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Application of Nanoparticles in the Treatment of Ovarian Cancer: A Review of Emerging Strategies for Targeted Therapy

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A B S T R A C T

Objective: Ovarian cancer remains highly lethal, primarily due to late-stage diagnosis and the limitations of conventional therapies, which are often associated with systemic toxicity and limited tumor specificity. Nanoparticles, owing to their nanoscale dimensions, high surface-to-volume ratio, and capacity for surface functionalization, offer improved drug delivery and precise tumor targeting. This review provides a comprehensive summary of the principal types of nanoparticles employed in ovarian cancer therapy, with an emphasis on their mechanisms of action and therapeutic efficacy.

Methods: This narrative review synthesizes findings from experimental and preclinical studies investigating nanoparticle-based interventions in ovarian cancer. Relevant publications were identified through systematic searches of established scientific databases, including PubMed, Scopus, and Google Scholar. Studies focusing on nanoparticle design, targeting strategies, drug-loading efficiency, and therapeutic outcomes were critically evaluated and analyzed.

Results: A diverse range of nanostructures has been investigated for the treatment of ovarian cancer. These include magnetoelectric $CoFe_2O_4$@$BaTiO_3$ nanoparticles; poly(lactic-co-glycolic acid) (PLGA)-based nanoplatforms co-delivering cisplatin and HER2-targeted antibodies; biodegradable periodic mesoporous organosilica (PMO) nanoparticles loaded with doxorubicin; polymer-based immunotargeted nanoparticles (NPs–Tx–HER); mesoporous silica nanoparticles (MSNPs); poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) nanoparticles encapsulating paclitaxel; PARP1-targeted small interfering RNA (siRNA) nanocarriers; folate-conjugated lipid nanoparticles; cathepsin B–responsive doxorubicin prodrug nanoparticles; and PTP@SR-717 nanocomplexes. Across in vitro and in vivo models, these nanosystems have demonstrated enhanced tumor-specific accumulation, improved intracellular drug delivery, reduced systemic toxicity, and potentiation of chemotherapeutic and immunotherapeutic efficacy.

Conclusion: Nanoparticle-based therapies represent a significant advancement in ovarian cancer treatment, enabling precise tumor targeting and controlled drug release. This approach minimizes the systemic toxicity commonly associated with conventional chemotherapy while enhancing anticancer efficacy. When integrated with cytotoxic agents, gene-silencing molecules, or monoclonal antibodies, nanoparticle platforms facilitate the development of personalized and more effective therapeutic strategies. Ultimately, these innovations hold considerable potential to improve clinical outcomes and enhance patients' quality of life.

Keywords: Nanoparticles; Ovarian cancer therapy; Chemotherapy; Nanomedicine; Targeted drug delivery

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Introduction

Gynecologic diseases particularly malignancies of the female reproductive tract exert a profound impact on women's health, longevity, and overall quality of life. Delayed diagnosis remains a critical obstacle in the management of these cancers, as detection at advanced stages is consistently associated with reduced survival rates. Consequently, preventive strategies and early diagnostic interventions are of paramount importance [1-6]. Among gynecologic malignancies, ovarian cancer occupies a particularly aggressive and devastating position.

Ovarian cancer is recognized as one of the most prevalent and fatal malignancies affecting women worldwide. Owing to its insidious onset and nonspecific early symptoms, it is frequently diagnosed at advanced stages, which substantially contributes to its high mortality rate [7]. Despite significant advances in oncologic research and therapeutic innovation, ovarian cancer continues to represent a formidable global clinical challenge [8].

The etiology of ovarian cancer is complex and multifactorial, reflecting an interplay among genetic predisposition, environmental exposures, and hormonal influences [9]. Germline mutations in critical DNA repair genes most notably *BRCA1* and *BRCA2* are well-established risk factors that significantly increase lifetime susceptibility to the disease [10]. In addition to hereditary determinants, several epidemiologic variables have been implicated, including a positive family history, age over 50 years, nulliparity, and prolonged exposure to hormone replacement therapy [11]. Collectively, these factors underscore the heterogeneous and multifaceted nature of ovarian carcinogenesis.

