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Analytical Review of Nanoparticles and Nano-Based Systems for Targeted Therapy of Endometrial Cancer: Insights from Cellular, Clinical and Animal Studies

Revisão analítica de nanopartículas e sistemas baseados em nanotecnologia para a terapia direcionada do câncer de endométrio: evidências provenientes de estudos celulares, animais e clínicos

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Abstract: Background: Endometrial cancer is among the most prevalent gynecological malignancies worldwide. Despite advances in conventional therapeutic approaches, treatment outcomes are often constrained by challenges such as systemic toxicity, therapeutic resistance, and insufficient target specificity. Nanomedicine has emerged as a promising strategy to overcome these limitations by enhancing both diagnostic accuracy and therapeutic efficacy. This review aimed to critically evaluate the current applications of nanoparticles and nano-engineered systems in the diagnosis and treatment of endometrial cancer and endometriosis.

Methods: An analytical review was conducted using literature retrieved from PubMed, Scopus, and Web of Science databases. Relevant studies published between 2010 and 2025 were systematically screened using predefined keywords related to nanotechnology, endometrial cancer, and endometriosis. Eligible publications included in vitro and in vivo preclinical investigations, animal studies, and comprehensive review articles. Data were extracted and synthesized through a qualitative thematic approach to identify major advances and emerging trends in nano-based diagnostic and therapeutic platforms.

Results: The reviewed evidence demonstrated that a wide range of nanoparticle formulations and nano-delivery systems, including NP@AZL, LDE, SPION@miR-326, CNP, FOL–PEG–PLGA loaded with paclitaxel, CXCR4-targeted nanotherapeutics, nMIL-100 (Fe), porphysomes, and tamoxifen-loaded solid lipid nanoparticles (Tamoxifen-SLN), exhibited considerable therapeutic and diagnostic potential. Across cellular, animal, and clinical models, these nanoplatforms effectively suppressed tumor cell proliferation, induced apoptosis, inhibited angiogenesis and metastatic progression, improved lymph node detection, and reduced the adverse effects commonly associated with conventional anticancer therapies.

Conclusion: Nano-based delivery systems and engineered nanoparticles represent a promising avenue for improving the precision and effectiveness of endometrial cancer management. By facilitating targeted drug delivery and enhancing diagnostic performance while minimizing systemic toxicity, these technologies may contribute substantially to the future development of personalized therapeutic strategies for endometrial malignancies.

Keywords: Nanomedicine; Endometrial Cancer; Nanoparticles; Nano-Based Systems; Targeted Therapy.

Resumo: O câncer endometrial está entre as neoplasias ginecológicas mais prevalentes em todo o mundo. Apesar dos avanços nas abordagens terapêuticas convencionais, os resultados clínicos ainda são frequentemente limitados por desafios como toxicidade sistêmica, resistência terapêutica e baixa especificidade para os tecidos-alvo. Nesse contexto, a nanomedicina tem emergido como uma estratégia promissora para superar essas limitações, aumentando tanto a precisão diagnóstica quanto a eficácia terapêutica. Esta revisão teve como objetivo avaliar criticamente as aplicações atuais de nanopartículas e sistemas nanoengenheirados no diagnóstico e tratamento do câncer endometrial e da endometriose.Foi realizada uma revisão analítica da literatura utilizando estudos recuperados das bases de dados PubMed, Scopus e Web of Science. Publicações relevantes, divulgadas entre 2010 e 2025, foram selecionadas sistematicamente por meio de palavras-chave previamente definidas relacionadas à nanotecnologia, câncer endometrial e endometriose. Foram incluídos estudos pré-clínicos in vitro e in vivo, investigações em modelos animais e artigos de revisão abrangentes. Os dados foram extraídos e sintetizados por meio de uma abordagem temática qualitativa, com o objetivo de identificar os principais avanços e tendências emergentes em plataformas diagnósticas e terapêuticas baseadas em nanotecnologia.As evidências analisadas demonstraram que uma ampla variedade de formulações nanoparticuladas e sistemas nanoestruturados de liberação de fármacos, incluindo NP@AZL, LDE, SPION@miR-326, CNP, FOL–PEG–PLGA carregado com paclitaxel, nanoterapias direcionadas ao CXCR4, nMIL-100 (Fe), porfisomas e nanopartículas lipídicas sólidas contendo tamoxifeno (Tamoxifen-SLN), apresentaram considerável potencial terapêutico e diagnóstico. Em modelos celulares, animais e clínicos, essas nanoplataformas foram capazes de reduzir a proliferação tumoral, induzir apoptose, inibir a angiogênese e a progressão metastática, melhorar a detecção de linfonodos e minimizar os efeitos adversos frequentemente associados às terapias antineoplásicas convencionais.Os sistemas de liberação baseados em nanotecnologia e as nanopartículas engenheiradas representam uma abordagem promissora para aprimorar a precisão e a eficácia do manejo do câncer endometrial. Ao possibilitar a entrega direcionada de fármacos, melhorar o desempenho diagnóstico e reduzir a toxicidade sistêmica, essas tecnologias podem contribuir significativamente para o desenvolvimento futuro de estratégias terapêuticas personalizadas para neoplasias endometriais.

