JOURNAL OF PHARMA INSIGHTS AND RESEARCH ISSN NO. 3048-5428

REVIEW ARTICLE

A Review on Phytochemical-Based Nano-systems for the Management of Ovarian Cancer

Sangeetha S*[1], Saravana Kumar A[2], Parthiban P[1], Nivetha G[1], Sangavi S[1], Vishnu Priya P[1], Yazhini R T[1]

[1] *Department of Pharmaceutical Chemistry, Vellalar College of Pharmacy, Thindal, Tamil Nadu, India*
[2] *Department of Pharmaceutical Biotechnology, Vellalar College of Pharmacy, Thindal, Tamil Nadu, India*

Publication history: Received on 9th January 2026; Revised on 18th February 2026; Accepted on 19th February 2026

Article DOI: 10.69613/n6b9hb12

Abstract: Ovarian cancer is the primary cause of gynecological cancer mortality due to delayed clinical presentation and the persistent emergence of multidrug resistance. Traditional platinum-taxane regimens often demonstrate limited efficacy in advanced stages, necessitating the development of innovative therapeutic modalities. Plant-derived bioactive compounds, including curcumin, resveratrol, and quercetin, possess potent antineoplastic properties but are restricted by poor aqueous solubility and rapid metabolic clearance. Integration with nanotechnology facilitates the creation of sophisticated delivery platforms, such as liposomes, polymeric nanoparticles, and metallic nanostructures, which enhance the pharmacokinetic profile and tumor-specific accumulation of these phytochemicals. These nano-enabled systems modulate critical oncogenic signaling pathways, including PI3K/AKT/mTOR, MAPK, and NF-κB, while inducing programmed cell death through mitochondrial-mediated and extrinsic apoptotic pathways. Beyond delivery, green synthesis techniques utilize plant extracts to fabricate metallic nanoparticles with intrinsic biological activity. Current evidence indicates that these formulations achieve superior therapeutic indices and effectively bypass efflux pump-mediated resistance. Despite significant preclinical success, clinical translation is governed by challenges in standardization, large-scale manufacturing, and the establishment of robust regulatory frameworks for botanical nanomedicines. These systems offer a pathway to improve survival rates and reduce systemic toxicity in patients with epithelial ovarian malignancies.

Keywords: Ovarian Carcinoma; Nanomedicine; Bioactive Phytochemicals; Targeted Drug Delivery; Molecular Oncology.

1. Introduction

Ovarian cancer stands as a major challenge in oncology, characterized by high fatality rates and a lack of specific early-stage symptoms. In 2020, global statistics reported over 313,000 new cases, positioning the disease as the fifth leading cause of cancer-related mortality among women [1]. The asymptomatic nature of early disease progression leads to a situation where approximately 70% to 80% of patients receive a diagnosis only at advanced stages, specifically FIGO stages III and IV, where the prognosis is significantly diminished [2]. Current diagnostic protocols involving serum biomarkers like CA-125 and transvaginal ultrasonography often lack the necessary sensitivity to detect the disease at a curative stage, resulting in late-phase presentations that are resistant to conventional interventions [1].

Standard therapeutic strategies typically involve aggressive debulking surgery followed by platinum-based chemotherapy. While initial responses are often favorable, a vast majority of patients experience recurrence and the development of chemoresistance, which drastically curtails long-term survival prospects [2]. The limitations of current pharmacology, particularly regarding systemic toxicity and poor drug penetration into peritoneal metastases, necessitate a transition toward more precise delivery systems. Nanotechnology offers a transformative solution by utilizing materials at the 1–100 nm scale to improve drug solubility, achieve sustained release, and facilitate tumor-specific accumulation through the enhanced permeability and retention effect [3].

Concurrent with these engineering advancements, plant-derived phytochemicals have surfaced as potent candidates for oncology. Molecules such as curcumin, epigallocatechin-3-gallate, and various ginsenosides demonstrate significant anti-inflammatory and pro-apoptotic activities. However, their natural forms suffer from poor bioavailability and rapid systemic elimination [3]. The intersection of nanocarrier technology with these natural products creates a synergistic platform capable of overcoming physiological barriers. Nano-enabled plant therapeutics represent a critical development in the pursuit of effective, low-toxicity cancer management By shielding bioactive molecules from degradation and directing them toward malignant cells via surface functionalization.

* Corresponding author: Sangeetha S

2. Pathology of Ovarian Cancer

2.1. Histopathological Classification

The global burden of ovarian cancer continues to escalate, influenced by demographic shifts and aging populations. Recent analysis suggests an age-standardized incidence rate of approximately 6.71 per 100,000 women, with significant regional variations dictated by socio-economic factors and access to screening [4]. While high-income regions show stabilizing rates, middle- and low-income regions face an increasing absolute number of cases, often complicated by late-stage diagnosis [5]. Projections indicate that the global burden will continue to rise through 2050, emphasizing the need for more accessible and effective treatment strategies [6].

Ovarian cancer is categorized as a heterogeneous group of malignancies rather than a single disease entity. Epithelial ovarian cancer represents the vast majority of cases, approximately 90%, and is further subdivided into distinct histological types. High-grade serous carcinoma is the most prevalent and aggressive form, often characterized by rapid dissemination across the peritoneal cavity [7]. Other subtypes, such as endometrioid, clear-cell, and mucinous carcinomas, exhibit unique molecular drivers and varying degrees of sensitivity to standard chemotherapy [7, 8]. The recognition of these distinct subtypes is crucial for the development of targeted nano-therapeutics, as each variant responds differently to pharmacological challenges [8].

2.2. Ovarian Tumorigenesis

The molecular basis of ovarian cancer involves a complex interplay of genetic mutations and dysregulated signaling cascades. In high-grade serous carcinoma, mutations in the TP53 gene are nearly universal, leading to significant genomic instability and a failure of DNA repair mechanisms [15]. The defects in homologous recombination, frequently resulting from BRCA1 or BRCA2 mutations, are present in a significant portion of patients, creating a therapeutic window for the use of DNA-damaging agents and specialized inhibitors [16].

Beyond genetic mutations, several intracellular pathways drive cell proliferation and survival. The PI3K/AKT/mTOR pathway is frequently hyperactivated, promoting metabolic reprogramming and resistance to apoptosis. Similarly, the MAPK pathway and NF-κB signaling contribute to the pro-inflammatory environment of the tumor, facilitating metastasis and immune evasion [17]. In subtypes like clear-cell carcinoma, mutations in ARID1A link chromatin remodeling defects to tumor progression [17]. The tumor microenvironment, consisting of fibroblasts, immune cells, and a dense extracellular matrix, further complicates the delivery of therapeutic agents by creating physical and biochemical barriers that traditional drugs cannot easily penetrate.

2.3. Limitations and Challenges in Conventional Management

The primary challenge in managing advanced ovarian cancer is the high rate of relapse. Despite optimal surgical cytoreduction and initial chemotherapy, many patients eventually develop resistance to platinum agents [11]. This resistance is multifactorial, involving the upregulation of drug efflux pumps, such as P-glycoprotein, and alterations in DNA repair pathways that nullify the effects of cytotoxic drugs [21]. The emergence of secondary mutations can restore DNA repair capacity in BRCA-deficient cells, leading to resistance against targeted maintenance therapies [21].

