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Green Synthesized Herbal Nanoparticles in Cancer Therapy: Emerging Trends, Current Challenges, and Future Perspectives

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Abstract

Cancer is a major global health challenge, and conventional treatments such as chemotherapy, radiotherapy, and surgery often face limitations including poor selectivity, severe side effects, and drug resistance. Green-synthesized herbal nanoparticles have emerged as a promising alternative because they combine the therapeutic potential of nanotechnology with the biocompatibility of plant-derived compounds. These nanoparticles are produced using herbal extracts that act as natural reducing and stabilizing agents, making synthesis more sustainable, cost-effective, and environmentally friendly. Compared with chemically synthesized nanocarriers, herbal nanoparticles may offer lower toxicity, improved surface functionality, and added antioxidant, anti-inflammatory, and anticancer properties. The review explains how reaction conditions such as pH, temperature, extract concentration, and reaction time influence nanoparticle size, shape, stability, and biological activity. Mechanistically, green-synthesized nanoparticles exert anticancer effects through cellular uptake, reactive oxygen species generation, mitochondrial dysfunction, DNA damage, cell cycle arrest, apoptosis activation, and inhibition of metastasis and angiogenesis. The review further discusses emerging trends such as active targeting, theranostics, combination therapy, and tumor microenvironment modulation. However, clinical translation is limited by batch variability, scalability issues, long-term safety concerns, and regulatory challenges. Future progress will likely depend on standardized synthesis, improved in vivo studies, and the integration of artificial intelligence and personalized medicine to develop reproducible and clinically useful nanoplatforms for cancer therapy.

Introduction

Cancer remains one of the most pressing global health challenges, with a continuously increasing burden across both developed and developing nations (Hussain et al., 2018). According to recent international epidemiological estimates, cancer contributes substantially to morbidity and mortality worldwide, reflecting its complex etiology, late diagnosis in many populations, and limited success of conventional therapeutic strategies (Lebech et al., 2017). Although chemotherapy, radiotherapy, and surgery remain the mainstays of cancer

management, these approaches are often constrained by serious limitations (Lambregts et al., 2011). Conventional chemotherapeutic agents frequently exhibit poor selectivity, leading to off-target toxicity in healthy tissues, which results in adverse effects such as myelosuppression, hepatotoxicity, nephrotoxicity, and cardiotoxicity (Talerman et al., 1980). In addition, the emergence of multidrug resistance, primarily through altered drug efflux, enhanced DNA repair, and evasion of apoptosis, significantly reduces therapeutic efficacy and contributes to treatment failure (Xie et al., 2020). These challenges have intensified the search for more precise, safer, and biologically compatible anticancer strategies (Mauro et al., 2020). In this context, nanomedicine has emerged as a transformative platform in oncology. Nanotechnology enables the design of nanoscale drug carriers capable of improving solubility, stability, circulation time, and intracellular delivery of therapeutic agents (Ma et al., 2012). One of the most widely discussed mechanisms supporting nanoparticle accumulation in tumors is the Enhanced Permeability and Retention effect, which arises from the abnormal vascular architecture and deficient lymphatic drainage of malignant tissues (Shi et al., 2021). This phenomenon allows nanoparticles to preferentially localize within tumor sites, thereby enhancing site-specific drug delivery while reducing systemic exposure. Beyond passive targeting, nanocarriers can also be engineered for active targeting, controlled release, and multimodal therapy, making them highly attractive for precision oncology (Pippa et al., 2017). Despite these advantages, the clinical translation of many synthetic nanocarriers remains limited by toxicity concerns, poor biocompatibility, and complex fabrication requirements (Madani et al., 2021). These limitations have stimulated a paradigm shift toward green nanotechnology, particularly green synthesis approaches that employ biological resources such as plant extracts, phytochemicals, and other natural reducing and stabilizing agents (Senapati et al., 2018). Compared with conventional chemical and physical methods, green synthesis offers a more sustainable, cost-effective, and environmentally benign route for nanoparticle production. Importantly, herbal-mediated nanoparticles often possess intrinsic bioactive compounds on their surface, which may contribute additional antioxidant, anti-inflammatory, and anticancer properties (Zhao et al., 2017). This synergy between nanomaterial engineering and phytochemistry creates a promising platform for safer and more effective cancer therapy. The use of biocompatible reagents also reduces the risk of residual toxic contaminants, thereby improving the translational potential of these nanosystems in biomedical applications (Thambiraj et al., 2018). The present review focuses on the emerging role of green-synthesized herbal nanoparticles in cancer therapy and aims to provide a comprehensive analysis of their therapeutic relevance, technological progress, and translational challenges (Patel et al., 2017). Unlike many existing reviews that discuss either nanomedicine in general or green synthesis in isolation, this article integrates both fields with a specific emphasis on herbal-based nanoparticle design for oncology applications (Qi et al., 2019). It critically examines recent advances in synthesis strategies, physicochemical characterization, anticancer mechanisms, and preclinical performance, while also addressing key barriers such as scalability, reproducibility, regulatory concerns, and long-term safety (Kalimuthu et al., 2018). By combining current knowledge with future research directions, this review highlights the novelty and scientific significance of green-synthesized herbal nanoparticles as a next-generation platform for cancer therapy (Kashyap et al., 2021). This figure1 presents the major biomedical and environmental applications of bio-