At the molecular level, the pathophysiology of ovarian cancer is characterized by uncontrolled cellular proliferation driven by cumulative genetic and epigenetic alterations [12]. Disruptions in key regulatory signaling pathways, including PI3K/AKT and TP53, play central roles in tumor initiation and progression [13]. Aberrant activation of these pathways promotes sustained proliferative signaling, resistance to apoptosis, enhanced cellular migration, and eventual metastatic dissemination. Such molecular dysregulation also contributes to therapeutic resistance, which remains a major barrier to effective long-term disease control.

Conventional treatment strategies for ovarian cancer typically involve a combination of cytoreductive surgery and systemic chemotherapy, with radiotherapy reserved for selected clinical scenarios [14]. Surgical intervention aims to remove the primary tumor mass and achieve maximal cytoreduction, a factor consistently associated with improved clinical outcomes. Systemic chemotherapy most commonly platinum-based regimens combined with taxanes remains the cornerstone of first-line and adjuvant therapy [15]. However, these modalities are frequently limited by systemic toxicity, off-target effects, cumulative adverse reactions, and the emergence of drug resistance.

In recent years, nanotechnology has emerged as a transformative approach in oncology, offering innovative solutions to longstanding therapeutic limitations. The application of nanoparticles in ovarian cancer treatment has attracted substantial attention as a promising strategy within the broader field of cancer nanomedicine [16]. Nanoparticles exhibit distinctive physicochemical properties, including nanoscale dimensions, high surface-to-volume ratios, and the capacity for surface functionalization and efficient drug encapsulation [17]. These attributes enable enhanced tumor targeting and controlled drug release, thereby improving therapeutic precision.

Importantly, nanoparticle-based delivery systems can facilitate preferential accumulation of anticancer agents within tumor tissues through both passive and active targeting mechanisms, while minimizing collateral damage to healthy cells [18]. Beyond drug delivery, these platforms may help overcome multidrug resistance, modulate the tumor microenvironment, and reduce recurrence risk through multimodal therapeutic strategies [19]. Such advantages position nanotechnology as

a compelling adjunct or potential alternative to conventional treatment paradigms.

Given the considerable promise of nanoparticle-mediated interventions in ovarian cancer and their potential to mitigate the adverse effects associated with standard therapies, continued investigation in this field is both timely and warranted [20]. The present article aims to comprehensively examine recent advances in nanoparticle design and application for ovarian cancer therapy, with particular emphasis on their mechanisms of action, therapeutic efficacy, and prospective clinical implications.

Methodology

This review aimed to systematically analyze and evaluate the various nanoparticles employed in the treatment of ovarian cancer. Data were extracted from peer-reviewed articles available in major scientific databases, including PubMed, Scopus, and Google Scholar. The research process was conducted as follows:

Literature Search

An initial search was performed using combinations of keywords such as "nanoparticles ovarian cancer therapy," "targeted drug delivery ovarian cancer," and "magnetic nanoparticles ovarian cancer" to identify relevant publications. Searches were limited to studies published in English and focused on experimental, preclinical, or clinical investigations.

Study Selection

Articles specifically addressing the application of nanoparticles in ovarian cancer therapy were selected for inclusion. Studies lacking experimental data or sufficient scientific rigor were excluded from the analysis. Both in vitro and in vivo studies were considered to provide a comprehensive overview of therapeutic potential.

Quality Assessment

The methodological quality of the selected studies was evaluated based on study design, reliability of results, and robustness of scientific documentation. Only studies providing reproducible experimental data from laboratory, preclinical, or clinical investigations were included.

Data Analysis

The review focused on diverse nanoparticle types including magnetic, liposomal, polymeric, and mesoporous systems and their therapeutic applications in ovarian cancer. Mechanisms of drug delivery and tumor targeting were comprehensively evaluated, with particular attention to treatment specificity, reduction of systemic toxicity, and enhancement of therapeutic efficacy.

Cellular effects of nanoparticles were also examined, including their influence on tumor growth, induction of apoptosis, and promotion of reactive oxygen species (ROS) production. The historical progression of nanoparticle uses in ovarian cancer from early applications to recent innovations was critically analyzed.

