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Biotechnological innovations in nano-medicines: potential of using medicinal plants in oncology

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ABSTRACT

Cancer continues to represent a formidable global health challenge, underscoring the urgent need for the development of cost-effective therapeutic strategies. The design of nanomedicines with precise targeting capability and enhanced bioavailability opens new opportunities in cancer therapy. Among all the nanoplatforms, plant-derived nanoparticles have attracted more attention because of their excellent biodegradability, biocompatibility, and low cytotoxicity. Bio-inspired nanocarriers use the abundance of phytochemical diversity present in medicinal plants to target multi-pathway signaling and counteract resistance mechanisms of cancer. The utilization of bioactive compounds from plants, including flavonoids, alkaloids, and polyphenols, leads to increased anti-cancer activity with fewer side effects. While these features are promising, there are several challenges to be overcome for successful clinical outcomes (stability, large-scale production, controlled drug release, etc.). Herein, different innovations are discussed related to plant-based nanomedicines, particularly in the context of sustainable and effective anti-cancer therapy. The ability of plant-based nanoparticles to modulate multiple cellular pathways represents a key advantage, as it can disrupt cancer progression and resistance mechanisms. What makes phytochemicals ideal candidates for targeted cancer therapies is that they naturally possess unique properties such as antioxidant, anti-inflammatory, and pro-apoptotic. Furthermore, Inhibition of tumor growth, suppression of metastasis, and enhanced immune responses, which will contribute to comprehensive cancer control, are achievable by the use of these plant-based bioactive compounds. Furthermore, the inherent biodegradability of plant-derived nanoparticles minimizes long-term toxicity concerns, aligning with the principles of sustainable medicine. Integrating nanotechnology with nature-originated therapeutic agents for producing plant-derived nanomedicines shows huge prospects in reshaping cancer treatment paradigms. This review highlights the confluence of phytochemicals and nanotechnology, focusing on novel formulations that target precision and patient care in cancer.

Highlights

- Plant-derived nanomedicines offer safe, biocompatible cancer therapy.
- Phytochemicals in nanoparticles target multiple cancer pathways effectively.
- PDNPs show natural biodegradability, reducing chronic toxicity risks.
- Plant nanovesicles overcome drug resistance and modulate tumor immunity.
- Sustainable plant sources enable green, scalable nanomedicine production.

1. Introduction

Recently, plant-derived nanomedicines (PDNs), which provide safety, biocompatibility, and therapeutic efficacy, have received great attention due to their potential in oncology and cancer therapy. These nanoparticles improve the stability, solubility, and targeted delivery of bioactive

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plant compounds such as curcumin, resveratrol, and epigallocatechin gallate (EGCG), thereby enhancing their anticancer activity (Pandey et al., 2025). PDNs can be composed of liposomes, polymeric carriers, or gold nanoparticles, which allow controlled release, lower toxicity, and enhanced treatment efficiency (Voliani et al., 2012). Plant-based nanomedicines also have the potential to be used in immunotherapy, photothermal therapy, and diagnostic imaging, which is a novel approach for improving the outcomes of cancer treatment. Polymeric nanoparticles are polymers synthesized from natural plant compounds such as polyphenols and flavonoids, which have several advantages over synthetic types, such as natural biodegradability, biocompatibility, safer degradation into non-toxic metabolites, and reduced chronic toxicity (Sathish et al., 2016). These nanoparticles also have antioxidant and anti-inflammatory properties, providing great potential for a sustainable, low-cost, green drug delivery system in cancer therapy (Lima et al., 2021). In addition, the functionalization of these nanoparticles with targeting agents enhances their specificity towards cancer cells, thus reducing the damage to healthy tissues and unwanted side effects. Numerous challenges persist in the development of plant-based nanomedicines, largely due to the inherent complexity of plant extracts, which comprise diverse bioactive constituents such as polyphenols, flavonoids, and terpenoids. Compounds derived from plants have high variability; as a result, they can be difficult to reproduce. Furthermore, being vulnerable to degradation in the formulation process is another drawback, which ultimately results in changes to the efficacy of the final formulation. Novel strategies such as protective nano-coating, green synthesis methodologies, and continuous-flow systems are needed to resolve and address these challenges (Cristaldi et al., 2020).

Enhancing bioavailability and ensuring specific targeted delivery are essential for improving therapeutic effects. Nanoparticles functionalized with ligands hold promise as solutions that may enhance the specificity of these therapies (Jahan et al., 2017).

While these benefits exist, the toxicological studies and regulatory barriers must be overcome; the generation of biodegradable materials, proper testing for safety, and regulatory guidelines will all have to be established and validated. For cancer therapy, plant-derived nanoparticles such as plant-derived nanovesicles (PDNVs) can target vital tumor progression pathways and hence avoid multidrug resistance. Finally, PDNVs with better stability, solubility, and delivery could encapsulate phytochemicals, such as quercetin and curcumin, to overcome resistance mechanisms and enhance immunotherapy outcomes (Liu et al., 2024; Cui et al., 2024).

These developments, together with the arrival and utilization of PDNs alongside radiotherapy, provide a sustainable, high-efficiency strategy to target tumors and enhance patient care outcomes. Phytochemicals are recognized as important candidates in the development of novel therapeutic agents because of their great potential utility in cancer, neurodegenerative diseases, and infectious disease management (Swetha et al., 2022).

2. Advancing cancer therapy through nanomedicines

2.1. Plant-derived nanomedicines for targeted and enhanced cancer therapy

Engineered at the nanoscale, nanomedicines are therapeutic systems meant to improve the pharmacokinetics, bioavailability, and targeted administration of pharmaceuticals by precisely interacting at the cellular and molecular levels, therefore allowing better treatment efficacy and lower adverse effects (Waheed et al., 2022).