Systemic toxicity remains a significant hurdle in the clinical setting. The high doses required to achieve therapeutic concentrations in the peritoneal cavity often led to severe hematological and gastrointestinal side effects, which limit the duration and intensity of treatment. Additionally, the molecular heterogeneity between patients, and even between different metastatic sites in the same patient, makes it difficult to predict therapeutic responses [22]. Conventional systemic delivery often fails to reach optimal concentrations in hypoxic tumor cores or within peritoneal nodules due to poor vascularization and high interstitial fluid pressure. These factors necessitate the development of localized, targeted delivery systems that can bypass systemic circulation and deposit active agents directly within the malignant tissue.

3. Fundamentals of Nanotechnology

3.1. Principles and Scale-Dependent Properties

Nanotechnology involves the engineering of functional systems at the molecular scale, typically within the range of 1 to 100 nanometers. At this dimension, materials exhibit unique physical and chemical properties that differ substantially from their bulk counterparts [23]. The high surface-to-volume ratio characteristic of nanoparticles allows for a high density of functional groups on the surface, which can be utilized for drug loading, chemical stabilization, and the attachment of targeting ligands. These properties make nanoparticles ideal candidates for overcoming the biological barriers that often limit the efficacy of conventional oncology drugs [24].

The behavior of matter at the nanoscale is governed by quantum effects and surface phenomena. Quantum confinement occurs when the size of a particle becomes comparable to the wavelength of its electrons, leading to discrete energy states and size-dependent optical and electronic properties. For instance, gold nanoparticles exhibit surface plasmon resonance, where the collective oscillation of free electrons results in intense light absorption and scattering, properties that are exploited in photothermal therapy and molecular imaging [23, 24]. These size-dependent effects allow for the precise tuning of nanoparticle characteristics to optimize their interaction with biological systems.

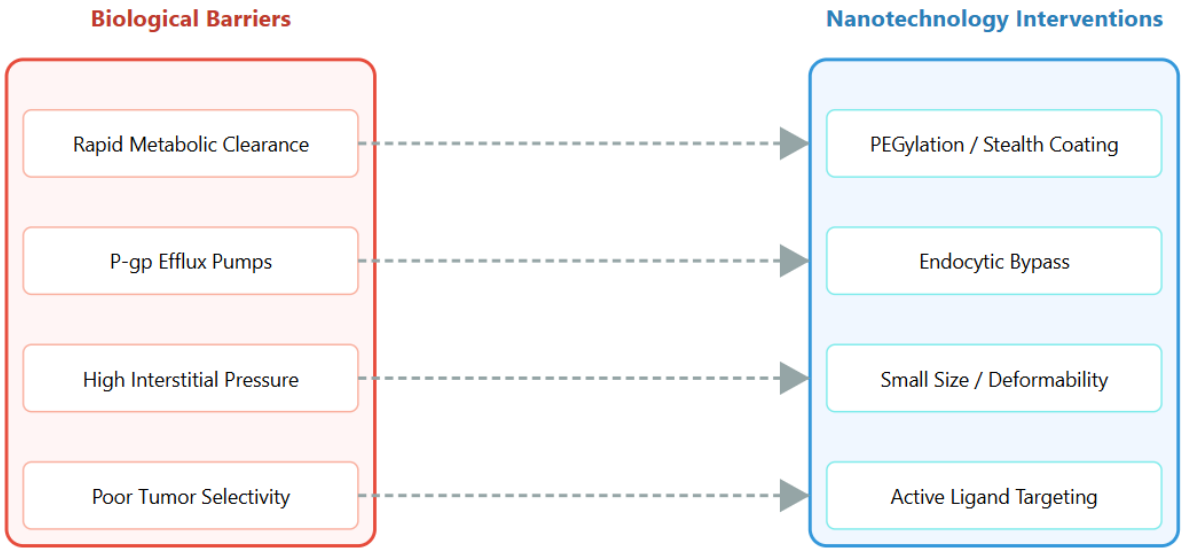

Figure 1. Overcoming Biological Barriers through Nanotechnology

3.2. Fabrication Methods for Nanocarriers

The synthesis of nanostructures for medical applications follows two primary methodologies: top-down and bottom-up approaches. Top-down fabrication involves the physical reduction of bulk materials into smaller components through techniques such as lithography or high-energy milling. While effective for creating precise patterns, these methods often require significant energy and may result in surface defects that affect the biocompatibility of the final product [24, 25].

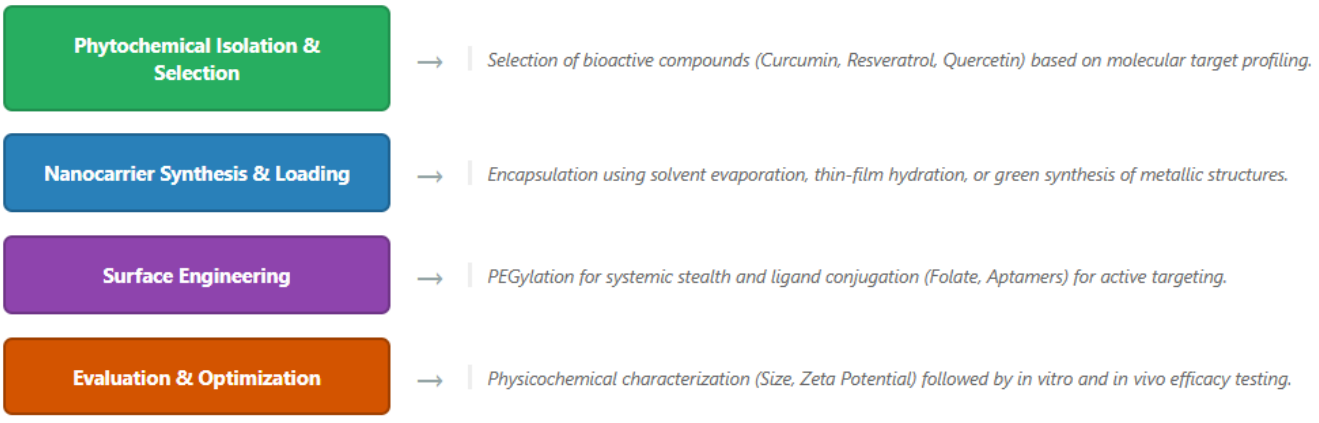

Figure 2. Fabrication of Functionalized Phytochemical Nanocarriers

In contrast, bottom-up synthesis involves the assembly of atoms or molecules into complex structures through chemical reactions or self-assembly. This approach is highly versatile and allows for the creation of organic nanocarriers, such as liposomes, micelles, and dendrimers. Self-assembly is a spontaneous process driven by thermodynamic equilibrium, where amphiphilic molecules organize into stable structures in aqueous environments [25]. This principle is fundamental in the development of lipid-based and polymeric nanoparticles, which are currently the most widely studied platforms for the delivery of plant-based therapeutics.

3.3. Classification of Therapeutic Nanoparticles

Nanocarriers utilized in cancer therapy are generally classified into organic and inorganic systems. Organic nanoparticles, including liposomes and polymeric structures, are valued for their biocompatibility and ability to carry diverse payloads. Liposomes consist of phospholipid bilayers that can encapsulate both hydrophilic drugs in the aqueous core and lipophilic compounds within the lipid membrane [23, 25]. Polymeric nanoparticles, often composed of biodegradable materials like PLGA, offer controlled drug release through the slow erosion of the polymer matrix.

