶⁴Cu or ⁶⁸Ga, with magnetic cores, such as Fe₃O₄, CoFe₂O₄, or MnO, in PET-MRI allowing for the concurrent recording of molecular function and high-resolution anatomical details

(MRI). The use of natural diminishing and capping agents reduces systemic toxicity improves radiolabelling stability and prevents nanoparticle aggregation. Compared with traditionally manufactured medicines, these bio-capped nanostructures have a longer circulatory duration, which is effective for tumor targeting and decreases immune recognition (70). Green nanocomposites made of Au, CuS or Ag combined with a carbon-derived or polymer matrix absorb near-infrared (NIR) light and transform it into ultrasonic signals for photoacoustic imaging, enabling high-contrast deep tissue imaging. The natural antioxidant properties of plant-derived compounds reduce ROS-induced deterioration during imaging, whereas biogenic coatings enhance optical absorption, biosafety and photothermal stability.

Bioactive compounds, such as polyphenols, flavonoids and proteins, form a natural organic shell around the nanoparticles. This shell stabilizes the

metallic or oxide core (Au, Ag, Fe₃O₄ and ZnO), preventing aggregation and improving optical clarity and fluorescence intensity. MRI and luminescence imaging, when used with magneto luminescent bimetallic nanocomposites, act as dual-imaging agents. Titanium dioxide and zinc oxide are ceramic-based nanocomposites that can be used for optical imaging and as contrast agents for CT scans because of their increased stability and biocompatibility (71). Titanium dioxide nanocomposites are useful for cancer diagnosis because they can target specific cancer cells. Various ceramic nanocomposites, such as carbon-based nanomaterials, including carbon nanotubes (CNTs), graphene, graphene oxide (GO) and carbon dots (CDs), can be integrated for multimodal imaging and engineered using different imaging agents because of their attractive electrical, mechanical and optical properties (72). CDs are used for their ability to emit their own fluorescent signal in fluorescence imaging technology and for their size, which is less than 10 nm and they exhibit excellent photoluminescence properties (73). Graphene and its compounds are mainly used to obtain anatomical information via MRI and optical imaging for contrast enhancement. The MXene polymer nanocomposites used in MRI applications act as contrast agents to enhance imaging and are also used as imaging agents (fluorophores, magnetic nanoparticles and radioisotopes) (65). These nanocomposites bind to molecular targets in diseased tissues, thereby improving the diagnostic accuracy. Additionally, MXene-based nanocomposites can be engineered for multimodal and responsive imaging, wherein their imaging properties can change in response to external stimuli.

Tissue Engineering

Tissue engineering requires a combination of molecular biology and material design because of the urgent need to provide temporary artificial substrates for cell seeding to facilitate the regeneration of tissues. In general, scaffolds should exhibit high porosity, appropriate pore size, biocompatibility and appropriate degradation rate (74). Nanoscale substances, such as proteins present in natural tissues, can instantly interact with cells. The fusion of molecular biology and material design in tissue engineering has resulted in short-term seeding of cell substrates. An appropriate pore size, biocompatibility and

degradation rate should be used to maintain stress and strain throughout the regeneration process, both in vitro and in vivo (64). Eco-friendly scaffolds fabricated from green-synthesized nanocomposites have emerged as a sustainable approach in tissue engineering and regenerative medicine applications. These scaffolds combine the structural advantages of biopolymers with the functional benefits of biogenic nanoparticles, resulting in biocompatible, biodegradable and biologically active materials (75). Green synthesis, which employs plant extracts, microbial metabolites, or natural polymers as reducing and stabilizing agents, eliminates toxic chemicals while introducing bioactive phytoconstituents that enhance cellular responses (76). In these scaffolds, polymeric matrix materials such as collagen, chitosan alginate, or cellulose constitute sustainable structures for the adhesion of cells and regeneration of tissues, whereas metal and metal oxide nanocomposites such as Ag, ZnO, TiO₂ and Fe₃O₄ provide mechanical enhancement, biological activity and antimicrobial protection. Biogenic capping molecules increase structural strength and prevent nanoparticle leaching by strengthening the bonds between surfaces and dispersing particles (77). Furthermore, green synthetic agents, such as anti-inflammatory and antioxidant agents, promote angiogenesis, wound recovery and cell division.