Nanomedicines that are derived from different plant sources represent a unique, safe, effective, and biocompatible drug delivery system for the treatment of cancer (Jahangirian et al., 2017). Various types of cancer nanomedicines are shown in Figure 1, which implement bioactive compounds derived from plants such as polyphenols, alkaloids, terpenoids, and flavonoids that have anticancer properties (Esmeeta et al., 2022). However, the bioavailability and cellular uptake of the desired bioactive compounds are low due to rapid degradation; by using nanotechnology techniques, overcoming these limitations will be possible. This process will happen through the use of nanoscale carriers such as liposomes, polymeric nanoparticles, gold nanoparticles, and solid lipid nanoparticles for encapsulating the mentioned plant-derived bioactive agents. The stability, solubility, and site-specific delivery of plant-derived agents to tumor locations will be enhanced by these nanoparticles, while systemic adverse effects will be limited (Patel et al., 2024). For example, nanoparticles that are loaded with Curcumin have shown enhanced therapeutic efficacy against various cancers, including breast, lung, and colon cancers (Yallapu et al., 2010). In other words, the efficiency will be increased because of the improved solubility of curcumin. Similarly, encapsulated resveratrol and epigallocatechin gallate (EGCG) in nanoparticles have shown significant improvements in their bioavailability encapsulated resveratrol and epigallocatechin gallate (EGCG) in nanoparticles have shown significant improvements in their bioavailability and anticancer activity (Yan et al., 2019).

Moreover, one of the key benefits of plant-based nanomedicines is the ability to deliver targeted therapy by using the tumor microenvironment (Zhang et al., 2017). One of the considerable advantages of using nanoparticles is that they can be customized to respond to specific acidic pH, redox gradients, or upregulated and increased enzyme expression that are prevalent at tumor sites (Tang et al., 2018). Gold nanoparticles conjugated with the phytochemicals derived from the plants exhibit selective cytotoxicity toward cancer cells without affecting normal tissues. Examples of these phytochemicals are quercetin and berberine (Sargazi et al., 2022). These nanoparticles enable drugs to be accumulated more effectively within the tumors via "Enhanced Permeability and Retention" (EPR) effects (Shinde et al., 2022). Furthermore, active components from plants can frequently have antioxidant and anti-inflammatory effects, reducing the risk of side effects induced by chemotherapy (Aravindaram et al., 2010). Recent studies have explored the use of plant-based nanosystems for co-delivery of multiple agents, combining phytochemicals with conventional chemotherapeutics to

achieve synergistic anticancer effects and overcome multidrug resistance (MDR) (Eftekhari et al., 2019).

Plant-derived nanomedicines, such as plant extracellular vesicles (PEVs), are fundamentally different from synthetic nanocarriers because they naturally integrate inherent bioactive components like lipids, proteins, and small RNAs with their delivery function. In contrast, synthetic systems, including liposomes, lipid nanoparticles (LNPs), and polymeric nanoparticles, mainly act as customizable carriers that are largely pharmacologically inactive. Research findings show that PEVs demonstrate excellent biocompatibility and minimal immune response while they remain stable in the digestive system, making them suitable for oral administration and cancer treatment applications. The production of PEVs faces challenges because different sources of materials, different types of cargo, and insufficient Good Manufacturing Practice (GMP) standards make it difficult to achieve large-scale manufacturing. In contrast, scientists now have the ability to create synthetic nanocarriers through which they can precisely control their size, binding capabilities, and drug release timing, but their progress remains limited, as proteins bind to them and the body clears them quickly while they fail to reach tumor sites effectively. (Zhang et al., 2025; Hoang et al., 2025).

Recent advances in plant-based nanomedicine are increasingly being linked to the sustainable agricultural production of medicinal plants, highlighting a closed-loop "agriculture–nanomedicine–environment" framework. Medicinal plants serve not only as sources of bioactive compounds for nanoparticle synthesis but also as renewable biomass (e.g., cellulose, lignin, and polyphenols), enabling the development of biodegradable nanomaterials that align with green chemistry principles. Importantly, the integration of nanotechnology into agricultural systems through nano-fertilizers, nano-pesticides, and biosensors enhances crop productivity, improves nutrient-use efficiency, and reduces excessive agrochemical release, thereby minimizing soil and water pollution (Zeng et al., 2025; Guo et al., 2025).

In parallel, plant-mediated nanoparticles have been shown to support precision agriculture by improving plant growth, stress tolerance, and disease resistance while maintaining ecological balance. This dual functionality establishes medicinal plant cultivation as both a source of therapeutic nanomaterials and a platform for environmentally sustainable agricultural practices. Consequently, the convergence of plant-based nanotechnology with agricultural biotechnology not only ensures a consistent and scalable supply of medicinal raw materials but also contributes to reduced environmental burden, resource efficiency, and the advancement of sustainable healthcare systems (Lakhani et al., 2025; Karnwal et al., 2024).

Table 1. The comparative table below represents different Nano-medicines and their applications, while mentioning the plant sources and chemical constituents. Accordingly, the different types of Nano-medicines, their source and applications can be compared together.