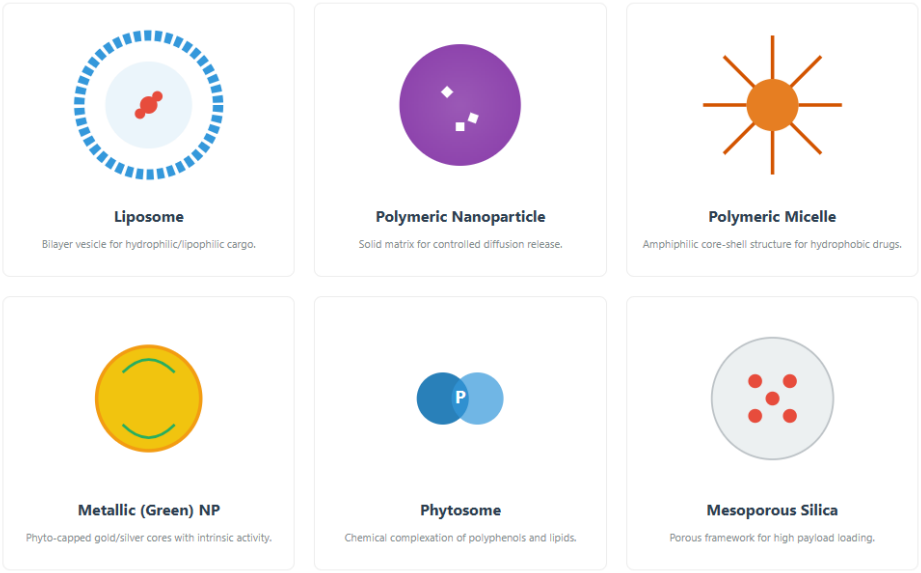

Figure 3. Structural Classification of Nano-Phytochemical Delivery Systems

Inorganic nanoparticles, such as gold, silver, and silica-based structures, provide unique functionalities for diagnostics and specialized therapies. Metallic nanoparticles are particularly useful for their stability and potential for synergistic effects when combined with phytochemicals. Silica-based systems, such as mesoporous silica nanoparticles, offer high loading capacities due to their porous architecture [25]. The selection of a specific nanoparticle type depends on the physicochemical properties of the therapeutic agent and the desired delivery mechanism, whether it be systemic circulation or localized peritoneal administration in ovarian cancer patients.

4. Plant-Based Therapeutics for Cancer Management

4.1. Drugs Already in Use with Clinical Success

Natural products derived from medicinal plants have historically provided the foundation for cancer chemotherapy. A significant portion of currently approved antineoplastic agents are either unaltered natural products or their semi-synthetic derivatives. The transition toward natural products is driven by the need for molecules with multi-target activity and lower systemic toxicity compared to synthetic cytotoxic agents [26]. The clinical success of plant-derived drugs is exemplified by the development of taxanes and vinca alkaloids, which have become pillars of modern oncology.

The medicinal significance of plants is underscored by the fact that nearly half of the new drugs approved over the last four decades have a natural origin [26]. These compounds often exhibit high patient tolerance and possess complex chemical structures that allow them to interact with specific cellular targets that are difficult to reach with small synthetic molecules. In the context of ovarian cancer, the integration of these bioactive compounds into nano-delivery systems aims to revitalize their therapeutic potential by addressing their inherent pharmacokinetic limitations.

4.2. Approved Phytochemical-Derived Antineoplastic Agents

Several plant-derived molecules are currently utilized as standard treatments for various malignancies, including ovarian cancer. Vinca alkaloids, such as vincristine and vinblastine isolated from *Catharanthus roseus*, act by binding to tubulin and inhibiting microtubule polymerization. This disruption prevents the formation of the mitotic spindle, leading to cell cycle arrest in the

metaphase and subsequent apoptosis [26, 27]. Taxanes, such as paclitaxel derived from the Pacific yew tree, operate through a complementary mechanism by stabilizing microtubules and preventing their depolymerization, which similarly triggers mitotic arrest [27].

Another critical class of plant-derived drugs includes podophyllotoxin derivatives like etoposide. These molecules target topoisomerase II, an enzyme essential for DNA replication and transcription. By stabilizing the transient complex between DNA and the enzyme, these drugs induce double-stranded DNA breaks that are lethal to rapidly dividing cancer cells [26]. While these drugs are highly effective, their use is often limited by systemic side effects and the development of resistance, highlighting the need for the next generation of nano-formulated phytochemicals that can deliver these or similar agents with greater precision.

4.3. Biological Mechanisms of Plant-Derived Compounds

The antineoplastic efficacy of phytochemicals stems from their ability to modulate multiple cellular processes simultaneously. Unlike many targeted synthetic drugs that focus on a single enzyme, bioactive plant compounds often exert a pleiotropic effect. They inhibit cell proliferation by inducing cell cycle arrest at the G1, S, or G2/M phases through the regulation of cyclins and cyclin-dependent kinases [28]. Many phytochemicals are potent inducers of apoptosis, activating both the intrinsic mitochondrial pathway through the regulation of Bcl-2 family proteins and the extrinsic pathway through death receptors [27, 28].

Table 1. Phytochemicals and Their Molecular Targets in Ovarian Cancer

Phytochemical	Primary Source	Major Molecular Targets	Biological Outcome in Ovarian Cancer
Curcumin	*Curcuma longa*	NF-κB, STAT3, PI3K/Akt/mTOR, Cyclin D1	Inhibition of proliferation, reversal of chemoresistance, and suppression of inflammatory cytokines.
Resveratrol	*Vitis vinifera*	SIRT-1, p53, Beclin-1, MMP-9	Induction of autophagy-mediated cell death and inhibition of metastatic potential.
Quercetin	*Allium cepa*	VEGF, Bcl-2/Bax ratio, Caspases-3/9	Inhibition of angiogenesis and induction of the intrinsic apoptotic pathway.
EGCG	*Camellia sinensis*	EGFR, MAPK, DNA Methyltransferases	Epigenetic modulation and suppression of growth factor-mediated signaling cascades.
Berberine	*Berberis* species	AMPK, P-glycoprotein, Survivin	Overcoming multidrug resistance and inhibition of cancer stem cell self-renewal.

Phytochemicals also interfere with oncogenic signaling cascades that are vital for tumor survival. Molecules like curcumin and resveratrol have been shown to inhibit the NF-κB and STAT3 pathways, which are major drivers of inflammation and chemoresistance in ovarian cancer [29, 30]. Additionally, these compounds can suppress angiogenesis by reducing the expression of vascular endothelial growth factor (VEGF) and inhibit metastasis by downregulating matrix metalloproteinases (MMPs) that degrade the extracellular matrix [29]. The multi-target nature of these molecules makes them particularly effective against the heterogeneous and adaptive nature of ovarian carcinomas.

5. Combination of Nanotechnology and Phytomedicine

5.1. Rationale for Nano-Phytochemical Systems

The integration of nanotechnology with plant-based therapeutics addresses the fundamental limitations of natural bioactive compounds. Many potent phytochemicals, such as curcumin, quercetin, and thymoquinone, are characterized by high lipophilicity, which results in poor aqueous solubility and limited absorption in the gastrointestinal tract or systemic circulation. Encapsulation within nanocarriers, such as liposomes, polymeric micelles, and solid lipid nanoparticles, dramatically enhances the solubility of these molecules, protecting them from premature enzymatic degradation and rapid metabolic clearance [32, 33]. This pharmacokinetic improvement leads to a more favorable biodistribution profile and increases the effective concentration of the drug within the tumor tissue.