synthesized nanoparticles along with their diverse structural morphologies. The nanoparticles exhibit significant antioxidant, antimicrobial, anti-inflammatory, and anticancer activities, while also being employed in bioremediation, targeted drug delivery, biomolecule labeling, and cosmetic and medical device applications.

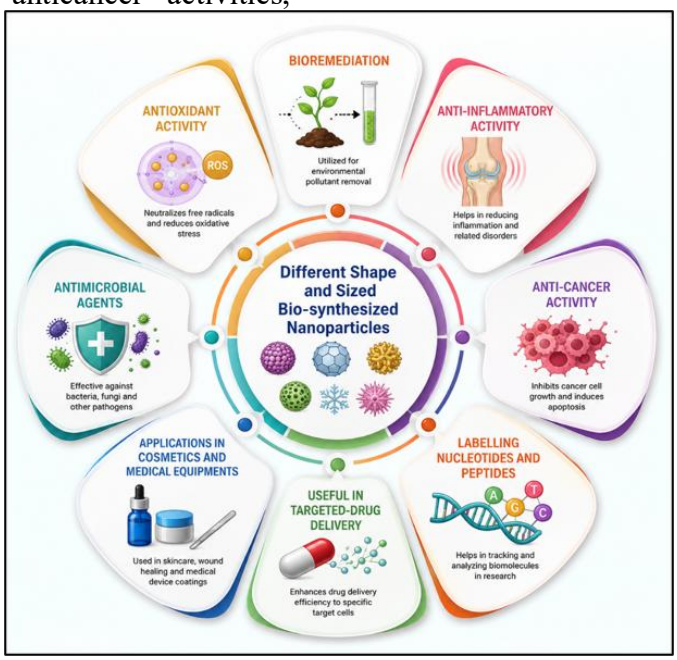

Figure 1. Diverse Biomedical and Environmental Applications of Bio-Synthesized Nanoparticles

Principles and Mechanisms of Green Synthesis using Herbal Extracts

Green synthesis of nanoparticles using herbal extracts is based on the ability of plant-derived biomolecules to simultaneously reduce metal ions and stabilize the newly formed nanostructures. In this biogenic approach, aqueous or hydroalcoholic extracts obtained from leaves, roots, bark, seeds, or flowers contain a complex mixture of secondary metabolites that function as natural bioreducing and capping agents (Tuasha et al., 2018). This strategy is considered superior to conventional chemical synthesis because it eliminates the need for hazardous reducing agents, minimizes toxic by-products, and improves the biocompatibility of the final nanomaterial (Khan et al., 2021). The process is therefore highly relevant for biomedical applications, particularly in cancer therapy, where safety and surface functionality are critical (Bhatt et al., 2025). The physicochemical features of the synthesized nanoparticles are strongly influenced by reaction conditions, and optimization is essential for obtaining reproducible products with desired biomedical properties (Saiful Yazan et al., 2016). pH is one of the most critical factors because it affects ionization of phytochemicals, metal precursor reactivity, and nucleation kinetics (Sargazi et al., 2020). Under alkaline conditions, deprotonation of hydroxyl groups often enhances electron donation and accelerates particle formation, whereas acidic conditions may slow reduction and alter morphology (Bhatt, Singh, et al., 2025). Temperature also plays a decisive role by modulating reaction rate, nucleation density, and crystal growth; higher temperatures generally promote faster synthesis and smaller particle size up to an optimal limit, beyond which instability or aggregation may occur (Hayat et al., 2021). Similarly, extract concentration determines the availability of reducing and capping