Nanomedicine Type	Plant Source	Active Component / Nanoparticle Composition	Application	Reference
Selenium nanoparticles	Ribes nigrum (black currant)	Selenium	Hypolipidemic and antioxidant activity in galactose-treated rats	(Al-Kurdy, 2020)
Silver nanoparticles	Nigella sativa	Silver	Reduction of triglycerides and LDL-C; antioxidant activity in male rats	(Ali et al., 2019)
Nanoemulsions	Hibiscus cannabinus (kenaf) seed oil	Phytosterols, saponins	Cholesterol-lowering and hepatoprotective effects in high-cholesterol diet-induced rats	(Cheong et al., 2018)
Nanocapsules	Copaifera spp. (copaiba oil)	β-caryophyllene	Treatment of pulmonary arterial hypertension; antioxidant and anti-inflammatory effects	(Campos et al., 2017)
Nanostructured lipid carriers	Curcuma longa (turmeric)	Curcumin	Treatment of skin disorders (psoriasis, dermatitis); anti-inflammatory and antimicrobial effects	(Wang et al., 2021; Yallapu et al., 2010)
Solid lipid nanoparticles	Kaempferia parviflora	Flavonoids	Enhanced transdermal delivery with potential anti-inflammatory effects	(Sutthanut et al., 2009)
Polymeric nanoparticles	Olea europaea (olive)	Polyphenols, oleuropein	Antibacterial, antifungal, antiviral, antioxidant, and antitumor activities	(Khanahmad et al., 2024)
Silver nanoparticles	Cynara scolymus (artichoke)	Silver	Anticancer activity via mitochondrial apoptosis in MCF-7 cells	(Erdogan et al., 2019)
Silver nanoparticles	Morinda citrifolia	Silver	Anticancer activity in HeLa cells	(Suman et al., 2013)
Silver nanoparticles	Actinidia deliciosa (kiwi)	Silver	Anticancer activity in HCT-116 cells	(Naraginti and Li, 2017)
Silver nanoparticles	Citrullus colocynthis	Silver	Inhibition of cancer cell proliferation in HEp-2 cells	(Satyavani et al., 2011)
Silver nanoparticles	Nigella sativa (leaves)	Silver	Reduction of cancer cell viability in mouse bone marrow cells	(Amooaghaie et al., 2015)
Silver nanoparticles	Melia dubia (leaves)	Silver	Anticancer activity in human breast cancer cell lines	(Kathiravan et al., 2014)
Plant-mediated nanoparticles	Jurinea dolomiaea (root and leaf)	Not reported	Anticancer activity in MCF-7 and HeLa cells	(Ahmed et al., 2019)
Gold nanoparticles	Various plant sources	Gold	Anticancer activity in multiple cell lines (HeLa, K-562, Vero, MDA-MB-231, A-549)	(Bhat et al., 2013)
Zinc oxide nanoparticles	Various plant sources	Zinc oxide	Induction of cytotoxicity via ROS generation and apoptosis in cancer cells	(Guo et al., 2013)
Plant-derived nanoparticles	Zingiber officinale (ginger)	Not reported	Inhibition of colorectal carcinogenesis and regulation of intestinal epithelial cell metabolism	(Cao et al., 2019)
Plant-derived nanoparticles	Panax ginseng	Not reported	Inhibition of melanoma growth via modulation of macrophage polarization	(Cao et al., 2019)
Lipid nanoparticles	Citrus paradisi (grapefruit)	Lipids	miRNA delivery to reduce liver metastasis via induction of M1 macrophages	(Teng et al., 2021)

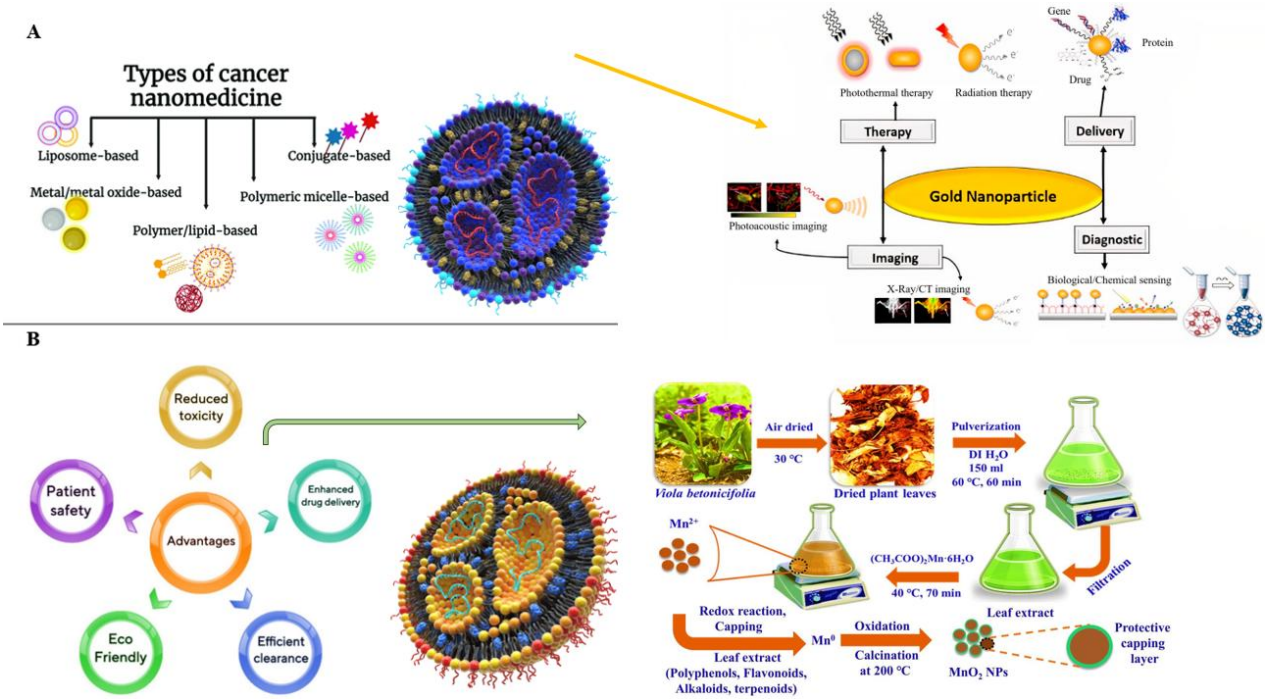


Figure 1. (A). Nanomedicines used in cancer therapy offer unique benefits. Liposome nanoparticles, which provide enhanced stability and increased targeted drug delivery. Metal nanoparticles like gold or silver are used for imaging, diagnosis, and therapies like photothermal therapy. Nanoparticles based on polymers/lipids allow controlled drug release and improve biocompatibility. Finally, conjugated-based nanoparticles combine a therapeutic agent with a targeting molecule to increase specificity (Mundekkad et al., 2022). (B). Advantages of biodegradability and biocompatibility in plant-based nanoparticles (PDNPs) such as MnO2 NPs are also shown in the figure above. These two properties of PDNPs are making them suitable to be used in sustainable cancer therapy (Hanna et al., 2025).

2.2. Innovations in immunotherapy, photothermal therapy, and cancer diagnostics

Recently, different plant-based nanomedicines are under investigation, specifically for immunotherapy and photothermal therapy. Chlorophyll derivatives like pheophorbide and hypericin exhibited strong photodynamic effects after being loaded into nanoparticle carriers, inducing selective generation of reactive oxygen species (ROS) and tumor apoptosis (Kubrak et al., 2022). In addition, saponins and polysaccharides derived from plants are capable of enhancing immune responses by stimulating macrophages and dendritic cells (Shen et al., 2024). Improving the antitumor immunity of the host will also be achievable (Wang et al., 2020). The unique integration of these phytochemicals with nanotechnology platforms can provide a novel approach in the development of multifunctional nanomedicines, which can simultaneously integrate targeted delivery, controlled release, and improved therapeutic activities. This makes plant-based nanomedicines a health-booster of the diet choice of the future (Shukla et al., 2023).