Palavras-chave: Nanomedicina; Câncer Endometrial; Nanopartículas; Sistemas Nanoestruturados; Terapia Alvo

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Introduction

Endometrial cancer is one of the most frequently diagnosed gynecological malignancies worldwide and arises primarily from the epithelial lining of the uterine endometrium (AMANT et al., 2005). The development of this disease is driven by a complex interplay of genetic, hormonal, metabolic, and environmental factors. Prolonged exposure to unopposed estrogen, obesity, diabetes mellitus, and a positive family history of cancer have been identified among the most important risk factors contributing to endometrial carcinogenesis (CROSBIE et al., 2022). At the molecular level, the disease is characterized by dysregulation of signaling pathways involved in cellular proliferation, apoptosis, differentiation, and cell-cycle control, ultimately leading to uncontrolled growth and malignant transformation of endometrial cells (PASSARELLO, KURIAN & VILLANUEVA, 2019). Diagnosis is typically established through a combination of clinical assessment, physical examination, imaging modalities such as transvaginal ultrasonography and magnetic resonance imaging (MRI), and histopathological confirmation obtained from endometrial biopsy specimens (BRAUN, OVERBEEK-WAGER & GRUMBO, 2016).

Current management strategies for endometrial cancer rely primarily on surgery, radiotherapy, and systemic therapies, including chemotherapy (DENSCHLAG, ULRICH & EMONS, 2011). Common chemotherapeutic regimens are largely based on platinum compounds, taxanes, and

antimetabolites, which have demonstrated efficacy in reducing tumor burden and controlling disease progression. Nevertheless, these agents are frequently associated with substantial limitations, including systemic toxicity, damage to healthy tissues, myelosuppression, gastrointestinal complications, and an increased susceptibility to infections (HILL & DIZON, 2012; HERRERA et al., 2014). Furthermore, the emergence of drug resistance and the limited selectivity of conventional therapies often compromise long-term therapeutic outcomes.

These challenges have stimulated growing interest in the development of more precise and less toxic treatment strategies. In addition to conventional chemotherapy, novel therapeutic approaches for disease management include the use of nanoparticles, probiotics, prebiotics, and synbiotics (DENSCHLAG et al., 211; MELLO, 2024).

In recent years, nanotechnology has emerged as a transformative field in biomedical research, offering innovative opportunities for cancer diagnosis and therapy (Alexis et al., 2008). Nanoparticles and nano-engineered delivery systems can selectively transport therapeutic agents, nucleic acids, and bioactive molecules to tumor tissues while minimizing exposure of healthy cells and organs (GMEINER & GHOSH, 2014). Such targeted delivery capabilities have the potential to enhance therapeutic efficacy, improve pharmacokinetic profiles, and reduce treatment-related adverse effects.

Beyond drug delivery, nanomaterials possess unique physicochemical characteristics that make them highly attractive for applications in early disease detection, molecular imaging, and theranostic platforms that integrate diagnostic and therapeutic functions within a single system (MOHANRAJ & CHEN, 2006). Through both passive targeting mechanisms, such as the enhanced permeability and retention (EPR) effect, and active targeting approaches involving specific molecular ligands, nano-based systems can improve drug accumulation within tumor tissues, overcome biological barriers, and mitigate mechanisms of therapeutic resistance (HORIKOSHI & SERPONE, 2013).