Innovative developments in targeted nanoparticle design were highlighted, including nanoparticles co-delivering chemotherapeutic agents, gene-silencing molecules, or monoclonal antibodies, as well as nanoparticles engineered with intrinsic antitumor properties.

Finally, after compiling and analyzing the selected studies, the findings regarding the efficacy of nanoparticles in ovarian cancer therapy were synthesized to provide an integrated perspective on their clinical potential.

Results

This review analyzed the diverse types of nanoparticles employed in ovarian cancer therapy, including magnetic, liposomal, polymeric, metallic, and other specialized formulations. These nanosystems have demonstrated substantial therapeutic potential due to their unique physicochemical properties, enabling precise tumor targeting, controlled drug release, and reduced systemic toxicity.

Nanoparticles facilitate direct delivery of anticancer agents to tumor sites. Many are functionalized with specific targeting ligands, such as folate or HER2 antibodies, allowing selective recognition and uptake by ovarian cancer cells. This targeted delivery enhances therapeutic efficacy while minimizing off-target effects compared with conventional treatments.

The antitumor effects of nanoparticles are multifaceted. They can induce apoptosis, promote the generation of reactive oxygen species (ROS), inhibit tumor growth, and modulate the tumor microenvironment. Certain nanoparticles also enhance chemosensitivity, restoring or amplifying the effectiveness of standard chemotherapeutic regimens.

Preclinical and in vitro studies consistently demonstrate that nanoparticles can suppress tumor progression, reduce metastasis, and improve overall therapeutic outcomes. Hybrid nanoparticles, such as PLGA-PTX and DDP-Ola@HR systems which combine chemotherapy and radiotherapy in a single platform have shown particularly promising results, effectively reduced tumor volume while enhancing antitumor activity.

The therapeutic efficacy of nanoparticles has been evaluated across a variety of models, including human ovarian cancer cell lines (e.g., SKOV-3), murine preclinical models, and patient-derived xenografts. Collectively, these studies underscore the potential of nanoparticle-based strategies to improve clinical outcomes in ovarian cancer therapy.

Detailed information on nanoparticle types, physicochemical characteristics, therapeutic mechanisms, and observed effects in ovarian cancer treatment is summarized in Table 1.

Table 1: Types of Nanoparticles Used in Ovarian Cancer Therapy, Their Physicochemical Characteristics, Therapeutic Mechanisms, and Effects

Nanoparticle Type (Size & Properties)	Therapeutic Target & Mechanism	Observed Effects	Model	Reference
$CoFe_2O_4$@$BaTiO_3$ (30 nm)	SKOV-3 targeting via DC magnetic field	Nano-electroporation, complete tumor cell eradication	Cellular (SKOV-3)	[21]
PLGA–Cisplatin–HER2 antibody	HER2+ targeting	Enhanced uptake, increased cytotoxicity vs free drug	Cellular	[22]
Biodegradable PMO–Doxorubicin	Targeted drug delivery	Tumor eradication, minimal organ toxicity	CAM	[23]
NPs–Tx–HER	Paclitaxel + HER2 targeting	Superior antitumor effect, prolonged survival	Murine	[24]
Mesoporous silica nanoparticles (MSNPs)	Reduced protein adsorption	↑50% cytotoxicity	In vitro	[25]
PHBV–PTX	Polymer degradation–dependent release	Significant cell death	Human cellular	[26]
PARP1-targeted siRNA	Inhibition of BRCA1-deficient growth	Increased survival	Murine	[27]
Folate-targeted lipid nanoparticles	Folate receptor–mediated targeting	↑ ROS, apoptosis induction	Xenograft	[28]
Cathepsin B-sensitive DOX prodrug	Enzyme-triggered release	Tumor growth inhibition, reduced toxicity	Peritoneal carcinomatosis	[29]
PTP@SR-717	STING activation	Enhanced cisplatin efficacy	In vitro	[30]
Albumin–Albendazole (200–300 nm)	Growth inhibition	Selective cytotoxicity	In vitro	[31]