Plant-based nanoparticles are also being investigated for their ability to improve diagnostic imaging in addition to their role in drug delivery (Zhou et al., 2022). For example, phytochemical-loaded nanoparticles loaded with imaging agents, such as quantum dots, gold nanoparticles, and iron oxide, have correlated real-time therapeutic responses with patients who benefited from nanoparticles using green tea extract or turmeric (Bange et al., 2018). Combining plant-based bioactives with imaging technology is beneficial in early detection of cancer as well as evaluation of nanocarriers' biodistribution, thus improving diagnostics and therapeutics (Esmeeta et al., 2022). A new area of research is focused on combined therapies using plant-derived nanomedicines to target metastatic cancers. Research has shown that the phytochemical-encapsulated nanoparticles are able to suppress angiogenesis, which is one of the mechanisms of metastasis (Mehan et al., 2022). As an example, nanoparticles containing genistein, a naturally occurring soy-derived isoflavone, have demonstrated the ability to suppress pathways associated with vascular endothelial growth factor (VEGF), thus limiting the growth of tumors (Kim et al., 2012).

3. Challenges and innovations in developing plant-based nanomedicines

Plant biotechnology is an area of extensive interest for the development of plant-based nanomedicines due to the unique feature of classifying plant-derived bioactive compounds with a nanotechnology platform (Mohammadzadeh et al., 2022). But, there are plenty of challenges that arise in this field, and a summary of them and the possible innovations to overcome these challenges is mentioned in Table 2. The first and foremost challenge is the complexity of plant extracts, as they have different phytochemical components with diverse molecular structures and biological activities (Altemimi et al., 2017). These phytochemicals may cooperate in unpredictable ways, complicating the attainment of consistent formulation and dosing. Moreover, the stability of these plant-based compounds is frequently affected and even lost when subjected to the processes involved in the preparation

of nanocarriers, and the reason is the sensitivity of these phytoconstituents to heat, pH changes, and light (Towers et al., 1984). To overcome these challenges, scientists explore extraction methods, protective nano-coating, and innovative encapsulation methods to maintain the bioactivity of these biomolecules. In the development of plant-based nanomedicines, one of the major challenges is the reproducibility of the production process and derivatives that is suitable for large-scale manufacture (Khan et al., 2018). Though making nanoparticles in a lab on a small scale usually works well, scaling up to make larger quantities can create issues (Patel et al., 2021). These issues result from variations in how the nanoparticles behave in terms of size, shape, and drug release, which, as a result, can undermine their potency. The natural variability in the plants themselves is also another considerable challenge. Plant type, seasonal fluctuations, or external environment all contribute to altering the consistency of the production process. It is important to note that research is being conducted in response to these issues; researchers are searching for new methods such as green synthesis (Hussain et al., 2016). This process involves the application of natural reducing and stabilizing agents, specifically extracts from plants, to enhance the uniformity of the nanoparticles while also promoting an eco-friendly environment. Moreover, they are developing continuous flow synthesis systems, a novel methodology that offers better control over the production process. This technique encourages more uniformity in the nanoparticles produced (Makgwane et al., 2014).

Furthermore, two other challenges are the bioavailability and targeted delivery that these plant-based nanomedicines face in their development process (Zolkepli et al., 2022). Several phytochemicals are characterized by poor solubility in water and low bioavailability, restricting their therapeutic potential. Nanocarrier systems, like liposomes, solid lipid nanoparticles, and polymeric nanoparticles, are used to enhance the solubility, stability, and controlled release of these materials (Bilia et al., 2019). Novel techniques for modifying surfaces have allowed such nanoparticles to both be delivered to specific cancer cells and increase drug absorption by the targeted tumor, limiting off-target effects. Ligand-functionalized nanoparticles that target overexpressed receptors on the surface of cancer cells have emerged as a promising approach to increase the specificity of different plant-induced nanomedicine treatments (Akhtar et al., 2014). Another consideration in the development of plant-based nanomedicines is toxicological concerns. Phytochemicals are generally considered safer than synthetic drugs, but some of them may exhibit cytotoxic effects at high concentrations (Lila et al., 2005).

In addition, the prolonged biocompatibility and possible bioaccumulation of nanocarriers are critical issues (Dinda et al., 2018). In solving these problems, investigations are being made regarding biodegradable and biocompatible materials including chitosan, alginate, and cellulose derivatives, for the fabrication of nanocarriers (Mokhtarzadeh et al., 2016). Also, advanced *in-vitro* and *in-vivo* testing models are developed to determine the safety profiles of these systems prior to clinical trials, broadly considering their toxicological implications. It is said that regulatory and commercial barriers are also important hurdles in the extensive application of plant-based nanomedicines. Existing regulatory frameworks may not sufficiently reflect the specific properties of these hybrid systems, resulting in an extended approval timescale (Sainz et al., 2015). A clear framework for quality control, safety assessments, and manufacturing protocols will need to be established and accepted by the relevant regulators. With the development of new strategies, the conjugation of nanotechnology with the broad therapeutic potential of medicinal plants can bring a new breakthrough in cancer treatment and other medicinal applications.