Given the increasing global burden of endometrial cancer and the remarkable potential of nanotechnology-based interventions, a comprehensive evaluation of current advances in this field is warranted.

Therefore, the present review aims to critically examine recent developments in the

application of nanoparticles and nano-based platforms for the targeted management of endometrial cancer. Emphasis is placed on their biological mechanisms of action, delivery strategies, therapeutic and diagnostic applications, and the major challenges that must be addressed to facilitate successful clinical translation

Methods

This study was conducted as an analytical review to evaluate the emerging applications of nanoparticles and nano-based systems in the targeted treatment of endometrial cancer.

A comprehensive literature search was performed across several national and international scientific databases, including Google Scholar, SID, ISC, PubMed, Scopus, and Web of Science. The search covered publications released between January 2010 and March 2025 to ensure inclusion of the most recent advances in nanomedicine and endometrial cancer research.

To maximize the comprehensiveness of the search strategy, a combination of relevant Medical Subject Headings (MeSH) terms and free-text keywords was employed. The primary search terms included “Endometrial Cancer,” “Nanoparticles,” “Nanocarriers,” “Nano-Based Drug Delivery Systems,” and “Endometriosis.”

These terms were combined using Boolean operators (AND, OR) to improve both the sensitivity and specificity of article retrieval.

Studies were considered eligible for inclusion if they investigated the application of nanoparticles or nano-engineered platforms in the diagnosis, treatment, or targeted drug delivery of endometrial cancer.

Eligible publications included in vitro experiments, in vivo preclinical studies, animal investigations, and review articles focusing on nanotechnology-based approaches in gynecologic oncology.

Articles lacking sufficient scientific evidence, duplicate publications, conference abstracts without full-text availability, and studies unrelated to the objectives of the review were excluded. Furthermore, studies focusing exclusively on other malignancies without providing relevant mechanistic or translational insights applicable to endometrial cancer were not considered.

The screening process was conducted in two sequential stages. Initially, the titles and abstracts of all retrieved records were independently evaluated for relevance to the review topic.

Publications that clearly failed to meet the inclusion criteria were excluded at this stage. Subsequently, the full texts of

heremaining articles were carefully examined to verify their eligibility and methodological relevance.

Following study selection, relevant information was extracted and synthesized using a descriptive–analytical approach. Attention was given to nanoparticle composition, targeting strategies, mechanisms of action, therapeutic outcomes, diagnostic applications, and reported limitations.

The collected evidence was then qualitatively analyzed to provide a comprehensive overview of recent developments, current challenges, and future perspectives regarding the use of nano-based technologies for the targeted management of endometrial cancer.

Results

The findings of this analytical review demonstrate that nanoparticles and nano-based systems play a significant role in enhancing targeted drug delivery, increasing drug accumulation within tumor tissues, and reducing systemic toxicity across in vitro, in vivo, and clinical models.

Most nanoparticle formulations exerted potent antitumor effects through multiple mechanisms, including induction of oxidative stress, inhibition of signaling pathways associated with cellular proliferation, and promotion of apoptosis.

In clinical and translational studies, nanoparticles have shown promise in improving diagnostic accuracy, especially in lymph node mapping, where they facilitated precise identification of metastatic nodes.

Additionally, the incorporation of nanocarriers into conventional chemotherapeutic regimens, such as paclitaxel, and hormonal inhibitors enhanced therapeutic efficacy while mitigating off-target effects and systemic side effects.

Overall, the accumulated evidence underscores the high potential of nanotechnology-based interventions in both therapeutic and diagnostic applications for endometrial cancer. A detailed summary of relevant studies, including cellular, animal, and clinical investigations, is provided in Table 1.

Table 1. Summary of in vitro, in vivo, and clinical studies evaluating the effects of nanoparticles on endometrial cancer.