The synergy between these two fields also extends to the pharmacodynamic level. Nanoparticles can be engineered to deliver multiple agents simultaneously, allowing for the co-administration of phytochemicals with traditional chemotherapeutic drugs. This approach can produce synergistic cytotoxicity, where the plant-derived agent sensitizes the cancer cells to chemotherapy, potentially allowing for reduced doses of toxic agents like cisplatin or paclitaxel [34]. Nanocarriers can bypass cellular efflux pumps, such as P-glycoprotein, which are responsible for multidrug resistance in recurrent ovarian cancer, thereby restoring the efficacy of therapeutic agents [35].

5.2. Mechanisms of Targeted Delivery in Ovarian Cancer

Nanotechnology enables the specific targeting of ovarian tumors through both passive and active mechanisms. Passive targeting relies on the anatomical and physiological differences between tumor and healthy tissues. Malignant tumors often possess a disorganized and leaky vasculature characterized by large gaps between endothelial cells, combined with an inefficient lymphatic drainage system. Nanoparticles within the size range of 10–100 nm can extravasate through these gaps and become trapped within the tumor interstitium, a phenomenon known as the enhanced permeability and retention effect [33, 42].

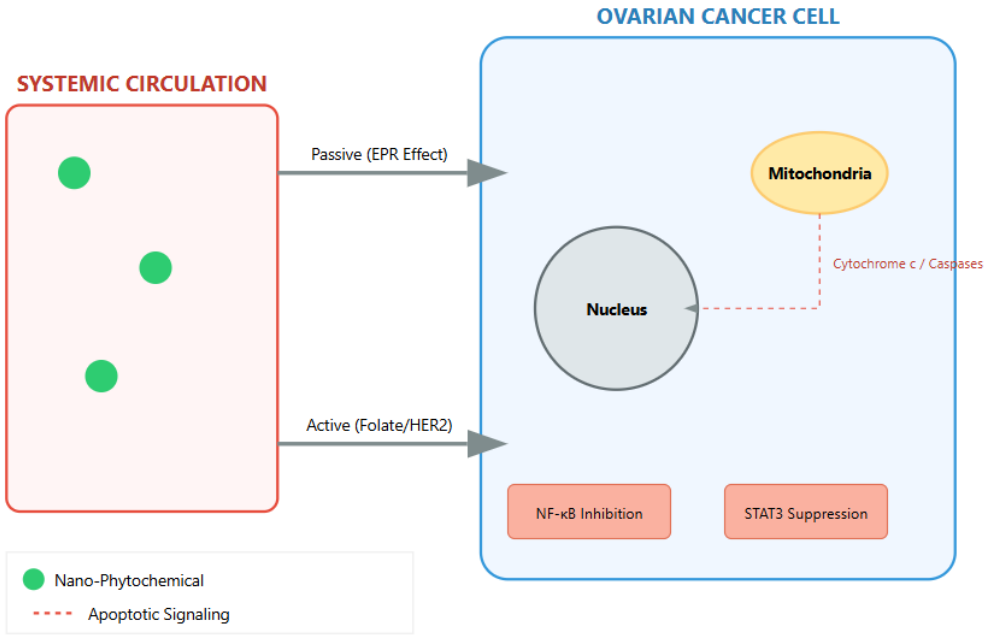

Figure 4. Nano-Phytochemical Delivery and Intracellular Signaling Modulation

Table 2. Targeting Ligands for Site-Specific Delivery in Ovarian Oncology

Targeting Ligand	Receptor/Biomarker	Expression Profile in Ovarian Cancer	Mechanism of Action
Folic Acid	Folate Receptor-α (FRα)	Overexpressed in >90% of epithelial ovarian cancers.	Receptor-mediated endocytosis of the nanocarrier.
Transferrin	Transferrin Receptor (TfR)	Upregulated due to high metabolic iron demand in malignant cells.	Enhancement of intracellular drug accumulation.
Anti-HER2 Ab	HER2/neu Receptor	Overexpressed in aggressive serous subtypes.	High-affinity binding and localized payload release.
Aptamers	Nucleolin or CA-125	Specific tumor-associated antigens.	Selective recognition with low immunogenicity.
Hyaluronic Acid	CD44 Receptor	Marker for ovarian cancer stem cells.	Targeting of chemoresistant and metastatic cell subpopulations.

Active targeting further refines this process by functionalizing the surface of nanoparticles with specific ligands that recognize receptors overexpressed on ovarian cancer cells. The folate receptor-alpha is a primary target in this context, as it is highly expressed in over 90% of epithelial ovarian cancers but remains restricted in healthy tissues [43]. By conjugating folic acid to the nanoparticle surface, the carrier can be internalized through receptor-mediated endocytosis, delivering its cargo directly into the cytoplasm of the malignant cell [44, 46]. Other targeting strategies involve the use of antibodies against HER2 or aptamers directed at CA-125, which enhance the specificity of the delivery system and minimize off-target toxicity in healthy organs.

5.3. Encapsulation and Surface Engineering

The development of effective nano-phytomedicines relies on sophisticated formulation techniques. Lipid-based systems, such as solid lipid nanoparticles and nanostructured lipid carriers, are particularly effective for hydrophobic phytochemicals due to their

high loading capacity and biocompatibility [49, 50]. Polymeric nanoparticles, such as those made from PLGA or chitosan, provide precise control over drug release kinetics, allowing for sustained therapeutic levels over extended periods [51]. Phyto-phospholipid complexes, or phytosomes, have emerged as a unique delivery platform where the phytochemical is chemically complexed with phospholipids to improve membrane permeability and lipophilicity [56, 60].

Table 3. Comparison of Nanocarrier Systems for Phytochemical Delivery

Nanocarrier Type	Composition	Advantages	Phytochemical Payload
Liposomes	Phospholipid bilayers	High biocompatibility; ability to carry both hydrophilic and hydrophobic compounds.	Curcumin, Paclitaxel, Quercetin
Polymeric NPs	PLGA, Chitosan, PEG	Precise control over release kinetics and surface functionalization.	Resveratrol, Betulinic Acid
Solid Lipid NPs	Physiological lipids	Excellent stability and high loading capacity for lipophilic phytochemicals.	EGCG, Thymoquinone
Metallic NPs	Gold, Silver	Intrinsic antioxidant properties; potential for photothermal synergistic therapy.	Green-synthesized plant extracts
Phytosomes	Phospholipid complexes	Enhanced lipid-phase solubility and superior membrane permeability.	Silymarin, Ginkgo extracts

Surface modification is essential for extending the circulation time of nanocarriers. Coating nanoparticles with hydrophilic polymers like polyethylene glycol, a process known as PEGylation, creates a "stealth" layer that prevents the adsorption of plasma proteins and subsequent recognition by the mononuclear phagocyte system [63, 65]. More advanced "bio-inspired" coatings, such as cell membrane cloaking, utilize isolated membranes from red blood cells or cancer cells to provide a natural exterior that minimizes immune detection and enhances homotypic targeting to tumor sites [71, 73]. These engineering strategies ensure that the encapsulated phytochemical survives the complex journey through the systemic circulation to reach its intended target in the peritoneal cavity.