4. Biodegradability and biocompatibility of plant-derived nanoparticles in sustainable cancer therapy

4.1. Biodegradable approach to cancer therapy

Plant-derived nanoparticles (PDNPs) have gained considerable attention in cancer treatment due to their natural biodegradability and biocompatibility (Karnwal et al., 2024). These compounds are derived from a variety of plant extracts, including polyphenols, flavonoids, and alkaloids, which collectively contribute to the distinctive chemical characteristics of PDNPs (Mohammadzadeh et al., 2022; Peng et al., 2023). Notably, these nanoparticles exhibit excellent biodegradability; as organic entities, they can be metabolized within the body into non-toxic byproducts (Hano et al., 2021). In contrast to synthetic nanoparticles that can bioaccumulate and cause chronic toxicity, PDNPs are metabolized via natural metabolic pathways; as a result, the likelihood of adverse responses will be decreased (Kakakhel et al., 2021). Moreover, PDNPs are synthesized from environmentally friendly principles of green chemistry that effectively avoid hazardous reagents. This not only ensures the safety of PDNPs with respect to the environment but also makes PDNPs compatible with living tissues, which is an important aspect of sustainable cancer therapy (Soltys et al., 2021). Furthermore, PDNPs exhibit therapeutic efficacy with excellent biocompatibility. Plant-derived nanoparticles show minimal immunogenicity owing to their natural sources; therefore, they are less likely to elicit inflammation or hypersensitivity responses (Sarvarian et al., 2022). PDNPs also have antioxidant and anti-inflammatory properties to reduce oxidative stress and inflammatory responses induced by treatment (Bi et al., 2024). Their surface chemistry enables them to be functionalized with targeting ligands, antibodies, or drugs, which improves the selectivity for cancer cells (Bandyopadhyay et al., 2023). This increased specificity minimizes off-target toxicity and enhances the therapeutic index. PDNPs from plants such as *Curcuma longa*, *Moringa oleifera*, and *Camellia sinensis* have been investigated in studies in which chemotherapeutic agents can be delivered with minimal injury to healthy tissues (Ng et al., 2022; Hamada et al., 2022; Tan et al., 2019). The biodegradability of the PDNPs is an important aspect that allows for their safe disposal from the body after the

treatment (Aswathi et al., 2023). Actually, the metabolism of such nanoparticles usually includes enzymatic degradation into smaller bioavailable molecules that can be easily excreted. Nanoparticles formed from biological macromolecules are generally biodegradable; for example, nanoparticles composed of plant polysaccharides or proteins can degrade into glucose or amino acids, which can then be metabolized efficiently (Wang et al., 2017). The degradation process ensures that PDNPs are completely cleared from the body and do not remain in the tissues, alleviating the concern about chronic toxicity. In addition, plant-based nanoparticles are less fibrotic or granuloma-forming, which are common complications in the case of poorly degradable materials (Nguyen et al., 2022). As a result, PDNPs offer an alternative for prolonged cancer therapies in a safer way, especially when repeated administration is needed.

4.2. Sustainable synthesis of plant-derived nanoparticles

The sustainable nature of PDNP synthesis also supports their application in cancer therapy. Current methods of nanoparticle synthesis are often associated with toxic solvents, high energy requirements, and hazardous products, but in contrast, plant-based nanoparticle synthesis adopts environmentally benign conditions, including aqueous plant extracts, room temperature reactions, and renewable resources (Duan et al., 2015; Madani et al., 2022). These approaches not only reduce the carbon footprint but also enhance the production of cost-effective nanoparticles (Altammar et al., 2023). It is demonstrated that the PDNPs have the potential to be used as a low-cost platform for developing advanced drug delivery systems for being used in oncology by utilizing plant-derived bioactive compounds (Khatik et al., 2022). The biodegradability and biocompatibility identify plant-based nanoparticles as excellent materials in sustainable cancer therapy. The capacity of these materials to effectively target disease sites offers great potential for their application in the delivery of therapeutic agents, and their low toxicity and environmentally friendly synthesis fit well with modern strategies aimed at safer and more effective cancer therapy (Shukla et al., 2023). By better understanding how to improve the stability, bioavailability, and targeting of PDNPs, future studies will open new opportunities to unleash the anticancer potential of these delivery systems. PDNPs represent a creative and suitable alternative to enhance cancer treatment results, guaranteed by less toxicity (An et al., 2025; Madani et al., 2022). As a result, 5 main advantages of biodegradability and biocompatibility in plant-based nanoparticles are available, as mentioned in Figure 1.

The sustainable synthesis of plant-derived nanoparticles (PDNPs) is increasingly aligned with environmentally responsible agricultural production of medicinal plants. Recent studies show that plant extracts act as natural reducing and stabilizing agents, enabling nanoparticle synthesis under green conditions while reducing toxic by-products and energy consumption. This approach supports the cultivation of medicinal plants as renewable bioresources, integrating nanotechnology with sustainable agriculture systems that promote soil health, reduced chemical inputs, and biodiversity. Moreover, plant-mediated nanoparticles have demonstrated roles in agriculture itself, including enhancing crop growth, stress tolerance, and nutrient efficiency with minimal environmental impact (Hanna et al., 2025; Lakhani et al., 2025). Such dual functionality establishes a circular and eco-friendly model in which medicinal plant cultivation supplies raw materials for nanomedicine while simultaneously contributing to sustainable agricultural practices and reduced environmental burden (Osman et al., 2024).

5. Plant-based nanomedicine multi-pathway targeting for breaking cancer resistance

5.1. Targeting cancer resistance through phytochemicals and nanovesicles

One of the main strategies with strong potential for overcoming cancer resistance is plant-based nanomedicine. This process occurs through the modulation of multiple pathways associated with tumor progression and mechanisms underlying drug resistance (Khan et al., 2018). This strategy utilizes the unique characteristics of plant-derived nanovesicles (PDNVs) as well as phytochemicals to enhance the therapeutic efficacy and reduce unwanted secondary effects of common cancer therapies. Plant-derived nanovesicles (PDNVs) are naturally occurring nanoparticles derived from plant extracellular vesicles containing intrinsic bioactive molecules (lipids, proteins, and nucleic acids) (Yu et al., 2020). These nanovesicles have been shown to modulate the tumor microenvironment (TME) and alter the cellular processes that are important signs of cancer progression (Liu et al., 2024). As it is mentioned in Figure 2, PDNVs can bring down the expression of anti-apoptotic proteins such as Bcl-2 and Bcl-xL and upregulate proteins such as Bax and Bak, which, as a result, will promote apoptosis of cancer cells (You et al., 2021; Sedky et al., 2023; Campbell et al., 2018). Moreover, PDNVs can disrupt inflammatory pathways via inhibition of NLRP3 inflammasome expression linked to chemoresistance (Marinho et al., 2021; Bagherniya et al., 2021). Phytochemicals are bioactive compounds of plant origin that are studied widely for their anticancer effects. Compounds like quercetin, curcumin, or catechins have been shown to modulate several signaling pathways in cancer cell survival, proliferation, and metastasis (Kapinova et al., 2018). Nonetheless, their clinical use is frequently limited by the poor bioavailability and stability of such phytochemicals. Nanotechnology solves this challenge through the encapsulation of such phytochemicals into nanoparticles for their enhanced solubility, stability, and selective delivery to the tumor sites (Odeh et al., 2014). For instance, suppressing drug resistance in breast cancer has been achieved by co-encapsulation of quercetin and doxorubicin into biotin receptor-targeting nanoparticles (Lv et al., 2016). The therapeutic application of plant-derived nanovesicles (PDNVs) and phytochemical-based nanomedicines is increasingly supported by the sustainable agricultural