Model/Population	**Nanoparticle /Intervention**	**Characteristics**	**Study Type**	**Key Findings**	**Mechanism /Interpretation**	**Ref.**
LOF p53 EC cells	PTX-loaded NPs + BIBF1120	~120 nm, 10% loading	In vitro/In vivo	Synergistic effect and synthetic lethality	Inhibition of angiogenesis and mitosis	Toczek et al., 2022
EC (Review)	AgNPs, AuNPs	Variable	Review	Accelerated wound healing	Anti-biofilm and anti-inflammatory effects	Toczek et al., 2022
EC (Ethnic disparities)	Nanoplatforms	—	Review	Reduced healthcare disparities	Precision medicine approach	Rowlands et al., 2024
EC (Systematic review)	Nanoparticles (NPs)	—	Systematic Review	Modulation of HIF/mTOR pathways	Regulation of tumor metabolism	Cai et al., 2021

IshikawaHG + PDCs	JX06-NPs + Metformin	Reduction-sensitive	In vitro/In vivo	Suppressed growth of resistant tumors	PDK1 inhibition	Yang et al., 2022
Obese EC patients	PLD liposome	PEGylated	Clinical PK study	Reduced drug exposure	Increased mononuclear phagocyte system (MPS) clearance	Starling et al., 2019
EC patients	Carbon nanoparticles (CNP) + ICG	50 mg	Clinical	100% sentinel lymph node (SLN) detection	Lymphatic mapping	Liang et al., 2021
EC (Review)	LNPs, LbL nanoparticles, liposomes	—	Review	Enhanced drug delivery	Improved immunotherapy efficacy	Murray, Swingle & Mitchell, 2025
Ishikawa cells + nude mice	DSF + CuCy NPs	0.5 μM	In vivo	Strong induction of apoptosis	Mitochondrial damage	Yang et al., 2024

HEC50co cells	CIP2b-NPs + PTX	PEGylated	In vivo	Strong synergistic antitumor activity	G2/M cell cycle arrest	Naguib et al., 2024
3D EC spheroids	HA-F127/SAHA nanoparticles	CD44-targeted	In vitro	Enhanced cellular uptake	CD44-mediated targeting	Edwards et al., 2021
AN3-CA cells	Fe3O4@Ag/ Guar Gum nanoparticles	IC50 = 87 µg/mL	In vitro	Significant cytotoxicity	ROS generation and metallic nanoparticle effects	Su et al., 2024
EC cell lines + PDCs	NP@AZL + MPA	Liposomal	In vivo	Induced endoplasmic reticulum stress	Ca^{2+} dysregulation	Huang et al., 2022
HuECSC cells	SPION-miR326	Magnetic nanoparticle	In vivo	Reduced tumorigenicity	STAT3/VEGF pathway inhibition	Bedin et al., 2019
EC	Carbon nanoparticle (CNP) SLN mapping	Carbon nanoparticle	Clinical	100% diagnostic accuracy	Lymphatic tracing	Gao et al., 2019

Stage I EC	SPIO tracer	Superparamagnetic iron oxide	Clinical	AUC = 0.90	Sentinel lymph node mapping	Zuo et al., 2019
EC	CNP-guided SLN biopsy	Carbon nanoparticle	Clinical	100% accuracy	Lymph node tracing	Jedryka et al., 2025
HEC-1A cells	FOL-PEG-PLGA + PTX	220 nm	In vivo	Increased apoptosis	Folate receptor-targeted delivery	Tao et al., 2023
Advanced EC	CXCR4-Toxin nanoparticles	Protein toxin-based	In vivo	Reduced metastasis	CXCR4-targeted therapy	Medina-Gutiérrez et al., 2022
KLE cells	nMIL-100(Fe)	MOF nanozyme	In vitro	Increased ROS production	Fenton reaction-mediated cytotoxicity	Gong et al., 2021
VX2 rabbit EC model	Porphysome	Fluorescent nanoparticle	In vivo	98% imaging accuracy	Image-guided surgery	Philp et al., 2019
Hec50co cells	PD98059-PLGA NPs + PTX	PEG-PAMAM	In vivo	Enhanced synergistic efficacy	MEK inhibition	Wiwatchaitawee

						et al., 2022
Rat uterus model	Tamoxifen-SLN	Lipid nanoparticle	In vivo	Reduced ERα and VEGF expression	Decreased oxidative stress	Javid et al., 2017
HEC1B cells	TQ-SeNPs	IC50 = 526 µg/mL	In vitro	Reduced cell proliferation	MAPK pathway inhibition	ulbay, ecme & han, 2023