molecules, influencing particle yield, polydispersity, and colloidal stability (Seca & Pinto, 2018). Reaction time further governs the extent of reduction and maturation of nanoparticles, with insufficient time producing incomplete synthesis and excessive time sometimes leading to secondary growth or aggregation. Therefore, systematic optimization of these parameters is necessary to produce nanoparticles with controlled size, shape, and functional performance (Hua et al., 2018). Comprehensive characterization is mandatory for any high-quality nanomaterials study, especially in Q1-level research. UV-Visible spectroscopy is used to confirm nanoparticle formation by detecting surface plasmon resonance, while Transmission Electron Microscopy (TEM) and High-Resolution TEM (HRTEM) provide direct visualization of morphology, size, and lattice fringes (Sadi & Shahidi Bonjar, 2017). X-Ray Diffraction (XRD) identifies crystalline phase, purity, and average crystallite size. Fourier Transform Infrared Spectroscopy (FTIR) reveals the functional groups involved in reduction and stabilization, thereby confirming phytochemical capping. Dynamic Light Scattering (DLS) measures hydrodynamic size distribution and polydispersity, whereas Zeta Potential assesses surface charge and predicts colloidal stability. X-Ray Photoelectron Spectroscopy (XPS) is especially useful for determining elemental composition, oxidation states, and surface chemistry (Hamidian et al., 2022).

Table 1. Transcriptomic Alterations Induced by Gold and Silver Nanoparticles in Experimental Model Organisms

Nanoparticle Type	**Exposure Dose**	**Experimental Model and Exposure Conditions**	**Developmental Stage at RNA Isolation**	**Transcriptomic Analysis Technique**	**Expression Pattern**	**Reference**
Citrate-functionalized gold nanoparticles (AuNPs)	5.9 mg/L	*Caenorhabditis elegans* L3 larvae exposed for 12 h	L3 larvae	Affymetrix *C. elegans* GeneChip	Predominantly upregulated	(Hua et al., 2018)
Uncoated gold nanoparticles (AuNPs)	0.1 and 0.2 mg/L (MUA/Au ratios: 0.5 and 3)	*C. elegans* embryos exposed for 72 h	Adult worms	Affymetrix *C. elegans* GeneChip	Both upregulated and downregulated genes	(Hayat et al., 2021)
Citrate-capped gold nanoparticles (AuNPs)	20 mg/L	Adult zebrafish liver following 96 h exposure	Adults	Affymetrix GeneChip Zebrafish Genome Array	Mixed upregulation and downregulation	(Khan et al., 2021)

Silver nanoparticles (AgNPs)	10 µg/mL	*C. elegans* exposed from L1 larval stage to adulthood for 72 h	Adults	RNA sequencing (*C. elegans*)	Both induced and suppressed genes	(Qi et al., 2019)
Silver nanoparticles (AgNPs)	50 µg/L	Adult zebrafish gill tissues exposed for 28 days	Adults	Agilent 4×44K Zebrafish Microarray	Over-represented transcripts	
Bare silver nanoparticles (AgNPs)	0.01 mg/L	Zebrafish larvae (6 days post-fertilization) exposed for 15 days	Larvae	Agilent Zebrafish (V3) Oligonucleotide Microarray	Upregulated and downregulated genes	(Patel et al., 2017)
Citrate-coated silver nanoparticles (AgNPs)	0.4 mg/L	Zebrafish embryos (24 h post-fertilization) exposed for 24 h	Embryos	Agilent 4×44K Zebrafish Microarray	Predominantly downregulated	(Senapati et al., 2018)

Classification of Green Synthesized Nanoparticles in Oncology

Green-synthesized nanoparticles are broadly classified according to their core composition and therapeutic utility in cancer nanomedicine (Shu et al., 2020). Among them, metallic nanoparticles, especially silver nanoparticles (AgNPs) and gold nanoparticles (AuNPs), are the most extensively investigated because of their strong surface plasmon resonance (SPR), ease of functionalization, and prominent anticancer potential (Sati et al., 2025). SPR is an optical phenomenon generated by collective oscillation of conduction electrons on the nanoparticle surface when exposed to incident light (Ahmad et al., 2024). In oncology, this property enhances photothermal conversion, imaging contrast, and drug delivery efficiency, thereby improving cancer cell targeting and therapeutic response (Rupanshi et al., 2025). Green-synthesized AgNPs and AuNPs have also shown cytotoxicity toward malignant cells while maintaining relatively better compatibility with normal tissues in several preclinical studies (Li et al., 2024).