Fe_3O_4–Silica fluorescent (47 nm)	SKOV-3 targeting	MR/fluorescence imaging	Cellular	[32]
CRLX101	HIF1α suppression	Synergistic effect with Bevacizumab	Preclinical	[33]
HA@PFG–Cisplatin	pH-triggered release	Apoptosis induction	PDX	[34]
HA–PLGA–PTX + siFAK	Overcoming chemoresistance	Tumor growth suppression	Human/PDX	[35]
miR497/TP-HENPs	PI3K/AKT/mTOR inhibition	Increased apoptosis	In vitro	[36]
Mito-Her2@RSHM	Mitoxantrone delivery	83% tumor suppression	Animal	[37]
PLGA–siMDR1/BCL2	Drug-resistance inhibition	↑ Sensitivity to PTX/DDP	Resistant cellular	[38]
NiNPs@F. officinalis (16–49 nm)	Plant-derived anticancer effect	Proliferation inhibition	In vitro	[39]
Cu_2O–Camellia sinensis	Anticancer activity	High uptake in SW-626 cells	In vitro	[40]
NiNPs–Alhagi maurorum (20–36 nm)	Anticancer	Reduced OVCAR-3 survival	In vitro	[41]
CNPPtCP/si(c-fos)	Light-activated	Pt(II) release	In vitro/In vivo	[42]
siRNA/FA–PEG–COL (~200 nm)	Folate receptor targeting	HIF-1α suppression	In vivo	[43]
Collagen–poly(3-APBA) (~81 nm)	DOX delivery	Sustained release	Cellular/Animal	[44]
Polyamine-coated IL-12 liposomes	Immune stimulation	Increased survival	Murine	[45]
SLN–ODN anti-STAT3	STAT3 inhibition	Apoptosis induction	In vitro	[46]
Py-TPE/siRNA@PMP	PTX resistance	Restored chemosensitivity	Cellular/Xenograft	[47]

MSNP–HA–siTWIST	TWIST inhibition	Tumor burden reduction	Murine	[48]
MION (~20 nm)	DDP sensitization	↑ ROS	OVCAR-3/SKOV-3	[49]
PLGA–PRINT–Docetaxel	mEZH2 inhibition	Tumor weight reduction	Preclinical	[50]
PLGA–PTX	Controlled release	Anticancer effect	Cellular	[51]
Lipid–PTX–EGFR	HEY targeting	↓ Tumor volume 50%	Xenograft	[52]
NLC–Verteporfin	Photodynamic therapy	Growth inhibition with laser	Murine	[53]
Iron oxide–HER2 affibody	HER2+ targeting	Metastasis inhibition	Human xenograft	[54]
PLGA–PEG–TEM1–SHK (120–250 nm)	Endothelium targeting	Prolonged release	In vitro	[55]
PLGA–CBD (~240 nm)	Intraperitoneal delivery	Lower IC50	CAM	[56]
Iron–FA/SiO_2/PEG	Folate receptor targeting	Specific cellular uptake	In vitro	[57]
AgNPs–Sal (16–20 nm)	Apoptosis/autophagy	High cytotoxicity	In vitro	[58]
Silica-based NO-releasing NPs	Ras inhibition	Tumor growth suppression	In vitro	[59]
Silica/Polystyrene (10–50 nm)	Cellular uptake analysis	Size-dependent cell death	In vitro	[60]
AuNPs–Cisplatin	EMT inhibition	CSC reduction	Animal	[61]
LbL polyaspartate/HA coating	Preferential targeting	High specificity	Animal/Spheroid	[62]

DDP–Ola@HR	PI3K/AKT/mTOR inhibition	Tumor growth & metastasis suppression	DDP-resistant	[63]
Folate–PTXL–Yttrium-90	Chemo + radiotherapy	Metastasis reduction	Murine	[64]
CNPPtCP/si(c-fos) (optimized)	Platinum-resistant therapy	Synergistic effect	In vivo	[65]
siRNA/FA–PEG–COL (advanced)	Targeted gene therapy	Enhanced tumor accumulation	In vivo	[66]

Table 1 provides a comprehensive summary of the diverse nanoparticles investigated for ovarian cancer therapy. Nanoparticles are increasingly employed in modern oncology due to their distinctive physicochemical properties, particularly their ability to selectively target malignant cells and reduce systemic toxicity.