Discussion

This analytical review highlights the significant potential of nanoparticles and nano-based systems in enhancing targeted therapy for endometrial cancer. The evidence indicates that drug-loaded nanoparticles, magnetic nanostructures, and nanocomposites can substantially improve anti-timor efficacy while minimizing the systemic toxicity associated with conventional chemotherapy. Specifically, formulations such as PTX-loaded nanoparticles, CIP2b-NPs, CXCR4-toxin nanoparticles, and NP@AZL demonstrated that simultaneous inhibition of angiogenesis and cell-cycle progression, combined with apoptosis induction and drug synergy, can significantly enhance therapeutic outcomes (TOCZEK et al., 2022; NAGUIB et al., 2024; TAO et al., 2023; MEDINA-GUTIÉRREZ et al., 2022; HUANG et al., 2022).

Preclinical studies consistently showed that nanoparticles enhance drug accumulation within tumor tissues while sparing healthy cells. For instance, PEGylated and folate-functionalized nanoparticles (FOL–PEG–PLGA + PTX) actively targeted tumor cells and selectively promoted apoptosis in in vivo models (Liang et al., 2011). Magnetic nanoparticles such as SPION carrying miR-326 and porphysomes not only exerted antitumor effects but also provided advanced diagnostic and imaging capabilities, thereby improving surgical precision and sentinel lymph node mapping (GAO et al., 2019; PHILP et al., 2019).

Cellular and animal studies further demonstrated that various molecular pathways, including MAPK, PDK1, STAT3/VEGF, and ROS-related pathways, including Fenton reaction mechanisms, are effectively modulated by targeted nanoparticles. Consequently, tumor cell proliferation is reduced, and apoptotic cell death is enhanced (JAVID et al., 2017; YANG et al., 2022; SU et al., 2024; GONG et al., 2021). These findings underscore the importance of designing multifunctional nanoparticles capable of simultaneously targeting key tumor pathways to optimize therapeutic responses.

Clinical investigations also revealed notable efficacy. The use of carbon nanoparticles (CNPs) and lipid-based delivery systems in patients with endometrial cancer improved lymph node detection, increased the accuracy of sentinel lymph node mapping, and reduced treatment-related side effects (LIANG et al., 2021; JEDRYKA et al., 2025; TAO et al., 2023). These results indicate that nanoparticle-based platforms hold significant promise not only in

preclinical models but also in clinical applications, enhancing both therapy and diagnostics.

Despite these advances, several challenges remain for the clinical translation of these technologies. Variability in nanoparticle design, including size, drug loading, and administration route, can influence therapeutic outcomes. Moreover, long-term patient studies evaluating systemic toxicity and immune responses are still limited. Successful clinical implementation will require standardized preclinical protocols and large-scale, well-designed clinical trials across diverse patient populations (MURRAY, SWINGLE & MITCHELL, 2025; STARLING et al., 2019).

In summary, the current evidence demonstrates that nanoparticles and nano-based systems with targeted and multifunctional properties represent a novel, low-toxicity strategy for the treatment and diagnosis of endometrial cancer.

Precise nanoparticle design incorporating active targeting, optimized pharmacokinetics, and multiple molecular mechanisms may improve therapeutic efficacy, reduce adverse effects, and pave the way for the development of personalized treatment approaches.

Conclusion

Nanomedicine and nano-based platforms play a critical role in the targeted management of endometrial cancer and endometriosis by enhancing drug accumulation within tumor tissues and improving therapeutic efficacy.

These systems minimize systemic side effects, protect healthy cells, and selectively target cancer cells. Their mechanisms of action include induction of apoptosis, inhibition of proliferative signaling pathways, suppression of angiogenesis, and control of metastatic progression, collectively strengthening the therapeutic response.

Clinically, nanoparticles have also been shown to improve diagnostic accuracy and sentinel lymph node identification. Therefore, the utilization of nanoparticles and nano-based drug delivery systems represents a promising, low-toxicity approach to advance both treatment and diagnostic precision in endometrial cancer.

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