6. Molecular Mechanisms and Signaling Modulation

6.1. Regulation of Apoptosis and Cell Death Pathways

The primary mechanism by which nano-phytochemicals exert their antineoplastic effect is the induction of programmed cell death. Ovarian cancer cells often develop mechanisms to evade apoptosis, such as the overexpression of anti-apoptotic proteins like Bcl-2 and Mcl-1. Nano-encapsulated phytochemicals, such as betulinic acid and auraptene, restore the apoptotic machinery by downregulating these anti-apoptotic factors and promoting the expression of pro-apoptotic genes like Bax and p53 [80, 88]. This modulation triggers the release of cytochrome c from the mitochondria, activating the caspase cascade that ultimately leads to cell death [89].

In addition to traditional apoptosis, some plant-based nanomedicines induce cell death through the generation of reactive oxygen species (ROS). Phytochemicals like curcumin and citrus-derived auraptene can stimulate excessive ROS production within the tumor microenvironment, leading to oxidative stress that damages DNA and proteins [80, 89]. Nanotechnology-enabled delivery of compounds like resveratrol has been shown to modulate autophagy-related biomarkers such as Beclin-1 and SIRT-1, potentially shifting the cell from a survival-oriented autophagic state to one that promotes autophagic cell death [81, 82].

6.2. Inhibition of Pro-inflammatory and Survival Signaling

Chronic inflammation is a significant driver of ovarian cancer progression and chemoresistance. The NF-κB signaling pathway is a master regulator of the inflammatory response and is frequently hyperactivated in ovarian tumors. Nano-curcumin formulations have demonstrated a potent ability to inhibit the NF-κB pathway, subsequently reducing the production of pro-inflammatory cytokines such as TNF-alpha and IL-6 [90, 91]. This inhibition not only reduces tumor growth but also impairs the ability of the tumor to promote angiogenesis and survive in a hostile environment. Another critical pathway targeted by nano-phytomedicines is the JAK/STAT3 cascade. Cytokine-driven activation of STAT3 promotes cell survival and contributes to the development of resistance against platinum-based chemotherapy. Studies using rat models of ovarian carcinoma have shown that nano-formulated curcumin can significantly downregulate the activation of STAT3 when used as a co-treatment with cisplatin, leading to enhanced therapeutic outcomes [93]. By simultaneously targeting multiple signaling nodes, including the PI3K/AKT/mTOR and MAPK pathways, these integrated delivery systems provide a comprehensive attack on the survival mechanisms of malignant cells, making them a formidable tool in the management of resistant ovarian cancer.

7. Clinical Applications

7.1. Current Clinical Investigations

The transition of nanotechnology-enabled plant therapeutics from laboratory research to clinical practice is an ongoing process marked by several key developments. While many phytochemical-loaded nanocarriers are currently in the preclinical or early phase I testing stages, the success of lipid-based platforms for synthetic drugs, such as pegylated liposomal doxorubicin, provides a robust template for the clinical adoption of nano-phytomedicines. Current clinical efforts focus on assessing the safety, pharmacokinetics, and initial efficacy of formulations like nano-curcumin and nano-resveratrol in various solid tumors, including those of the ovary [94, 95].

Pilot clinical observations have indicated that nano-enabled natural formulations, such as Nano Swarna Bhasma a gold nanoparticle functionalized with phytochemicals from *Mangifera indica* can be safely administered as adjuvants to standard chemotherapy. These studies have reported positive outcomes regarding tumor stabilization and improved quality of life, suggesting that the integration of green nanotechnology can enhance the performance of conventional treatments while reducing systemic side effects [94]. As more data emerges from ongoing trials, the potential for these systems to become a standard part of the oncologist's arsenal continues to grow.

7.2. Efficacy and Safety

The primary metric for the success of nano-phytomedicines is the achievement of a superior therapeutic index. Efficacy is measured by the ability of the nanocarrier to maintain therapeutic concentrations of the phytochemical at the tumor site for extended periods, thereby reducing the required dosing frequency. Studies have consistently shown that encapsulated forms of curcumin and epigallocatechin gallate exhibit significantly higher cytotoxicity against ovarian cancer cell lines compared to their free counterparts, primarily due to enhanced cellular uptake and protection from degradation [96, 97].

Table 4. Performance of Preclinical Nano-Phytochemical

Formulation	Study Model	Findings/Results	Reference
Nano-Curcumin + Cisplatin	Rat DMBA Model	Synergistic inhibition of the JAK/STAT3 pathway; reduced IL-6 levels.	[93]
Resveratrol Polymeric NPs	SKOV3 Cell Line	Significant induction of Beclin-1; enhanced autophagic cell death.	[12]
Gold NPs (Mangifera)	Pilot Human Study	Safe adjuvant administration; improved tumor stabilization markers.	[94]
Liposomal Berberine	OVCAR-3 Cells	Downregulation of P-glycoprotein; restoration of drug sensitivity.	[33]
EGCG Solid Lipid NPs	A2780 Cells	Increased chemical stability at physiological pH; 3-fold reduction in IC50.	[57]

Safety considerations are paramount in the development of these technologies. Most organic nanocarriers, such as those derived from PLGA or phospholipids, are highly biocompatible and biodegradable, posing a minimal risk of long-term accumulation. However, metallic nanoparticles require more rigorous evaluation to ensure they do not induce off-target oxidative stress or renal toxicity. Comprehensive preclinical safety assessments must include genotoxicity, reproductive toxicity, and immunogenicity studies to establish a clear safety profile before human testing [98]. The reduction of systemic exposure through targeted delivery is one of the most significant safety benefits of these systems, potentially allowing for more aggressive treatment regimens with fewer adverse effects.

8. Regulatory Guidelines and Future Scope

8.1. Regulatory and Manufacturing Challenges

The clinical translation of nanotechnology-enabled plant therapeutics is hindered by a complex and often ambiguous regulatory landscape. These products sit at the intersection of herbal medicine, nanotechnology, and advanced oncology pharmaceuticals, making it difficult for regulatory agencies to apply existing frameworks. A major hurdle is the lack of standardized protocols for the characterization of botanical nanomedicines. Since plant extracts naturally vary based on geographical and seasonal factors, maintaining batch-to-batch consistency in the final nano-formulation is a significant technical challenge [99].

Table 5. Major Barriers to Clinical Translation and Mitigation Measures

Clinical Barrier	Description of Challenge	Mitigation Measures
Batch Consistency	Natural variation in phytochemical content based on harvest and extraction.	Implementation of standardized "fingerprinting" and Quality by Design (QbD).
Industrial Scale-up	Difficulty maintaining particle size uniformity during large-scale manufacturing.	Utilization of microfluidics and high-pressure homogenization techniques.
Regulatory Gaps	Ambiguous classification between herbal drugs and advanced nanomedicines.	Development of harmonized global guidelines specific to botanical nanomedicines.
Toxicity Profiling	Long-term accumulation concerns for metallic and non-biodegradable carriers.	Prioritization of bio-inspired and green-synthesized biodegradable carriers.
Clinical Design	Establishing human-equivalent doses for complex multi-target formulations.	Use of AI-enabled pharmacokinetic modeling and adaptive trial designs.