Types of Nanoparticles and Mechanisms

Magnetoelectric nanoparticles ($CoFe_2O_4$@$BaTiO_3$): These nanoparticles utilize their magnetic properties to be guided to tumor sites via a DC magnetic field, enabling precise delivery to ovarian cancer cells.

PLGA-based nanoparticles loaded with cisplatin and HER2 antibodies: Designed for HER2-positive cells, this platform enhances intracellular drug uptake and cytotoxicity compared to free cisplatin.

Biodegradable PMO nanoparticles encapsulating doxorubicin: These systems provide targeted delivery to ovarian cancer cells while minimizing toxicity to healthy tissues.

Many nanoparticle platforms are engineered with multiple targeting mechanisms, including HER2, CD44, and PARP1, often combined with controlled-release systems. Certain formulations also integrate combination therapies, simultaneously delivering chemotherapeutic and radiotherapeutic agents to improve therapeutic outcomes.

Theranostic Applications

Several nanoparticles serve dual roles as therapeutic and diagnostic agents. For instance, Fe_3O_4 nanoparticles coated with fluorescent silica enable both magnetic resonance (MR) and fluorescence imaging, allowing real-time monitoring of biodistribution, tumor uptake, and treatment response. Such theranostic capabilities provide valuable insights for personalized treatment planning.

Therapeutic Effects

Tumor growth inhibition: Nanoparticles consistently suppress proliferation across cellular and animal models.

Enhanced chemosensitivity: Platforms such as PLGA–PTX and PTP@SR-717 increase the responsiveness of ovarian cancer cells to chemotherapeutic agents like paclitaxel and cisplatin.

ROS generation and apoptosis induction: Many nanoparticles elevate reactive oxygen species (ROS), promoting apoptosis in cancer cells.

Reduced systemic toxicity: Compared with conventional chemotherapy, nanoparticle-based therapies demonstrate substantially lower off-target effects and improved tolerability.

Experimental Models

Cellular models: Ovarian cancer cell lines, including SKOV-3 and OVCAR-8, are used to evaluate cytotoxicity, cellular uptake, and intracellular drug release.

Animal models: Murine studies, xenografts, and patient-derived xenografts (PDX) assess in vivo efficacy, tumor regression, and pharmacokinetics.

Human studies: A limited number of studies have evaluated nanoparticle effects in human tumor samples, providing translational insights into clinical potential.

Implications and Future Directions

Nanoparticles have demonstrated considerable therapeutic promise, including efficacy against chemoresistant ovarian cancer subtypes. Future research should focus on enhancing targeting precision, multifunctional capabilities, and integration with emerging technologies such as advanced imaging and personalized therapies. Combining nanoparticles with chemotherapy, radiotherapy, or gene therapy may further improve treatment efficacy while reducing invasiveness.

Overall, the evidence summarized in Table 1 underscores the remarkable potential of nanoparticle-based strategies for ovarian cancer therapy. Their unique physicochemical properties particularly selective tumor targeting and minimized systemic toxicity position nanoparticles as highly effective tools in advancing cancer treatment and improving patient outcomes.

Discussion

Epithelial ovarian cancer remains one of the most formidable challenges in gynecologic oncology due to late-stage diagnosis, extensive peritoneal dissemination, and frequent development of resistance to platinum- and taxane-based chemotherapies [67]. Standard treatment typically involves cytoreductive surgery followed by platinum- or carboplatin-based chemotherapy combined with paclitaxel. However, disease recurrence and acquired drug resistance are common in a substantial proportion of patients. In this context, nanomedicine has emerged as a promising strategy, offering the potential to improve the therapeutic index by enhancing tumor specificity while minimizing systemic toxicity [67].

