

# Nanoparticle-Based Drug Delivery Systems to Overcome Multidrug Resistance in Ovarian Cancer

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## DESCRIPTION

Ovarian cancer remains a formidable clinical challenge, ranking as one of the deadliest gynecological malignancies worldwide. Despite advances in surgical techniques and chemotherapy regimens, the overall prognosis for ovarian cancer patients remains poor, primarily due to the development of Multidrug Resistance (MDR). MDR significantly limits the effectiveness of chemotherapeutic agents such as platinum compounds and taxanes, leading to tumor relapse and treatment failure. In this context, nanoparticle-based drug delivery systems have emerged as a promising strategy to circumvent MDR mechanisms and enhance therapeutic efficacy in ovarian cancer. Multidrug resistance in ovarian cancer is multifactorial, involving overexpression of drug efflux pumps (e.g., P-glycoprotein), alterations in drug targets, enhanced DNA repair and evasion of apoptosis. These mechanisms reduce intracellular drug accumulation and promote survival of resistant cancer cells. Conventional chemotherapy formulations face significant hurdles in overcoming these barriers, highlighting the need for innovative delivery platforms capable of improving drug bioavailability, targeting specificity, and intracellular retention.

Nanoparticles, typically ranging from 1 to 100 nanometers in size, offer unique physicochemical properties that enable efficient drug encapsulation, protection from degradation and controlled release. Their small size allows Enhanced Permeability and Retention (EPR) effect-mediated passive accumulation in tumor tissues. Moreover, nanoparticles can be engineered to carry multiple agents simultaneously, including chemotherapeutics, MDR modulators and gene-silencing molecules, thus enabling combination therapies tailored to combat resistance. Active targeting strategies further enhance nanoparticle specificity by conjugating ligands such as folate, transferrin, or antibodies that recognize ovarian cancer-specific surface receptors. This targeted delivery increases cellular uptake via receptor-mediated endocytosis, improving intracellular drug concentration while minimizing off-target toxicity. For example, folate receptor- $\alpha$  is overexpressed in many ovarian cancers and folate-decorated nanoparticles have demonstrated superior delivery and cytotoxicity in preclinical models.

Several types of nanoparticles have been investigated for overcoming MDR in ovarian cancer. Liposomes, polymeric nanoparticles, dendrimers and inorganic nanoparticles each offer distinct advantages. Liposomal formulations, such as liposomal doxorubicin, are already approved for clinical use and have shown improved pharmacokinetics and reduced cardiotoxicity compared to free drug. Polymeric nanoparticles enable stimuli-responsive drug release, such as pH or redox-triggered mechanisms, to release cargo specifically in the tumor microenvironment. Importantly, nanoparticles can be designed to co-deliver chemotherapeutic drugs alongside MDR modulators such as siRNA targeting P-glycoprotein or inhibitors of drug efflux pumps. This dual delivery approach has demonstrated promising results in preclinical studies by restoring chemosensitivity and enhancing apoptosis in resistant ovarian cancer cells.

Beyond drug delivery, nanoparticles can be harnessed for diagnostic imaging and theranostic applications, facilitating early detection and real-time monitoring of therapeutic response. For instance, magnetic or fluorescent nanoparticles allow visualization of tumor accumulation and distribution, supporting personalized treatment adjustments.

Despite these promising developments, clinical translation of nanoparticle-based therapies faces challenges. Manufacturing complexity, scalability and regulatory hurdles require standardized protocols to ensure reproducibility and safety. Furthermore, biological barriers such as immune clearance and heterogeneous tumor microenvironment impact nanoparticle bio distribution and efficacy. Comprehensive preclinical studies and well-designed clinical trials are essential to validate the safety and therapeutic benefits of nanoparticle platforms in overcoming MDR. Integration of nanoparticle drug delivery with existing treatment regimens offers a rational pathway toward improving ovarian cancer outcomes.

## CONCLUSION

Nanoparticle-based drug delivery systems represent a cutting-edge strategy to tackle multidrug resistance in ovarian cancer,

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addressing one of the most significant barriers to successful treatment. By enabling targeted, controlled and combinational delivery of chemotherapeutics and resistance modulators, nanoparticles have the potential to revolutionize ovarian cancer therapy. While challenges in clinical translation persist, ongoing advancements in nanotechnology, material science and cancer biology continue to refine these platforms. Collaborative efforts across disciplines will be important to overcome existing

limitations and accelerate the development of safe and effective nanoparticle therapeutics. Ultimately, harnessing nanoparticle-based drug delivery to circumvent MDR could transform the treatment landscape for ovarian cancer, improving patient survival and quality of life. Continued investment in research and clinical validation is imperative to realize this potential and bring innovative Nano medicine approaches from bench to bedside.