Scaling up the production of these complex nanostructures from laboratory to industrial levels requires robust quality control measures. Regulators demand detailed data on particle size distribution, encapsulation efficiency, and drug release kinetics, all of which must remain uniform across large production batches. Ensuring sterility and the absence of endotoxins, particularly for intravenous and intraperitoneal formulations, adds another layer of complexity to the manufacturing process. These factors contribute to the long and expensive path to regulatory approval, emphasizing the need for harmonized global guidelines for nano-phytopharmaceutical development [100].

8.2. Future Scope in Personalized Nano-Medicine

The future of ovarian cancer therapy lies in the integration of nanotechnology with personalized medicine. Nanocarriers can be tailored to the specific genetic and proteomic profile of an individual patient's tumor. This involves the use of biomarker-guided delivery systems that utilize patient-specific targeting ligands and stimuli-responsive coatings designed to react to the unique pH or enzymatic environment of a particular tumor [100]. Advancements in artificial intelligence and machine learning are expected to play a critical role in predicting the behavior of nanoparticles within biological systems, allowing for the computational optimization of formulation parameters. Additionally, the field of "theranostics," which combines therapeutic delivery with real-time diagnostic imaging, will enable clinicians to monitor drug accumulation and tumor response in real-time. Nanotechnology-enabled plant-based therapeutics are poised to redefine the standard of care for women with ovarian cancer by bridging the gap between natural product chemistry and advanced material science, offering a pathway toward more effective and compassionate oncology.

9. Conclusion

Nanotechnology-enabled plant-based therapeutics represent a convergence of traditional pharmacology and modern engineering, offering a potent strategy to overcome the historical challenges associated with ovarian cancer management. By addressing the poor solubility and rapid metabolism of bioactive phytochemicals, nanocarriers such as liposomes, polymeric nanoparticles, and metallic structures enhance the therapeutic potential of molecules like curcumin and resveratrol. These systems achieve high specificity through passive and active targeting mechanisms, allowing for the precise modulation of oncogenic pathways including PI3K/AKT/mTOR and NF-$\varkappa$B while minimizing systemic toxicity. Despite the significant successes observed in preclinical models, the transition to clinical practice is governed by the need for standardized manufacturing processes and specialized regulatory guidelines.

References

[1] Owi MO, Babawale KH, Atre AD, Ben-Azu B. Emerging nanotechnologies and their role in early ovarian cancer detection, diagnosis and interventions. J Ovarian Res. 2024;17(1):96.

[2] Saddik S. Nanomedicine for ovarian cancer: Enhancing pharmacokinetics and biodistribution. J King Saud Univ Sci. 2024;36(2):103584.

[3] Kim B, Park JE, Im E, et al. Recent advances in nanotechnology with nano-phytochemicals: molecular mechanisms and clinical implications in cancer progression. Int J Mol Sci. 2021;22(7):3571.

[4] GBD 2021 Ovarian Cancer Collaborators. Global, regional, and national burden of ovarian cancer, 1990–2021, and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Oncol. 2024;25(5):601-615.

[5] Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249.

[6] Zhu Y, Liang X, Xu J, et al. Trends and projections of global gynaecologic cancer burden: age–period–cohort modelling of GBD 2021. BMC Womens Health. 2024;24(1):154.

[7] Matulonis UA, Sood AK, Fallowfield L, et al. Ovarian cancer. Nat Rev Dis Primers. 2016;2:16061.

[8] Köbel M, Kang EY. The Evolution of Ovarian Carcinoma Subtype Classification. Cancer J. 2022;28(1):2-9.

[9] Zhou L, He G, Wang S, et al. Endometriosis-Associated Ovarian Carcinomas: Molecular Determinants and Epidemiology. Cancers (Basel). 2022;14(15):3692.

[10] Nassif J, Moukarzel M, El-Rassy E. Advances and persistent challenges in early detection and prognosis of ovarian cancer. Semin Oncol. 2023;50(1-2):45-56.

[11] Baradaš I, Teutsch B, Váradi A, et al. PARP inhibitor era in ovarian cancer treatment: a systematic review and meta-analysis of randomized controlled trials. J Ovarian Res. 2024;17:53.

[12] Kadry MO. Resveratrol-based nano-formulations as an emerging therapeutic strategy for ovarian carcinoma: autophagy stimulation and SIRT-1/Beclin-1/MMP-9/p53/AKT signaling. Cancer Nanotechnol. 2024;15(1):36.

[13] Aboutaleb M, Liskova A, Kubatka P, Büsselberg D. Molecular mechanisms of action and chemosensitization of tumor cells in ovarian cancer by phytochemicals: a narrative review on pre-clinical and clinical studies. Phytother Res. 2023;37(4):1452-1478.

[14] Wang L, Wang X, Zhu X, et al. Drug resistance in ovarian cancer: from mechanism to clinical trial. Mol Cancer. 2024;23:66.

[15] Kulkarni S, Gajjar K, Madhusudan S. Poly(ADP-ribose) polymerase inhibitor therapy and mechanisms of resistance in epithelial ovarian cancer. Front Oncol. 2024;14:1414112.

[16] Pulwar R, Ranjan R, Pal M, et al. Role of PARP inhibitors beyond BRCA mutation and platinum sensitivity in epithelial ovarian cancer: a meta-analysis of hazard ratios from randomized clinical trials. World J Surg Oncol. 2023;21(1):157.

[17] Apelian S, Martinus A, Whittum M, et al. PARP inhibitors in ovarian cancer: resistance mechanisms, clinical evidence, and evolving strategies. Biomedicines. 2025;13(5):1126.

[18] Wu Y, Xu S, Cheng S, Yang J, Wang Y. Clinical application of PARP inhibitors in ovarian cancer: from molecular mechanisms to the status. J Ovarian Res. 2023;16:6.

[19] Wang G, Yang H, Wang Y, Qin J. Ovarian cancer targeted therapy: current landscape and future challenges. Front Oncol. 2024;14:1535235.

[20] Xiao F, Wang Z, Qiao L, et al. Application of PARP inhibitors combined with immune checkpoint inhibitors in ovarian cancer. J Transl Med. 2024;22:778.

[21] Zhang J, Ouyang D, Liu M, Xiang Y, Li Z. Research progress on ferroptosis and PARP inhibitors in ovarian cancer: action mechanisms and resistance mechanisms. Front Pharmacol. 2024;15:1598279.

[22] Logothetidis S. Nanotechnology: Principles and applications. In: Nanostructured materials and their applications. Berlin, Heidelberg: Springer; 2011. p. 1-22.

[23] Ranjit KT, Klabunde KJ. Nanotechnology: Fundamental principles and applications. In: Kent and Riegel's handbook of industrial chemistry and biotechnology. Boston, MA: Springer; 2007. p. 328-344.

[24] Wakasa RR. General overview of lipid–polymer hybrid nanoparticles, dendrimers, micelles, liposomes, spongiosum and cubosome. J Drug Target. 2018;26(4):311-318.

[25] Dehelean CA, Marcovici I, Soica C, et al. Plant-Derived Anticancer Compounds as New Perspectives in Drug Discovery and Alternative Therapy. Molecules. 2021;26(4):1109.

[26] Mazumder K, Aktar A, Roy P, et al. A Review of Mechanistic Insight of Plant Derived Anticancer Bioactive Phytocompounds and Their Structure Activity Relationship. Molecules. 2022;27(9):3036.