production of medicinal plants and environmentally friendly processing strategies. Recent studies demonstrate that PDNVs are naturally produced by plant cells and can be sourced from widely cultivated medicinal and food crops, providing abundant, renewable, and environmentally sustainable raw materials for nanomedicine development. In parallel, emerging research emphasizes that plant-derived nanovesicles are eco-friendly and low-toxicity delivery systems, aligning with green synthesis approaches that reduce chemical waste and energy consumption (Wang et al., 2025). Moreover, integrating medicinal plant cultivation with nano-enabled extraction and processing supports circular bioeconomy models by utilizing plant biomass and agricultural residues efficiently, thereby minimizing environmental impact while ensuring scalable production (Devarajan et al., 2026).

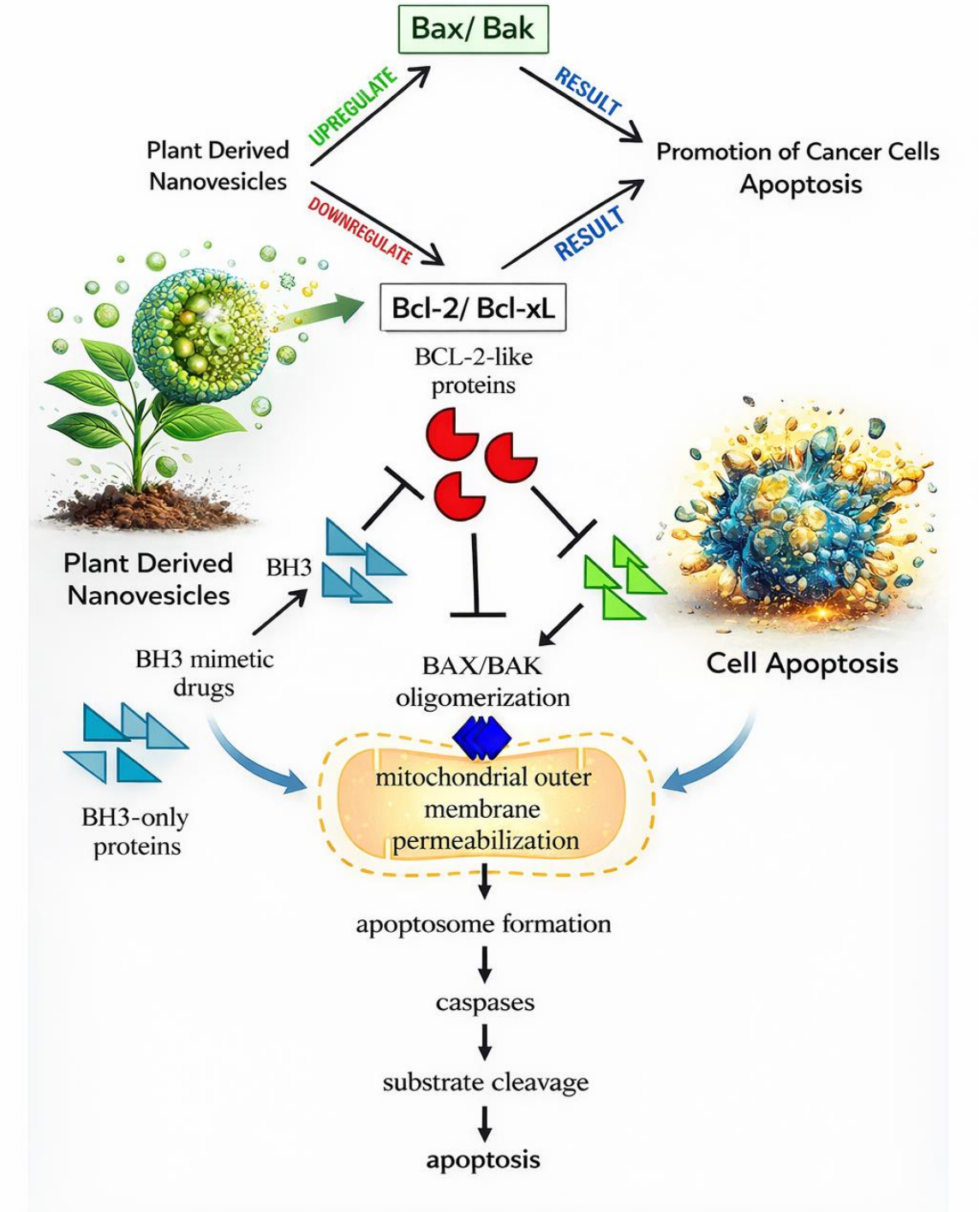


Figure 2. In the figure above, it is schematically shown how Plant-Derived Nanovesicles (PDNVs) can promote the apoptosis of cancerous cells through upregulating Bax and Bak proteins while downregulating Bcl-2 and Bcl-xL proteins. The figure once more indicates the importance of plant-derived nanovesicles in oncology and cancer treatment.