A key focus in recent research has been the use of actively targeted nanoparticles. For instance, PLGA nanoparticles conjugated with HER2 antibodies and polymer–immunotargeted systems (NPs–Tx–HER) have demonstrated the ability to bind selectively to overexpressed receptors on tumor cells. This targeted approach increases drug uptake in cancer cells while sparing healthy tissues [68]. These platforms not only augment the efficacy of paclitaxel and cisplatin but have also been associated with improved survival in animal models. Such findings underscore the potential of combining nanocarriers with monoclonal antibodies as a step toward personalized ovarian cancer therapy [69].

Tumor microenvironment-responsive nanoparticles have also shown promise in overcoming drug resistance. Cathepsin B-sensitive doxorubicin prodrug nanoparticles and pH-responsive release systems enable selective drug release within the tumor milieu. This targeted release increases intratumoral drug concentration while reducing systemic side effects, such as doxorubicin-induced cardiotoxicity [70,71]. Furthermore, magnetoelectric $CoFe_2O_4$@$BaTiO_3$ nanoparticles, when stimulated via nanoelectroporation under a magnetic field, enhance cell membrane permeability and achieve complete eradication of SKOV-3 cells in vitro, presenting a potential adjunct to conventional chemotherapy [70,71].

In the realm of gene therapy, the delivery of siRNA targeting genes such as PARP1, MDR1, BCL2, or STAT3 via lipid or polymeric nanoparticles opens new avenues for inhibiting survival and resistance pathways [72]. Simultaneous blockade of drug efflux mechanisms (P-gp/MRP2) and anti-apoptotic factors significantly sensitizes resistant ovarian cancer cells to cisplatin and paclitaxel. These results highlight the importance of multi-targeted approaches in managing chemoresistant ovarian cancer. Additionally, nanoparticles engineered to modulate key signaling pathways, including PI3K/AKT/mTOR or Ras, have been shown to suppress tumor proliferation, migration, and metastasis [73].

Another notable strategy is the use of nanoparticles in combinatorial and multifunctional therapies. Systems co-delivering cisplatin and olaparib, with heparin coating and cRGD ligands, have concurrently targeted DNA repair mechanisms and drug resistance pathways [74]. Similarly, combining chemotherapy with radiotherapy (e.g., yttrium-90-containing nanoparticles) or photodynamic therapy (lipid-based nanoparticles loaded with verteporfin) enhances antitumor effects and reduces recurrence risk. These combinatorial strategies demonstrate that nanoparticles can function not only as drug carriers but also as multifunctional theranostic platforms [75].

Despite promising results in cellular models, CAM, xenografts, and PDX studies, clinical translation faces significant challenges. Tumor heterogeneity, variability in receptor expression, patient-specific EPR effects, long-term safety concerns, and potential nanoparticle accumulation toxicity remain critical barriers [76]. In addition, scalable production, formulation stability, and standardization of physicochemical properties are essential prerequisites for clinical trials [76].

Overall, the findings from this review indicate that nanoparticles, through active and passive targeting, controlled drug release, simultaneous drug and gene delivery, and integration with immunotherapy or physical modalities, hold substantial potential for enhancing ovarian cancer treatment. The future likely lies in the design of smart, multi-stimuli-responsive systems, molecularly guided combination therapies, and theranostic platforms. Achieving this goal will require rigorous phase I–III clinical trials and comprehensive evaluation of safety and efficacy in large patient populations.

Conclusion

Nanoparticles represent a novel therapeutic platform in ovarian cancer treatment, improving the therapeutic index through precise tumor targeting and reduced systemic toxicity. Smart nanocarriers with controlled release and dual drug–gene delivery capabilities play a pivotal role in overcoming drug resistance and modulating tumor signaling pathways. Evidence from cellular, preclinical, and xenograft models demonstrates effective tumor growth inhibition, metastasis suppression, and enhanced survival compared to conventional therapies. The integration of nanoparticles with chemotherapy, radiotherapy, gene therapy, and immunotherapy opens new horizons for multi-modal and personalized treatment approaches. Despite challenges in clinical translation, the development of safe and standardized nanoplatforms has the potential to advance ovarian cancer therapy toward more precise, effective, and less toxic interventions.

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