A second major category includes metal oxide nanoparticles, such as zinc oxide nanoparticles (ZnONPs), iron oxide nanoparticles (IONPs), and copper oxide nanoparticles (CuONPs). These nanomaterials are valued for their redox activity, catalytic behavior, and ability to induce apoptosis through oxidative stress, mitochondrial dysfunction, and DNA damage in tumor cells (Magar et al., 2024). Among them, IONPs are particularly important because of their magnetic properties, which make them suitable for magnetic resonance imaging and hyperthermia-based cancer therapy. In hyperthermia, an external alternating magnetic field causes IONPs to generate localized heat, leading to selective tumor cell death and improved sensitivity to chemotherapeutic agents (Falke et al.,

2024). Green synthesis of these oxides improves surface biocompatibility and reduces residual toxicity associated with conventional fabrication routes (Gherasim et al., 2020). Another important subgroup is herbal nanoformulations, in which pure phytocompounds such as curcumin and paclitaxel are encapsulated into biopolymeric nanoparticles like chitosan and alginate (Bhosale et al., 2025). These formulations are designed to overcome the major pharmacological limitations of natural products, including poor aqueous solubility, rapid metabolism, low bioavailability, and limited tumor accumulation. Encapsulation improves pharmacokinetic performance, protects the active compound from premature degradation, and enables sustained or stimuli-responsive release at the tumor site (Li et al., 2001). Therefore, herbal nanoformulations represent a clinically relevant bridge between natural product chemistry and targeted nanotherapy (Bhushan et al., 2017).

Table 2. Plant-Derived Green-Synthesized Nanoparticles and Their Anticancer Mechanisms Against Different Cancer Cell Lines

Plant Source	**Characterization Techniques**	**In Vitro Cancer Model**	**Proposed Anticancer Mechanism**	**Reference**
Pinus roxburghii	UV–Vis spectroscopy, FTIR, XRD, EDX, SAED, FESEM, HRTEM	A549 (lung adenocarcinoma), PC-3 (prostate carcinoma)	Promoted mitochondria-mediated apoptosis through ROS generation, mitochondrial membrane depolarization, DNA damage, cell cycle arrest, and caspase-3 activation.	(Gherasim et al., 2020)
Phyllanthus emblica	UV–Vis, TEM, FTIR, SEM-EDX, XRD, DLS, Zeta potential, TGA, HRTEM	A549 (lung cancer)	Triggered oxidative stress by elevating intracellular ROS, resulting in DNA damage and apoptotic cell death.	(Ahmad et al., 2024)
Cynara scolymus (Artichoke)	UV–Vis, FTIR, SEM, DLS, EDX	MCF-7 (breast cancer)	Suppressed cancer cell migration by upregulating Bax while downregulating the anti-apoptotic Bcl-2 protein.	(Sati et al., 2025)
Moringa oleifera	XRD, FTIR, HRTEM, EDX, PL	HT-29 (human colorectal cancer)	Exhibited cytotoxic effects primarily through induction of programmed cell death (apoptosis).	(Rupanshi et al., 2025)