5.2. Overcoming tumor microenvironment and multidrug resistance in cancer therapy:

The tumor microenvironment has an important role in cancer progression and therapy resistance. The TME has diverse components, such as cancer-associated fibroblasts, immune cells, and extracellular matrix; it communicates excessive signals with tumor cells to facilitate tumor growth and escape from immune surveillance (Sun et al., 2016). It can be said that PDNVs that play an important role in regulating the TME by modifying stromal immunity and the immune response against tumor cells can be used against cancer therapy resistance (Chen et al., 2023). For example, nanovesicles derived from tea flowers induce oxidative stress and mitochondrial damage in cancer cells, leading to cell cycle arrest and apoptosis (Chen et al., 2022). Multidrug resistance (MDR) is a major obstacle for effective cancer treatment and leads to failure of chemotherapy. PDNVs represent a new strategy to combat MDR by enabling the delivery of cytotoxic agents and antibiotics directly to resistant cancer cells while also modulating mechanisms of drug resistance (Ahmadifar et al., 2024; Kadriya et al., 2024). One such strategy is the use of heparin-modified lemon-derived nanovesicles for the delivery of the drug doxorubicin into doxorubicin-resistant cells via caveolin-mediated endocytosis, which overcomes the drug efflux pumps and decreases the intracellular ATP levels that are essential for the action of the drug efflux (Chen et al., 2023). The potential of utilizing plant-based nanomedicine as part of anticancer therapy is a way to approach the multifactorial and heterogeneous nature of the cancer resistance problem. This strategy aims to improve the potency of anticancer agents, diminish side effects and confront difficulties presented by the tumor microenvironment and multidrug resistance through harnessing natural bioactive compounds in plants and applying nanotechnology for targeted delivery. Comprehensive studies and clinical trials are needed to address the potential of plant-based nanomedicine to dismantle cancer resistance and improve patient outcomes. Recent advancements have explored the utilization of plant-based nanomedicine in improving the outcomes of immunotherapy using the immune-stimulating potential of specific plant-based nanovesicles; these nanovesicles can enhance T-cell activation, augment antigen presentation, and also enhance the infiltration of immune cells into solid tumors (Jung et al., 2022). For instance, grape-derived extracellular vesicles have been shown to carry immunomodulatory agents. Delivery of the agents to the tumor significantly improved the response rates to checkpoint inhibitors. In addition to directly targeting cancer cells, this strategy improves the host immunity, thus decreasing the likelihood of tumor recurrence or resistance (Nguyen et al., 2023; Nemati et al., 2022). Additionally, the synergistic therapeutic effects of traditional radiotherapy methods combined with plant-based nanomedicine in cancer therapy have been remarkable. Nanoparticles derived from specific plants also possess radiosensitizing characteristics, increasing the susceptibility of tumor cells to radiation-induced DNA damage (Sisin et al., 2023). As an example, Curcumin-loaded nanoparticles will increase ROS generation in irradiated cancer cells, amplifying DNA strand breaks and promoting cell death. Consequently, combinatorial approaches provide a holistic strategy to combat the very complex framework of cancer resistance, leading to enhanced patient survival and treatment outcomes (Minafra et al., 2019; Duse et al., 2019).

6. Phytochemicals found in medicinal plants and their other powerful therapeutic potentials

Active compounds naturally present in medicinal plants called phytochemicals have shown significant therapeutic effects (Nwozo et al., 2023). Actually, phytochemicals are secondary metabolites of plants that can perform important functions for the plant, such as different activities against pathogens, environmental stressors, and herbivore protection (Velu et al., 2018). Alkaloids, flavonoids, terpenoids, phenolics, and saponins are examples of the important and prominent classes of phytochemicals that each exhibit unique biochemical properties with pharmacological potential. For example, alkaloids such as cisplatin, vinblastine, and vincristine are derived from *Catharanthus roseus*, which has been extensively used in cancer treatments (Arora et al., 2010). Quercetin and kaempferol, which are from the flavonoid class, have strong antioxidative and anti-inflammatory activities (Al-Khayri et al., 2022; Alam et al., 2020). It is demonstrated that Most phytochemicals target multiple cellular pathways and thus can be important agents in the prevention of chronic diseases associated with various dysfunctions, including cardiovascular diseases, neurodegenerative disorders, and also different types of cancers (Shuvalov et al., 2023). The anticancer potential of phytochemicals has attracted interest in the past few decades. Numerous phytocompounds exert strong cytotoxic action against cancer cells by promoting apoptosis, preventing proliferation, and inhibiting tumor angiogenesis. For example, curcumin, which is obtained from *Curcuma longa*, was found to be highly efficient in modulating some crucial signaling pathways, including NF-κB and STAT3, which are crucial for cancer cell proliferation and survival (Wang et al., 2021; Shehzad et al., 2013). Resveratrol from grapes has also been widely examined for its repressive effect on cell proliferation within various tumors through its multiple molecular targets, including the p53 and Bcl-2 proteins (Cal et al., 2003; Tinhofer et al., 2001). Moreover, phytochemicals frequently modulate synergistically when used in combination with conventional chemotherapeutic agents, improving overall treatment outcomes and minimizing negative and unwanted side effects. All these advantages make the phytochemicals a promising candidate to be used in oncology for prevention and treatment of various cancers (Gao et al., 2022).

6.1. Therapeutic potential of phytochemicals from cancer to neurodegenerative diseases and antimicrobial resistance

Phytochemicals are also under investigation for their neuroprotective effects and properties, leading to potential therapeutic options for neurodegenerative disorders, including Alzheimer's or Parkinson's disease (Velmurugan