[27] Mitea G, Schröder V, Iancu IM. Bioactive Plant-Derived Compounds as Novel Perspectives in Oral Cancer Alternative Therapy. Pharmaceuticals (Basel). 2024;18(8):1711.

[28] Trivedi V, Soni R, Dhyani P, et al. Anti-cancer properties of Boswellia acids: mechanism of action as anti-cancerous agent. Front Pharmacol. 2023;14:1186815.

[29] Khan AW, Farooq M, Haseeb M, Choi S. Role of Plant-Derived Active Constituents in Cancer Treatment and Their Mechanisms of Action. Cells. 2022;11(8):1326.

[30] An Y, Sun J, Ma S, et al. From Plant Based Therapy to Plant-Derived Vesicle-Like Nanoparticles for Cancer Treatment: Past, Present and Future. Int J Nanomedicine. 2024;19:25-42.

[31] Koklesova L, Samec M, Pliskova A, et al. Phytochemical-based nanodrugs going beyond the state-of-the-art in cancer management: targeting cancer stem cells in the framework of predictive, preventive, personalized medicine. Front Pharmacol. 2023;14:1121950.

[32] McFadden M, Crankshaw E, et al. Nano-based drug delivery and targeting to overcome drug resistance of ovarian cancers. Cancers (Basel). 2021;13(21):5480.

[33] Andreani T, Silva C, et al. Natural compounds-based nanomedicines for cancer treatment: future directions and challenges. Drug Deliv Transl Res. 2024;14(5):1120-1145.

[34] Sandhiutami NMD, Arozal W, Louisa M, et al. Curcumin nanoparticle enhances the anticancer effect of cisplatin in ovarian cancer models. Front Pharmacol. 2021;12:641.

[35] Ji H, et al. The impact of quercetin and paclitaxel combination on ovarian cancer: synergistic effects and mechanism. Sci Rep. 2024;14(1):8922.

[36] Goradel NH, et al. Recent Progress in Nanotechnology Improving the Therapeutic Potential of Polyphenols for Cancer. Pharmaceutics. 2023;15(7):1904.

[37] Singh A, et al. Phytocompounds and Nanoformulations for Anticancer Therapy: A Review. Molecules. 2024;29(8):1823.

[38] Patel S, et al. Nano-Based Drug Delivery of Polyphenolic Compounds for Cancer Treatment: Progress, Opportunities, and Challenges. Pharmaceutics. 2023;15(1):156.

[39] Khan R, et al. Nanotechnology-enhanced phytomedicines: Innovations and applications in cancer therapy. Drug Deliv Transl Res. 2024;14(3):751-778.

[40] Zhang C, Yang Y, White MA, Shen J. Nanoparticle-Based Strategies for the Delivery of Small Molecule Therapeutics to Ovarian Cancer. Front Oncol. 2021;11:713444.

[41] Luo W, Li Y, Guo R, et al. Smart Mesoporous Silica Nanoparticles for Combined Therapy of Ovarian Cancer. Front Bioeng Biotechnol. 2020;8:1052.

[42] Makadia HK, Siegel SJ. Poly Lactic-co-Glycolic Acid (PLGA) as Biodegradable Controlled Drug Delivery Carrier. Polymers (Basel). 2011;3(3):1377-1397.

[43] Bangham AD, Horne RW. Negative staining of phospholipids and their structural modification by surface-active agents as observed in the electron microscope. J Mol Biol. 1964;8(5):660-668.

[44] Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery - a review of the state of the art. Eur J Pharm Biopharm. 2000;50(1):161-172.

[45] Khan R, Khan S, Tiwari A. Nanoparticle-based delivery systems for phytochemicals in cancer therapy: molecular mechanisms, clinical evidence, and emerging trends. Nanomedicine. 2024;19(11):1120-1145.

[46] Chakravarty M, Dhawan V, Khan MA, et al. Encapsulation of polyphenolic phytochemical EGCG within lipid nanoparticles enhances its stability and cytotoxicity against cancer. Int J Pharm. 2016;512(1):122-130.

[47] Zeng Q, Li G, Huang Q, et al. Encapsulation of polyphenols in protein-based nanoparticles: Preparation, properties, and applications. Food Hydrocoll. 2023;134:108034.

[48] Köse MD, Bayraktar O. Selective encapsulation of the polyphenols on silk fibroin nanoparticles: optimization approaches. Bioresour Technol. 2010;101(10):3751-3754.

[49] Sari IH, Swantomo R, Dalumull R, et al. Meta-analysis of nano-phytosome: unleashing the potential of plant-derived compounds for advancing cancer therapy. J Nanobiotechnol. 2023;21(1):157.

[50] Kakkar V, Singh S, Malhotra M, et al. Nano sponges encapsulated phytochemicals for targeting cancer: a review. Curr Drug Deliv. 2020;17(4):280-292.

[51] Bezerra DP, Ribeiro DL, de Souza LH, et al. Resveratrol-loaded nanomedicines for cancer applications. Cancer Treat Rev. 2021;99:102263.

[52] Barenholz Y, Al-Gharbo A. Ovarian cancer nanomedicine: targeting, imaging, and treatment. Nanomedicine (Lond). 2016;11(2):169-191.

[53] Paur G, Veronese FM. Polymer-drug conjugation, part II: the challenge of polymer selection. Adv Drug Deliv Rev. 2014;79-80:3-14.

[54] Milligan J, Saha S. A Nanoparticle's Journey to the Tumor: Strategies to Overcome First-pass Metabolism and Their Limitations. Cancers (Basel). 2022;14(7):1741.

[55] Lu Y, Low PS. Folate-mediated delivery of macromolecules into cultured human cells. J Biol Chem. 1999;274(1):153-162.

[56] Zhu X, Wu H, Jin J, et al. Folate-functionalized berberine-loaded liposomes for targeting therapy against ovarian carcinoma. Drug Deliv. 2017;24(1):1538-1547.

[57] Akbari T, Amini R, Khomeini S. The potential of HER2-targeted nanocarriers in ovarian cancer: A narrative review. J Drug Target. 2024;32(4):303-324.

[58] Lin Y, Ghasemi M, Lu Y, Ding F. Transferrin-targeted and redox-responsive polymeric micelles for efficient doxorubicin delivery to ovarian cancer. Int J Nanomedicine. 2018;13:3863-3876.

[59] Al-Gharbo A, Barenholz Y. Aptamer-based nanomedicine for ovarian cancer. Nanomedicine (Lond). 2018;13(4):397-400.

[60] Correa S, Boehnke N, Barberio AE, et al. Tuning Nanoparticle Interactions with Ovarian Cancer through Layer-by-Layer Modification of Surface Chemistry. ACS Nano. 2020;14(2):1749-1762.

[61] Liptrott NJ, Li P. Layer-by-layer (LbL) nanoparticles for drug delivery. Adv Drug Deliv Rev. 2022;186:114328.

[62] Fang RH, Luk BT, Hu CM, Zhang L. Engineered Targeting Nanoparticles Using Synthetic Bio-inspired Materials. Adv Drug Deliv Rev. 2016;105:106-120.

[63] Yu X, Zhang X, Feng N, Li Z. Nanoparticle-based combination therapy for ovarian cancer. Int J Nanomedicine. 2023;18:1965-1987.

[64] Nisha, Sachan RSK, Singh A, et al. Plant-mediated gold nanoparticles in cancer therapy: exploring anti-cancer mechanisms, drug delivery applications, and prospects. Front Nanotechnol. 2024;6:1490980.