Tamarindus indica	UV–Vis, FTIR, EDS, SEM, TEM	MCF-7 (breast cancer)	Induced apoptotic cell death, thereby reducing cancer cell viability.	(Kashyap et al., 2021)
Achillea biebersteinii	UV–Vis, FTIR, TEM, DLS, EDX	MCF-7 (breast cancer)	Activated caspase-dependent apoptosis accompanied by increased Bax and decreased Bcl-2 expression.	(Lebech et al., 2017)
Punica granatum	UV–Vis, FTIR, DLS, EDX, SEM, XRD	HeLa (cervical cancer)	Significantly decreased cellular viability, indicating pronounced cytotoxic activity.	(Falke et al., 2024)
Gloriosa superba	UV–Vis, HRTEM, EDX, DLS, XRD	MCF-7 (breast cancer)	Interacted with cellular DNA and proteins, leading to enhanced cytotoxicity and apoptotic cell death.	(Roco et al., 1999)
Teucrium polium	UV–Vis, FTIR, SEM, XRD	MNK45 (gastric cancer)	Displayed potent cytotoxicity by promoting apoptotic pathways in cancer cells.	(Lee et al., 2010)
Melia dubia	UV–Vis, XRD, EDS, SEM	KB (human oral carcinoma)	Demonstrated significant antiproliferative activity against KB cancer cells.	(Chang et al., 1999)
Cucumis prophetarum	UV–Vis, FTIR, DLS, XRD, SEM, EDX	A549, MDA-MB-231, HepG2, MCF-7	Exhibited broad-spectrum antiproliferative activity across multiple human cancer cell lines.	(Konop et al., 2016)
Rosa damascena	UV–Vis, FTIR, DLS, SEM, HRTEM, XRD, EDX	A549 (lung adenocarcinoma)	Promoted apoptosis through ROS overproduction and disruption of mitochondrial membrane integrity.	(Li et al., 2001)

Mechanisms of Anticancer Activity

Green-synthesized nanoparticles exert anticancer effects through a multifactorial and highly coordinated set of cellular and molecular mechanisms (Konop et al., 2016). After administration, these nanostructures are internalized by cancer cells mainly through endocytosis, including clathrin-mediated, caveolae-mediated, and macropinocytotic pathways; importantly,

the phytochemical capping layer derived from herbal extracts can enhance membrane interaction, improve colloidal stability, and modulate surface charge, thereby influencing cellular uptake and facilitating endosomal escape (Barillo et al., 2014). Once inside the cell, many green nanoparticles induce a surge in reactive oxygen species, which is considered one of the principal apoptotic triggers in tumor cells. Excessive ROS overwhelms the endogenous antioxidant defense system, causing oxidative stress, lipid peroxidation, protein oxidation, and loss of redox homeostasis, ultimately driving malignant cells toward programmed cell death (Clement & Jarrett, 1994). A key downstream event of this oxidative injury is mitochondrial dysfunction, characterized by collapse of the mitochondrial membrane potential, disruption of electron transport, and release of cytochrome c into the cytosol (Alexander et al., 2009). Cytochrome c then activates the intrinsic apoptotic cascade, leading to caspase activation and irreversible cellular demise (Medici et al., 2019). In parallel, some green nanoparticles interact directly with nuclear DNA or indirectly generate DNA lesions through oxidative stress, resulting in genotoxicity, impaired replication, and activation of DNA damage checkpoints (Quadri et al., 2025). This often culminates in cell cycle arrest at the G0/G1, S, or G2/M phase, thereby preventing proliferation and giving the cell time to undergo repair or apoptosis (You et al., 2012). At the molecular level, green nanoparticles modulate apoptotic signaling by upregulating pro-apoptotic proteins such as Bax and the executioner and initiator caspases, particularly caspase-3 and caspase-9, while downregulating anti-apoptotic proteins such as Bcl-2. This shift in the Bax/Bcl-2 ratio favors mitochondrial outer membrane permeabilization and amplifies the apoptotic response (Castellano et al., 2007). In addition to direct cytotoxicity, these nanomaterials also exhibit anti-angiogenic and anti-metastatic properties (Chen & Schluesener, 2008). They suppress the expression of vascular endothelial growth factor, thereby limiting neovascularization required for tumor growth, and inhibit matrix metalloproteinases, which are essential for extracellular matrix degradation, invasion, and metastatic dissemination (Fong et al., 2005). Collectively, these mechanisms make green-synthesized nanoparticles promising multifunctional agents for targeted cancer therapy, combining oxidative stress induction, mitochondrial disruption, genomic injury, apoptosis activation, and suppression of tumor progression (Sunilbhai et al., 2022).