et al., 2018). This means that the use of phytochemicals is not just limited to oncology but also other fields. Compounds such as epigallocatechin gallate (EGCG) derived from green tea and ginsenosides found in *Panax ginseng* have been shown to counteract oxidative stress, diminishing neuroinflammation and inhibiting amyloid-beta aggregation (Fei et al., 2020; Yadav et al., 2021). These mechanisms are key regulators for improving cognition and preventing Alzheimer's disease, or even slowing it down. Some phytochemicals like berberine also showed potential to balance neurotransmitter levels; it also plays an important role in synaptic plasticity, resulting in improved neurological outcomes (Vuddanda et al., 2010). Their ability to cross the blood-brain barrier further highlights their relevance in neurotherapeutics. Phytochemicals also have powerful antimicrobial effects, making them very valuable in the battle against multidrug-resistant pathogens (Barbieri et al., 2017). Various bioactive compounds, including allicin from garlic and eugenol from cloves, have shown broad-spectrum antibacterial and antifungal activities. These compounds exert their effects by compromising microbial cell membranes. This action is because of inhibiting biofilm formation and also blocking critical enzymatic reactions by these plant-based bioactive compounds (Senarathna et al., 2023). As antibiotic resistance continues to rise, phytochemicals become a new and promising alternative for managing different kinds of infections. In addition, their minimal risk of developing resistance makes them a promising target for novel antimicrobial agents (Borges et al., 2015). Phytochemicals have various advantageous pharmacological properties, but beyond that, they are also widely used as synthetic nanomedicines to improve the bioavailability and stability of different drugs (Aqil et al., 2013). As it was mentioned before, nanocarrier systems, including liposomes, nanoparticles, and micelles, offer controlled and targeted delivery of phytochemicals that will address challenges surrounding solubility, stability, and cellular uptake (Wang et al., 2014). Incorporation of curcumin into nanoparticles has resulted in enhanced anticancer activity due to increased cellular retention and reduced systemic toxicity (Ombredane et al., 2021). This technology has led to the development of new drug delivery systems that utilize the inherent strength of phytochemicals and enhance the therapeutic outcome. The therapeutic potential of medicinal plant-derived phytochemicals encompasses a wide range of diseases, including oncology, neurology, and infectious disease management. Since they can modulate multiple cellular pathways with unique mechanisms of action, they are critical in drug discovery and development (Rahman et al., 2021). Synergistic interactions of phytochemicals and nanoformulation of phytochemicals for enhanced bioavailability are a promising approach for innovative modern medicine that deserves further study. By leveraging the full power of these naturally occurring compounds, natural bioactive compounds can help the scientific community tackle some of the most difficult health issues such as cancer. The therapeutic application of phytochemicals and plant-derived nanovesicles (PDNVs) is increasingly supported by sustainable agricultural production of medicinal plants and environmentally responsible sourcing strategies. Recent evidence indicates that PDNVs are naturally produced by a wide range of edible and medicinal plants (e.g., ginger, ginseng, garlic, and turmeric), providing abundant, renewable, and scalable raw materials for nanomedicine development. Importantly, these plant-based nanovesicles originate from normal plant physiological processes and contain intrinsic bioactive molecules involved in plant growth and defense, linking their production directly to agricultural practices and crop management (Li et al., 2025; Wang et al., 2025). Furthermore, recent reviews emphasize that PDNVs offer "environmentally sustainable sources of raw materials" compared to synthetic or animal-derived systems, supporting their integration into green production pipelines and circular bioeconomy models. Consequently, the cultivation of medicinal plants under sustainable agricultural systems not only ensures a consistent supply of phytochemicals and nanovesicles for advanced therapeutics but also minimizes environmental impact, reinforcing the synergy between nanomedicine innovation and ecological sustainability (Zheng et al., 2025).

7. Conclusion and future directions

The use of plant-derived nanoparticles (PDNs) is essential in combating various types of cancers as they are not only safe and biocompatible but also show increased drug efficacy. Nanoparticles enhance the stability, solubility, and targeted delivery of bioactive plant constituents (curcumin, resveratrol, and EGCG), which is a significant and effective pathway for achieving anticancer activity. PDNs are based on the use of sophisticated platforms, such as liposomes, gold particles, and polymeric vehicles for the controlled release of plant-derived bioactive compounds while reducing toxicity and enhancing efficacy. In addition to their direct anticancer effects, plant-derived nanomedicines have potential applications in immunotherapy, photothermal therapy, and diagnostic imaging, offering a multifaceted approach to enhancing patient outcomes. PDNs have different advantageous properties such as natural biodegradability and non-toxic breakdown of plant compounds like polyphenols and flavonoids, which can lower the risk of chronic toxicity. Moreover, the antioxidant and anti-inflammatory potential of nanoparticles makes them attractive green, cheap candidates to be used in oncology. Functionalizing PDNs with targeting agents can increase the selectivity for cancer cells, leading to minimal toxicity against healthy tissues and, as a result, decreasing the unwanted side effects on the body. However, all the promising potential of medicinal plants is still influenced by the complexity and inconsistency of their extracts, along with challenges in formulation stability and bioavailability. To overcome the challenges, efforts are directed towards nano-coating techniques, green synthesis methods, or ligand-functionalized nanoparticles. Moreover, regulatory issues and toxicological safety need careful attention, using biodegradable materials and comprehensive testing techniques. In addition, plant-derived nanovesicles

(PDNVs) can deliver phytochemicals that modulate tumor progression (e.g., quercetin and curcumin) and target multidrug resistance, as well as augment immunotherapy and radiotherapy responses. This study suggests that plant-derived nanomedicines, with their versatile pharmacological activities and multi-targeting applications among different therapeutic areas, including cancer, neurodegenerative diseases, and infectious diseases, will play a significant role in the development of new therapeutic agents and improve clinical management and patient outcomes. Looking ahead, the progress of plant-derived nanomedicines will depend less on introducing new nano-carriers and more on making them reliable, reproducible, and clinically meaningful. A central priority is the rigorous standardization of botanical materials, ensuring consistent chemotypes, controlled extraction conditions, and well-defined quality attributes so that variability in plant composition does not compromise nanoformulation performance or therapeutic predictability. Equally important is the rational design of nanocarriers based on clear pharmacokinetic and pharmacodynamic principles rather than assumptions of passive tumor accumulation. Future systems should integrate stimulus-responsive release, precise surface engineering, and quantitative modeling to improve biodistribution, tumor penetration, and controlled drug exposure. At the same time, emerging platforms such as plant-derived nanovesicles require deeper mechanistic investigation to clarify their intrinsic bioactivity, immune-modulatory properties, and long-term safety. Advanced analytical tools, including multi-omic profiling, single-cell analysis, and spatial imaging, can help elucidate how these systems interact with tumor microenvironments and host immunity. Finally, successful translation will require early alignment with regulatory standards, scalable and green manufacturing strategies, and comprehensive toxicological assessment. By integrating biological insight, engineering precision, and regulatory foresight, the next generation of plant-based nanomedicines can move from promising experimental constructs to robust therapeutic platforms suitable for clinical application. In addition to these therapeutic advances, future progress in phytochemical- and PDNP-based nanomedicine will increasingly depend on the sustainable agricultural production of medicinal plants and environmentally responsible sourcing strategies. Establishing standardized cultivation systems such as controlled-environment agriculture, precision farming, and plant cell culture technologies will be essential to ensure consistent phytochemical yield, quality, and reproducibility for clinical applications. Moreover, integrating green extraction methods and valorization of agricultural residues into nanoparticle synthesis can support circular bioeconomy models, reducing waste and minimizing environmental impact. Future research should therefore focus on optimizing agronomic conditions, developing scalable and eco-friendly supply chains, and aligning medicinal plant production with sustainability frameworks, ultimately enabling a reliable, cost-effective, and environmentally conscious pipeline for next-generation plant-based therapeutics.

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