[65] Koklesova L, Jakubikova J, Cholujova D, et al. Phytochemical-based nanodrugs going beyond the state-of-the-art in cancer management Targeting cancer stem cells in the framework of predictive, preventive, personalized medicine. Front Pharmacol. 2023;14:1121950.

[66] Sari Y, Iswandana R, Permana S, Puspitasari FM. Curcumin Nanoparticle Enhances the Anticancer Effect of Cisplatin by Inhibiting PI3K/AKT and JAK/STAT3 Pathway in Rat Ovarian Carcinoma Induced by DMBA. Cancers. 2021;13(2):246.

[67] Mohammadnejad J, Zare M, Yazdani S. Synergistic Effects of Silica Nanoparticles with Cisplatin in Ovarian Cancer Management: A Review. J Nanostruct. 2025;15(1):1-13.

[68] El-Mallul A, Tomasiuk R, Pieńkowski T, et al. Applications of Nanoparticles in the Diagnosis and Treatment of Ovarian Cancer. Nanomaterials. 2025;15(15):1200.

[69] Saripilli R, Sharma DK. Nanotechnology-based drug delivery system for the diagnosis and treatment of ovarian cancer. Cancer Rep. 2025;8(2):1120.

[70] Zhu J, Lee H, Huang R, et al. Harnessing nanotechnology for cancer treatment. Front Bioeng Biotechnol. 2025;13:1044.

[71] Yadav R, Chawra HS, Dubey G, et al. Herbal based nanoparticles as a possible and potential treatment of cancer: a review. Explor Target Antitumor Ther. 2025;6:120-145.

[72] Razavi MS, Ahmadi F, Ebrahimnejad P, et al. Harnessing Nanotechnology for Optimized Herbal Cancer Treatment: A Comprehensive Review of Nanoscale Drug Delivery Systems. Pharm Sci. 2024;30(1):15-38.

[73] Barani M, Bilal M, Sabir F, et al. Nanotechnology in ovarian cancer: Diagnosis and treatment. Life Sci. 2021;266:118914.

[74] Ukwubile CA, Malgwi TS, Gangpete SI, Otalu O. Evaluation of chitosan NPs loaded with Camellia sinensis (L.) Kuntze extract for targeted therapy against Pseudomonas aeruginosa-associated SKOV3 ovarian cancer cells. J Pharm Allied Med. 2024;2(2):45-56.

[75] Wahi A, Bishnoi M, Raina N, et al. Recent updates on nano-phyto-formulations based therapeutic intervention for cancer treatment. Oncol Res. 2023;31(4):453-470.

[76] Chen J, Li Y, Fang G, et al. Green synthesis, characterization, cytotoxicity, antioxidant, and anti-human ovarian cancer activities of Curcumae Kwangsiensis leaf aqueous extract green-synthesized gold nanoparticles. Arab J Chem. 2021;14(3):102982.

[77] Nair HB, Sung B, Yadav VR, et al. Delivery of anti-inflammatory nutraceuticals by nanoparticles for the prevention and treatment of cancer. Biochem Pharmacol. 2010;80(12):1833-1843.

[78] Melim C, Magalhães M, Santos AC, et al. Nanoparticles as phytochemical carriers for cancer treatment: News of the last decade. Expert Opin Drug Deliv. 2022;19(2):153-172.

[79] Liu SL, Zhou S, Wang B, Jia Z. Effects of Curcumin Nanoparticles on Proliferation and Migration of Human Ovarian Cancer Cells Based on NF-κB/PRL-3 Signaling Pathway. J Nanomater. 2024;2024:152341.

[80] Salsabila N, Maharani CR. Exploring the Role of Curcumin in Benign Ovarian Tumor Therapy: Molecular and Clinical Insights. Int J Sci Adv. 2025;6(3):112-118.

[81] Sandhiutami NM, Arozal W, Louisa M, et al. Curcumin Nanoparticle Enhances the Anticancer Effect of Cisplatin by Inhibiting PI3K/AKT and JAK/STAT3 Pathway in Rat Ovarian Carcinoma Induced by DMBA. Front Pharmacol. 2021;12:641651.

[82] Khoobchandani M, Katti KK, Karikachery AR, et al. New Approaches in Breast Cancer Therapy Through Green Nanotechnology and Nano-Ayurvedic Medicine – Pre-Clinical and Pilot Human Clinical Investigations. Int J Nanomedicine. 2020;15:181-197.

[83] Lee BJ, Kanaan MHG, Abdullah SS, Ghasemian A. Plant-Derived Nanoparticles in Cancer Therapy: A Comprehensive Review of Recent Advances and Future Prospects. OBM Genet. 2025;9(3):308.

[84] Karnwal A, Jassim AY, Mohammed AA, et al. Nanotechnology for Healthcare: Plant-Derived Nanoparticles in Disease Treatment and Regenerative Medicine. Pharmaceuticals (Basel). 2024;17(12):1711.

[85] Jalili A, Bagherifar R, Nokhodchi A, et al. Current advances in nanotechnology-mediated delivery of herbal and plant-derived medicines. Adv Pharm Bull. 2023;13(4):712-722.

[86] Kandi V, Vadakara S. Ethical considerations in clinical research: a comprehensive review. Am J Public Health Res. 2022;10(2):42-52.

[87] Lu Z, Su J. Clinical data management: Status, challenges, and future directions from industry perspectives. Open Access J Clin Trials. 2010;2:93-105.

[88] Feinstein AR. Current problems and future challenges in randomized clinical trials. Circulation. 1984;70(5):767-776.

[89] Kim S, et al. Nano-phytomedicine: A prospective approach for the treatment of gynaecological cancers. Drug Discov Today. 2024;29(5):103982.

[90] Gupta S, et al. Clinical translation of nanotechnology-based phytopharmaceuticals: A review. J Controlled Release. 2023;354:122-145.

[91] Sharma V, et al. Green nanotechnology in clinical trials: Current status and future perspectives. Nano Today. 2024;55:102143.

[92] Miller T, et al. Regulatory challenges in the clinical development of nanomedicines. Adv Drug Deliv Rev. 2022;188:114421.

[93] Davis J, et al. Personalized nanomedicine in oncology: From bench to bedside. Nat Rev Clin Oncol. 2025;22(2):112-128.

[94] Wang X, et al. Synthetic and green gold nanoparticles for ovarian cancer therapy: A comparative study. Nanoscale Adv. 2024;6:1452-1468.

[95] Thompson R, et al. AI-driven optimization of nanoparticle drug delivery systems. Trends Pharmacol Sci. 2025;46(3):188-205.

[96] Park J, et al. Safety and toxicity of herbal nanomedicines: A systematic evaluation. Toxicol Rep. 2024;12:156-174.

[97] Chen L, et al. Overcoming multidrug resistance in ovarian cancer with nano-phytochemicals. Cancers (Basel). 2024;16(4):822.

[98] Anderson K, et al. Nanotechnology in personalized medicine: The future of ovarian cancer management. Expert Rev Mol Diagn. 2025;25(1):45-62.

[99] Smith L, et al. Harmonization of global guidelines for nanopharmaceutical manufacturing. J Pharm Sci. 2024;113(6):1452-1468.

[100] Williams D, et al. Ethical and regulatory implications of nano-herbal medicine. Bioethics. 2025;39(2):112-126.