Fibrous scaffolds are a good choice for imitating the nanostructure of the extracellular matrix because they have a more ideal shape than porous scaffolds and hydrogels (78). The nanofibers resemble collagen fiber networks, with diameters varying between 50 and 500 nm. Nanofiber scaffolds have been used in tissue engineering for the heart, cartilage, bone, ligaments, skeletal muscles, skin and nerves. They are also used to transport drugs, proteins and DNA to specific locations in the body (79). Eco-friendly scaffolds can be customized for medication administration, such as dressing wounds and regenerating the skin, bone and neural tissue. Examples of future efforts include the creation of responses to stimuli and 3D-printed green nanocomposite scaffolds with regulated breakdown and biofunctional release.

Regenerative Medicine

Hydrogels constructed from biomimetic structures show high accuracy in host cell colonization. NPs

can release chemokines (80). Hence, hydrogel-synthesized nanomaterials exhibit greater biological activity than nanomaterials synthesized using other sources (81). Hydrogels are highly favourable for cell adherence, protein retention and cell expansion. Additionally, it is similar to the extracellular matrix of tissues because of its composition and structure and it has a hydrated 3D network (82). Its use in tissue engineering scaffolds has increased because of its efficiency in holding cells, biological structures and ability to change its network configuration (83). The porous structure of scaffolds allows nutrient delivery, gas penetration, cell attachment and communication (84). The use of nanomaterials from inorganic compounds in tissue engineering involves synthetic and natural polymer networks (85). Metal oxide nanoparticles, hydroxyapatite (Hap) and calcium phosphate nanoparticles are examples of organic nanomaterials made from components found in biological tissues and have potential biological activity (86). NPs improve the signal conductivity, mechanics, biological engineering and conductivity and polymeric substances increase the flexibility and stability of nanocomposite materials. Polymeric nanoparticles improve and repair myocardial infarction via conductivity.

Challenges and Limitations of Nanotechnology

New research technologies have certain limitations and challenges due to a lack of knowledge about them. As nanotechnology is considered a new technology in the field of innovation, it offers certain opportunities for researchers because of its wide range of applications in the research sector. Owing to the complexity of manufacturing, toxicity analysis, scalability, lack of standardization and real-time monitoring techniques, nanotechnology has created a large gap in research. In the medical and environmental domains, toxicity and scalability pose challenges in nanocatalysis and enzyme immobilization assays. The complexity of fabrication and short operational lifespan of nanotechnology have created limitations in biosensor nanotechnology (87). The risks of metal nanoparticles in clinical use, including their lack of durability under real-world stressors, biosafety concerns, biocompatibility, toxicity, fabrication complexity, stability, shelf life, long-term behavior

uncertainty, high production cost and environmental concerns, pose significant challenges. The risks of organ damage, immune response, poor reproducibility, moisture/enzymatic degradation, lack of chronic toxicity data, expensive synthesis methods and toxic nanoparticle residues are limitations of this method (88).

Conclusion

Sustainable nanocomposites represent a transformative advancement in biomedicine, bridging the gap between nanotechnology innovation and environmental responsibility. Despite major breakthroughs, nanotechnology remains limited by its scalability, toxicity, environmental impact and fabrication difficulties. To overcome these barriers, the proper development of biodegradable and eco-friendly nanomaterials and the standardization of nanocomposites for use in different sectors via a new protocol are required. Their adjustable physicochemical characteristics reduce biological and ecological hazards while enabling a variety of multipurpose applications, such as photothermal treatment, biosensing, targeted drug delivery, bioimaging and antibacterial activity. Both therapeutic and commercial translation are still hampered by issues such as large-scale manufacturing, long-term biocompatibility, dependability and potential cytotoxicity of eco-friendly synthesis techniques. In addition to meeting environmental regulations, the use of plant-derived phytochemicals and compounds obtained from microbes for synthesis provides the final nanocomposites with unique biological properties. Next-generation nanocomposites with improved structural integrity, physiological sensitivity and customized functional behavior should be the focus of future studies. Additionally, the creation of intelligent, multipurpose, stimuli-responsive systems that combine medicinal and detection capabilities (theranostics) is key to sustainable development of nanocomposites. Advancements in bioinspired synthesis, surface engineering and machine learning-based material design will further refine their safety, targeting efficiency and scalability. For clinical acceptability, focusing on sustainability, long-term biosafety evaluations and regulatory standardization is essential. The combination of targeted nanomedicine, hybrid