Emerging Trends in Green Nanotherapy

Emerging trends in green nanotherapy are reshaping modern oncology by moving beyond simple drug carriage toward highly selective, multifunctional, and biologically intelligent treatment systems (Yang et al., 2019). One of the most important advances is active targeted delivery, in which green-synthesized nanoparticles are surface-functionalized with ligands such as aptamers, monoclonal antibodies, peptides, or small molecules like folic acid to recognize overexpressed receptors on tumor cells (Stephen et al., 2020). This receptor-mediated targeting improves cellular selectivity, enhances intracellular accumulation, and reduces systemic toxicity by concentrating the therapeutic payload at the diseased site rather than in healthy organs (Phan & Haes, 2019). In parallel, theranostics has emerged as a powerful strategy that integrates diagnosis and therapy within a single nanoplatform (Buerki-Thurnherr et al., 2018). For example, green-synthesized iron oxide nanoparticles can serve as magnetic resonance imaging contrast agents while simultaneously enabling hyperthermia, targeted drug delivery, or magnetic field-guided therapy (Abreu et al., 2021). This dual functionality allows real-time monitoring of biodistribution, tumor

response, and treatment efficacy, making precision oncology more feasible and clinically informative (Ramos-Gomes et al., 2020). Another major trend is the development of synergistic combination therapies, where green nanoparticles are used alongside conventional or energy-based modalities to amplify anticancer efficacy. In chemoradiotherapy, nanoparticles may act as radiosensitizers by increasing intracellular oxidative stress, disrupting DNA repair pathways, and enhancing radiation-induced cytotoxicity (Nethi et al., 2020). Likewise, in photothermal therapy (PTT) and photodynamic therapy (PDT), green nanoparticles can convert near-infrared light into localized heat or generate reactive oxygen species upon irradiation, thereby producing highly selective tumor ablation with minimal collateral damage (Gao et al., 2016). These combinations are particularly valuable because they can overcome resistance mechanisms that limit the effectiveness of single-agent treatment and may allow dose reduction of toxic chemotherapeutics. Importantly, green synthesis adds an additional layer of safety and sustainability to these platforms by minimizing hazardous residues and improving biocompatibility (Peng & Liang, 2019). A further frontier in green nanotherapy is the modulation of the tumor microenvironment (TME), which is increasingly recognized as a key determinant of cancer progression, immune evasion, and therapeutic resistance. Green nanoparticles can be engineered to reprogram tumor-associated macrophages from a pro-tumorigenic M2 phenotype toward an anti-tumorigenic M1 phenotype, thereby strengthening local immune surveillance and suppressing tumor growth (Rostami & Sazgarnia, 2019). They may also help address tumor hypoxia, a condition that drives angiogenesis, metastasis, and resistance to radiotherapy and PDT. By delivering oxygen-generating agents, hypoxia-responsive drugs, or catalytic components that modulate redox balance, green nanoplatforms can improve oxygenation and restore treatment sensitivity (McNeilly et al., 2021).

Current Challenges and Translational Bottlenecks

Current challenges and translational bottlenecks remain the major barrier between promising laboratory findings and clinical application of green-synthesized nanoparticles in oncology. One of the most critical issues is batch-to-batch variability, which arises because plant extracts are inherently complex and their phytochemical composition changes with geographical origin, seasonal variation, soil conditions, harvesting time, extraction solvent, and even plant species or cultivar (Gomes et al., 2021). Since these phytoconstituents act as both reducing and stabilizing agents, any fluctuation in their concentration can alter nanoparticle size, morphology, surface charge, crystallinity, and biological activity, making reproducibility difficult (Pokropivny & Skorokhod, 2007). A second major concern is long-term nanotoxicity and bioaccumulation, as many studies remain limited to short-term in vitro assays or preliminary animal experiments. There is still insufficient understanding of how these nanoparticles behave in vivo over time, including their absorption, distribution, metabolism, excretion, organ retention, and possible accumulation in the liver, spleen, kidneys, or brain (Goodilin et al., 2019). The absence of robust pharmacokinetic and pharmacodynamic profiling makes it difficult to predict chronic toxicity, immune interactions, or delayed adverse effects, especially for repeated-dose cancer therapy. Another significant bottleneck is scalability and manufacturing, because most green synthesis protocols are optimized at milligram or small batch laboratory scale, where reaction conditions can be tightly controlled (Fang et al., 2019). However, translation to industrial production requires uniform mixing, consistent extract quality,

sterility, process automation, and cost-effective purification, all of which are difficult to maintain when moving to pilot-scale reactors or bioreactor systems. The transition from bench-top synthesis to large-scale manufacturing often leads to changes in particle characteristics, yield, and reproducibility. Finally, regulatory hurdles continue to slow clinical translation because current FDA and EMA frameworks do not always clearly address nanomaterials produced through complex biological routes (Kraegeloh et al., 2018). Herbal-mediated nanoparticles occupy a gray zone between conventional nanomedicine and biologically derived products, creating uncertainty about acceptable characterization standards, toxicity endpoints, quality control requirements, and batch release criteria. In the absence of harmonized international guidelines, researchers face difficulties in designing regulatory-compliant preclinical studies and obtaining approval for clinical testing. Therefore, solving these translational bottlenecks will require standardized plant sourcing, rigorous physicochemical characterization, validated in vivo safety studies, scalable manufacturing platforms, and clearer regulatory pathways to ensure that green-synthesized nanoparticles can move safely and effectively toward cancer therapy (Leza et al., 2020).

Future Perspectives

The future of green nanotherapy is expected to be shaped by the convergence of computational science, precision medicine, and highly standardized synthesis platforms. One of the most promising directions is the integration of artificial intelligence and machine learning into nanoparticle design and optimization. By using computational biology, predictive modeling, and data-driven algorithms, researchers can estimate the interactions between phytoconstituents and metal ions, identify the most effective reducing and capping agents, and optimize critical synthesis variables such as pH, temperature, reaction time, and extract concentration. This approach can substantially reduce trial-and-error experimentation, improve reproducibility, and accelerate the development of nanoparticles with controlled size, morphology, stability, and anticancer efficacy. In parallel, personalized nanomedicine is likely to become a defining feature of next-generation cancer therapy. Since tumors differ widely among patients in terms of receptor expression, mutational profile, redox status, and microenvironmental characteristics, future green nanoparticles may be tailored according to patient-specific biomarkers. Such customization could allow receptor-targeted delivery, biomarker-responsive release, and individualized dosing strategies, thereby improving therapeutic selectivity while minimizing toxicity. This precision-oriented framework is especially important in oncology, where interpatient variability often determines treatment outcome. Another important evolution is Green Synthesis 2.0, which refers to the transition from crude plant extracts toward purified phytochemical-mediated nanoparticle synthesis. Although crude extracts are attractive because they are cheap and readily available, their compositional variability can compromise batch consistency, mechanistic clarity, and regulatory acceptance. Purified compounds such as flavonoids, polyphenols, terpenoids, or alkaloids can provide better control over reaction chemistry, improve reproducibility, and facilitate standardization of physicochemical properties. This shift is likely to be essential for clinical translation, because regulatory agencies require robust quality control, defined composition, and scalable manufacturing processes. Collectively, these future perspectives indicate that the field is moving from empiric green fabrication toward intelligent, personalized, and regulation-ready nanoplatforms. The

next generation of green nanoparticles will probably not only be environmentally sustainable but also computationally optimized, biomarker-guided, and clinically translatable, thereby bridging the gap between laboratory innovation and real-world cancer care.

Conclusions

Green-synthesized herbal nanoparticles represent a highly promising and innovative approach in modern cancer therapy. By integrating nanotechnology with plant-derived bioactive compounds, they offer a safer, more sustainable, and potentially more effective alternative to conventional anticancer strategies. Their green fabrication avoids hazardous chemicals, reduces toxic residues, and improves biocompatibility, which is especially valuable in biomedical applications. These nanoparticles not only serve as drug carriers but also contribute intrinsic anticancer activity through antioxidant, pro-apoptotic, anti-inflammatory, and anti-metastatic effects. Their ability to generate reactive oxygen species, disrupt mitochondrial function, induce DNA damage, and trigger apoptosis makes them powerful candidates for selective tumor cell killing. In addition, advances in active targeting, theranostics, combination therapy, and tumor microenvironment modulation have expanded their potential far beyond simple drug delivery. However, despite strong preclinical evidence, several challenges remain before clinical application becomes routine. These include variability in plant extracts, poor batch-to-batch reproducibility, limited large-scale manufacturing, insufficient long-term safety data, and unclear regulatory pathways. Therefore, future research must focus on standardized synthesis protocols, rigorous physicochemical and biological characterization, comprehensive in vivo toxicological studies, and scalable production methods. The integration of artificial intelligence, biomarker-based personalization, and purified phytochemical-mediated synthesis may further improve precision, reproducibility, and translational success. Overall, green-synthesized herbal nanoparticles hold great promise as next-generation nanotherapeutics that can bridge the gap between natural product chemistry and advanced oncology, offering hope for more targeted, effective, and less toxic cancer treatment.

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