imaging methods (PET-MRI, photoacoustic imaging) and sustainable nanocomposites may provide tailored treatment regimens with minimal side effects. Real-time diagnostic and theragnostic applications may be made possible by combining green nanocomposites with smart materials such as biosensors, stimuli-responsive polymers and MXenes. To translate these compounds from the laboratory to clinical use, comprehensive *in vivo* studies and regulatory harmonization are essential. Multidisciplinary collaboration across materials science, nanotechnology, pharmacology and clinical sciences will be key to unlocking the full potential of green nanocomposites as safe, sustainable and efficient platforms for future medicinal and environmental applications.

Sustainable nanocomposites are taking shape as one of the attractive options in the intersection of nanotechnology, biomedicine and environmental sustainability, thus presenting the opportunity to solve many problems associated with the traditional nanomaterials production and application. The combination of biodegradable polymers, phyto-derivatives and microbial elements makes it possible to form nanocomposites with adjustable physicochemical properties, enhanced biocompatibility etc. Hence, green synthesis can decrease the usage of harmful substances in the process, lower the amount of generated waste and facilitate the environmental compatibility of nanomaterials production. However, the move from laboratory to practical and clinical application is hindered by several challenges such as variability of batches, insufficient control over particle size and shape, limited ability to produce nanomaterials in big quantities and inconsistency in their biological behaviour, long-term toxicity issues, environmental persistence of the materials and lack of scientific understanding of nano-bio interactions. Also, the varying synthesis methods and the method of their characterization complicate the comparison of research and create barriers from the viewpoint of acceptance of the technology by regulatory practices.

The focus of future studies should be to formulate standardized, reproducible, cost-effective and feasible green synthesis methods alongside setting globally accepted norms for the identification of physicochemical properties, assessment of toxicity, evaluation of environmental dangers and

confirmation of compliance. Special attention should be given to bioinspired synthesis, surface modification, degradation control and intelligent material design, aiming at obtaining the expected biological effect and characteristics. Involvement of stimuli-responsive polymers, biosensors, MXenes and other innovative materials can facilitate the creation of multifunctional theranostics enabling simultaneous diagnostics, specific treatment and real-time monitoring. Furthermore, machine learning-based approaches can highly speed up the process of predicting and optimizing composition, structure, toxicity and biological behaviour of nanocomposite materials, thus decreasing experimental expenditures and improving the quality of the design. Overall laboratory, clinical, pharmacokinetic and ecological studies, as well as life cycle assessment of nanocomposite materials, should be conducted in order to confirm their sustainability and translational potential.

Abbreviations

CMNCs: Ceramic Matrix Nanocomposites, CNMCF: Carbon nitride/methyl pyrophosphoride Copper/folic acid, CNTs: Carbon Nanotubes, CS: Chitosan, MMNCs: Metal Matrix Nanocomposites, MMONs: Metal and metal oxide nanocomposites, MMP: Matrix metalloproteinase, MOF: Metal Organic Framework, PCL: Polycaprolactone, PMNCs: Polymer Matrix Nanocomposites.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

Data Availability

No new datasets were generated or analyzed during the preparation of this review article. All information discussed is derived from published literature cited in the reference list.

Declaration of Artificial Intelligence (AI) Assistance

Artificial intelligence (AI)-assisted tools were used solely to improve the language, grammar and readability of the manuscript. The authors reviewed, verified and take full responsibility for the accuracy, originality and scientific content of the final manuscript.

Ethics Approval

This review article is based exclusively on previously published literature and does not involve any studies with human participants, animals, or identifiable personal data conducted by the authors. Therefore, ethics approval was not required.

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